Pd–Tetrahydrosalan-Type Complexes as Catalysts for Sonogashira Couplings in Water: Efficient Greening of the Procedure

Krisztina Voronova,*[a] Levente Homolya,[a] Antal Udvardy,[a] Attila C. Bényei,[a] and Ferenc Joó*[a, b]

New sulfonated tetrahydrosalen-type ligands and their water-soluble palladium(II) complexes have been synthesized. The palladium(II) complexes catalyze the Sonogashira coupling (23 examples) of various aryl halides (including chloroarenes) with terminal alkynes, with good to excellent conversions under mild conditions (80 °C, air, no Cu^I cocatalyst) in aqueous–organic mixtures and turnover frequencies of up to 2790 h^{-1}. Under optimized reaction conditions to minimize environmental con-

tamination, diphenylacetylenes can be isolated in 76–98 % yield. The aqueous catalyst solution can be recycled four times with decreasing activity; however, yields between 93 and 98 % can still be achieved with extended reaction times. Several water-insoluble products can be isolated in excellent yield by simple filtration and purification by washing with water; this method is used, for the first time, for this type of C—C coupling procedure.

Introduction

Cross-coupling reactions are of utmost importance in the metal-catalyzed formation of carbon–carbon bonds. One of the best methods for the formation of C(sp^2)–C(sp) bonds is the reaction of vinyl or aryl halides with alkynes.[1] The reaction has been widely used for the synthesis of various complex organic compounds, such as polymers,[2] liquid crystals,[3] compounds of natural origin,[4] pharmaceuticals,[5] and many others.[1,6] Originally, Sonogashira coupling was performed with relatively high amounts of palladium(0)–tertiary phosphine catalysts and with copper(I)-containing cocatalysts in the presence of base.[7] Owing to the air sensitivity of the Pd^0 catalyst and phosphine ligands, the reaction had to be performed with the exclusion of air; in addition, the copper(I)-based cocatalysts facilitated the formation of unwanted butadiyne byproducts through Glaser coupling.[8] In the last 30 years, many improvements have been made in the reaction conditions: various new cata-

lysts have been introduced (some of them with less oxygen sensitive N-donor ligands), copper-free variants of the reaction have been developed, and various solvents have also been applied.[1,9]

The use of water is becoming more and more pronounced in synthesis due to the favorable green properties of this solvent. Water is nontoxic and nonflammable; this makes it attractive compared with common organic solvents. In addition, water is suitable for the construction of biphasic systems,[10] in which a water-soluble catalyst can be recovered by phase separation once the reaction ends. Water-soluble catalysts have been used for diverse reactions, such as hydrogenation,[11] hydroformylation,[12] and various cross-coupling reactions.[13] It is important to mention that, despite the reactions being run in water, in many cases, the products are isolated by extraction with organic solvents, so the overall process cannot be regarded as environmentally friendly. To overcome this deficiency, in several new processes, the isolation of the products is achieved by filtration or decantation.[14]

In aqueous organometallic catalysis the most widely used catalysts are metal complexes of tertiary phosphines and N-heterocyclic carbenes, although N- and/or O-donor ligands may also play a crucial role. Less attention has been devoted to the study of complexes with multidentate N,O-donor ligands, which includes the various N,N′-bis(salicylidene)ethylenediamine (salen) ligands.

Complexes of salen[15] were mainly investigated in nonaqueous solutions for catalysis of reactions such as oxidation,[16] epoxidation,[17] opening of epoxide rings,[18] and hydrogenation.[19] In aqueous solutions, salen complexes serve as catalysts for oxidation[20] and coupling reactions,[21] but there are also

[a] K. Voronova,+ L. Homolya, Dr. A. Udvardy, Dr. A. C. Bényei, Prof. F. Joó
Department of Physical Chemistry
University of Debrecen, Egyetem tér 1
H-4032 Debrecen (Hungary)
E-mail: voronova.krisztina@science.unideb.hu

[b] Prof. F. Joó
MTA-DE Homogeneous Catalysis and
Reaction Mechanisms Research Group
P.O.B. 7, H-4010 Debrecen, (Hungary)
E-mail: joo.ferenc@science.unideb.hu

[+] Current address:
Department of Chemistry, University of the Pacific
3601 Pacific Avenue, Stockton, CA 95211 (USA)

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examples for catalysis of kinetic resolution[22] and N-arylation.[23]

In aqueous solutions, salen undergoes hydrolysis,[24] especially at higher temperatures. This is a clear disadvantage in catalysis. The hydrogenation of salen yields tetrahydrosalen or salan with much higher stability in aqueous systems. Complexes of salan with palladium, chromium, aluminum, zirconium, hafnium, titanium, iron, and niobium have already been used as catalysts of reactions such as oxidation[25] and polymerization.[26] The solubility of salan and its complexes in water can be increased by attaching sulfonate or phosphonate substituents to the aromatic rings of the ligand.[24a,b,27]

Although there are several reports in the literature on aqueous–biphasic Sonogashira couplings,[28] the number of Pd[II] catalysts with N- or N,O-donor ligands is small. A relevant example is the Pd[II]–salen-type complex containing triphenylphosphonium substituents used by Bakherad and co-workers.[21e] This complex was an active catalyst in the reaction of aryl iodides and terminal alkynes under aerobic conditions in water at 60 °C in the presence of sodium lauryl sulfate surfactant and Cs_2CO_3. Relatively high catalyst loadings ($[S]/[C] = [100]/[1]$) were required to perform the coupling in good to excellent yields in reaction times of 6–12 h. No reactions of aryl bromides and chlorides were reported and recycling of the catalyst was not tested. In another study, Wang and co-workers accomplished Sonogashira coupling promoted by a Pd[II]–2,2′-dipyridylamine complex in the absence of copper under mild conditions (water, 25 °C, 6 h, N_2 atmosphere).[29] Aryl iodides and terminal alkynes were coupled with good to excellent yields by using triethylamine (TEA) as a base (39 examples).

Previously, we reported an improved synthesis of sulfonated salan (sulfosalan, HSS, Scheme 1, **1**) and its palladium(II) complex (**4**). The latter showed high catalytic activity and good chemical stability in the redox isomerization of allylic alcohols in aqueous systems.[24a] Encouraged by these results, we extended our investigations to the synthesis of more salan-type ligands with different bridging units between the two nitrogen atoms.
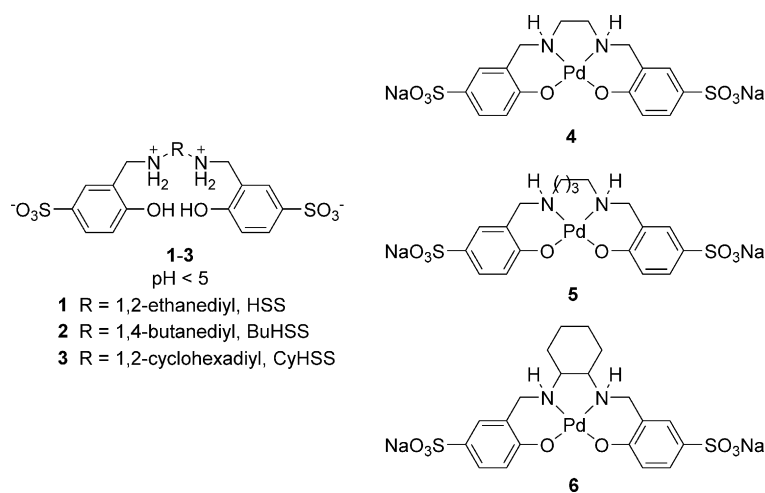
Herein, we report on the synthesis of new sulfonated tetrahydrosalen-type ligands (BuHSS (**2**), CyHSS (**3**); Scheme 1) obtained by direct sulfonation of the corresponding tetrahydrosalens. Palladium(II) complexes of these ligands (**4**–**6**) were then used for the catalysis of Sonogashira coupling of aryl halides with alkynes. With these new catalysts, the abovementioned coupling reactions can be performed with high efficiency in water and in the presence of air without a copper-based cocatalyst and, in many cases, product isolation can be achieved by simple filtration, which avoids the use of organic solvents. In such a way, this carbon–carbon cross-coupling process largely meets the requirements of green and sustainable chemistry.

Results and Discussion

Synthesis and characterization of sulfosalan-type ligands and their Pd[II] complexes

The synthesis of sulfonated tetrahydrosalen[24a] (sulfosalan, HSS (**1**); Scheme 1) was adapted for the synthesis of BuHSS (**2**) and CyHSS (**3**). Briefly, salicylaldehyde was treated with the appropriate diamine (ethylenediamine, 1,4-butylenediamine, or 1,2-cyclohexyldiamine), the product diimines were reduced with $NaBH_4$, and the resulting amines were sulfonated in a mixture of concentrated H_2SO_4 and fuming sulfuric acid (oleum). After dilution of the sulfonation mixture and adjusting the pH to 5, the zwitterionic forms of the free acid ligands (**1**–**3**; Scheme 1) were obtained. These are sparingly soluble in water, in contrast to the sodium salts, which are soluble. Ligands **1**–**3** were characterized by ^{1}H and ^{13}C NMR spectroscopy, ESI-TOF mass spectrometry, and elemental analysis.

X-ray quality crystals of **2** were obtained by layering 2-propanol on a solution of **2** prepared with 0.1 M KOH. An ORTEP view of **2** is shown in Figure 1. The bond lengths and angles are in good agreement with those of similar molecules found in the literature.[24,30a] The asymmetric unit contains half of the molecule and shows $C2$ symmetry (Figure S16 in the Supporting Information). In the unit cell, there are four potassium counterions for the two phenolate and two sulfonate groups. All K^+ ions are coordinated to seven oxygen atoms with K—O distances in the range of 2.78–3.11 Å. A search of the Cambridge Structural Database[30b] (CSD, Version 5.35, Update November 2013) indicated that the C2—O2 distance of 1.299(8) Å represented a deprotonated phenolic OH group; the crystal was obtained from a strongly basic solution. Bond length data also prove single bonds between N1 and neighboring carbon atoms.

In the crystal lattice, BuHSS is positioned in parallel layers between the inorganic layers composed of K^+ and H_2O (Figure S17 in the Supporting Information). The solid-state structure of **2** represents a polymer held together with electrostatic and van der Waals interactions as well as hydrogen bonds. Similar layered structures are found in crystals of the nickel–sulfosalen complex determined by Rogez et al.,[24c] and in other compounds containing sulfonate groups, for

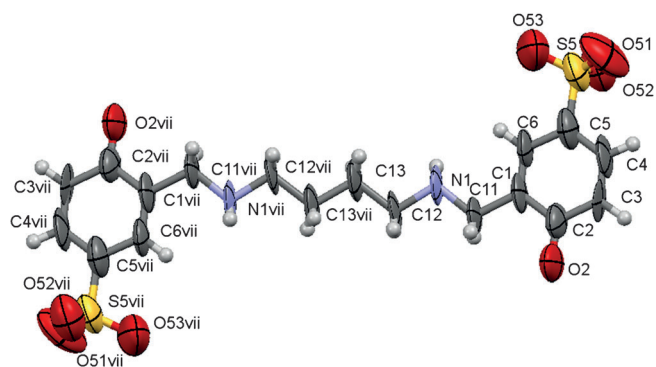

Scheme 1. Sulfosalan-type ligands HSS (**1**), BuHSS (**2**), and CyHSS (**3**) along with their Pd[II] complexes [Pd(HSS)] (**4**), [Pd(BuHSS)] (**5**), and [Pd(CyHSS)] (**6**).

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Figure 1. An ORTEP view of **2** at the 50% probability level; the numbering scheme is also shown. Water molecules and potassium counterions are omitted for clarity. Symmetry code (vii): $-x+1/2, -y+1/2, -z+1/2$. Selected bond lengths [Å] and angles [°]: C2–O2 1.299(8), C5–S5 1.749(7), S5–O51 1.459(5), S5–O52 1.452(5), S5–O53 1.459(5), C11–N1 1.472(7), C12–N1 1.484(3); C1-C11-N1 114.2(5), C11-N1-C12 109.3(5), N1-C12-C13 110.7(5).

Table 1. Optimization of the amount of catalyst in the Sonogashira coupling of iodobenzene and phenylacetylene.[a]

Entry	[Substrate]/[Pd(BuHSS)] Ratio	Yield[b] [%]	TOF[c] [h^{-1}]
1	100	67	134
2	500	60	600
3	1000	42	840
4	2000	31	1240
5	3000	27	1620
6	4000	19	1520
7	5000	10	1000

[a] Reaction conditions: iodobenzene (5×10^{-4} mol), phenylacetylene (7.5×10^{-4} mol, 1.5 equiv), TEA (2×10^{-3} mol), water (3 mL), 30 min, 80 °C, air. [b] Yield determined by GC on the basis of the amount of starting iodobenzene. [c] TOF: turnover frequency, which is defined as (mol of product)$\times$[(mol of catalyst)$\times$h]$^{-1}$.

instance, in the crystal of *meta*-monosulfonated triphenylphosphine.[31]

The palladium–sulfosalan complexes **4–6** were obtained by stirring an aqueous solution of ammonium tetrachloropalladate and the respective sulfosalan sodium salt at 60 °C for 10 h. The yellow, air-stable products could be precipitated by the addition of absolute ethanol. The complexes are soluble in water and their aqueous solutions can be stored for months with no sign of decomposition or loss of catalytic activity. These compounds were characterized by elemental analysis, ^{1}H and ^{13}C NMR spectroscopy, and ESI-MS spectrometry (see the Experimental Section and Supporting Information). The obtained data are in agreement with the structures shown in Scheme 1.

Catalytic activity of water-soluble Pd^{II}–tetrahydrosalen complexes in Sonogashira coupling

The new Pd^{II}–sulfosalan complexes were studied as catalysts for biphasic Sonogashira coupling in the presence of a base. The catalyst was dissolved in water and the organic phase was comprised of the substrate, product, and water-immiscible base (if any). Table S2 in the Supporting Information shows results for the effect of various inorganic and organic bases (entries 1–14) on the yield of Sonogashira coupling of phenylacetylene and iodobenzene catalyzed by [Pd(BuHSS)]. The highest conversion was achieved with TEA (74%; Table S2 in the Supporting Information, entry 14) with an optimum TEA to substrate (iodobenzene) ratio of four (Table S2 in the Supporting Information, entries 14–19).

As expected, decreasing the catalyst concentration in the aqueous phase (i.e., increasing the [substrate]/[catalyst] ratio) led to a decrease in the yield of diphenylacetylene (Table 1); however, high turnover frequencies were obtained, even at [S]/[C]=5000. The TOF changed according to a maximum curve and the highest TOF observed was 1620 h^{-1} at [S]/[C]=3000 (Table 1, entry 5). Under these conditions, the reaction proceeded rapidly to about 70% conversion followed by lower

but steady progress until completion in 4 h (Figure S13 in the Supporting Information). Under the conditions outlined in Table 1 entry 5, the reaction was also attempted in the presence of CuI with [Cu]/[Pd]=2. Strong inhibition by copper(I) was observed and instead of 27% yield only 0.5% diphenylacetylene was obtained together with 1% 1,4-diphenyl-1,3-butadiyne. Such an effect of Cu^I was observed previously by Schoenebeck et al.[32a] and by Gelman and Buchwald.[32b]

In the 40–120 °C range, the yield of diphenylacetylene showed a strong temperature dependence (Table 2). With [S]/[C]=3000, the maximum TOF of 2190 h^{-1} was observed at 120 °C. It is gratifying that the reaction also proceeded—albeit slowly—at low temperatures (e.g., at 40 °C, Table 2, entry 1); this is an important condition in reactions of heat sensitive compounds.
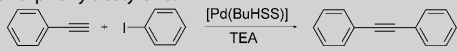
Table 2. Sonogashira coupling of iodobenzene and phenylacetylene as a function of temperature.[a]

Entry	T [°C]	Yield [%][b]
1	40	14
2	40	58[c]
3	60	40
4	80	51
5	100	63
6	120	73

[a] Reaction conditions: [Pd(BuHSS)] (1.67×10^{-7} mol), iodobenzene (5×10^{-4} mol; substrate), phenylacetylene (7.5×10^{-4} mol, 1.5 equiv), TEA (2×10^{-3} mol), water (3 mL), 60 min, air. [b] Yield determined by GC on the basis of the amount of starting iodobenzene. [c] 10 h.

With the aim of increasing the solubility of the organic components in water, the reaction was also run in the presence of tetrahydrofuran (THF) as a cosolvent. Small amounts of THF did not change the conversion; however, at water/THF=2/1 a significant decrease in yield was observed (Figure S14 in the Supporting Information).

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Table 3. Recycling of the catalyst in the Sonogashira coupling of iodo-benzene and phenylacetylene.[a]
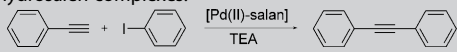
Entry	Number of cycles	Yield [%][b]	TON[c]
1	1	51	1530
2	2	27	2340
3	3	20	2940
4	4	11	3270

[a] Reaction conditions: [Pd(BuHSS)] (1.67×10^{-7} mol), iodobenzene (5×10^{-4} mol), phenylacetylene (7.5×10^{-4} mol, 1.5 equiv), TEA (2×10^{-3} mol), water (3 mL), 60 min, 80 °C, air. [b] Yield determined by GC on the basis of the amount of starting iodobenzene. [c] TON: turnover number, defined as (mol of product)/(mol of catalyst).

Recycling of the [Pd(BuHSS)]-containing aqueous phase in biphasic Sonogashira coupling was also studied (Table 3). Although the yields decreased steadily, the catalyst was still active in the 4th cycle with a TOF = 330 h^{-1}. The drop in activity may be due to accumulation of inorganic halide ([Et$_3$NH]I) in the catalyst-containing aqueous phase, similar to the effect of NaCl on [Pd(HSS)]-catalyzed redox isomerization of allylic alcohols.[24a]

[Pd(HSS)], [Pd(BuHSS)], and [Pd(CyHSS)] showed comparable activities, of which [Pd(CyHSS)] is the most effective catalyst (Table 4). Nevertheless, the TOF values did not differ significantly (1380–1650 h^{-1}).

Table 4. Sonogashira coupling of iodobenzene and phenylacetylene with Pd^{II}–tetrahydrosalen complexes.[a]

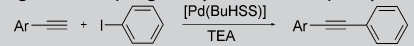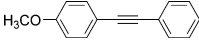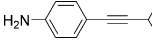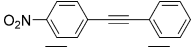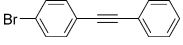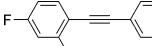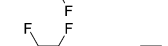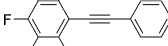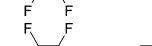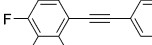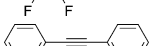| Entry	Catalyst	Yield [%][b]	TOF [h^{-1}]
1	[Pd(HSS)]	46	1380
2	[Pd(BuHSS)]	51	1530
3	[Pd(CyHSS)]	55	1650

[a] Reaction conditions: catalyst (1.67×10^{-7} mol), iodobenzene (5×10^{-4} mol), phenylacetylene (7.5×10^{-4} mol, 1.5 equiv), TEA (2×10^{-3} mol), water (3 mL), 60 min, 80 °C, air. [b] Yield determined by GC on the basis of the amount of starting iodobenzene.

The scope of the reaction was studied under optimized conditions of the coupling of phenylacetylene and aryl iodides with various substituents (Table 5). Aryl iodides with electron-withdrawing substituents showed higher reactivity, for example, 1-iodo-4-nitrobenzene and 1-bromo-4-iodobenzene gave excellent yields (Table 5, entries 4 and 5) and in case of the bromo derivative the TOF reached 2790 h^{-1}. However, multiply substituted iodobenzenes, such as 2,4-difluoroiodobenzene or iodopentafluorobenzene, reacted less efficiently (Table 5, entries 6 and 7). Iodoaromatics with electron-donating substituents, such as 4-iodoanisole (Table 5, entry 2) and iodoaniline (Table 5, entry 3), showed diminished reactivity and the coupling of 1-iodonaphtalene with phenylacetylene (Table 5,

Table 5. Sonogashira coupling of aryl iodides and phenylacetylene.[a]

Entry	Product	Yield [%][b]
1		51
2	H$_3$CO–	35
3	H$_2$N–	34
4	O$_2$N–	87
5	Br–	93
6		37
7		11
8		42[c]
9		6
10		36[c]
11		44

[a] Reaction conditions: [Pd(BuHSS)] (1.67×10^{-7} mol), aryl iodide (5×10^{-4} mol), phenylacetylene (7.5×10^{-4} mol, 1.5 equiv), TEA (2×10^{-3} mol), water (3 mL), 60 min, 80 °C, air. [b] Yield determined by GC on the basis of the amount of starting aryl iodide. [c] 6 h.

entry 11) also gave somewhat lower yields relative to the reaction of iodobenzene. Under the applied mild conditions, even 2-iodopyridine could be coupled with phenylacetylene. In the standard reaction time of 1 h the yield was only 6% (Table 5, entry 9); however, after 6 h we obtained 36% yield of the coupled product. Although for electronic reasons 2-iodopyridine is expected to react faster than iodobenzene, this low reactivity may reflect the effect of nitrogen coordination to palladium. A similar decrease in conversion was also observed in the case of pentafluoroiodobenzene (Table 5, entries 7 and 8).

Various terminal alkynes were coupled with iodobenzene (Table 6). 4-Ethynyltoluene was less reactive than phenylacetylene, whereas 4-ethynylanisole and 1-bromoethynylbenzene gave higher conversions under the same conditions (Table 6, entry 3 versus entries 2 and 4). When iodobenzene was coupled with the water-soluble propargyl alcohol, only 8% conversion was obtained in 1 h; however, the catalyst was not poisoned and had not decomposed because in 6 h the conversion attained 60% (Table 6, entries 7 and 8). Similarly, 4-ethynylpyridine reacted slowly but steadily (3% conversion in 1 h versus 15% in 6 h; Table 6, entries 5 and 6).

Bromo- and chloroaryl derivatives are usually less reactive than the corresponding iodo compounds. To determine the activity of water-soluble Pd^{II}–salan complexes in a biphasic reaction of such substrates, the coupling of various bromo- and

Table 6. Sonogashira coupling of iodobenzene and terminal alkynes.[a]

Entry	Product	Yield [%][b]
1		51
2	H₃CO...	60
3	H₃C...	25
4	Br...	59
5	N...	3
6	N...	15[c]
7	HO...	8
8	HO...	60[c]

[a] Reaction conditions: [Pd(BuHSS)] (1.67×10^{-7} mol), iodobenzene (5×10^{-4} mol), terminal alkyne (7.5×10^{-4} mol, 1.5 equiv), TEA (2×10^{-3} mol), water (3 mL), 60 min, 80 °C, air. [b] Yield determined by GC on the basis of the amount of starting iodobenzene. [c] 6 h.

chloroarenes with phenylacetylene was studied with the [Pd-(BuHSS)] catalyst. The reactions run smoothly at 80 °C and no formation of any byproducts was observed. The results are presented in Table 7. At a [S]/[C] = 500 ratio, bromoarenes gave good to excellent yields, although over a longer reaction time (20 h). Dibromobenzenes were particularly reactive (Table 7, entries 4–6) with conversions in the 85–89 % range. 4-Bromoani-

Table 7. Sonogashira coupling of aryl halides and phenylacetylene.[a]

X = Cl, Br

Entry	Aryl halide	Product	Yield [%][b]
1	Br		64
2	Cl—Br	Cl—	66
3	H₃CO—Br	H₃CO—	46
4	Br, Br		86
5	Br, Br		89
6	Br—Br	Br—	85
7	Br		16
8[c]	Cl		22
9[c]	Cl, Cl		69

[a] Reaction conditions: [Pd(BuHSS)] (1×10^{-6} mol), aryl halide (5×10^{-4} mol), phenylacetylene (7.5×10^{-4} mol, 1.5 equiv), TEA (2×10^{-3} mol), water (3 mL), 20 h, 80 °C, air. [b] Yield determined by GC on the basis of the amount of starting aryl halide. [c] 5×10^{-6} mol [Pd(BuHSS)].

sole and 1-bromonaphtalene showed lower reactivity than that of bromobenzene (Table 7, entries 3 and 7 versus entry 1). To achieve substantial conversion of chloroarenes, the amount of catalyst had to be increased to 1 mol %; under such conditions chlorobenzene was coupled with phenylacetylene with 22 % conversion, whereas 1,2-dichlorobenzene reacted with 69 % conversion (Table 7, entries 8 and 9).

The data obtained so far do not allow solid conclusions to be drawn on the reaction mechanism with the new Pd^II–sulfosalan catalysts. The generally accepted mechanistic scheme[1c] cannot be simply applied to this system. The substituent effects are in accordance with an initial oxidative addition of the Ar—X substrate onto the catalyst. Because the initial form of the catalysts involves Pd^II ion reduction to Pd⁰, which is likely to be brought about by TEA or the alkyne substrates in reaction mixtures when inorganic bases, such as KOH, are used. Furthermore, in the coordinatively saturated catalysts, for example, in [Pd(HSS)] at least one free coordination site has to be created by decoordination of one of the phenolate oxygen atoms. Our earlier DFT calculations on the reaction of [Pd(HSS)] and H₂ showed that such phenolate decoordination was feasible.[24a]

It is also known that in several cases palladium-containing catalysts degrade under the conditions of C—C coupling reactions, which are catalyzed by palladium nanoparticles (Pd NPs) formed in such degradation processes. Furthermore, ripening of Pd NPs may decrease their activity over longer reaction times; this could rationalize the drop in catalyst activity in our recycling experiments, too. During the reactions, we did not observe the formation of precipitates or any other sign of particle formation, and there was no baseline increase in the UV/Vis spectra of the catalyst-containing aqueous phase. To gain more information on possible NP catalysis in our systems, we performed a standard mercury test and performed dynamic light scattering (DLS) measurements. When the standard reaction of iodobenzene and phenylacetylene was performed in the presence of mercury, conversion to diphenylacetylene dropped from 51 to 36 %. In contrast, DLS measurements on the resulting aqueous and organic phases did not show the presence of NPs. Nevertheless, based on these observations, the formation of NPs and their participation in catalysis cannot be excluded. Clearly, further work is needed to gain an insight into the reaction mechanism of Sonogashira coupling with Pd^II–sulfosalan catalysts, including the establishment of the true nature of the catalyst (molecular vs. NP).

Copper-free Sonogashira coupling in the presence of air with no need for organic bases and solvents: Towards a green procedure

In aqueous-phase organometallic catalysis, products are usually isolated by extraction with organic solvents. This is a fast and effective method in the case of small-scale reactions for determining reaction parameters (reaction kinetics, activity and selectivity of the catalyst, etc.). However, to eliminate pollution of the environment, it is of paramount importance to devise methods for product isolation with no need to use toxic or-

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ganic solvents. In the following, we describe a possible solution of this problem, which, to the best of our knowledge, has not been applied before for Sonogashira couplings.

Sonogashira coupling procedures characteristically involve a 10–100 % excess of the alkyne to achieve high reaction rates together with full conversion of the aryl halide. Additionally, when a Cu^I cocatalyst is used, the formation of butadiyne derivatives often leads to substantial substrate loss. As a consequence, the coupled product should be purified by chromatography or other techniques.

To overcome these difficulties, we first checked the effect of using equimolar amounts of aryl halide and alkyne (Table S4 in the Supporting Information). In the coupling of phenylacetylene with iodobenzene, the yield obtained in 1 h decreased from 58 to 35 % when the [alkyne]/[aryl halide] ratio decreased from 2/1 to 1/1. Encouraged by the finding that no side products were formed, in the rest of the studies we used longer reaction times (unoptimized) to achieve 100 % conversion (as determined by GC).

In most cases, the water-insoluble products precipitated from the aqueous reaction mixture. Upon cooling, the products solidified and could be isolated by simple filtration. Thorough washings with cold water yielded analytically pure products, the identity and purity of which were checked by ^{1}H and ^{13}C NMR spectroscopy and GC, respectively.

Table 8 shows the yields of diphenylacetylene derivatives obtained by the above method in Sonogashira couplings of several aryl iodides and terminal alkynes with the [Pd(BuHSS)] catalyst. This simple method, which led to full conversion of the starting compounds (applied in 1/1 ratio) and did not require extraction by an organic solvent for product isolation, led to the products being isolated in excellent yields.

Replacement of TEA by a less harmful base was also deemed necessary for a greener procedure. For this purpose KOH was chosen because, of the inorganic bases, it was the most effective (Table S2 in the Supporting Information). However, in this case, the coupling reaction was not complete, even when using a higher catalyst loading (1 mol %) and a reaction time of 24 h. Additionally, the products stuck to the magnetic stirrer bar so strongly that they could only be removed by dissolution in organic solvents. These difficulties could be overcome simply by adding a surfactant, sodium dodecylsulfate (SDS), to the reaction mixture. The reactions became fast enough to achieve 100 % conversion (as determined by GC) in 24 h, and the products could be easily collected by filtration. Table 9 shows the excellent yields of diphenylacetylene derivatives obtained by this method. It should be added, however, that thorough washings with cold water were needed to remove the surfactant from the products.

The aqueous catalyst solutions obtained upon filtering out the products were recycled for further reactions. To achieve high conversions in the preparative-scale processes, we applied longer reaction times from run to run. In such a way, the product was isolated in 93–98 % yield, as exemplified by the coupling of 1-iodo-4-nitrobenzene and phenylacetylene (Table 10). Furthermore, the overall TON of the catalyst reached 8640 by the end of the 3rd cycle.

**Table 8.** Sonogashira coupling of aryl iodides and terminal alkynes in water.[a]

$$Ar-I + \text{≡}-\text{C}_6\text{H}_4-R \xrightarrow[\text{TEA}]{[\text{Pd(BuHSS)}]} Ar-\text{≡}-\text{C}_6\text{H}_4-R$$

Entry	Product	Reaction time [h][b]	Isolated yield [%]
1	O$_2$N—C$_6$H$_4$—≡—C$_6$H$_5$	4	97
2	O$_2$N—C$_6$H$_4$—≡—C$_6$H$_4$—CH$_3$	12	98
3	O$_2$N—C$_6$H$_4$—≡—C$_6$H$_4$—OCH$_3$	12	97
4	O$_2$N—C$_6$H$_4$—≡—C$_6$H$_4$—Br	12	99
5	Br—C$_6$H$_4$—≡—C$_6$H$_5$	8	88
6	Br—C$_6$H$_4$—≡—C$_6$H$_4$—CH$_3$	12	95
7	Br—C$_6$H$_4$—≡—C$_6$H$_4$—OCH$_3$	12	93
8	Br—C$_6$H$_4$—≡—C$_6$H$_4$—Br	8	97
9	C$_6$H$_5$—≡—C$_6$H$_4$—Br	8	76[c]
10	H$_3$CO—C$_6$H$_4$—≡—C$_6$H$_4$—Br	12	90[c]
11	F,F—C$_6$H$_3$—≡—C$_6$H$_4$—Br	12	88[c]
12	naphthyl—≡—C$_6$H$_4$—Br	12	85[c]
13	naphthyl—≡—C$_6$H$_4$—OCH$_3$	12	89[c]
14	H$_3$CO—C$_6$H$_4$—≡—C$_6$H$_4$—OCH$_3$	12	96[c]
15	C$_6$H$_5$—≡—C$_6$H$_4$—CH$_3$	12	91[c]

[a] Reaction conditions: [Pd(BuHSS)] (3.34×10^{-7} mol), aryl iodide (1×10^{-3} mol), terminal alkyne (1×10^{-3} mol, 1 equiv), TEA (4×10^{-3} mol), water (3 mL), 80 °C, air. [b] Reaction times are not optimized. [c] 1.00×10^{-6} mol [Pd(BuHSS)].

Table 9. Sonogashira coupling of aryl iodides and terminal alkynes in water.[a]

$$R^1-\text{C}_6\text{H}_4-I + \text{≡}-\text{C}_6\text{H}_4-R^2 \xrightarrow[\text{KOH, SDS}]{[\text{Pd(BuHSS)}]} R^1-\text{C}_6\text{H}_4-\text{≡}-\text{C}_6\text{H}_4-R^2$$

Entry	Product	Isolated yield [%][b]
1	O$_2$N—C$_6$H$_4$—≡—C$_6$H$_5$	90
2	O$_2$N—C$_6$H$_4$—≡—C$_6$H$_4$—CH$_3$	98
3	O$_2$N—C$_6$H$_4$—≡—C$_6$H$_4$—OCH$_3$	91
4	Br—C$_6$H$_4$—≡—C$_6$H$_5$	93
5	Br—C$_6$H$_4$—≡—C$_6$H$_4$—CH$_3$	95
6	Br—C$_6$H$_4$—≡—C$_6$H$_4$—OCH$_3$	93

[a] Reaction conditions: [Pd(BuHSS)] (1×10^{-5} mol), aryl iodide (1×10^{-3} mol), terminal alkyne (1×10^{-3} mol, 1 equiv), KOH (4×10^{-3} mol), SDS (5×10^{-6} mol), water (3 mL), 24 h, 80 °C, air. [b] Reaction times are not optimized.

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Table 10. Recycling of the catalyst in the Sonogashira coupling of 1-iodo-4-nitrobenzene and phenylacetylene.[a]
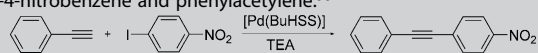
Number of cycles	Reaction time [h][b]	Isolated yield [%]	TON [h^{-1}]
1	4	97	2910
2	12	93	5700
3	36	98	8640

[a] Reaction conditions: [Pd(BuHSS)] (3.34×10^{-7} mol), 1-iodo-4-nitrobenzene (1×10^{-3} mol), phenylacetylene (1×10^{-3} mol, 1 equiv), TEA (4×10^{-3} mol), water (3 mL), 80 °C, air. [b] Reaction times are not optimized.

Conclusions

We reported the synthesis of sulfonated tetrahydrosalen-type ligands (sulfosalans, **1**–**3**) and their palladium(II) complexes (**4**–**6**). The syntheses are straightforward and yield stable ligands and palladium(II) complexes that can be stored in aqueous solution in the presence of air for months with no apparent sign of decomposition. Complexes **4**–**6** showed excellent catalytic activity in the Sonogashira coupling of aryl halides and terminal alkynes in aqueous–organic biphasic systems. The hydrophilic nature of **4**–**6** allowed us to run the reactions in biphasic mixtures of water-insoluble reactants and aqueous solutions of the catalysts; this allowed elimination of the use of organic solvents.

Based on these findings, we devised a simple preparative-scale method for the synthesis of diphenylacetylene derivatives by Sonogashira coupling. Because the reaction did not require a copper(I) cocatalyst, no formation of butadiyne byproducts was observed. With equimolar quantities of the aryl halide and terminal alkyne, 100% conversion could be achieved with sufficiently long reaction times (4–24 h) and did not leave unreacted substrates (as opposed to reactions run in excess of alkyne). Insolubility in water of the coupled products allowed their simple isolation by filtration and purification by washing with water. TEA could be replaced with KOH; however, in this case, a micelle-forming agent, SDS, was required to speed up the reaction and facilitate filtration of the products. Altogether, the procedure befits several principles of green chemistry.

Experimental Section

Materials and methods

All reagents were obtained commercially and used as received. The ^{1}H and ^{13}C NMR spectra of samples were recorded on a Bruker Avance 360 MHz spectrometer. Coupling constants are reported in Hz. ESI mass spectra were recorded on a Bruker micrOTOFQ ESI-TOF mass spectrometer. Reaction mixtures in the Sonogashira coupling were analyzed by GC (Agilent 7890A gas chromatograph; HP-5 30 m × 0.32 mm × 0.25 μm; FID; carrier gas nitrogen) and ^{1}H NMR spectroscopy. Elemental analysis was performed on an Elementar varioMicro cube instrument (CHNS). DLS measurements were made on a Malvern Zetasizer Nano ZS instrument.

Single-crystal X-ray structure determinations

A colorless prism crystal (0.35 mm × 0.3 mm × 0.15 mm) of **2** was mounted on top of a glass capillary by using epoxy glue. Diffraction intensity data collection was performed at 293(2) K on a Bruker-Nonius MACH3 diffractometer equipped with a point detector using graphite-monochromated Mo$_{K\alpha}$ radiation ($\lambda =$ 0.71073 Å). The structure was solved by using the SIR-92 program[33] and refined by a full-matrix least-squares method on F^2, with all non-hydrogen atoms refined with anisotropic thermal parameters by using the SHELXL-97 package.[34] Publication material was prepared with the WINGX-suite.[35] Hydrogen atoms were located geometrically and refined in the rigid mode, except water hydrogen atoms, which could be found in the difference electron density map. The distance between the hydrogen and oxygen atoms had to be restrained in the final stage of the refinement of the orientation of water molecules; hence the description of the hydrogen-bond web is uncertain. The remaining electron density peak represented an alternative position of one of the water hydrogen atoms and checkcif resulted in a few B and C level errors because of the uncertain positioning of water protons.

Crystallographic and experimental details are summarized in Table S1 in the Supporting Information. CCDC 989166 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Preparation of sulfosalans 1–3

Ligands were prepared as previously described for the preparation of HSS.[24a] Accordingly, salen-type compounds were first obtained through the condensation reaction of salicylaldehyde and the corresponding diamine; these were then reduced with NaBH$_4$. The resulting amines were sulfonated in fuming sulfuric acid. Adjusting the acidity of the sulfonation mixtures to pH 5 led to the precipitation of disulfonated salan-type ligands as the free acids in their zwitterionic forms.

***N,N′*-Bis(salicylidene)-1,2-ethylenediamine**: Yield: 10.12 g, 74% (38 mmol); ^{1}H NMR (360 MHz, [D$_6$]DMSO, 25 °C): $\delta =$ 3.96 (s, 4H; -CH$_2$-CH$_2$-), 6.90 (q, ^3J(H,H) $=$ 7.9 Hz, 4H; CH$_{arom}$), 7.35 (t, ^3J(H,H) $=$ 7.5 Hz, 2H; CH$_{arom}$), 7.46 (d, ^3J(H,H) $=$ 7.5 Hz, 2H; CH$_{arom}$), 8.62 ppm (s, 2H; CH$=$N).

***N,N′*-Bis(2-hydroxybenzyl)-1,2-ethylenediamine**: Yield: 10.14 g, 98% (37 mmol); ^{1}H NMR (360 MHz, [D$_6$]DMSO, 25 °C): $\delta =$ 3.38 (s, 4H; -CH$_2$-CH$_2$-), 4.14 (s, 4H; CH$_2$-NH), 6.87 (t, ^3J(H,H) $=$ 7.0 Hz, 2H; CH$_{arom}$), 7.02 (d, ^3J(H,H) $=$ 7.8 Hz, 2H; CH$_{arom}$), 7.21 (t, ^3J(H,H) $=$ 7.6 Hz, 2H; CH$_{arom}$), 7.46 ppm (d, ^3J(H,H) $=$ 6.7 Hz, 2H; CH$_{arom}$).

HSS (1): Yield: 135 mg, 97% (0.23 mmol); ^{1}H NMR (360 MHz, D$_2$O, 25 °C): $\delta =$ 2.67 (s, 4H; -CH$_2$CH$_2$-), 3.58 (s, 4H; CH$_2$-NH), 6.52 (d, $^3J =$ 8.6 Hz, 2H; CH$_{arom}$), 7.36 (dd, $^3J_1 =$ 8.6 Hz, $^4J_2 =$ 2.1 Hz, 2H; CH$_{arom}$), 7.41 ppm (d, $^3J =$ 2.1 Hz, 2H; CH$_{arom}$); ^{13}C NMR (90 MHz, D$_2$O, 25 °C): $\delta =$ 168.7, 127.7, 126.8, 126.3, 126.2, 118.4, 48.7, 47.3 ppm; ESI-MS: m/z calcd for C$_{16}$H$_{16}$Na$_2$N$_2$O$_8$S$_2$Pd: 431.059 $[M-2$Na$+$H]$^{1-}$; found: 431.064 (for the correct isotope distribution, see Figure S2 in the Supporting Information); elemental analysis calcd (%) for C$_{16}$H$_{18}$Na$_2$N$_2$O$_8$S$_2$·2H$_2$O (512.38): C 37.51, H 4.33, N 5.47, S 12.52; found: C 37.55, H 4.68, N 5.48, S 13.23.

***N,N′*-Bis(salicylidene)-1,4-butylenediamine**: Yield: 13.90 g, 92% (47 mmol); ^{1}H NMR (360 MHz, [D$_6$]DMSO, 25 °C): $\delta =$ 1.73 (s, 4H; -CH$_2$-CH$_2$-), 3.66 (s, 4H; -N-CH$_2$-), 6.90 (t, ^3J(H,H) $=$ 8.3 Hz, 4H; CH$_{arom}$), 7.35 (t, ^3J(H,H) $=$ 7.7 Hz, 2H; CH$_{arom}$) 7.44 (d, ^3J(H,H) $=$ 7.9 Hz, 2H; CH$_{arom}$), 8.58 ppm (s, 2H; CH$=$N).

***N,N′*-Bis(2-hydroxybenzyl)-1,4-butylenediamine**: Yield: 4.44 g, 87% (15 mmol); ^{1}H NMR (360 MHz, [D$_6$]DMSO, 25 °C): $\delta =$ 1.75 (s,

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4H; -CH$_2$-CH$_2$-), 2.92 (s, 4H; CH$_2$-NH), 4.07 (s, 4H; CH$_2$-NH), 6.86 (t, ^3J(H,H) = 7.5 Hz, 2H; CH$_{arom}$), 7.00 (d, ^3J(H,H) = 8.1 Hz, 2H; CH$_{arom}$), 7.26 (t, ^3J(H,H) = 7.9 Hz, 2H; CH$_{arom}$), 7.43 ppm (d, ^3J(H,H) = 7.5 Hz, 2H; CH$_{arom}$).

BuHSS (2): Yield: 905 mg, 59% (1.97 mmol); ^{1}H NMR (360 MHz, D$_2$O, 25 °C): δ = 1.49 (s, 4H; -CH$_2$CH$_2$-), 2.56 (s, 4H; -CH$_2$-NH), 3.60 (s, 4H; CH$_2$-NH), 6.55 (d, ^3J = 8.5 Hz, 2H; CH$_{arom}$), 7.40 (dd, $^3J_1$ = 8.6 Hz, $^4J_2$ = 2.2 Hz, 2H; CH$_{arom}$), 7.44 ppm (s, 2H; CH$_{arom}$); ^{13}C NMR (90 MHz, D$_2$O, 25 °C): δ = 168.8, 127.9, 126.3, 126.2, 118.4, 48.8, 48.0, 26.6 ppm; ESI-MS: m/z calcd for C$_{18}$H$_{22}$Na$_2$N$_2$O$_8$S$_2$: 459.090 [M−2Na+H]$^-$; found: 459.087 (for the correct isotope distribution, see Figure S6 in the Supporting Information); elemental analysis calcd (%) for C$_{18}$H$_{24}$N$_2$O$_8$S$_2$·H$_2$O (478.46): C 45.19, H 5.48, N 5.86, S 13.40; found: C 45.46, H 5.33, N 6.17, S 13.39.

N,N′-**Bis(salicylidene)-1,2-cyclohexanediamine**: Yield: 15.48 g, 94% (48 mmol); ^{1}H NMR (360 MHz, [D$_6$]DMSO, 25 °C): δ = 1.48–1.93 (m, 10H; CH$_{ring}$), 6.87 (m, 4H; CH$_{arom}$), 7.36 (m, 4H; CH$_{arom}$), 8.50 (s, 1H; CH=N), 8.59 ppm (s, 1H; CH=N).

N,N′-**Bis(2-hydroxybenzyl)-1,2-cyclohexanediamine**: Yield: 5.12 g, 83% (15 mmol); ^{1}H NMR (360 MHz, [D$_6$]DMSO, 25 °C): δ = 1.23–1.76 (m, 10H; CH$_{ring}$), 4.08 (s, 4H; CH$_2$-NH), 6.85 (t, ^3J(H,H) = 7.0 Hz, 2H; CH$_{arom}$), 7.01 (d, ^3J(H,H) = 6.6 Hz, 2H; CH$_{arom}$), 7.22 (t, ^3J(H,H) = 7.5 Hz, 2H; CH$_{arom}$), 7.45 ppm (d, ^3J(H,H) = 7.0 Hz, 2H; CH$_{arom}$).

CyHSS (3): Yield: 480 mg, 32% (0.99 mmol); ^{1}H NMR (360 MHz, D$_2$O, 25 °C): δ = 1.06 (m, 4H; CH$_{ring}$), 1.50 (m, 2H; CH$_{ring}$), 1.83 (m, 2H; CH$_{ring}$), 2.28 (m, 2H; CH$_{ring}$), 3.55 (m, 4H; CH$_2$-NH), 6.45 (d, ^3J = 8.4 Hz, 2H; CH$_{arom}$), 7.32 (d, ^3J = 8.7 Hz, 2H; CH$_{arom}$), 7.37 ppm (s, 2H; CH$_{arom}$); ^{13}C NMR (90 MHz, D$_2$O, 25 °C): δ = 169.1, 128.0, 127.1, 126.3, 126.1, 118.5, 118.4, 46.5 ppm; ESI-MS: m/z calcd for C$_{20}$H$_{24}$Na$_2$N$_2$O$_8$S$_2$: 485.105 [M−2Na+H]$^-$; found: 455.105 (for the correct isotope distribution, see Figure S10 in the Supporting Information); elemental analysis calcd (%) for C$_{20}$H$_{24}$Na$_2$N$_2$O$_8$S$_2$·5H$_2$O (620.54): C 38.71, H 5.52, N 4.51, S 10.34; found: C 38.88, H 5.59, N 4.43, S 10.66.

Preparation of Pd–sulfosalans 4–6

Complexes were prepared as previously described[24a] for the preparation of [Pd(HSS)] by stirring equimolar amounts of (NH$_4$)$_2$[PdCl$_4$] and the corresponding ligand in an aqueous solution at pH 7.5 (adjusted with NaOH) for 10 h at 60 °C followed by precipitation with ethanol.

[Pd(HSS)] (4): Yield: 135 mg, 97% (0.23 mmol); ^{1}H NMR (360 MHz, D$_2$O, 25 °C): δ = 2.78 (d, ^3J(H,H) = 8.0 Hz, 2H; -CH$_2$CH$_2$-), 2.94 (d, ^3J(H,H) = 8.0 Hz, 2H; -CH$_2$CH$_2$-), 3.46 (d, ^3J(H,H) = 13.0 Hz, 2H; CH$_2$-NH), 4.15 (d, ^3J(H,H) = 13.2 Hz, 2H; CH$_2$-NH), 6.81 (d, ^3J(H,H) = 8.9 Hz, 2H; CH$_{arom}$), 7.41 (s, 2H; CH$_{arom}$), 7.45 ppm (d, ^3J(H,H) = 9.2 Hz, 2H; CH$_{arom}$); ^{13}C NMR (90 MHz, D$_2$O, 25 °C): δ = 165.1, 129.2, 128.1, 127.6, 123.6, 118.9, 53.2, 53.0 ppm; ESI-MS: m/z calcd for C$_{16}$H$_{16}$Na$_2$N$_2$O$_8$S$_2$Pd: 266.970 [M−2Na]$^{2-}$; found: 266.967 (for the correct isotope distribution, see Figure S4 in the Supporting Information); elemental analysis calcd (%) for C$_{16}$H$_{16}$Na$_2$N$_2$O$_8$S$_2$Pd·10H$_2$O (778.83): C 24.68, H 4.92, N 3.60, S 8.23; found: C 24.68, H 4.55, N 3.65, S 8.60.

[Pd(BuHSS)] (5): Yield: 140 mg, 96% (0.23 mmol); ^{1}H NMR (360 MHz, D$_2$O, 25 °C): δ = 1.61 (m, 2H; -CH$_2$CH$_2$-), 2.27 (m, 4H; CH$_2$-NH), 2.45 (m, 2H; -CH$_2$CH$_2$-), 3.33 (d, ^2J = 13.6 Hz, 2H; CH$_2$-NH), 4.13 (d, ^2J = 13.6 Hz, 2H; CH$_2$-NH), 6.85 (d, ^3J = 8.3 Hz, 2H; CH$_{arom}$), 7.44 (s, 2H; CH$_{arom}$), 7.52 ppm (d, ^3J = 7.9 Hz, 2H; CH$_{arom}$); ^{13}C NMR (90 MHz, D$_2$O, 25 °C): δ = 164.6, 129.7, 128.0, 123.2, 118.4, 51.6, 51.5, 25.3 ppm; ESI-MS: m/z calcd for C$_{18}$H$_{20}$Na$_2$N$_2$O$_8$S$_2$Pd: 280.986 [M−2Na]$^{2-}$; found: 280.984 (for the correct isotope distribution, see Figure S8 in the Supporting Information); elemental analysis

calcd (%) for C$_{18}$H$_{20}$Na$_2$N$_2$O$_8$S$_2$Pd·3H$_2$O (662.84): C 32.62, H 3.95, N 4.23, S 9.68; found: C 32.78, H 3.80, N 4.18, S 9.76.

[Pd(CyHSS)] (6): Yield: 135 mg, 89% (0.21 mmol); ^{1}H NMR (360 MHz, D$_2$O, 25 °C): δ = 1.12 (m, 4H; CH$_{ring}$), 1.65 (m, 2H; CH$_{ring}$), 2.39–2.71 (m, 4H; CH$_{ring}$), 3.63 (m, 2H; CH$_2$-NH), 4.00 (m, 2H; CH$_2$-NH), 5.55 (m, 2H; CH$_{arom}$), 6.83 (m, 2H; CH$_{arom}$), 7.47 ppm (m, 4H; CH$_{arom}$); ^{13}C NMR (90 MHz, D$_2$O, 25 °C): δ = 157.6, 134.3, 128.1, 127.8, 115.9, 50.2, 45.7, 24.1 ppm; ESI-MS: m/z calcd for C$_{20}$H$_{22}$Na$_2$N$_2$O$_8$S$_2$Pd: 293.990 [M−2Na]$^{2-}$; found: 293.990 (for the correct isotope distribution, see Figure S12 in the Supporting Information); elemental analysis calcd (%) for C$_{20}$H$_{22}$Na$_2$N$_2$O$_8$S$_2$Pd·6H$_2$O (742.94): C 32.33, H 4.61, N 3.77, S 8.63; found: C 32.08, H 4.51, N 3.84, S 8.60.

General procedure for the Sonogashira cross-coupling reaction

The coupling reactions were performed under air in a 25 mL flask equipped with a rubber septum. The reaction mixture was prepared by mixing aryl halide (0.5 mmol), terminal alkyne (0.5–0.75 mmol), base (0.5–3.0 mmol), a solution of the catalyst in water (0.1×10^{-3}–5.0×10^{-3} mmol Pd), and water (total volume of solvent 3 mL). The reaction vessel was immersed into a thermostated bath (40–80 °C) and the mixture was stirred for 15–210 min. At room temperature, the products were extracted with chloroform (1 mL), dried over MgSO$_4$, and subjected to gas chromatography. In the recycling experiments, after extraction the catalyst-containing aqueous phase was used in the next run.

General procedure for the preparation of Sonogashira coupling products without organic solvents

The coupling reactions were performed under air in a 25 mL flask equipped with a rubber septum. The reaction mixture was prepared by mixing aryl halide (1 mmol), terminal alkyne (1 mmol), TEA or KOH (4 mmol), a solution of the catalyst in water (3.34×10^{-4}–1.00×10^{-2} mmol Pd), and water (total volume of solvent 3 mL). When KOH was used as a base, SDS (5×10^{-3} mmol) was also added. The reaction mixture was stirred for 4–24 h at 80 °C then cooled to 4 °C before the product was filtered. After washing the residue several times with deionized water, the analytically pure product was obtained.

[1] a) *Applied Cross-Coupling Reactions* (Ed.: Y. Nishihara), Springer, Heidelberg, **2013**; b) J. G. de Vries, *Top. Organomet. Chem.* **2012**, *42*, 1–34; c) R. Chinchilla, C. Nájera, *Chem. Soc. Rev.* **2011**, *40*, 5084–5121; d) *Palladium-Catalyzed Coupling Reactions* (Ed.: Á. Molnár), Wiley-VCH, Weinheim, **2013**; e) D. L. Gray in *Name Reactions for Homologations* (Ed.: J. J. Lee), Wiley, Hoboken, NJ, **2009**, pp. 100–132; f) K. Sonogashira, *J. Orga-*

nomet. Chem. **2002**, *653*, 46–49; g) K. Sonogashira in *Handbook of Organopalladium Chemistry for Organic Synthesis* (Ed.: E. Negishi), Wiley, Hoboken, NJ, **2002**, pp. 493–529; h) R. Chinchilla, C. Nájera, *Chem. Rev.* **2014**, *114*, 1783–1826.

[2] a) X. Ma, X. Jiang, S. Zhang, X. Huang, Y. Cheng, C. Zhu, *Polym. Chem.* **2013**, *4*, 4396–4404; b) H. Lee, H. W. Park, J. Y. Chang, *Macromol. Res.* **2013**, *21*, 1274–1280; c) M.-Y. Jiang, Q. Wang, Q. Chen, X.-M. Hu, X.-L. Ren, Z.-H. Li, B.-H. Han, *Polymer* **2013**, *54*, 2952–2957.

[3] a) H. Chen, P. Liu, H. Li, S. Daniel, Z. Zeng, *Tetrahedron* **2013**, *69*, 5129–5135; b) Y.-M. Zhang, D. Wang, Z.-C. Miao, S.-K. Jin, H. Yang, *Liquid Crystals* **2012**, *39*, 1330–1339; c) K. C. Majumdar, S. Mondal, N. De, R. K. Sinha, N. Pal, B. Roy, *Tetrahedron Lett.* **2010**, *51*, 521–524; d) H. Shang, R. Hua, Q. Zheng, J. Zhang, X. Liang, Q. Zhu, *Appl. Organomet. Chem.* **2010**, *24*, 473–476; e) H. Gallardo, R. Cristiano, A. A. Vieira, R. A. W. Neves Filho, R. M. Srivastava, *Synthesis* **2008**, *4*, 605–609; f) J. F. Tannaci, M. Noji, J. L. McBee, T. D. Tilley, *J. Org. Chem.* **2008**, *73*, 7895–7900.

[4] a) B. Z. Lu, H.-X. Wei, Y. Zhang, W. Zhao, G. Li, V. Farina, C. H. Senanayake, *J. Org. Chem.* **2013**, *78*, 4558–4562; b) A. Yepremyan, T. G. Minehan, *Org. Biomol. Chem.* **2012**, *10*, 5194–5196; c) A. Larivée, J. B. Unger, M. Thomas, C. Wirtz, C. Dubost, S. Handa, A. Fürstner, *Angew. Chem. Int. Ed.* **2011**, *50*, 304–309; *Angew. Chem.* **2011**, *123*, 318–323; d) A. Français, A. Leyva-Pérez, G. Etxebarria-Jardi, J. Peña, S. V. Ley, *Chem. Eur. J.* **2011**, *17*, 329–343; e) B. Gockel, N. Krause, *Eur. J. Org. Chem.* **2010**, 311–316.

[5] a) J. Magano, J. R. Dunetz, *Chem. Rev.* **2011**, *111*, 2177–2250; b) M. A. Berliner, E. M. Cordi, J. R. Dunetz, K. E. Price, *Org. Process Res. Dev.* **2010**, *14*, 180–187; c) S. Yu, A. Haight, B. Kotecki, L. Wang, K. Lukin, D. R. Hill, *J. Org. Chem.* **2009**, *74*, 9539–9542.

[6] a) T. Patonay, I. Pazurik, A. Ábrahám, *Aust. J. Chem.* **2013**, *66*, 646–654; b) A. S. Dudnik, V. Gevorgyan, *Angew. Chem. Int. Ed.* **2010**, *49*, 2096–2098; *Angew. Chem.* **2010**, *122*, 2140–2142; c) E. Negishi, L. Anastasia, *Chem. Rev.* **2003**, *103*, 1979–2018.

[7] a) K. Sonogashira, Y. Tohda, N. Nagihara, *Tetrahedron Lett.* **1975**, *16*, 4467–4470; b) R. Singh, G. Just, *J. Org. Chem.* **1989**, *54*, 4453–4457; c) R. Rossi, A. Carpita, M. G. Quirici, M. L. Gaudenzi, *Tetrahedron* **1982**, *38*, 631–637; d) G. C. Nwokogu, *J. Org. Chem.* **1985**, *50*, 3900–3908.

[8] C. Glaser, *Ber. Dtsch. Chem. Ges.* **1869**, *2*, 422–424.

[9] a) R. U. Islam, S. K. Mahato, S. K. Shukla, M. J. Witcomb, K. Mallick, *ChemCatChem* **2013**, *5*, 2453–2461; b) L.-H. Zou, A. J. Johansson, E. Zuidema, C. Bolm, *Chem. Eur. J.* **2013**, *19*, 8144–8152; c) M. Bakherad, A. Keivanloo, S. Samangooei, M. Omidian, *J. Organomet. Chem.* **2013**, *740*, 78–82; d) X. Wang, J. Zhang, Y. Wang, Y. Liu, *Catal. Commun.* **2013**, *40*, 23–26; e) K. Neilde, M. D. Crozet, T. Terme, P. Vanelle, *Synthesis* **2013**, *45*, 1349–1356; f) J. Huang, W. Wang, H. Li, *ACS Catal.* **2013**, *3*, 1526–1536; g) J. F. Cívicos, D. A. Alonso, C. Najera, *Adv. Synth. Catal.* **2013**, *355*, 203–208; h) A. Jiblaoui, C. Baudequin, V. Chaleix, G. Ducourthial, F. Louradour, Y. Ramondenc, V. Sol, S. Leroy-Lhez, *Tetrahedron* **2013**, *69*, 5098–5103; i) A. R. Hajipour, H. Rahimi, F. Rafiee, *Appl. Organomet. Chem.* **2012**, *26*, 727–730; j) P. Karthikeyan, P. N. Muskawar, S. A. Aswar, P. R. Bhagat, S. K. Sythana, *Appl. Organomet. Chem.* **2012**, *26*, 562–569; k) L. Yang, P. Guan, P. He, Q. Chen, C. Cao, Y. Peng, Z. Shi, G. Pang, Y. Shi, *Dalton Trans.* **2012**, *41*, 5020–5025; l) T.-T. Hung, C.-M. Huang, F.-Y. Tsai, *ChemCatChem* **2012**, *4*, 540–545; m) C. Torborg, A. Zapf, M. Beller, *ChemSusChem* **2008**, *1*, 91–96.

[10] a) *Aqueous-Phase Organometallic Catalysis: Concepts and Applications, 2nd ed.* (Eds.: B. Cornils, W. A. Herrmann), Wiley-VCH, Weinheim, **2005**; b) F. Joó, *Aqueous Organometallic Catalysis*, Kluwer, Dordrecht, **2001**; c) *Metal-Catalyzed Reactions in Water* (Eds.: P. H. Dixneuf, V. Cadierno), Wiley-VCH, Weinheim, **2013**.

[11] a) P. A. Chaloner, M. A. Esteruelas, F. Joó, L. A. Oro, *Homogeneous Hydrogenation*, Kluwer, Dordrecht, **1994**; b) F. Joó in *Science of Synthesis: Water in Organic Synthesis* (Ed.: S. Kobayashi), Thieme, New York, **2012**, pp. 95–119; c) F. Joó, Á. Kathó in *Handbook of Homogeneous Hydrogenation, Vol. 3* (Eds.: J. G. de Vries, C. J. Elsevier), Wiley-VCH, Weinheim, **2007**, Chap. 38, pp. 1327–1359.

[12] a) *Applied Homogeneous Catalysis with Organometallic Compounds* (Eds.: B. Cornils, W. A. Herrmann), Wiley-VCH, Weinheim, **1996**; b) M. Beller, B. Cornils, C. D. Frohning, C. W. Kohlpaintner, *J. Mol. Catal. A* **1995**, *104*, 17–85; c) P. W. N. M. van Leeuwen, C. Claver in *Rhodium Catalyzed Hydroformylation*, Kluwer, Dordrecht, **2000**; d) B. Cornils, *Top. Curr. Chem.* **1999**, *206*, 133–152.

[13] a) M. A. Zolfigol, V. Khakyzadeh, A. R. Moosavi-Zare, A. Rostami, A. Zare, N. Iranpoor, M. H. Beyzavi, R. Luque, *Green Chem.* **2013**, *15*, 2132–2140; b) A. Kumbhar, S. Jadhav, S. Kamble, G. Rashinkar, R. Salunkhe, *Tetrahedron Lett.* **2013**, *54*, 1331–1337; c) K. H. Shaughnessy, *Metal-Catalyzed Cross-Couplings of Aryl Halides to Form C—C Bonds in Aqueous Media in Metal-Catalyzed Reactions in Water* (Eds.: P. H. Dixneuf, V. Cadierno), Wiley-VCH, Weinheim, **2013**, pp. 1–46; d) N. Chatterjee, S. Sarkar, R. Pal, A. K. Sen, *Tetrahedron Lett.* **2013**, *54*, 3748–3751; e) L. Wu, X. Zhang, Z. Tao, *Catal. Sci. Technol.* **2012**, *2*, 707–710; f) V. Polshettiwar, A. Decottignies, C. Len, A. Fihri, *ChemSusChem* **2010**, *3*, 502–522; g) K. H. Shaughnessy, R. B. DeVasher, *Curr. Org. Chem.* **2005**, *9*, 585–604; h) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009–3066.

[14] a) N. A. Isley, F. Gallou, B. H. Lipshutz, *J. Am. Chem. Soc.* **2013**, *135*, 17707–17710; b) A. Ohtaka, *Chem. Rec.* **2013**, *13*, 274–285; c) A. N. Marziale, S. H. Faul, T. Reiner, S. Schneider, J. Eppinger, *Green Chem.* **2010**, *12*, 35–38; d) V. Polshettiwar, B. Baruwati, R. S. Varma, *Chem. Commun.* **2009**, 1837–1839; e) V. Polshettiwar, R. S. Varma, *Chem. Eur. J.* **2009**, *15*, 1582–1586; f) M. Kidwai, S. Saxena, M. K. R. Khan, S. S. Thukral, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4295–4298; g) W.-C. Lee, B. J. Frost, *Green Chem.* **2012**, *14*, 62–66.

[15] P. Pfeiffer, E. Breith, E. Lübbe, T. Tsumaki, *Justus Liebigs Ann. Chem.* **1933**, *503*, 84–130.

[16] a) E. Watanabe, A. Kaiho, H. Kusama, N. Iwasawa, *J. Am. Chem. Soc.* **2013**, *135*, 11744–11747; b) K. Pamin, G. Pozzi, E. Tabor, W. Bukowski, J. Poltowicz, *Catal. Commun.* **2013**, *39*, 102–105; c) N. Levi, R. Neumann, *ChemPlusChem* **2012**, *77*, 977–981.

[17] a) A. Bhunia, M. A. Gotthardt, M. Yadav, M. T. Gamer, A. Eichhöfer, W. Kleist, P. W. Roesky, *Chem. Eur. J.* **2013**, *19*, 1986–1995; b) N. C. Maity, G. V. S. Rao, K. J. Prathap, S. H. R. Abdi, R. I. Kureshy, N. H. Khan, H. C. Bajaj, *J. Mol. Catal. A* **2013**, *366*, 380–389; c) E. N. Jacobsen, W. Zhang, A. R. Muci, J. R. Ecker, L. J. Deng, *J. Am. Chem. Soc.* **1991**, *113*, 7063–7064; d) E. N. Jacobsen, W. Zhang, M. L. Guler, *J. Am. Chem. Soc.* **1991**, *113*, 6703–6704.

[18] a) K. Venkatasubbaiah, Y. Feng, T. Arrowood, P. Nickias, C. W. Jones, *ChemCatChem* **2013**, *5*, 201–209; b) A. M. DiCiccio, G. W. Coates, *J. Am. Chem. Soc.* **2011**, *133*, 10724–10727; c) L. E. Martinez, J. L. Leighton, D. H. Carsten, E. N. Jacobsen, *J. Am. Chem. Soc.* **1995**, *117*, 5897–5898.

[19] a) E. Tas, A. Kilic, M. Durgun, I. Yilmaz, I. Özdemir, N. Gurbuz, *J. Organomet. Chem.* **2009**, *694*, 446–454; b) S. Kowalak, R. C. Weiss, K. J. Balkus Jr., *J. Chem. Soc. Chem. Commun.* **1991**, 57–58; c) G. Henrici-Olivé, S. Olivé, *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 549–550; *Angew. Chem.* **1974**, *86*, 561–562.

[20] a) X. Wang, G. Wu, F. Wang, K. Ding, F. Zhang, X. Liu, Y. Xue, *Catal. Commun.* **2012**, *28*, 73–76; b) M. Allard, R. Ricoux, R. Guillot, J.-P. Mahy, *Inorg. Chim. Acta* **2012**, *382*, 59–64; c) A. Salanti, M. Orlandi, E. Tolppa, L. Zoia, *Int. J. Mol. Sci.* **2010**, *11*, 912–926; d) B. Bahramian, V. Mirkhani, S. Tangestaninejad, M. Moghadam, *J. Mol. Catal. A: Chemical* **2006**, *244* 1–2, 139–145; e) A. Haikarainen, J. Sipilä, P. Pietikäinen, A. Pajunen, I. Mutikainen, *J. Chem. Soc. Dalton Trans.* **2001**, *7*, 991–995.

[21] a) L. Yu, X. Zhou, D. Wu, H. Xiang, *J. Organomet. Chem.* **2012**, *705*, 75–78; b) M. J. Matos, S. Vazquez-Rodriguez, F. Borges, L. Santana, E. Uriarte, *Tetrahedron Lett.* **2011**, *52*, 1225–1227; c) S. R. Borhade, S. B. Waghmode, *Indian J. Chem.* **2010**, *49B*, 565–572; d) P. Liu, X.-J. Feng, R. He, *Tetrahedron* **2010**, *66*, 631–636; e) M. Bakherad, A. Keivanloo, B. Bahramian, M. Hashemi, *Tetrahedron Lett.* **2009**, *50*, 1557–1559; f) S. R. Borhade, S. B. Waghmode, *Tetrahedron Lett.* **2008**, *49*, 3423–3429.

[22] a) R. Tana, Y. Donga, M. Penga, W. Zhenga, D. Yina, *Appl. Catal. A* **2013**, *458*, 1–10; b) C. Li, J. Zhao, R. Tan, Z. Peng, R. Luo, M. Peng, D. Yin, *Catal. Commun.* **2011**, *15*, 27–31; c) S. Sahoo, P. Kumar, F. Lefebvre, S. B. Halligudi, *Appl. Catal. A* **2009**, *354*, 17–25; d) Z. Li, Z. Tang, X. Hu, X. Xia, *Chem. Eur. J.* **2005**, *11*, 1210–1216.

[23] a) Z. Wu, L. Zhou, Z. Jiang, D. Wu, Z. Li, X. Zhou, *Eur. J. Org. Chem.* **2010**, 4971–4975; b) Y. Wang, Z. Wu, L. Wang, Z. Li, X. Zhou, *Chem. Eur. J.* **2009**, *15*, 8971–8974; c) M. L. Kantam, T. Ramani, L. Chakrapani, *Synth. Commun.* **2008**, *38*, 626–636.

[24] a) K. Voronova, M. Purgel, A. Udvardy, A. C. Bényei, Á. Kathó, F. Joó, *Organometallics* **2013**, *32*, 4391–4401; b) I. Correia, J. Costa Pessoa, L. F. Veiros, T. Jakusch, A. Dörnyei, T. Kiss, M. M. C. A. Castro, C. F. G. C. Geraldes, F. Avecilla, *Eur. J. Inorg. Chem.* **2005**, 732–744; c) É. Delahaye, M. Diop, R. Welter, M. Boero, C. Massobrio, P. Rabu, G. Rogez, *Eur. J. Inorg. Chem.* **2010**, 4450–4461.

These are not the final page numbers! ↗↗

[25] a) K. Matsumoto, H. Egami, T. Oguma, T. Katsuki, *Chem. Commun.* **2012**, *48*, 5823–5825; b) T. Kunisu, T. Oguma, T. Katsuki, *J. Am. Chem. Soc.* **2011**, *133*, 12937–12939; c) K. P. Bryliakov, E. P. Talsi, *Eur. J. Org. Chem.* **2011**, 4693–4698; d) H. Egami, T. Oguma, T. Katsuki, *J. Am. Chem. Soc.* **2010**, *132*, 5886–5895.

[26] a) S. Song, H. Ma, Y. Yang, *Dalton Trans.* **2013**, *42*, 14200–14211; b) E. D. Cross, L. E. N. Allan, A. Decken, M. P. Shaver, *J. Polym. Sci. Part A* **2013**, *51*, 1137–1146; c) J. Liu, Y. Y. Bao, Y. Liu, W. M. Ren, X. B. Lu, *Polym. Chem.* **2013**, *4*, 1439–1444; d) D. J. Darensbourg, R. R. Poland, A. L. Strickland, *J. Polym. Sci. Part A* **2012**, *50*, 127–133; e) L. Ding, Z. Chu, L. Chen, X. Lü, B. Yan, J. Song, D. Fan, F. Bao, *Inorg. Chem. Commun.* **2011**, *14*, 573–577.

[27] I. Correia, Á. Dörnyei, T. Jakusch, F. Avecilla, T. Kiss, J. Costa Pessoa, *Eur. J. Inorg. Chem.* **2006**, 2819–2830.

[28] a) P. Klumphu, B. H. Lipshutz, *J. Org. Chem.* **2014**, *79*, 888–900; b) R. Zhou, W. Wang, Z.-j. Jiang, H.-y. Fu, X.-l. Zheng, C.-c. Zhang, H. Chena, R.-x. Li, *Catal. Sci. Technol.* **2014**, *4*, 746–751; c) A. S. Roy, J. Mondal, B. Banerjee, P. Mondal, A. Bhaumik, S. M. Islam, *Appl. Catal. A* **2014**, *469*, 320–327; d) M. Bakherad, *Appl. Organomet. Chem.* **2013**, *27*, 125–140; e) M. Lamblin, L. Nassar-Hardy, J.-C. Hierso, E. Fouquet, F.-X. Felpin, *Tetrahedron* **2010**, *66*, 1064–1069; f) C. A. Fleckenstein, H. Plenio, *Green Chem.* **2008**, *10*, 563–570; g) S. Roy, H. Plenio, *Adv. Synth. Catal.* **2010**, *352*, 1014–1022.

[29] H. Zhong, J. Wang, L. Li, R. Wang, *Dalton Trans.* **2014**, *43*, 2098–2103.

[30] a) J-M. Lo, H.-H. Yao, T.-H. Lu, *Acta Crystallogr. Sect. C* **1997**, *53*, 1327–1329; b) F. R. Allen, *Acta Crystallogr. Sect. B* **2002**, *58*, 380–388.

[31] Á. Kathó, A. C. Bényei, F. Joó, M. Sági, *Adv. Synth. Catal.* **2002**, *344*, 278–282.

[32] a) M. Aufiero, F. Proutiere, F. Schoenebeck, *Angew. Chem. Int. Ed.* **2012**, *51*, 7226–7230; *Angew. Chem.* **2012**, *124*, 7338–7342; b) D. Gelman, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2003**, *42*, 5993–5996; *Angew. Chem.* **2003**, *115*, 6175–6178.

[33] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, *J. Appl. Crystallogr.* **1993**, *26*, 343–350.

[34] G. M. Sheldrick, *Acta Crystallogr. Sect. A* **2008**, *64*, 112–122.

[35] L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837–838.

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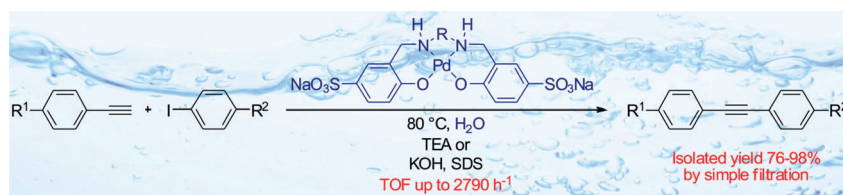
K. Voronova,* L. Homolya, A. Udvardy,
A. C. Bényei, F. Joó*

■■ – ■■

Pd–Tetrahydrosalan-Type Complexes as Catalysts for Sonogashira Couplings in Water: Efficient Greening of the Procedure

Exclusive partnership: Water-soluble sulfonated tetrahydrosalen complexes of palladium(II) efficiently catalyze the Sonogashira coupling of aryl halides and terminal alkynes in aqueous–organic biphasic mixtures under mild conditions. Instead of extraction with organic solvents, several of the products can be isolated in high purity by simple filtration.

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