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# Solvent-free palladium-catalyzed addition of diaryl dichalcogenides to alkynes

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Solvent-free palladium-catalyzed addition of diaryl disulfides and diselenides to terminal alkynes makes it possible to achieve high stereoselectivity and almost 100% yields in ≈10 min using only 0.1 mol.% catalyst. Both $Pd(PPh_3)_4$ and easily available $Pd(OAc)_2$ and $PdCl_2$ can be used in the reaction with an excess of triphenylphosphine. The catalyst and triphenylphosphine are readily recycled for repeated use. The study of the mechanism of the solvent-free catalytic reaction indicates that the process involves binuclear palladium complexes.

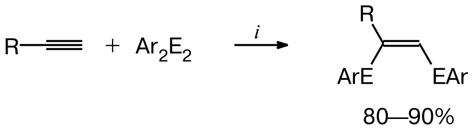
**Key words:** vinyl sulfides, vinyl selenides, stereoselective addition, solvent-free reaction, homogeneous catalysis, palladium complexes.

In modern organic chemistry, a special attention is given to the development of economical and ecologically safe methods of synthesis. One of the main concept of "green chemistry" is aimed at minimizing the amount of toxic compounds used in chemical reactions, in particular, organic solvents. This decreases the amount of toxic waste and also provides a more economically favorable procedure for synthesis, especially for catalytic reactions that require thoroughly purified and dehydrated solvents treated in an inert atmosphere.

The development of synthetic methods appropriate for solvent-free reactions is a dynamically advancing area of modern chemistry.**[1,2]** This methodology is shown**[3—9]** to be successfully applied for transformations catalyzed by metal complexes (Sudzuki and Heck reactions, C—N bond formation). In many cases, microwave irradiation is needed to perform synthesis under solvent-free conditions.**[10—13]**

We have recently shown**[14]** that the $Pd(PPh_3)_4$-catalyzed addition of diaryl dichalcogenides ($Ar_2E_2$, E = S, Se) to acetylenic hydrocarbons can occur in the absence of a solvent. Diaryl dichalcogenides add to the triple bond of alkynes in melt with a high stereoselectivity ($Z/E > 97/3$). The process is catalyzed by palladium complexes with phosphine ligands and does not require microwave irradiation (Scheme 1).

**Scheme 1**



E = S, Se

**Reagents and conditions:** *i.* [Pd]/$PPh_3$, Δ, without solvent.

Unlike addition in melt, an analogous reaction in solution is well studied.**[15—18]** The process is usually carried out in benzene or toluene at 80 °C in the presence of 2—3 mol.% $Pd(PPh_3)_4$ as the catalyst. As shown by the detailed study of the mechanism of this reaction,**[17,18]** the oxidative addition of diaryl dichalcogenides to $Pd^0$ affords binuclear metal complexes **2** and **3** (Scheme 2), which can further be transformed into polymer **4**.**[15,19]** The structures of the binuclear complexes were established by X-ray diffraction analysis,**[20—23]** and their formation under the catalytic conditions in benzene or toluene was confirmed by $^{31}P\{^1H\}$ NMR spectroscopy.**[17,18]**

The results of further studies of the solvent-free addition reaction are presented in this work. In particular, it is of great interest to find an alternative for the $Pd^0$-based catalyst, reveal a possibility of regeneration of triphenylphosphine, test the catalytic reaction using more examples, and study the reaction mechanism.

We have found that in the $Ar_2E_2/PPh_3$ melt at 140 °C diaryl dichalcogenides ($Ar_2E_2$, E = S, Se) add to alkynes in almost 100% yields for 10 min with the use of only 0.1 mol.% $Pd(OAc)_2$ or $PdCl_2$ as the catalyst (Table 1). The stereochemistry of the compounds synthesized was established by NOESY NMR spectroscopy. A high stereo-

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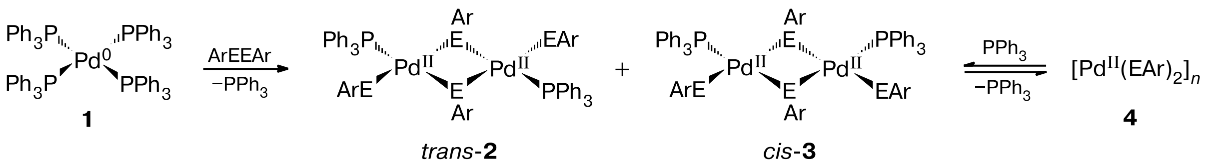
**Scheme 2**



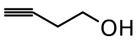
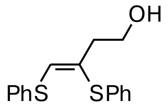
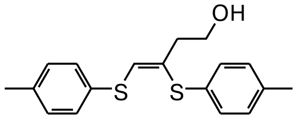
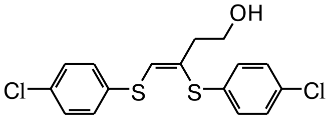
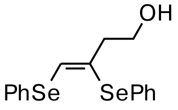
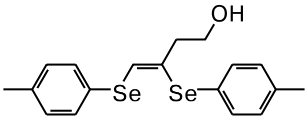
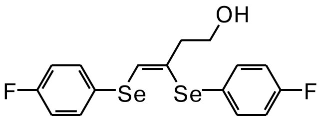
selectivity of addition ($Z/E > 97/3$) and 80—90% yields of the purified reaction products (according NMR spectroscopy, the conversion of $Ar_2Se_2$ was 90—99%) were achieved for a wide range of alkynes and diaryl dichalcogenides. The catalytic reaction in melt exhibits the same efficiency for disulfides and diselenides, unlike a similar process in a solvent, where disulfides are more reactive.[18]

The key point in a solvent-free reaction is the presence of an excess of triphenylphosphine in melt. Triphenylphosphine prevents the polymerization of the active form of the catalyst. In the absence of $PPh_3$, an insoluble dark brown precipitate of $[Pd(EAr)_2]_n$ is formed in the system (Scheme 2), and dichalcogenides do not add to the triple bond.

An important advantage of the procedure developed is a wide scope of palladium complexes that can be used as precursors of the active form of the catalyst. In addition to the traditionally used $Pd(PPh_3)_4$ complex, the addition can be catalyzed by $Pd(OAc)_2$ and $PdCl_2$ without a decrease in the yield of the reaction products.

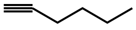
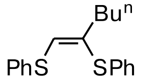
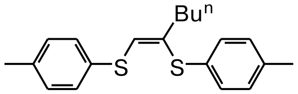
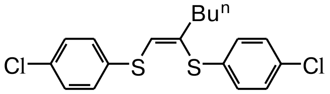
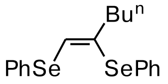
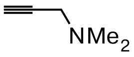
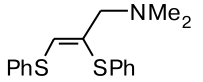
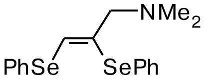
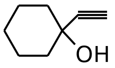
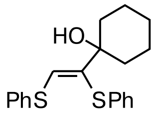
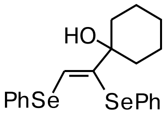
To study the mechanism of the catalytic reaction, we performed the $^{31}P\{^1H\}$ NMR investigation directly in melt. It turned out that the dissolution of $Pd(PPh_3)_4$ and $Pd(OAc)_2$ in the $Ph_2S_2/PPh_3$ melt produced the same binuclear *cis-/trans-*$[Pd_2(SPh)_4(PPh_3)_2]$ complexes (see Scheme 2) with the signals $\delta_P = 29.1$ and 30.4 in a ratio of ~2 : 1 (similar complexes are formed in a $C_6D_6$ solution, $\delta_P = 29.4$ and 30.8).[17,18] A small difference in the measured chemical shifts indicates similar solvating proper-

**Table 1.** Addition of diaryl dichalcogenides to alkynes catalyzed by the palladium complexes

| Alkyne | $Ar_2E_2$ | Product | Yield* (%) |
|---|---|---|---|
|  | $Ph_2S_2$ |  | 90 |
|  | $(p\text{-}MeC_6H_4)_2S_2$ |  | 92 |
|  | $(p\text{-}ClC_6H_4)_2S_2$ |  | 88 |
|  | $Ph_2Se_2$ |  | 87 |
|  | $(p\text{-}MeC_6H_4)_2Se_2$ |  | 85 |
|  | $(p\text{-}FC_6H_4)_2Se_2$ |  | 85 |

(*to be continued*)

**Table 1** (*continued*)

| Alkyne | $Ar_2E_2$ | Product | Yield* (%) |
|---|---|---|---|
|  | $Ph_2S_2$ |  | 80 |
|  | $(p\text{-}MeC_6H_4)_2S_2$ |  | 90 |
|  | $(p\text{-}ClC_6H_4)_2S_2$ |  | 86 |
|  | $Ph_2Se_2$ |  | 80 |
|  | $Ph_2S_2$ |  | 85 |
|  | $Ph_2Se_2$ |  | 80 |
|  | $Ph_2S_2$ |  | 90 |
|  | $Ph_2Se_2$ |  | 91 |

* The yield after chromatography.

ties of the $Ph_2S_2/PPh_3$ melt and aromatic solvents. This seems to be one of the key factors for the successful solvent-free reaction to occur. The signals of the binuclear $Pd_2(SPh)_4(PPh_3)_2$ complexes were also detected in the $^{31}P\{^1H\}$ NMR monitoring of the corresponding catalytic reactions. The NMR study indicates that the catalytic addition in melt involves binuclear complexes as for the reaction in solution.

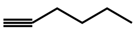
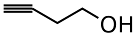
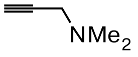
It is noteworthy that, when the catalytic reaction occurs in solution, the use of palladium chloride complexes requires their pre-activation by the $ArEH/NEt_3$ additives.[18] No additional reagents are needed for the reaction in melt. Most likely, in melt the chloride ligands are replaced under the effect of high temperatures or trace amounts of ArEH, which are present in $Ar_2E_2$.

The solvent-free reaction has several incontestable advantages over the traditional reaction in solution. A high thermal stability of the catalyst in melt makes it possible to perform the reaction at higher temperature and to shorten substantially the reaction time (from 8—12 h at 80 °C to 10 min at 140 °C). In addition, the reaction is significantly accelerated due to the concentration effect. According to our measurements, the rate of solvent-free addition of diphenyl disulfide to hex-1-yne is more than sixfold higher than that in 5 mL of toluene (both reactions were carried out at 80 °C using 1 mmole of $Ph_2S_2$).

As a result, 0.1 mol.% catalyst is enough for the solvent-free reaction instead of 2—3 mol.% for the reaction in solution. Even when 0.001 mol.% catalyst is used in the addition of diphenyl disulfide to but-3-yn-1-ol in melt (140 °C), the 70% yield is observed after 5 h. In the experiments in which the amounts of $Ar_2E_2$ differed by an order of magnitude ($1.0 \cdot 10^{-3}$—$1.0 \cdot 10^{-2}$ moles), the yields of products and stereoselectivity of the reaction were the same. An important factor is the possibility to use $Pd(OAc)_2$ and $PdCl_2$, which are cheap and stable in air, instead of expensive and readily oxidizable $Pd(PPh_3)_4$. The solvent-free addition of diaryl dichalcogenides can also be performed in high yields under microwave irradiation. However, in this case, the isolation of a product is more difficult due to caking of the reaction mixture.

The system under study has a unique feature: the catalyst and ligand can be regenerated for repeated use. After the end of the catalytic reaction in melt, about 90% cata-

**Table 2.** Catalytic addition of $Ph_2S_2$ to alkynes using the regenerated catalyst

| Cycle | Alkyne | Yield of product[a] (%) | Regenerated catalyst[b] (%) | Regenerated $PPh_3$[b] (%) |
|---|---|---|---|---|
| *1* |  | 98 | 92 | 70 |
| *2* |  | 96 | 87 | 50 |
| *3* |  | 97 | 90 | 55 |

[a] Measured by NMR spectroscopy after the end of the reaction.

[b] Calculated per the initial amount.

lyst and 50—70% triphenylphosphine can be regenerated by a simple procedure of flash chromatography (Table 2). Triphenylphosphine cannot be regenerated completely because of its partial oxidation to triphenylphosphine oxide. The regeneration procedure repeated triply did not noticeably decrease the catalytic activity of the isolated palladium complexes (see Table 2). In particular, after the addition of $Ph_2S_2$ to hex-1-yne (cycle *1*, see Table 2), the regenerated catalyst was repeatedly used for the addition of $Ph_2S_2$ to but-3-yn-1-ol (cycle *2*, see Table 2). After the repeated isolation of the catalyst, it was also used in the reaction with *N*,*N*-dimethylpropargylamine (cycle *3*, see Table 2). In all cases, high yields (96—98%) and selectivities of the reactions were observed. The $^{31}P\{^1H\}$ NMR spectrum of the regenerated catalyst in deuterated benzene exhibited signals at 29.4 and 30.8 ppm corresponding to the binuclear *cis-/trans-*$[Pd_2(SPh)_4(PPh_3)_2]$ complexes.[17,18] Thus, in the presence of an excess of triphenylphosphine, the catalytically active palladium complexes are highly stable and do not decompose after regeneration.

## Experimental

Diaryl dichalcogenides and alkynes were commercially available and used after spectral monitoring of purity ($^1H$ and $^{13}C$ NMR). Solvents were purified according to standard procedures. All syntheses were carried out in an argon atmosphere. Reaction mixtures were heated in a temperature-controlled oil bath.

NMR spectra were recorded on a Bruker DRX500 spectrometer with working frequencies of 500, 125, and 95 MHz for the $^1H$, $^{13}C$, and $^{77}Se$ nuclei, respectively. For recording $^1H$ NMR spectra, signals of residual protons of solvents were used as standards. External standards $Ph_2Se_2/CDCl_3$ (463.0 ppm) and $H_3PO_4/H_2O$ (0 ppm) were used for $^{77}Se$ and $^{31}P$ NMR spectra, respectively. $^{77}Se$ NMR spectra were recorded using the $^1H—^{77}Se$ HMQC inverse procedure.[24] NOESY spectra were recorded as described previously.[18] All measurements were performed at room temperature.

**Solvent-free addition of diaryl dichalcogenides to alkynes (general procedure).** The reaction was carried out in a sealed or hermetically closed tube. A mixture of $Ar_2E_2$ ($1.0 \cdot 10^{-3}$ mol), $PPh_3$ ($1.5 \cdot 10^{-4}$ mol), and a catalyst ($Pd(OAc)_2$, $Pd(PPh_3)_4$, or $PdCl_2$) ($1.0 \cdot 10^{-6}$ mol) was heated at 140 °C until complete melting and shaken to form a homogeneous dark black melt (1—3 min). The melt was cooled to ~20 °C until solidification, alkyne ($1.5 \cdot 10^{-3}$ mol) was added, and the tube was sealed (or hermetically closed). The reaction mixture was kept for 10 min at 140 °C in a thermostat. Heating resulted in the formation of a homogeneous dark brown melt, whose color changed during the reaction to light brown or yellow.

**Isolation and purification of products.** After completing the reaction, unreacted alkyne was removed *in vacuo*, and the product was purified by flash chromatography.[25] Gradient elution was carried out with a mixture of light petroleum and ethyl acetate (0—10%). After chromatography, the solvent was evaporated *in vacuo*, and the resulting products were dried *in vacuo*.

The structures of the reaction products were confirmed by $^1H$, $^{13}C$, and $^{77}Se$ NMR spectroscopy (comparing with the published spectral data[14—18]) and by mass spectrometry. The addition products of $Ph_2S_2$ and $Ph_2Se_2$ to *N*,*N*-dimethylpropargylamine were isolated in the form of oxalate as described previously. Their structures were established by X-ray diffraction analysis.[17,18]

**Regeneration of the catalyst and triphenylphosphine after the reaction (general procedure).** After completing the reaction in melt ($1.0 \cdot 10^{-3}$ mole of $Ar_2E_2$, $1.5 \cdot 10^{-4}$ mole of $PPh_3$, $3.0 \cdot 10^{-5}$ mole of the catalyst, and $1.0 \cdot 10^{-3}$ mole of an alkyne), the reaction mixture was adsorbed on silica gel, and chromatographic purification was performed as described above. Triphenylphosphine was eluted in the first fractions (light petroleum), and the product was isolated by gradient elution (ethyl acetate 0—10%). The palladium complexes were eluted in the last fractions with a light petroleum—ethyl acetate (1 : 1) mixture. After the solvent was removed and the residue was dried *in vacuo*, triphenylphosphine and palladium complexes were obtained as white crystals and brown oil, respectively (identified by $^1H$ and $^{31}P$ NMR spectroscopy).[14,18]

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