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Potassium selenocyanate as an efficient selenium source in C–Se cross-coupling catalyzed by copper iodide in water

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ABSTRACT

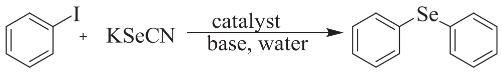
An efficient and conceptually new protocol for C–Se cross coupling of potassium selenocyanate with aryl halides via copper-catalyzed cascade reaction has been developed in water. Utilizing this protocol, a variety of aryl and heteroaryl halides were reacted with potassium selenocyanate to afford the corresponding diaryl selenides in moderate to good yields.

Diaryl selenides have proven to be valuable building blocks in organic synthesis[1,2] and also serve as potential drug candidates.[3] Many compounds bearing this core unit have revealed diverse and interesting biological activities, such as antioxidant, antitumor, anticancer, anti-infective, enzyme inhibiting, glutathione peroxidase mimicking, immunomodulating etc.[4] They have also been widely used in chemo-, regio-, and stereoselective reactions and apart from this, selenium is known as a fundamental element in life sciences.[5]

However, the classical version of this C-Se cross coupling reaction requires photochemical or harsh reaction conditions, for example, the use of polar and toxic solvents like HMPA and high reaction temperatures.[6] To overcome these drawbacks, transition metals such as palladium,[7] nickel,[8] copper,[9] iron,[10] indium,[11] and lanthanum[12] based catalytic systems have been studied for the synthesis of diaryl selenides. These reactions usually involve the coupling of aryl halides with either diaryl diselenides or aryl selenols. Our recent report depicts the copper catalyzed synthesis of diaryl selenides in excellent yields using selenourea as a selenium source using DMSO as solvent.[13] The majority of the reported protocols proceed in organic solvents and nowadays, their disposal is a major problem for the chemical industry. Moreover, organic solvents are expensive, toxic, flammable and not recyclable. Thus, it is desirable to find a novel catalytic system for the synthesis of diaryl selenides by using water as solvent.

Recently, organic reactions in water have attracted much attention because water is the most economical, safe, non-toxic,

Table 1
Screening of copper catalyzed synthesis of diaryl selenides in water[a]



Entry	Copper source	Ligand	Base	Temp (°C)	Yield[b] (%)
1	CuI	L1	CS_2CO_3	rt	Trace
2	CuI	L1	CS_2CO_3	80	50
3	CuI	L1	CS_2CO_3	100	70
4	CuI	L2	CS_2CO_3	100	75
5	CuI	L3	CS_2CO_3	100	65
6	CuI	L4	CS_2CO_3	100	91
7	CuI	L5	CS_2CO_3	100	85
8	CuI	L6	CS_2CO_3	100	79
9	$Cu(OAc)_2$	L4	CS_2CO_3	100	71
10	$CuSO_4 \cdot 5H_2O$	L4	CS_2CO_3	100	59
11	CuI	L4	CS_2CO_3	100	51
12	CuI	L4	K_2CO_3	100	73
13	CuI	L4	KOH	100	50
14	CuI	L4	K_3PO_4	100	65
15	–	L1	CS_2CO_3	100	–
16	CuI	–	CS_2CO_3	100	Trace
17	CuI	L4	–	100	Trace

[a] Reactions and conditions: iodobenzene (1.0 mmol), potassium selenocyanate (1.2 mmol), catalyst (10 mol %), ligand (10 mol %), base (2.0 equiv), water (3.0 mL), 24 h, 100 °C
[b] Isolated yield.

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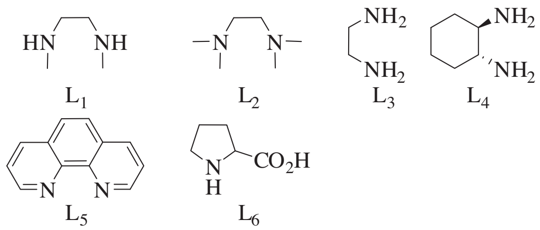
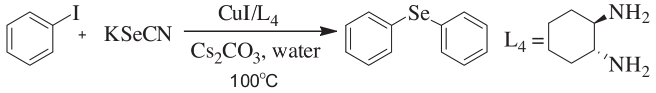


Scheme 1. Copper catalyzed synthesis of diaryl selenides in optimized conditions. In all of the cases the cross-coupling of water.

environmentally friendly and most readily available reaction medium.[14] In the course of our continuing investigations in the field of cross-coupling reactions[15] we report, herein, a new approach for the synthesis of diaryl selenides via C–Se cross coupling of potassium selenocyanate with aryl halides catalyzed by copper iodide in water. To the best of our knowledge, this is the first protocol explored for the synthesis of diaryl selenides via C–Se cross-coupling of potassium selenocyanate with aryl halides catalyzed by CuI as a catalyst in combination with trans 1,2-diaminocyclohexane as ligand in water.[16]

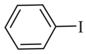
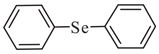
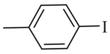
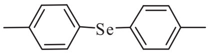
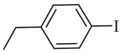
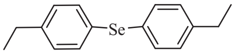
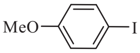
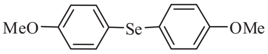
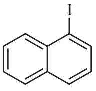
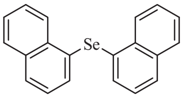
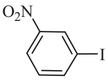
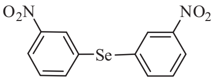
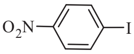
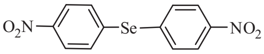
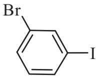
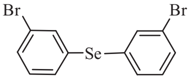
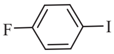
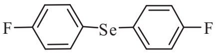
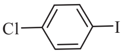
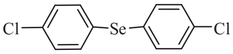
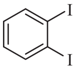
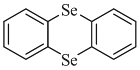
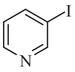
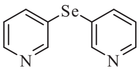
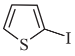
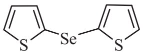
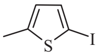
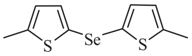
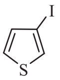
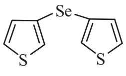
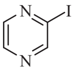
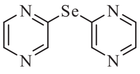
Initially, iodobenzene and potassium selenocyanate were chosen as the model substrates to optimize the reaction conditions such as various copper sources, bases, ligands and temperature (Table 1). First, several catalysts and ligands were screened and CuI and L4 were proven to be preeminent for this cross coupling reaction (Table 1, entry 6). The effect of bases was also investigated, and Cs_2CO_3 was found to be most effective in water (Table 1, entry 6). The control experiment confirmed that the reaction did not occur in the absence of catalyst (Table 1, entry 15) as well as the base (Table 1, entry 17). Only trace amount of the expected product was formed in the absence of the ligand (Table 1, entry 16). The reaction when conducted at room temperature and 80 °C, the yields observed were very low (Table 1, entries 1 and 2). The ideal temperature for the reaction was found to be 100 °C. The best result was obtained when the reaction was pursued at 100 °C using 10 mol % of the CuI/10 mol % of the *trans* 1,2-diaminocyclohexane in the presence of Cs_2CO_3 (2.0 equiv) in water Scheme 1.



To explore the scope of this novel transformation, we examined the cross-coupling of various substituted aryl iodides with potassium selenocyanate. As shown in Table 2, different aryl iodides were transformed into the corresponding diaryl selenides with good isolated yields.[17,18] The results have shown that substitution

Table 2
Copper catalyzed synthesis of symmetrical diaryl selenides in water[a]

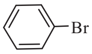
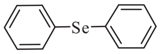
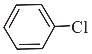
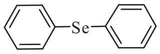
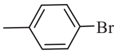
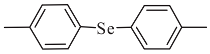
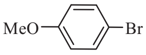
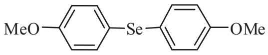
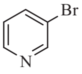
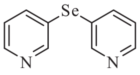
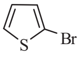
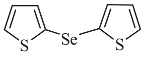
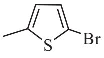
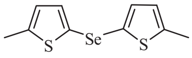
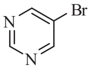
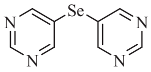
$$\text{Ar–I} + \text{KSeCN} \xrightarrow[\text{24 h, 100 °C}]{\text{CuI, L4, H}_2\text{O}} \text{Ar–Se–Ar}$$

Entry	Arylhalides	Product	Yield[b] (%)
1			91
2			88
3			86
4			90
5			82
6			75
7			77
8			81
9			78
10			79
11			61[c]
12			74
13			79
14			81
15			77
16			76

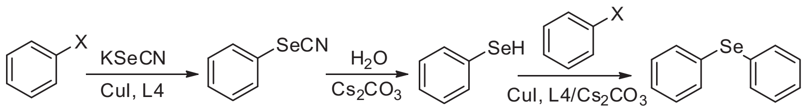
[a] Reactions and conditions: aryl iodide (1.0 mmol), potassium selenocyanate (1.2 mmol), CuI (10 mol %), L4 (10 mol %) Cs_2CO_3 (2.0 equiv), water (3.0 mL), 24 h, 100 °C.
[b] Isolated yield.
[c] Potassium selenocyanate (2.4 mmol).

Table 3
Copper catalyzed synthesis of symmetrical diaryl selenides in water[a]

$$\text{Ar–X} + \text{KSeCN} \xrightarrow[\text{H}_2\text{O, 40 h, 100 °C}]{\text{CuI, L4, Cs}_2\text{CO}_3} \text{Ar–Se–Ar}$$

Entry	Arylhalides	Product	Yield[b] (%)
1			45[c] 81
2			Trace
3			72
4			79
5			65
6			59
7			62
8			70

[a] Reactions and conditions: aryl halides (1.0 mmol), potassium selenocyanate (1.2 mmol), CuI (10 mol %), L4 (10 mol %) Cs_2CO_3 (2.0 equiv), water (3.0 mL), 40 h, 100 °C.
[b] Isolated yield.
[c] After 24 h.



Scheme 2. A plausible mechanism for the CuI catalyzed C–Se cross-coupling of aryl halides with potassium selenocyanate.

played a major role in governing the reactivity of the substrate. This protocol efficiently coupled iodo benzenes having electron donating groups (eg. Me, Et and OMe) with potassium selenocyanate to produce the corresponding products in good yields (Table 2, entries 2, 3, 4), whereas in the presence of electron withdrawing group (NO2) a slight decrease in the yield of the diaryl selenides (Table 2, entries 6 and 7) was observed. Interestingly, when 1,2-diiodobenzene was reacted with potassium selenocyanate, the desired product was obtained in moderate yield (Table 2, entry 11). Utilizing these conditions, heterocyclic compounds, such as 3-iodopyridine and 2-iodo/5-methyl-2- iodo thiophene also afforded the corresponding products in high yields (Table 2, entries 12–16).

In order to evaluate the scope of the process, a variety of substituted aryl bromides and chlorides were tested under the same reaction conditions (Table 3). In the case of aryl bromides, the reaction with potassium selenocyanate furnished the corresponding diaryl selenide derivatives in moderate yields (Table 3 entries 1, 3–8) whereas in the case of aryl chlorides, trace amount of coupling product was observed (Table 3, entry 2).

Further more, C–Se cross-coupling of heterocyclic bromides such as 3-bromopyridine, 5-methyl-2-bromothiopene and 5-bromopyrimidine gave moderate to good yields (Table 3, entries 5–8). Iodo benzene was found to be the more reactive substrate than bromo and chloro benzenes.

A plausible mechanism for the CuI catalyzed C–Se cross-coupling of aryl halides with potassium selenocyanate is shown in Scheme 2. First, the aromatic halide is activated by the Cu(I) complex, which further reacts with potassium selenocyanate leading to the formation of aryl selenocyanate. Then, aryl selenocyanate is hydrolyzed to generate benzeneselenol under the basic conditions. Then the newly generated benzeneselenol intermediate reacts with the aryl halide in the presence of copper catalyst to afford the C–Se coupling product.[18]

In conclusion, we have developed an experimentally simple and inexpensive copper iodide catalyzed C–Se cross coupling of aryl halides with potassium selenocyanate as a selenium surrogate in water without inert atmosphere. Various aryl halides underwent cross-coupling with potassium selenocyanate to give the corresponding products in high yields.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.05.068.

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16. Copper-catalyzed Cross-coupling reactions in aqueous media, see: (a) Teo, Y.-C.; Chua, G.-L. *Chem. Eur. J.* **2009**, *15*, 3072; Teo, Y.-C.; Yong, F.-F.; Poh, C.-Y.; Yan, Y.-K.; Chua, G.-L. *Chem. Commun.* **2009**, 6258; Peng, J.; Ye, M.; Zong, C.; Hu, F.; Feng, L.; Wang, X.; Wang, Y.; Chen, C. *J. Org. Chem.* **2011**, *76*, 716; Wang, F.; Fu, H.; Jiang, Y.; Zhao, Y. *Green Chem.* **2008**, *10*, 452; Wang, Y.; Wu, Z.; Wang, L.; Li, Z.; Zhou, X. *Chem. Eur. J.* **2009**, *15*, 8971; Liang, L.; Li, Z.; Zhou, X. *Org. Lett.* **2009**, *11*, 3294; Li, X.; Yang, D.; Jiang, Y.; Fu, H. *Green Chem.* **2010**, *12*, 1097.
17. *General procedure for the synthesis of diaryl selenides.* Aryl halide (1.0 mmol), CuI (10 mol %), L4 (10 mol %), Cs_2CO_3 (2.0 equiv) and potassium selenocyanate (1.2 mmol) were charged in a 10 ml round bottom flask with a condenser under air, followed by the addition of water (3.0 mL). The reaction mixture was heated in an oil bath at 100 °C and stirred at this temperature for 24 h. The progress of the reaction was monitored by TLC. After the reaction was complete, the reaction mixture was allowed to cool, and treated with ethyl acetate. The combined organic extracts were dried with anhydrous Na_2SO_4. The solvent and volatiles were completely removed under vacuum to give the crude product, which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 9:1) to afford the corresponding coupling product in excellent yields. All the products were characterized by ^1H and ^{13}C NMR, MS and compared with the literature values.
*Data of representative examples. Bis(4-ethylphenyl)selane (*Table 2*, entry 3).* Light yellow oil; IR (neat): ν 3057, 2930, 2836, 1559, 1461, 1061, 937, 846, 735 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, TMS): $\delta = 7.34$ (d, 4H, $J = 8.12$ Hz), 7.06 (d, 4H, $J = 8.12$ Hz), 2.59 (q, 4H, $J = 7.54$ Hz), 1.22 (t, 6H, $J = 7.54$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$, TMS): $\delta = 133.0$, 132.9, 128.8, 127.9, 28.4, 15.4; Mass (ESI): m/z 290 [M+1]; Anal. Calcd for $C_{16}H_{18}Se$ (289): C, 66.43; H, 6.27. Found: C, 66.37; H, 6.19.

*Dinaphthalen-1-ylselane (*Table 2*, entry 5).* Yellow liquid; IR (neat): *ν* 3091, 2928, 1588, 1390, 1077, 968, 848 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$, TMS): δ = 8.05- 8.02 (m, 4H), 7.79–7.65 (m, 4H), 7.55- 7.40 (m, 4H), 7.15 (t, 2H, *J* = 7.93 Hz); ^{13}C NMR (50 MHz, CDCl$_3$, TMS): δ = 137.2, 133.9, 131.9, 128.8, 128.3, 127.5, 126.6, 125.6; Mass (ESI): *m*/*z* 335[M+1]; Anal. Calcd for $C_{20}H_{14}Se$ (334): C, 72.07; H, 4.23. Found: C, 72.01; H, 4.18.

*Bis(3-bromophenyl)selane (*Table 2*, entry 7):*Colorless oil; IR (Neat): *ν* 3062, 2857, 1599, 1443, 1042, 910, 823, 746 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$, TMS): δ = 7.31–7.12 (m, 6H), 6.99–6.93 (m, 2H); ^{13}C NMR (50 MHz, CDCl$_3$, TMS): δ = 164.6, 161.2, 130.6, 128.6, 119.9, 114.7; Mass (ESI): *m*/*z* 391 [M+1]; Anal. Calcd for $C_{12}H_8Br_2Se$ (390): C, 36.87; H, 2.06. Found: C, 36.81; H, 1.99.

*Dipyrimidin-5-ylselane (*Table 3*, entry 8).* Colorless oil; IR (neat): *ν* 3092, 2960, 1597, 1444, 1068, 865, 738 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$, TMS): δ = 7.51(s, 2H), 7.25(s, 4H); ^{13}C NMR (50 MHz, CDCl$_3$, TMS): δ = 132.9, 129.0, 127.5; Mass (ESI): *m*/*z* 239 [M+1]; Anal. Calcd for $C_8H_6N_4Se$ (238): C, 40.52; H, 2.55; N, 23.63. Found: C, 40.46; H, 2.45; N, 23.57.

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