

9.11.4 Selenophenes (Update 2010)

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General Introduction

The present chapter is intended to update the first report on selenophenes in *Science of Synthesis* (see Section 9.11) and will briefly summarize essential, more recent findings concerning this heterocyclic system in the first decade of the new millennium.

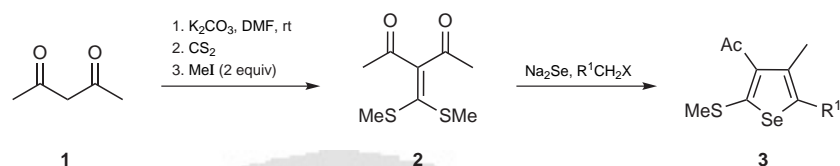
In 2009–2010, applications of selenophene-based materials in organic electronics and photonics were reviewed extensively.^[1,2] Selenophene-containing π -conjugated compounds have been proposed as organic magnetic materials.^[3]

During the decade 2000–2010, a quite comprehensive review article concerning all aspects of selenophene chemistry^[4] appeared, together with overviews in specialized journals.^[5–16]

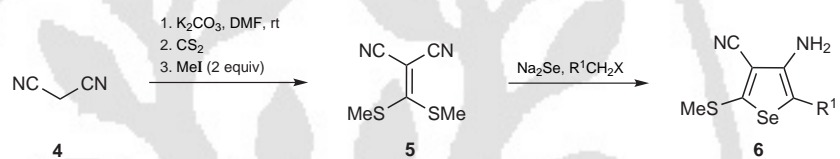
9.11.4.1 Synthesis by Ring-Closure Reactions**9.11.4.1.1 By Formation of Two Se—C Bonds and One C—C Bond****9.11.4.1.1.1 Fragments C—C—C, C, and Se****9.11.4.1.1.1.1 Method 1:
From Ketene Dithioacetals and Sodium Selenide**

Fully substituted selenophenes, such as **3**, can easily be synthesized in a three-component reaction involving ketene dithioacetal **2**, sodium selenide, and an activated methylene compound (Scheme 1). The ketene dithioacetal is formed in a base-assisted reaction of pentane-2,4-dione (**1**) with carbon disulfide in dimethylformamide followed by methylation. Treatment of the ketene dithioacetal **2** with sodium selenide and 1 equivalent of an activated halide generates moderate to good yields of substituted selenophenes **3**. When malononitrile (**4**) is used as starting material, selenophenes **6** are formed in significantly lower yields (Scheme 1).

for references see p 96

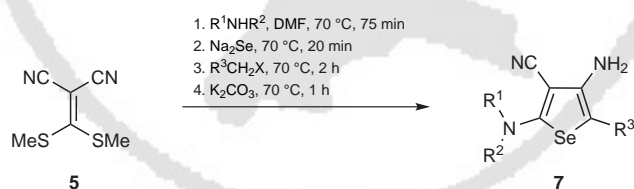
Scheme 1 Preparation of Selenophenes from Dithioacetals^[17]

R ¹	X	Yield (%) of 3 from 2	Ref
CO ₂ Et	Br	26	[17]
Ac	Cl	32	[17]
CN	Cl	55	[17]
Bz	Br	40	[17]



R ¹	X	Yield (%) of 6 from 5	Ref
Ac	Cl	9	[17]
Bz	Br	10	[17]

Selenophenes with a dialkylamino substituent can be prepared directly by a sequential one-pot, four-step procedure. This method is more efficient than the S_NAr pathway via the corresponding 2-(methylsulfanyl)thiophenes, and with selection of the appropriate secondary amine and activated halide (2 equiv), offers an easy access to new tetrasubstituted 4-aminoselenophene-3-carbonitriles **7** (Scheme 2).^[18]

Scheme 2 Synthesis of Substituted 4-aminoselenophene-3-carbonitriles^[18]

R ¹	R ²	R ³	X	Yield (%)	Ref
	(CH ₂) ₄	Ac	Cl	88	[18]
	(CH ₂) ₅	4-ClC ₆ H ₄ CO	Br	38	[18]
	(CH ₂) ₂ NBn(CH ₂) ₂	CN	Cl	19	[18]

2,3,4,5-Tetrasubstituted Selenophenes 3 and 6; General Procedure:^[17]

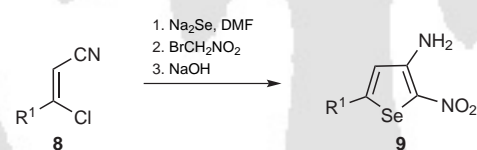
A 100-mL, three-necked, round-bottomed flask equipped with a magnetic stirrer, condenser, and septum was charged with freshly prepared Na₂Se (10.0 mmol, 1.0 equiv) in DMF (30 mL). The ketene dithioacetal (10.0 mmol, 1.0 equiv) was added and the mixture was stirred for 2 h at 50 °C. The halide (10.0 mmol, 1.0 equiv) was then added dropwise and the mixture was stirred for a further 1 h before adding dried K₂CO₃ (1.38 g, 1.0 equiv). The reaction was quenched with H₂O (100 mL) after having stirred for 3 h at 50 °C. The precipitated crude product was collected by filtration and purified by recrystallization (iPrOH); yield: 9–55%.

4-Aminoselenophen-3-carbonitriles 7; General Procedure:^[18]

2-[Bis(methylsulfanyl)methylene]malononitrile (**5**; 10.0 mmol) was dissolved in DMF (15 mL). The secondary amine (10.0 mmol) was added and the mixture was heated at 70 °C for 75 min. Then, fresh Na₂Se (10.0 mmol) was added and the mixture was heated for 20 min at 70 °C. Activated halide (20.0–30.0 mmol) was added dropwise at 70 °C. The mixture was heated at 70 °C for 2 h and then K₂CO₃ (10.0 mmol) was added. The mixture was stirred at 70 °C for an additional 1 h and then poured onto H₂O (100 mL) with good stirring. The precipitate was collected by filtration, washed with H₂O, and dried at rt until constant weight. The isolated solid was recrystallized (MeCN); yield: 19–88%.

9.11.4.1.1.1.2 **Method 2:**
From β-Chloroacrylonitriles and Sodium Selenide

To access selenophen-3-amines, β-chloroacrylonitriles can serve as an alternative starting material. Treatment of β-chloroacrylonitriles **8** with sodium selenide and bromonitromethane in a one-pot, three-step procedure yields the substituted 2-nitroselenophen-3-amines **9** in good yields (Scheme 3). The starting material **8** can be generated by a Vilsmeier–Haack–Arnold reaction, oximation, and dehydration.

Scheme 3 Synthesis of Substituted 2-Nitroselenophen-3-amines^[19]

R ¹	Yield (%)	mp (°C)	Ref
4-Tol	58	246–248	[19]
4-MeOC ₆ H ₄	66	228–230	[19]
4-ClC ₆ H ₄	57	274–276	[19]
<i>t</i> -Bu	62	136–138	[19]

2-Nitroselenophen-3-amines 9; General Procedure:^[19]

Na₂Se (10.0 mmol) was suspended in DMF (10 mL) and stirred at 60 °C for 30 min. After that time, the corresponding β-chloroacrylonitrile **8** (10.0 mmol) dissolved in DMF (5 mL) was added. After the mixture had been heated at 60 °C for 2 h, it was cooled to 0 °C and bromonitromethane (10.0 mmol) was added slowly dropwise. After complete addition, the mixture was heated for 2 h at 60 °C. The reaction was followed by TLC (CH₂Cl₂) and after full conversion, NaOH (10.0 mmol) in H₂O (7 mL) was added and the mixture was left to

for references see p 96

stir for 1 h at the same temperature. The mixture was poured onto H₂O (150 mL), and the precipitate was collected by filtration, washed with H₂O, dried at rt until constant weight, and recrystallized (EtOH); yield: 57–66%.

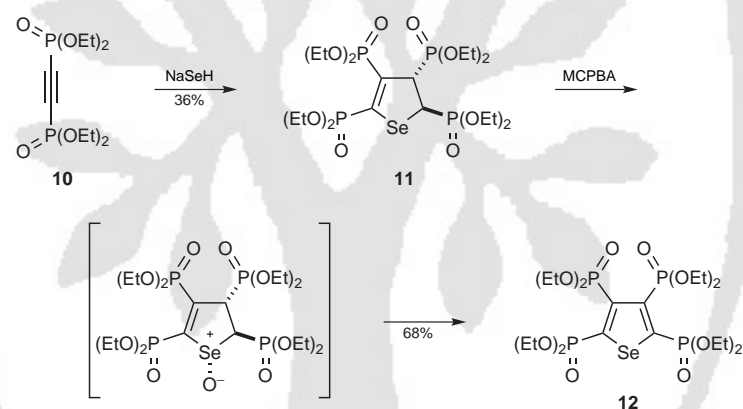
9.11.4.1.1.2 Fragments C–C, C–C, and Se

9.11.4.1.1.2.1 Method 1:

From Diphosphorylacetylene and Sodium Hydroselenide

A general method for the preparation of selenophenes (or thiophenes) is the aromatization of the corresponding dihydroselenophene (or dihydrothiophene),^[20–23] but typical oxidizing agents such as *o*- or *p*-chloranil or 2,3-dichloro-5,6-dicyanobenzo-1,4-quinone^[23] fail for this reaction. However, treatment of the tetraphosphoryl-2,3-dihydroselenophene **11** with 3-chloroperoxybenzoic acid in dichloromethane affords the selenophene **12** bearing four phosphoryl groups (Scheme 4).^[24] The desired tetraphosphoryl-2,3-dihydroselenophene **11** can be generated by the reaction of acetylene **10** with sodium hydroselenide, prepared in situ from selenium powder and sodium borohydride. In detail, sodium hydroselenide undergoes addition to two molecules of bis(diethoxyphosphoryl)acetylene (**10**) followed by cyclization to give the 2,3-dihydroselenophene species **11**.

Scheme 4 Synthesis of a Tetraphosphorylselenophene^[24]



2,3,4,5-Tetrakis(diethoxyphosphoryl)-*trans*-2,3-dihydroselenophene (11):^[24]

To a suspension of Se powder (136 mg, 1.72 mmol) in EtOH (3 mL) was added a soln of NaBH₄ (81.2 mg, 2.15 mmol) in EtOH (2.5 mL) at 0 °C. The mixture was stirred for 30 min at 0 °C, warmed to rt, and concentrated under reduced pressure. To the NaSeH thus obtained was added Et₂O (5 mL) and a soln of acetylene **10** (1.11 g, 3.73 mmol) in Et₂O (4 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h and at 20 °C for 23 h. The mixture was concentrated under reduced pressure, and purified by column chromatography (silica gel, EtOAc/acetone/EtOH); yield: 460 mg (36%).

2,3,4,5-Tetrakis(diethoxyphosphoryl)selenophene (12):^[24]

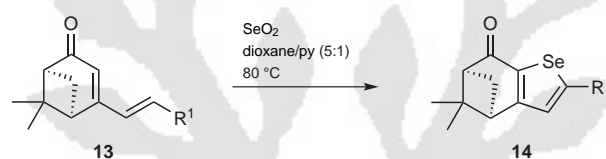
A soln of 65% MCPBA (42.9 mg, 0.160 mmol) in CH₂Cl₂ (1 mL) was added to a soln of 2,3-dihydroselenophene **11** (104 mg, 0.154 mmol) in CH₂Cl₂ (2 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h and at 20 °C for 22 h. The mixture was directly submitted to column chromatography (silica gel, EtOAc/acetone/EtOH) to give selenophene **12** as a colorless oil; yield: 70.5 mg (68%).

9.11.4.1.2 **By Formation of Two Se—C Bonds**9.11.4.1.2.1 **Fragments C—C—C—C and Se**9.11.4.1.2.1.1 **Method 1:
Reaction of C₄ Building Blocks with Sources of Selenium**9.11.4.1.2.1.1.1 **Variation 1:
Reaction of Conjugated 1,3-Dienes with Selenium Dioxide**

The conversion of 1,4-dilithio- or 1,4-diiodobuta-1,3-dienes into selenophenes is well established. Diselenium dibromide and lithium selenide are useful sources of selenium for the synthesis of selenophenes in this way.^[25,26]

A novel method for the preparation of selenophenes **14** has been disclosed.^[27] This efficient one-step synthesis of selenophenes can be realized by the reaction of selenium dioxide with 1,3-dienes such as **13** containing an activating carbonyl group at the C1 position (Scheme 5).

Scheme 5 Synthesis of Selenophenes Starting from Conjugated 1,3-Dienes^[27]



R ¹	Time (h)	Yield (%)	mp (°C)	Ref
Ph	15	86	102–104	[27]
4-ClC ₆ H ₄	18	45	124–127	[27]
4-MeOC ₆ H ₄	12	63	136–139	[27]
2,4-(MeO) ₂ C ₆ H ₃	10	55	127–129	[27]
2,4,5-(MeO) ₃ C ₆ H ₂	10	65	113–115	[27]
2,4,6-(MeO) ₃ C ₆ H ₂	10	90	167–170	[27]
4-Me ₂ NC ₆ H ₄	3	48	>180	[27]

9,9-Dimethyl-4-(2,4,6-trimethoxyphenyl)-5-selenatricyclo[6.1.1.0^{2,6}]deca-2(6),3-dien-7-one [14, R¹ = 2,4,6-(MeO)₃C₆H₂]; **Typical Procedure:**^[27]

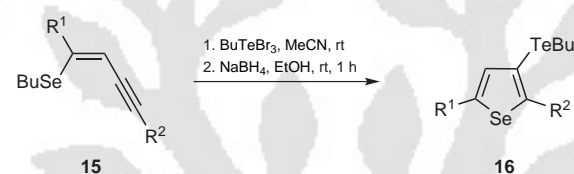
To a stirred soln (open to air) of diene **13** [R¹ = 2,4,6-(MeO)₃C₆H₂; 100 mg, 0.32 mmol] in 1,4-dioxane/pyridine (5:1; 6 mL) was added SeO₂ (390 mg, 3.50 mmol). The mixture was vigorously stirred at 80 °C for 10 h and then cooled to rt. The reaction was subsequently quenched with H₂O, washed with aq CuSO₄, extracted with Et₂O (4 ×), and dried (MgSO₄). Evaporation of the solvent followed by flash column chromatography (silica gel, hexane/Et₂O 4:1) provided selenophene **14** [R¹ = 2,4,6-(MeO)₃C₆H₂]; yield: 130 mg (90%); mp 167–170 °C; ¹H NMR (CDCl₃, δ): 0.87 (s, 3H), 1.58 (s, 3H), 2.37 (d, 1H, J = 9.5 Hz), 2.78 (t, 1H, J = 5.8 Hz), 3.04 (dt, 1H, J = 9.2, 5.8 Hz), 3.15 (t, 1H, J = 5.8 Hz), 3.87 (s, 3H), 3.92 (s, 6H), 6.23 (s, 2H), 7.91 (s, 1H); ¹³C NMR (CDCl₃, δ): 23.7, 27.6, 43.6, 47.6, 56.1, 56.4, 58.1, 58.8, 91.8, 108.0, 129.4, 134.0, 148.7, 158.9, 161.6, 162.9, 198.3; ⁷⁷Se NMR (CDCl₃, δ): 632.7.

for references see p 96

9.11.4.1.3 **By Formation of One Se—C Bond**9.11.4.1.3.1 **Fragment Se—C—C—C**9.11.4.1.3.1.1 **Method 1:
Electrophilic Cyclization of Z-Selanylenynes**9.11.4.1.3.1.1.1 **Variation 1:
Reaction with Butyltellurium Tribromide**

The electrophilic cyclization of *Z*-selanylenynes **15** using butyltellurium tribromide as an electrophilic source is a general one-pot method for the synthesis of 3-(butyltellanyl)selenophene derivatives **16** (Scheme 6).^[28] The cyclization reactions proceed cleanly under mild reaction conditions and a variety of 3-(butyltellanyl)selenophenes **16** are obtained in moderate to excellent yields. Unsymmetrical selanylenynes also give good results.

Scheme 6 Formation of Selenophenes from *Z*-Selanylenynes^[28]



R ¹	R ²	Time (h)	Yield (%)	Ref
Ph	Ph	1	91	[28]
4-Tol	4-Tol	2	82	[28]
Bu	Bu	0.5	81	[28]
Ph	Bu	3	87	[28]
H	Ph	4	85	[28]
H	Bu	3	83	[28]

3-(Butyltellanyl)selenophenes 16; General Procedure:^[28]

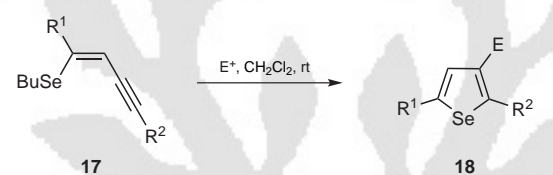
To a soln of the appropriate *Z*-selanylenyne **15** (0.500 mmol) in MeCN (5 mL) was added BuTeBr₃ (0.233 g, 0.55 mmol). The mixture was allowed to stir at rt for the time shown in Scheme 6. After that, EtOH (5 mL) and NaBH₄ (37.0 mg, 1.0 mmol) were added with vigorous stirring (gas evolution was observed during this addition). The mixture was stirred at rt for an additional 1 h, diluted with EtOAc (20 mL), and washed with H₂O (10 mL) and brine (3 × 10 mL). The organic layer was dried (MgSO₄) and concentrated under reduced pressure to give the crude product, which was purified by flash chromatography (silica gel, hexane); yield: 51–91%.

9.11.4.1.3.1.1.2 **Variation 2:
Reaction with Other Electrophiles**

Treatment of *Z*-selanylenynes with different electrophilic sources such as iodine, iodine monochloride, benzeneselenenyl bromide, and benzeneselenenyl chloride in dichloromethane induces a cyclization reaction (Scheme 7). The use of starting materials with methyl, ethyl, or butyl groups at the selenium atom results in the formation of products in high yields after short reaction times. With selanylenynes having a *tert*-butyl or benzyl

group, selenophenes are formed in good yields, but with longer reaction times. In cases where a phenyl group is attached to the selenium atom, the cyclization fails. The efficiency of the selenophene formation significantly depends on steric effects and the cyclization reaction occurs only with selanylenynes having a selenium–sp³-carbon bond. Additionally, the solvent plays an important role. The optimum solvent is dichloromethane, but good yields can also be obtained when tetrahydrofuran, diethyl ether, methanol, hexane, or acetonitrile are used; however, these reactions proceed more slowly. The optimum conditions for the electrophilic cyclization reaction are a combination of 1 equivalent of *Z*-selanylenyne **17**, 1.1 equivalents of the electrophilic source, and dichloromethane as solvent, at room temperature. The reactions of selanylenynes **17** having aryl and alkyl groups, either symmetrically or unsymmetrically substituted, give the selenophene derivatives **18** in good yields; however, the yields are lower for selanylenynes containing a hydroxy function. The resulting selenophene iodides **18** (E = I) are useful intermediates in many transition-metal-catalyzed processes, such as Sonogashira,^[29,30] Suzuki,^[31] Stille,^[32] Heck,^[33] and Ullmann^[34–38] cross couplings (see Section 9.11.4.3.2).

Scheme 7 Electrophilic Cyclization of *Z*-Selanylenynes^[29]



R ¹	R ²	E	E ⁺	Time (min)	Yield (%)	Ref
Ph	Ph	I	I ₂	5	93	[29]
			ICl	5	90	[29]
Ph	Ph	SePh	PhSeBr	10	80	[29]
			PhSeCl	15	76	[29]
4-Tol	4-Tol	I	I ₂	5	94	[29]
			ICl	10	93	[29]
Bu	Bu	I	I ₂	15	90	[29]
			ICl	15	89	[29]
Ph	Bu	I	I ₂	10	90	[29]
			ICl	15	89	[29]
H	Ph	I	I ₂	15	82	[29]
			ICl	15	80	[29]
H	Bu	I	I ₂	20	81	[29]
			ICl	20	81	[29]

3-Iodoselenophenes **18** (E = I); General Procedure:^[29]

To a soln of the appropriate *Z*-selanylenyne **17** (0.50 mmol) in CH₂Cl₂ (3 mL) was added gradually I₂ or ICl (1.1 equiv) dissolved in CH₂Cl₂ (7 mL). The mixture was allowed to stir at rt for the time shown in Scheme 7. Excess I₂ or ICl was removed by washing with sat. aq Na₂S₂O₃. The product was then extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were dried (MgSO₄) and concentrated under reduced pressure to give the crude

for references see p 96

product, which was purified by flash chromatography (silica gel, EtOAc/hexane); yield: 76–94%.

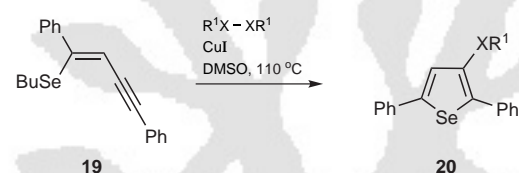
3-(Phenylselanyl)selenophenes **18** (E = SePh); General Procedure:^[29]

To a soln of the appropriate *Z*-selanylenyne **17** (0.50 mmol) in CH₂Cl₂ (3 mL) was added gradually PhSeBr or PhSeCl (1.1 equiv) dissolved in CH₂Cl₂ (7 mL). The mixture was allowed to stir at rt for the time shown in Scheme 7. The mixture was washed with H₂O (40 mL) and extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were dried (MgSO₄) and concentrated under reduced pressure to give the crude product, which was purified by flash chromatography (silica gel, hexane); yield: 76–80%.

9.11.4.1.3.1.1.3 Variation 3: Copper(I) Iodide Catalyzed Cyclization

Copper-catalyzed cyclization of selanylenyne **19** with diaryl dichalcogenides is an alternative route to obtain 3-substituted selenophenes **20** in good to excellent yields (Scheme 8).^[39] The reaction works well for a variety of diaryl dichalcogenides. Electronic effects of the substituents in the aromatic ring as well as steric effects seem to be negligible.

Scheme 8 Synthesis of Selenophenes via Copper-Catalyzed Cyclization^[39]



R ¹	X	Yield (%)	Ref
Ph	Se	86	[39]
4-ClC ₆ H ₄	Se	89	[39]
Mes	Se	65	[39]
Ph	Te	77	[39]
4-ClC ₆ H ₄	Te	78	[39]

2,5-Diphenyl-3-(phenylselanyl)selenophene (**20**, R¹ = Ph; X = Se); Typical Procedure:^[39]

A mixture of enyne **19** (0.50 mmol) and (PhSe)₂ (1.1 equiv) in DMSO (3 mL) was reacted with CuI (10 mol%) at 110 °C for 10 h; yield: 86%.

9.11.4.1.4 By Formation of One C—C Bond

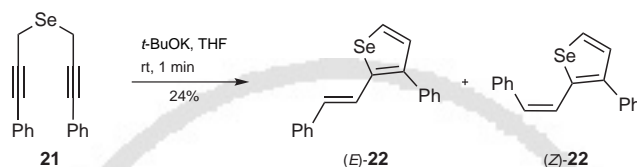
9.11.4.1.4.1 Fragment C—C—C—Se—C

9.11.4.1.4.1.1 Method 1: Cyclization of a Dipropargyl Selenide

Dipropargylic systems bridged by selenium, such as **21**, react with potassium *tert*-butoxide in anhydrous tetrahydrofuran at room temperature to form 2-vinylselenophenes. The cyclization of selenide **21** yields the products (*E*)- and (*Z*)-**22** (36:64 ratio), regardless

of the base concentration (Scheme 9).^[40] The overall process can be rationalized as an anionic cyclization/aromatization reaction.

Scheme 9 Synthesis of 2-Vinylselenophenes^[40]



3-Phenyl-2-[(*E*)-2-phenylvinyl]selenophene [(*E*)-22] and 3-Phenyl-2-[(*Z*)-2-phenylvinyl]selenophene [(*Z*)-22]:^[40]

To a stirred soln of *t*-BuOK (1.0 equiv) in dry THF (5 mL) was added in one portion a soln of the dipropargylic compound **21** (0.50 mmol) in dry THF (10 mL). After the mixture had been stirred for 1 min at rt, it was diluted with H₂O/CH₂Cl₂ (1:1; 80 mL) and the organic layer was washed with 3% HCl (2 × 50 mL), H₂O (3 × 50 mL), and brine (1 × 50 mL). The organic layer was dried (MgSO₄) and the solvent was removed under reduced pressure. The compounds (*E*)- and (*Z*)-**22** were obtained as an inseparable mixture and purified by column chromatography (silica gel, hexane); total yield: 24%.

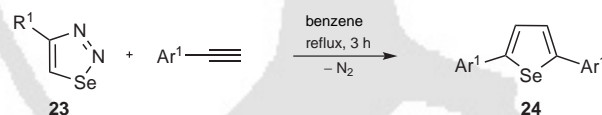
9.11.4.2 Synthesis by Ring Transformation

9.11.4.2.1 Method 1:

Thermal Decomposition of Selenadiazoles in the Presence of Arylacetylenes

2,5-Diarylselenophenes can be prepared by thermal decomposition of 1,2,3-selenadiazoles in the presence of arylacetylenes (Scheme 10). Heating selenadiazole **23** in the presence of 2 equivalents of an arylacetylene proceeds without selectivity giving a mixture of three different symmetrical and unsymmetrical selenophenes in low yields. A single 2,5-diarylselenophene **24** can be obtained when using a 10-fold excess of the arylacetylene.

Scheme 10 2,5-Diarylselenophenes from Thermal Decomposition of Selenadiazoles in the Presence of Arylacetylenes^[41]



R ¹	Ar ¹	Yield (%)	Ref
Ph		80	[41]
2-thienyl		42	[41]

for references see p 96

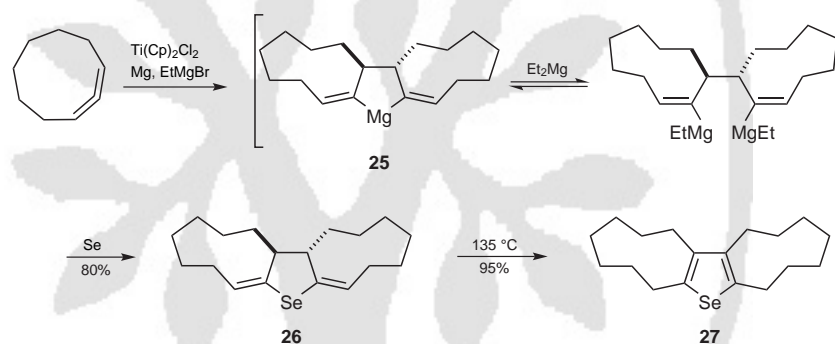
2,5-Bis(6-methyl-3-pyridyl)selenophene (24, Ar¹ = 6-Methyl-3-pyridyl);**Typical Procedure:**^[41]

A mixture of 4-phenyl-1,2,3-selenadiazole (**23**, R¹ = Ph; 104 mg, 0.50 mmol) and 5-ethynyl-2-methylpyridine (0.590 g, 5.0 mmol) in benzene (2 mL) (**CAUTION: carcinogen**) was refluxed for 3 h. The pure product was isolated by column chromatography (silica gel, EtOAc); yield: 80%; mp 91–93 °C; ¹H NMR (CDCl₃, δ): 2.55 (s, 6H), 7.12 (d, 2H, J = 8.3 Hz), 7.43 (s, 2H), 7.55 (dd, 2H, J = 8.2, 2.2 Hz), 8.68 (d, 2H, J = 2.2 Hz); ¹³C NMR (CDCl₃, δ): 24.1, 115.9, 123.3, 125.9, 137.5, 146.2, 152.4, 157.7.

9.11.4.2.2

Method 2:**Formal Exchange of Magnesium with Selenium**

A remarkable synthetic route to selenophene **27** starts from cyclonona-1,2-diene.^[42] Cyclo-magnesiation using ethylmagnesium bromide in the presence of metallic magnesium (a halogen ion acceptor) and a catalytic amount of titanium complex leads to the corresponding magnesacycle **25**. Compound **26** is then accessible in 80% yield by treating magnesatricyclononadecadiene **25** in situ with selenium metal. The conversion into pure tricyclic selenophene **27** requires heating to 135 °C (Scheme 11).

Scheme 11 Synthesis of a Tricyclic Selenophene Starting from a Cyclic 1,2-Diene^[42]**1,2,3,4,5,6,7,9,10,11,12,13,14,15-Tetradecahydrodicyclonona[b,d]selenophene (27):**^[42]

Cyclonona-1,2-diene (10.0 mmol), $\text{Ti}(\text{Cp})_2\text{Cl}_2$ (0.50 mmol), Mg powder (10.0 mmol), Et_2O (10 mL), and EtMgBr (ethereal soln; 20.0 mmol) were added with stirring to a glass reactor in a dry argon atmosphere at 0 °C. The mixture was brought to ~20 °C and then stirred for 4 h to give compound **25**. Then, benzene (10 mL) (**CAUTION: carcinogen**) and Se (12.0 mmol) were added at 0 °C and the mixture was heated for 6 h at 40 °C. The mixture was treated with 7–10% HCl . The reaction products were extracted with hexane and dried (MgSO_4). The volatile solvents were removed under reduced pressure. The diene **26** was separated by column chromatography (silica gel, hexane); yield: 80%; R_f 0.43 (hexane).

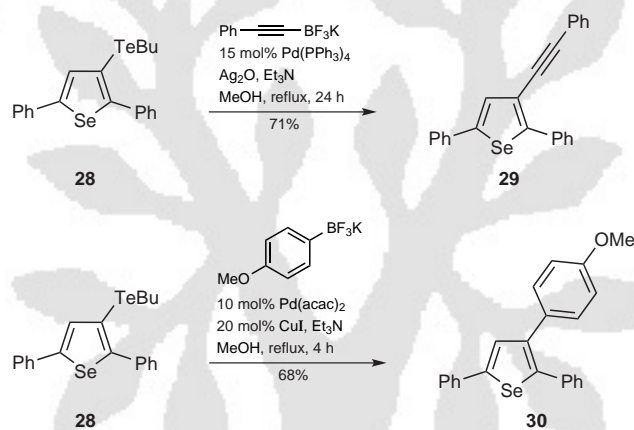
Diene **26** was placed in a glass ampule and heated for 6 h at 130 °C to give compound **27**; yield: 95%; bp 191–193 °C/1 Torr.

9.11.4.3 Synthesis by Substituent Modification

9.11.4.3.1 Substitution of Metals

9.11.4.3.1.1 Method 1:
Substitution Reactions Involving Organoboron Derivatives

The 3-(butyltellanyl)selenophene **28** behaves similarly to its iodo or bromo analogues. For instance, Suzuki cross-coupling reactions of compound **28** with alkynyl- or aryltrifluoroborates proceed smoothly to give 3-substituted selenophenes **29** and **30**, respectively, in satisfactory yields (Scheme 12).^[28] Since the yields of the Suzuki cross coupling with a butyltellanyl group at the 3-position are very similar to the corresponding iodine derivatives,^[43] these compounds provide an alternative intermediate in the preparation of highly substituted selenophenes.

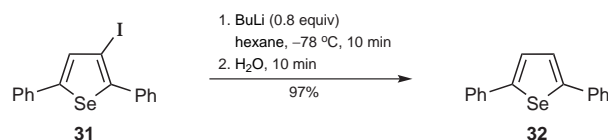
Scheme 12 Palladium-Catalyzed Cross-Coupling Reactions^[28]

9.11.4.3.2 Substitution of Heteroatoms

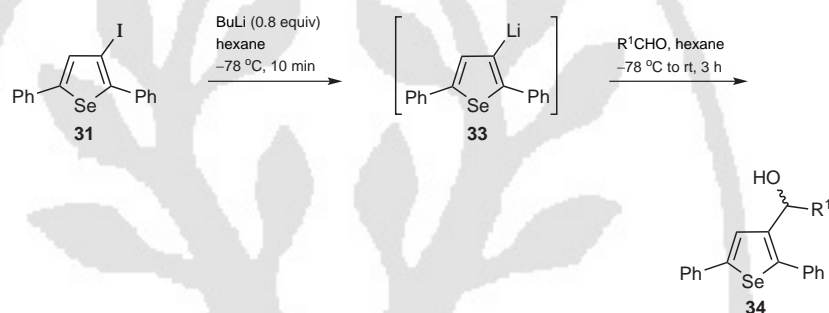
9.11.4.3.2.1 Method 1:
Substitution of Halogens by Lithium

Metal–halogen exchange reactions are of great importance in synthetic organic chemistry, particularly with respect to the formation of new C–C bonds. For instance, 3-lithiothiophene derivatives can be prepared by metal–halogen exchange of 3-bromothiophenes with butyllithium.^[44,45] Such well-known metal–halogen exchange reactions can be extended to an intermediate 3-lithio-2,5-diphenylselenophene (**33**).^[29] Both the solvent and temperature of the reaction are of importance. Performing the reaction of iodoselephenone **31** in tetrahydrofuran with addition of 1.0 equivalent of butyllithium at -78°C , leads to a mixture of *Z*- and *E*-selanylenynes, instead of the targeted product **32**; however, the iodide **31** can be converted into the desired 2,5-diphenylselenophene (**32**) by switching from tetrahydrofuran to hexane. When decreasing the amount of lithium reagent from 1.0 to 0.8 equivalents and using low temperatures, better yields of compound **32** are observed (Scheme 13).

for references see p 96

Scheme 13 Halogen–Metal Exchange^[29]

In addition, 3-iodoselenophenes (e.g., **31**) can be transformed into more complex products using a metal–halogen exchange reaction with butyllithium and trapping the intermediate formed with aldehydes, furnishing the desired secondary alcohols **34** in good yields (Scheme 14).^[29]

Scheme 14 Reactions of Intermediate 3-Lithio-2,5-diphenylselenophene with Aldehydes^[29]

R^1	Yield (%)	Ref
Ph	82	[29]
4-Tol	86	[29]
4-MeOC ₆ H ₄	70	[29]
4-ClC ₆ H ₄	74	[29]
Cy	67	[29]
(CH ₂) ₅ Me	62	[29]

2,5-Diphenylselenophene (32):^[29]

To a two-necked, round-bottomed flask, under argon, containing a soln of iodoseleophene **31** (102 mg, 0.25 mmol) in hexane (2 mL) at $-78\text{ }^{\circ}\text{C}$ was added 2.5 M BuLi in hexane (80.0 μL , 0.20 mmol) in one portion. The mixture was stirred at rt for 10 min. H_2O (2 mL) was added, and the mixture was diluted with hexane (20 mL) and washed with brine ($3 \times 20\text{ mL}$). The organic phase was dried (MgSO_4), and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (silica gel, hexane); yield: 55.0 mg (97%, based on BuLi).

3-(1-Hydroxyalkyl)-2,5-diphenylselenophenes 34; General Procedure:^[29]

To a two-necked, round-bottomed flask, under argon, containing a soln of iodoseleophene **31** (102 mg, 0.25 mmol) in hexane (2 mL) at $-78\text{ }^{\circ}\text{C}$ was added 2.5 M BuLi in hexane (80.0 μL , 0.200 mmol) in one portion. The mixture was stirred for 10 min, and then a soln of the appropriate aldehyde (0.30 mmol) in hexane (1 mL) at $-78\text{ }^{\circ}\text{C}$ was added. The mixture was allowed to stir at rt for 3 h. After this time, the mixture was diluted with

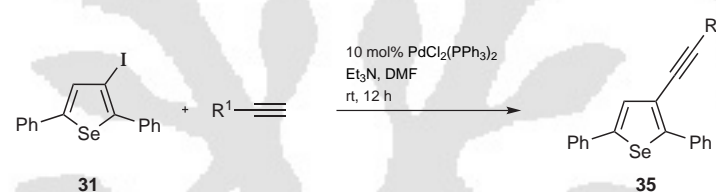
EtOAc (20 mL) and washed with sat. aq. NH_4Cl (20 mL) and H_2O (3×20 mL). The organic phase was separated, dried (MgSO_4), and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, EtOAc/hexane); yield: 62–87%.

**9.11.4.3.2.2 Method 2:
Metal-Assisted Cross Coupling of Haloselenophenes**

**9.11.4.3.2.2.1 Variation 1:
Coupling with Alkynes**

3-Iodoselenophene derivatives such as **31** undergo direct Sonogashira–Hagihara cross-coupling reactions with terminal alkynes in the presence of a catalytic amount of dichlorobis(triphenylphosphine)palladium(II) in dimethylformamide with triethylamine as the base under cocatalyst-free conditions (Scheme 15). This copper-free Sonogashira cross-coupling reaction can be performed with propargylic alcohols and propargylic ethers, as well as alkyl-, vinyl-, and arylalkynes to furnish the corresponding 3-alkynylselenophenes **35** in good to excellent yields.^[46]

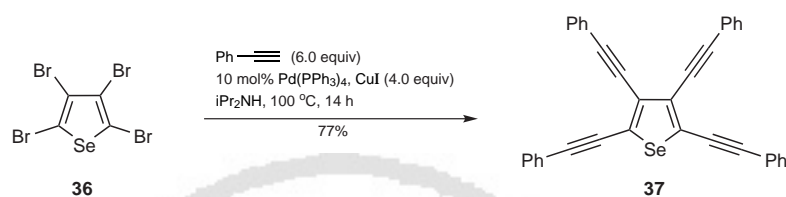
Scheme 15 Cross-Coupling Reaction of 3-Iodoselenophene and Alkynes^[46]



R^1	Yield (%)	Ref
CMe_2OH	91	[46]
CH_2OEt	67	[46]
$(\text{CH}_2)_4\text{Me}$	97	[46]
Ph	94	[46]
<i>t</i> -Bu	70	[46]

2-Haloselenophenes also undergo direct cocatalyst-free Sonogashira cross-coupling reactions with several terminal alkynes, and can be converted into 2-alkynylselenophenes in good yields. This reaction also works well for a variety of terminal alkynes (e.g., propargylic alcohols, protected propargylic alcohols, propargylic amines, alkyl- and arylalkynes) in the presence of dichlorobis(triphenylphosphine)palladium(II), triethylamine, dimethylformamide, and in the absence of any supplementary additive.^[47] Moreover, the Sonogashira reaction of tetrabromoselenophene (**36**) with phenylacetylene offers access to the first tetraalk-1-nylselenophene **37** (Scheme 16).^[48]

for references see p 96

Scheme 16 Synthesis of Tetra(phenylethynyl)selenophene^[48]**3-Alk-1-ynyl-2,5-diphenylselenophenes 35; General Procedure:**^[46]

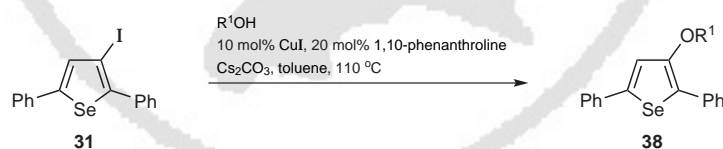
To a Schlenk tube, under an atmosphere of argon, containing the 3-iodoselenophene **31** (0.50 mmol) in DMF (2.5 mL) was added PdCl₂(PPh₃)₂ (35.0 mg, 50.0 μmol). The resulting soln was stirred for 5 min at rt. After this time, a terminal alkyne (1.50 mmol) dissolved in Et₃N (1 mL) was added dropwise, and the mixture was allowed to stir at rt for 12 h. After this time, the mixture was diluted with CH₂Cl₂ (20 mL) and washed with brine (3 × 20 mL). The organic phase was separated, dried (MgSO₄), and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, EtOAc/hexane 1:8); yield: 67–97%.

Tetrakis(phenylethynyl)selenophene (37):^[48]

An oven-dried Schlenk flask was charged with Pd(PPh₃)₄ (35.0 mg, 10 mol%), tetrabromoselenophene (**36**; 0.30 mmol), phenylacetylene (153 mg, 1.50 mmol), and CuI (229 mg, 1.20 mmol). The Schlenk flask was evacuated and subsequently flushed with argon. To the mixture was added iPr₂NH (12 mL) by syringe. After stirring of the soln at 0 °C for 4 h, the mixture was heated under reflux for 8 h. The mixture was allowed to cool to ambient temperature and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, heptane). Product **37** was isolated as a yellow solid; yield: 123 mg (77%); mp 80–81 °C.

9.11.4.3.2.2.2 Variation 2: Coupling with Alcohols

The reactions of 3-iodoselenophene **31** with alcohols in dry toluene, using a catalytic system of copper(I) iodide/1,10-phenanthroline and cesium carbonate as base, gives Ullmann-type products **38** in good isolated yields (Scheme 17).^[29]

Scheme 17 Copper-Catalyzed Coupling Reactions with Alcohols^[29]

R ¹	Yield (%)	Ref
Bu	67	[29]
(CH ₂) ₇ Me	64	[29]

3-Alkoxy-2,5-diphenylselenophenes 38; General Procedure:^[29]

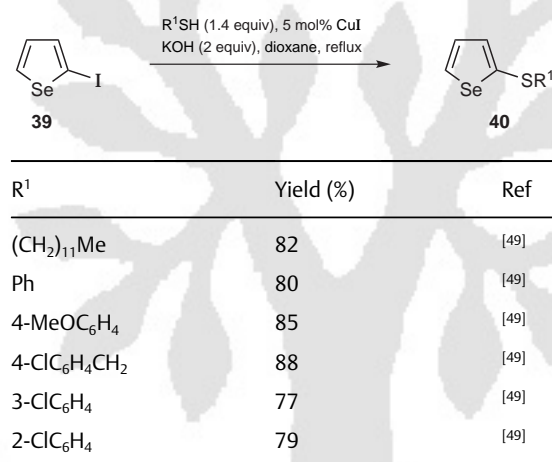
To a Schlenk tube, under argon, containing CuI (9.5 mg, 50 μmol) in dry toluene (1.5 mL) was added 1,10-phenanthroline (18.0 mg, 0.10 mmol). The resulting soln was stirred for

30 min at rt. After this, 3-iodo-2,5-diphenylselenophene (**31**; 0.204 g, 0.50 mmol) was added, and the resulting soln was stirred for an additional 15 min at rt. Then, Cs₂CO₃ (0.325 g, 1.00 mmol) and the appropriate alcohol (1.50 mmol) were added and the mixture was heated at 110 °C for 12 h. The soln was cooled to rt, diluted with CH₂Cl₂ (20 mL), and washed with sat. aq NH₄Cl (3 × 20 mL). The organic phase was separated, dried (MgSO₄), and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, EtOAc/hexane); yield: 64–67%.

9.11.4.3.2.2.3 Variation 3: Coupling with Thiols

Not only alcohols react with haloselenophenes in a copper-catalyzed coupling reaction but also thiols. The coupling of thiols with 2-haloselenophenes, such as **39**, by copper(I) can be used to obtain 2-sulfanylselenophenes **40** in good yields (Scheme 18).^[49] In the absence of any supplementary additives, the reaction can be performed with both electron-donating and electron-withdrawing substituents on the thiol.

Scheme 18 Copper-Catalyzed Thiol Cross Coupling^[49]



2-Sulfanylselenophenes **40**; General Procedure:^[49]

A two-necked, round-bottom flask equipped with a magnetic stirrer bar and under argon was charged sequentially with CuI (5 mol%), thiol (0.700 mmol), KOH (1.00 mmol), 2-iodoselenophene (**39**; 0.500 mmol), and dioxane (5 mL). The mixture was stirred at rt for 10 min, then refluxed for 8–10 h. After this time, the mixture was filtered through a pad of alumina, eluting with EtOAc (50 mL). The organic phase was concentrated under vacuum and the residue was purified by flash chromatography; yield: 77–88%.

for references see p 96

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