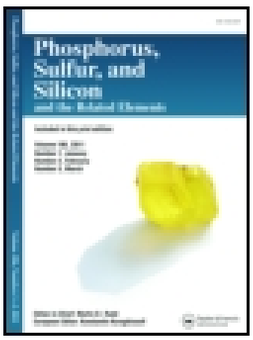

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# Synthesis of 4-aryl-7-methoxy-9-thia-[1,3,4a]triazafluorene-2-selones via a three-component condensation of 6-methoxybenzothiazol-2-ylamine, potassium selenocyanate and an acyl chloride

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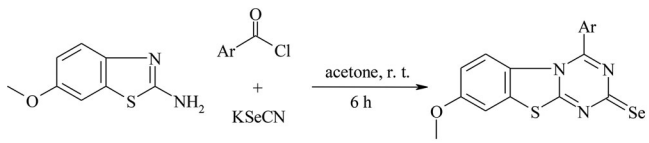
**ABSTRACT**

A simple, one-pot synthesis of six 4-aryl-7-methoxy-9-thia-[1,3,4a]triazafluorene-2-selones has been achieved in moderate to good yields via a three-component condensation of 6-methoxybenzothiazol-2-ylamine, potassium selenocyanate and variously substituted benzoyl chlorides in acetone at room temperature.

**GRAPHICAL ABSTRACT**

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4-Aryl-7-methoxy-9-thia-[134a]triazafluorene-2-selones; benzoyl chlorides; potassium selenocyanate; 6-methoxybenzothiazol-2-ylamine

## Introduction

Bridgehead nitrogen heterocycles are of interest because they constitute an important class of natural and synthetic products, many of which exhibit useful biological activity.[1,2] Many triaza analogs of polycyclic aromatic compounds that feature a bridgehead nitrogen have a long history of widespread use as precursors to construct functional materials such as antibacterial agents, pesticides, active dyes, encapsulation resins of integrated circuits, and structural adhesives for advanced carbon-fiber composites in the aerospace industry.[3–7] As a result, a number of reports of their synthesis have appeared in the literature,[8–12] but most of them require forcing conditions, long reaction times and complex synthetic pathways.

In chemistry, a selenone is the structural analog of a ketone where selenium replaces oxygen. Selenium-77, is one of the isotopes of selenium that is stable and naturally occurring, so selone-containing chemicals can be analyzed by nuclear magnetic resonance spectroscopy (NMR). They can be used as chiral derivatizing agents for $^{77}$Se-NMR.[13] Chiral oxazolidineselones can be used for stereoselective control of aldol reactions, analogous to the Evans aldol reaction that uses oxazolidinones, which allows $^{77}$Se-NMR to be used to determine the diastereomeric ratio of the aldol product.[14]

In contrast to analogous structures with lighter chalcogens, selones exhibit greater steric and electronic stabilization.[15] Selenobenzophenone reversibly dimerizes. It is known to undergo cycloaddition with 1,3-dienes in a reaction similar to the Diels-Alder reaction.[16]

The current interest in selenium-containing organic compounds stems from their remarkable synthetic and biological functions.[17–21] The first synthesis of acyl isoselenocyanates, which were generated by the reaction of acyl chlorides and potassium selenocyanate, has been described by Douglas.[22] Recently, a few synthesis of heterocycles from acyl isoselenocyanates were reported.[23–25] Herein, we describe a synthesis of a new series of 4-aryl-7-methoxy-9-thia-[1,3,4a]triazafluorene-2-selones using a reported method.[23]

## Results and discussion

A recent report[23] described the synthesis of a series of aryl triazanaphthalene-selones by the reaction at room temperature in solvent acetone between 2-aminopyridine, an acyl chloride and potassium selenocyanate (KSeCN). We thought that a synthesis of some benzo analogs of the aryl triazanaphthalene-selones, 4-aryl-7-methoxy-9-thia-[1,3,4a]triazafluorene-2-selones (**4**) might be simply achieved by a similar reaction in which 2-aminopyridine was replaced by 6-methoxybenzothiazol-2-ylamine (**1**) (Scheme 1).

So it proved, and a series of six such compounds were prepared in good yields by using a variety of substituted

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benzoyl chlorides (**2**; Ar = various) in reaction with 6-methoxybenzothiazol-2-ylamine (**1**) and KSeCN (**3**) (Table 1).

The structures of compounds **4a-g** were deduced from their elemental analysis and their IR, $^1$H NMR, 13C NMR and mass spectra. The $^1$H NMR spectrum of compound **4a** was simple and exhibited a single sharp line readily recognized as arising from a methoxy ($\delta = 3.84$ ppm). Aromatic protons resonate as multiples at $\delta = 7.05$–$7.26$ ppm. The mass spectra of compounds **4a–f** are fairly similar and display molecular ion peaks. For example, the mass spectrum of compound (**4a**) showed a molecular ion peak at 372 confirming that it is a (1:1:1) adduct of, 6-methoxybenzothiazol-2-ylamine, benzoyl chloride and potassium selenocyanate. The IR spectrum of compound **4a** also supported the suggested structure exhibiting strong absorption bands at 1595 cm$^{-1}$ for the C = N and 1290 cm$^{-1}$ for the C = Se groups. The 13C NMR spectrum of compound **4a** showed 14 distinct resonances in agreement with the proposed structure. The selone 13C resonances of compounds **4** were observed at 165.3–169.6 ppm.[26]

The mechanism of the reaction is probably similar to that published by Yavari *et al.*[23]

It is conceivable that the reaction starts with formation of acyl isoselenocyanate **5** followed by addition of 6-methoxybenzothiazol-2-ylamine **1** to generate **6**. The cyclization of intermediate **6** affords **7**, which is converted into **4** by elimination of water (Scheme 2).

## Experimental

Melting points were determined with an Electrothermal 9100 apparatus and are uncorrected. Elemental analysis for C and H were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. NMR spectra were obtained on a Brucker DRX 500 Avance spectrometer ($^1$H NMR at 500 Hz, 13C NMR at 125 Hz) in $d_6$-DMSO using TMS as an internal standard. Chemical shifts ($\delta$) are given in ppm. All of the chemicals used in this study were purchased from Merck and Fluka (Buchs, Switzerland) and were used without further purification. The Supplemental Materials contains sample

Caution! All of the reactions involving selenium-containing compounds should be carried out in a well-ventilated hood.

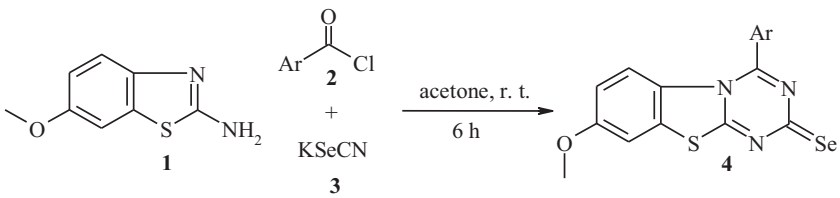
### General procedure

To a solution of potassium selenocyanate (1 mmol) in dry acetone (3 mL) was added acyl chloride (1 mmol) in dry acetone (3 mL). The reaction mixture was stirred at r.t. for 10 min. 6-methoxybenzothiazol-2-ylamine (1 mmol) in dry acetone (4 mL) was added to the mixture. The progress of the reaction was monitored by TLC. After completion of the reaction, the resulting precipitate was collected by filtration on a Buchner funnel and washed with cold water (20 mL)

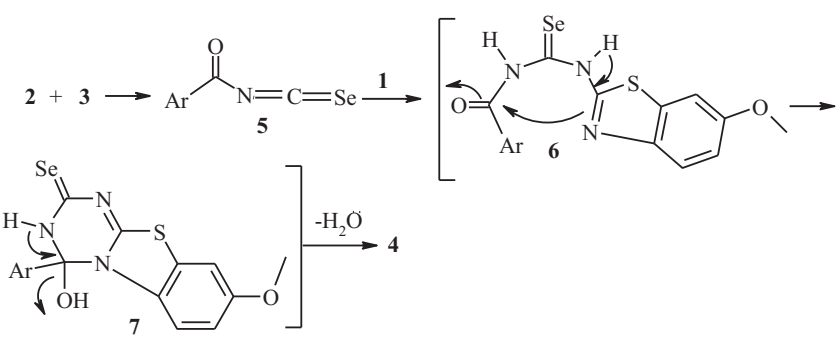
**Table 1.** Yields of a series of 4-aryl-7-methoxy-9-thia-[1,3,4a]triazafluorene-2-selones (**4**) prepared from 6-methoxybenzothiazol-2-ylamine (**1**), an acyl chloride (**2**) and KSeCN (**3**) (Scheme 1).

| 4 | Ar | %Yield[b] | m.p. (°C) |
|---|---|---|---|
| **a** | $C_6H_5$ | 78 | 118–120 |
| **b** | 4-C1$C_6H_4$ | 83 | 189–191 |
| **c** | 4-Br$C_6H_4$ | 81 | 196–198 |
| 4 | Ar | %Yield[b] | m.p. (°C) |
| **d** | 3-$O_2NC_6H_4$ | 92 | 181–183 |
| **e** | 4-$O_2NC_6H_4$ | 90 | 225–227 |
| **f** | 4-$CH_3C_6H_4$ | 75 | 128–130 |

[*]Yields refer to the pure isolated products




**Scheme 1.** Three-component condensation of 6-methoxybenzothiazol-2-ylamine, variously substituted benzoyl chlorides and potassium selenocyanate.




**Scheme 2.** Proposed mechanism for 4.

and recrystallized from EtOH to afford the pure title compounds.

### 4-Phenyl-7-methoxy-9-thia-[1,3,4a]triazafluorene-2-selone (4a)

Yellow powder; m.p. 118–120 °C; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 1664, 1595, 1556, 1462, 1290, 1117; $^1$H NMR(ppm): $\delta$ 3.84 (3H, s, $OCH_3$), 7.05–8.26 (8H, m, 8CH aromatic); 13C NMR(ppm): $\delta$ 55.45 ($OCH_3$), 104.5, 114.8, 120.8, 128.1, 128.3, 128.4, 128.6, 129.1, 132.5, 132.6, 155.2, 156.1 and 167.1; Anal. Calcd. for $C_{16}H_{11}N_3OSSe$: C, 51.62; H, 2.98; N, 11.29. Found: C, 51.75; H, 3.09; N, 11.40%; MS (m/z, %): 372 (6).

### 4-(4-Chlorophenyl)-7-methoxy-9-thia-[1,3,4a] triazafluorene-2-selone (4b)

Yellow powder; m.p. 189–191 °C; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 1658, 1596, 1563, 1471, 1311, 1148; $^1$H NMR(ppm): $\delta$ 3.81 (3H, s, $OCH_3$), 7.03–8.13 (7H, m, 7CH aromatic); 13C NMR(ppm): $\delta$ 55.46 ($OCH_3$), 104.6, 114.9, 120.8, 128.1, 128.4, 128.5, 129.2, 129.5, 130.9, 137.5, 156.1, 156.6 and 166.3; Anal. Calcd. for $C_{16}H_{10}ClN_3OSSe$: C, 47.25; H, 2.48; N, 10.33. Found: C, 47.36; H, 2.60; N, 10.42%; MS (m/z, %): 406 (8).

### 4-(4-Bromophenyl)-7-methoxy-9-thia-[1,3,4a] triazafluorene-2-selone (4c)

Yellow powder; m.p. 196–198 °C; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 1662, 1584, 1541, 1382, 1280, 1144; $^1$H NMR(ppm): $\delta$ 3.81 (3H, s, $OCH_3$), 7.05-8.04 (7H, m, 7CH aromatic); 13C NMR(ppm): $\delta$ 55.74 ($OCH_3$), 104.1, 115.2, 120.9, 124.6, 128.0, 128.9, 129.4, 132.1, 141.1, 149.7, 156.4, 157.4 and 167.6; Anal. Calcd. for $C_{16}H_{10}BrN_3OSSe$: C, 42.59; H, 2.23; N, 9.31. Found: C, 42.68; H, 2.35; N, 9.41%; MS (m/z, %): 451 (4).

### 4-(3-Nitrophenyl)-7-methoxy-9-thia-[1,3,4a] triazafluorene-2-selone (4d)

Yellow powder; m.p. 181–183 °C; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 1659, 1596, 1552, 1424, 1338, 1266, 1125; $^1$H NMR(ppm): $\delta$ 3.81 (3H, s, $OCH_3$), 7.03-8.94 (7H, m, 7CH aromatic); 13C NMR(ppm): $\delta$ 55.27 ($OCH_3$), 104,4, 114.8, 120.4, 122.8, 126.6, 127.8, 128.6, 129.9, 132.2, 133.5, 134.2, 147.4, 155.8, 156.0, 168.4; Anal. Calcd. for $C_{16}H_{10}N_4O_3SSe$: C, 46.05; H, 2.42; N, 13.43. Found: C, 46.18; H, 2.53; N, 13.59%; MS (m/z, %): 417 (11).

### 4-(4-Nitrophenyl)-7-methoxy-9-thia-[1,3,4a] triazafluorene-2-selone (4e)

Yellow powder; m.p. 225-227 °C; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 1664, 1597, 1557, 1521, 1455, 1334, 1267, 1149; $^1$H NMR(ppm): $\delta$ 3.82 (3H, s, $OCH_3$), 7.06–8.84 (7H, m, 7CH aromatic); 13C NMR(ppm): $\delta$ 55.29 ($OCH_3$), 104.5, 114.9, 120.4, 123.2, 127.4, 128.5, 129.5, 132.2, 137.6, 149.3, 155.7, 156.1, and 165.3; Anal. Calcd. for $C_{16}H_{10}N_4O_3SSe$: C, 46.05; H, 2.42; N, 13.43. Found: C, 46.15; H, 2.55; N, 13.53%; MS (m/z, %): 417 (9).

### 4-p-Tolyl-7-methoxy-9-thia-[1,3,4a]triazafluorene-2-selone (4f)

Yellow powder; m.p. 128-130 °C; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 1666, 1604, 1550, 1468, 1273, 1116; $^1$H NMR(ppm): $\delta$ 2.40 (3H, s, $CH_3$), 3.82 (3H, s, $OCH_3$), 7.04–8.15 (7H, m, 7CH aromatic); 13C NMR(ppm): $\delta$ 20.7 ($CH_3$), 55.29 ($OCH_3$), 104.3, 114.6, 120.6, 127.9, 128.8, 129.0, 129.8, 139.4, 142.3, 142.7, 143.5, 155.9 and 169.6; Anal. Calcd. for $C_{17}H_{13}N_3OSSe$: C, 52.85; H, 3.39; N, 10.88. Found: C, 52.94; H, 3.60; N, 11.01%; MS (m/z, %): 386 (5).

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