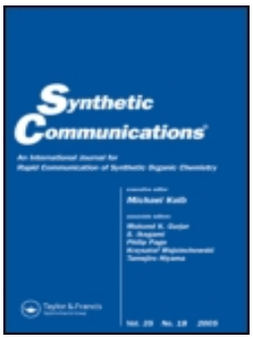

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Solid-State Synthesis of 1,3-Selenazoles Employing $CuPy_2Cl_2$ as a Lewis Acid Catalyst

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Abstract: 1,3-Selenazoles were Synthesized from 3-bromo acetyl coumarin and selenourea in the presence of $CuPy_2Cl_2$ under solvent-free conditions at ambient temperature. The pure products were identified by spectral data.

Keywords: α-Bromo ketone, $CuPy_2Cl_2$, 1,3-selenazole, selenourea

INTRODUCTION

1,3-Selenazoles are very important in synthetic organic chemistry because of their interesting reactivity[1] and potential biological interest.[2] For the construction of selenium containing heterocyclic compounds, a number of synthetic routes have been developed. 1,3-Selenazoles were mainly synthesized by the application of the Hantzsch procedure.[3] Therefore, the development of new methods for the synthesis of the selenium-containing high-value building blocks by replacing the thermal reaction conditions and organic solvents, most of which are flammable and toxic, is of considerable current interest.

In continuation of our exploration of new catalysts, we characterize $CuPy_2Cl_2$[4] as an efficient Lewis acid catalyst; it is water tolerant and reusable and can effectively promote some of the organic reactions such as the Pechmann condensation,[5] Biginelli reaction,[6] and synthesis of benzoxanthenes[7] in good yields.

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This article describes the synthesis of 1,3-selenazoles starting from α-bromo ketones and selenourea in the presence of $CuPy_2Cl_2$.

RESULTS AND DISCUSSION

In an effort to improve the yields of the condensation reaction of α-bromo ketones and selenourea, various solvents were screened, and the results are summarized in Table 1. Ethanol provided good yields and proved to be the solvent of choice, whereas chloroform and water afforded lower yields. It was interesting to realize that 3-bromo acetyl coumarin and selenourea (mixed at the ratio of 1:1.2) in the presence of $CuPy_2Cl_2$ (0.01 mmol) react in a mortar without solvent very efficiently. The results showed that the reactions were completed within 30 min of grinding, and the desired products were obtained in excellent yields. The same method applied to the reaction of bromo acetyl benzene and selenourea. We tried to prepare the selenazoles by using 3-bromo acetyl coumarin and selenourea without using any catalyst, but we obtained only 55% yield. Therefore, a catalyst is needed for the reaction.

The products prepared by the solid-state reaction were characterized by IR, ^{1}H NMR, and mass spectral data and compared with the products obtained from the liquid-state reaction. The results showed that the reaction under solid-state conditions was benign to the environment, completed with higher yields, and has a more convenient workup.

EXPERIMENTAL

All the melting points were uncorrected. The progress of the reaction was monitored by thin-layer chromatography (TLC). IR spectra (KBr) were recorded on a Shimadzu FTIR model 8010 spectrometer and the

Table 1. $CuPy_2Cl_2$-catalyzed synthesis of 3-(2-amino-1,3-selenazol-4-yl)-2H-chromen-2-one in different solvents

Entry	Solvent	Yield (%)
1	EtOH	93
2	$CHCI_3$	86
3	H_2O	75

Note. Reaction conditions: 3-bromo acetyl coumarin (1 mmol), selenourea (1.2 mmol), and $CuPy_2Cl_2$ in presence of solvent were stirred at the room temperature for 45 min.

^{1}H NMR spectra on a Varian Gemini 200-MHz spectrometer using TMS as internal standard. The C, H, and N analysis of the compound was done on a Carlo Erba model EA1108. Mass spectra were recorded on a Jeol JMS D-300 spectrometer. All solvents and reagents were purchased from Aldrich and Fluka firms.

Typical Procedure for Synthesis of 1,3-Selenazoles

$CuPy_2Cl_2$ (0.01 mmol) was added to a mixture of α-bromo ketone (1 mmol) and selenourea (1.2 mmol) in a mortar and ground with a pestle at room temperature until the reaction was completed (progress of the reaction was observed by TLC) (Tables 2 and 3). After completion of the reaction, water (5 ml) was added to the reaction mixture and extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, the solvent was evaporated under reduced pressure, and the resulting product was further purified by column chromatography (hexane/ethyl acetate 7:3). The aqueous layer containing the catalyst could be evaporated under reduced pressure (50 mm Hg pressure at 85 °C) to give a blue solid. This could be reused for the next reaction with only modest loss in activity.

Spectral Data

4-Phenyl-1,3-Selenazol-2-Amine (Table 3, Entry 1)

IR (KBr): 707, 770, 1011, 1279, 1322, 1480, 1528, 1594, 3258, 3419 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 5.62$ (br, s, 2H), 7.15–7.45 (m, 4H), 7.75 (d, 2H). Mass (EI): $m/z = 224$. Anal. Calcd. for $C_9H_8N_2Se$: C, 48.44, H, 3.61; N, 12.55. Found: C, 48.37; H, 3.72; N, 12.66.

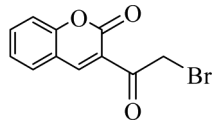
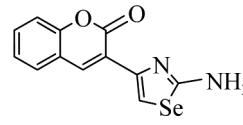
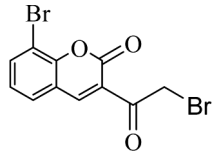
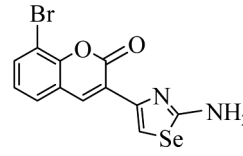
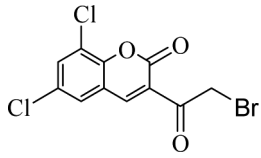
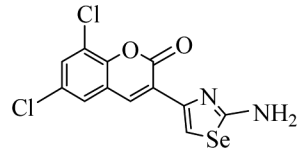
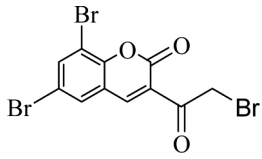
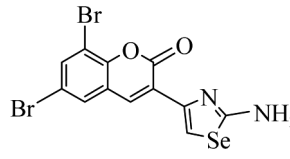
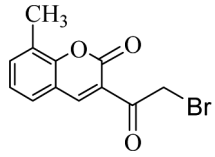
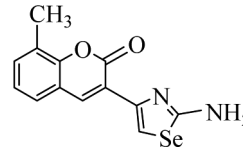
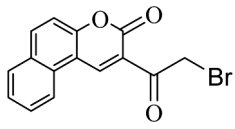
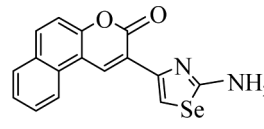
4-*p*-Tolyl-1,3-selenazol-2-amine (Table 3, Entry 2)

IR (KBr): 723, 826, 1021, 1181, 1285, 1326, 1528, 1633, 2929, 3119, 3385 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 2.35$ (s, 3H), 5.68 (br, s, 2H), 7.10–7.25 (m, 3H), 7.65 (d, 2H). Mass (EI): $m/z = 237$. Anal. Calcd. for $C_{10}H_{10}N_2Se$: C, 50.64; H, 4.25; N, 11.81. Found: C, 50.52 H, 4.20; N, 11.91.

4-(4-Chlorophenyl)-1,3-selenazol-2-amine (Table 3, Entry 3)

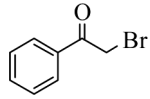
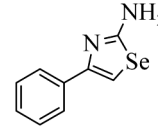
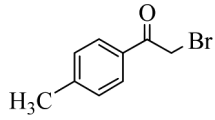
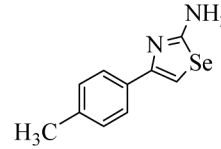
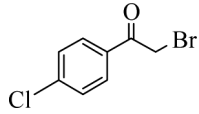
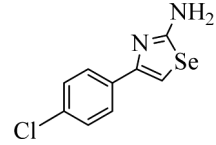
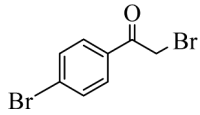
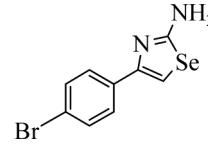
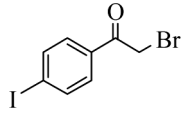
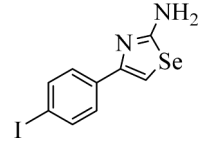
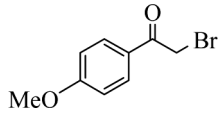
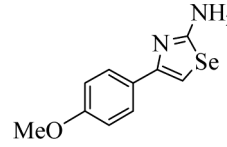
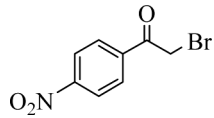
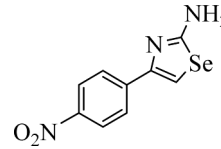
IR (KBr): 683, 725, 831, 1022, 1085, 1187, 1329, 1393, 1475, 1542, 1637, 2921, 3145, 3295, 3451 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 5.27$ (br, s, 2H), 7.28 (s, 1H), 7.33–7.45 (d, 2H), 7.60–7.72 (d, 2H). Mass

Table 2. Synthesis of 3-(2-amino-1,3-selenazol-4-yl)-2H-chromen-2-ones by the solid-state method

Entry	3-Bromo acetyl coumarin	Product[a]	Time (min)	Yield (%)[b]	Mp (°C)
1			25	96	280
2			20	95	172
3			25	92	98
4			23	96	140
5			25	90	166
6			30	87	190

[a]All the products were confirmed by ^{1}H NMR, IR, and mass spectral data.
[b]Isolated yields after purification.

Table 3. Synthesis of 4-pheny1-1,3-selenazol-2-amines by the solid-state method

Entry	Bromo acetyl benzene	Product[a]	Time (min)	Yield (%)[b]	Mp (°C)
1			20	95	132[11]
2			18	95	166[11]
3			20	92	155[11]
4			18	94	132[11]
5			20	92	188[11]
6			20	95	173[11]
7			20	96	250[11]

[a]All the products were confirmed by ^{1}H NMR, IR, and mass spectral data and compared with those of authentic samples.

(EI): $m/z = 258$. Anal. Calcd. for $C_9H_7ClN_2Se$: C, 41.97; H, 2.74; N, 10.88. Found: C, 41.89; H, 2.60; N, 10.80.

4-(4-Bromophenyl)-1,3-Selenazol-2-Amine (Table 3, Entry 4)

IR (KBr): 652, 691, 725, 822, 1010, 1025, 1181, 1322, 1397, 1478, 1541, 1635, 3128, 3287, 3440 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 5.29$ (br, s, 2H), 7.23 (s, 1H), 7.42–7.51 (d, 2H), 7.63–7.72 (d, 2H). Mass (EI): $m/z = 303$, Anal. Calcd. for $C_9H_7BrN_2Se$: C, 35.79; H, 2.34; N, 9.28. Found: C, 35.87; H, 2.25; N, 9.15.

4-(4-Iodophenyl)-1,3-selenazol-2-amine (Table 3, Entry 5)

IR (KBr): 650, 685, 729, 831, 1009, 1015, 1181, 1315, 1392, 1468, 1531, 1635, 3118, 3283, 3429 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 5.37$ (br, s, 2H), 7.23 (s, 1H), 7.46–7.57 (d, 2H), 7.62–7.71 (d, 2H), Mass (EI): $m/z = 349$. Anal. calcd. for $C_9H_7IN_2Se$: C, 30.97; H, 2.02; N, 8.03. Found: C, 30.91; H, 2.09; N, 7.92.

4-(4-Methoxyphenyl)-1,3-Selenazol-2-Amine (Table 3, Entry 6)

IR (KBr): 720, 817, 1023, 1050, 1191, 1327, 1540, 1655, 3361 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 3.82$ (s, 3H), 5.61 (br, s, 2H), 6.82–7.04 (m, 3H), 7.20–7.32 (d, 2H), Mass (EI): $m/z = 253$, Anal. calcd. for $C_{10}H_{10}N_2OSe$: C, 47.44; H, 3.98; N, 11.07. Found: C, 47.52; H, 3.91; N, 11.03.

4-(4-Nitrophenyl)-1,3-Selenazol-2-Amine (Table 3, Entry 7)

IR (KBr): 707, 845, 1015, 1107, 1325, 1467, 1498, 1540, 1592, 1637, 1735, 2851, 2926, 3392 cm^{-1}. ^1H NMR (DMSO-d_6, 200 MHz): $\delta = 5.25$ (br, s, 2H), 7.25 (s, 1H), 7.42–7.53 (d, 2H), 7.63–7.72 (d, 2H). Mass (EI): $m/z = 268$. Anal. calcd. for $C_9H_7N_3O_2Se$: C, 40.31. H, 2.63; N, 15.67. Found: C, 40.25; H, 2.72. N, 15.59.

3-(2-Amino-1,3-Selenazol-4-yl)-2H-Chromen-2-One (Table 2, Entry 1)

IR (KBr): 782, 1172, 1693, 1737, 3385 cm^{-1}. ^1H NMR (DMSO-d_6, 200 MHz): $\delta = 5.37$ (br, s, 2H), 7.20–7.85 (m, 4H), 8.17 (s, 1H), 8.65 (s, 1H). Mass (EI): $m/z = 292$ (M^+). Anal. calcd. for $C_{12}H_8N_2O_2Se$: C, 49.50; H, 2.77; N, 9.62. Found: C, 49.41; H, 2.72; N, 9.68.

3-(2-Amino-1,3-Selenazol-4-yl)-8-Bromo-2H-Chromen-2-One (Table 2, Entry 2)

IR (KBr): 787, 1185, 1675, 1719, 3375 cm^{-1}. ^1H NMR (DMSO-d_6, 200 MHz): $\delta = 5.45$ (br, s, 2H), 7.31–7.87 (m, 3H), 8.25 (s, 1H), 8.71 (s, 1H). Mass (EI): $m/z = 370$ (M^+). Anal. calcd. for $C_{12}H_7BrN_2O_2Se$: C, 38.95; H, 1.91; N, 7.57. Found: C, 38.81; H, 1.85; N, 7.62.

3-(2-Amino-1,3-Selenazol-4-yl)-6,8-Dichloro-2H-Chromen-2-One (Table 2, Entry 3)

IR (KBr): 775, 1165, 1690, 1740, 3392 cm^{-1}. ^1H NMR (DMSO-d_6, 200 MHz): $\delta = 5.25$ (br, s, 2H), 7.35–7.85 (m, 2H), 8.10 (s, 1H), 8.55 (s, 1H). Mass (EI): $m/z = 360$ (M^+), Anal. calcd. for $C_{12}H_6Cl_2N_2O_2Se$: C, 40.03; H, 1.68; N, 7.78. Found: C, 40.09; H, 1.61; N, 7.75.

3-(2-Amino-1,3-Selenazol-4-yl)-6,8-Dibromo-2H-Chromen-2-One (Table 2, Entry 4)

IR (KBr): 775, 1165, 1690, 1740, 415 cm^{-1}. ^1H NMR (DMSO-d_6, 200 MHz): $\delta = 5.32$ (br, s, 2H), 7.21–7.79 (m, 2H), 8.31 (d, 1H), 8.77 (s, 1H). Mass (EI): $m/z = 449$ (M^+), Anal. calcd. for $C_{12}H_6Br_2N_2O_2Se$: C, 32.10; H, 1.35; N, 6.24. Found: C, 32.17; H, 1.31; N, 6.29.

3-(2-Amino-1,3-Selenazol-4-yl)-8-Methyl-2H-Chromen-2-One (Table 2, Entry 5)

IR (KBr): 761, 1181, 1680, 1733, 3399 cm^{-1}. ^1H NMR (DMSO-d_6, 200 MHz): $\delta = 2.38$ (s, 3H), 5.45 (br, s, 2H), 7.15–7.65 (m, 3H), 8.25 (s, 1H), 8.51 (s, 1H). Mass (EI): $m/z = 305$ (M^+); Anal. calcd. for $C_{13}H_{10}N_2O_2Se$: C, 51.16; H, 3.30; N, 9.18. Found: C, 51.19; H, 3.35; N, 9.13.

2-(2-Amino-1,3-Selenazol-4-yl)-3H-Benzo[f]chromen-3-One (Table 2, Entry 6)

IR (KBr): 755, 1182, 1685, 1721, 3373 cm^{-1}. ^1H NMR (DMSO-d_6, 200 MHz): $\delta = 5.41$ (br, s, 2H), 6.92–7.45(m, 3H), 7.57 (d, 2H), 8.06 (d, 2H), 8.59(s, 1H). Mass (EI): $m/z = 341$ (M^+), Anal. Calcd. for $C_{16}H_{10}N_2O_2Se$: C, 56.32; H, 2.95; N, 8.21. Found: C, 56.38; H, 2.81; N, 8.24.

CONCLUSIONS

In conclusion, we have developed an efficient method for the synthesis of 1,3-selenazoles in good yields with high purity by a solid-state reaction. The notable factors of this reaction are an extremely simple experimental procedure, mild reaction conditions, environmentally friendly synthesis with no product wastes or toxic solvents, and a reusable catalyst.

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