An efficient synthesis of 1,3-dialkylimidazole-2-selenones

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An efficient method for the synthesis of 1,3-dialkylimidazole-2-selenones involves the reaction of 1,3-dialkylimidazole salts with selenium in the presence of potassium carbonate in ethanol or acetone under refluxing conditions to afford the products in good to excellent yields.

Keywords: 1,3-dialkylimidazole salts, 1,3-dialkylimidazole-2-selenones, selenium, potassium carbonate, ethanol, acetone

1,3-Dialkylimidazole-2-selenones are chalcogen derivatives of N-heterocyclic carbenes, and are useful precursors for the synthesis of various N, Se-containing heterocycles.[1,2] 1,3-dialkylimidazole-2-selenones have been synthesised by reacting the corresponding iodide and bromide salts with selenium powder in methanol in the presence of potassium carbonate.[3–6] 1,3-Dialkylimidazole salts react with selenium in the presence of strong bases such as KH and NaH to give the corresponding 1,3-dialkylimidazole-2-selenones.[7] In addition, 1,3-dialkylimidazole salts also react with Na_2Se_2 at room temperature in dry THF using potassium tert-butoxide as a base to afford the target products.[8,9] Both Roy[10] and Guziec[11] reported that treatment of imidazole with BuLi and selenium powder also gave 1,3-dialkylimidazole-2-selenones under Schlenk conditions. However, most of the known methods for the preparation of imidazole-2-selenones suffer from disadvantages such as use of strong bases and harsh reaction conditions, long reaction time, low yields or complicated work-up.

Results and discussion

In the course of our ongoing studies on selenium-containing compounds,[12–15] we found that 1,3-dialkylimidazole-2-selenones catalysed the carbonylation of organic amines and ethanolamine using carbon monoxide as a reagent to give ureas and 2-oxazolidinone[16] We then investigated the reactions of 1,3-disubstituted imidazole salts with selenium in the presence of K_2CO_3 under refluxing conditions and found that these reactions led to 1,3-dialkylimidazole-2-selenones easily in ethanol or acetone. We now report an efficient synthesis of 1,3-dialkylimidazole-2-selenones (Scheme 1).

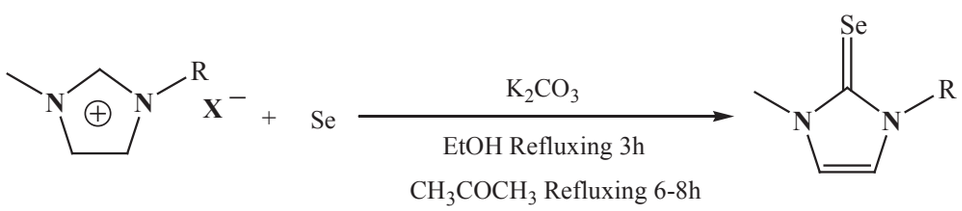
1-Butyl-3-methylimidazolidine chloride (**1a**) was treated with equivalent selenium in the presence of two equivalents of potassium carbonate in ethanol or acetone under reflux to give 1-butyl-3-methylimidazole-2-selenone (**1b**) conveniently (entries 1 and 2 in Table 1). We also investigated the effect of different bases in acetone under similar conditions and found K_2CO_3 is the best reagent for this reaction (entries 2–4 in Table 1). In addition, when two equivalents of potassium carbonate were used, the reaction yield was the highest (entries 2, 4 and 5 in Table 1). When DMF and CH_3OH were used as the solvents, although the reaction could occur in 97% and 94% yields (entries 7 and 8 in Table 1), their products could not be separated easily and gave off an unpleasant smell. The reaction proceeded to some extent in THF and toluene (entries 9 and 10 in Table 1).

The reactions of other 1,3-dialkylimidazolium salts were also investigated and the results are summarised in Table 2. From Table 2 we can see that 1,3-dialkylimidazolium chlorides, bromides and tetrafluoroborates react with selenium easily to produce 1,3-dialkylimidazole-2-selenones in high yields (89–97%) in ethanol or acetone (entries 1–8 in Table 2). The effect of steric hindrance on the 3-position of the imidazole rings did not significantly influence the yields of the products (entries 1–5 in Table 2). When 1,3-dialkylimidazolium iodide salts were used as the substrate, the yields of the selenation reactions were higher in ethanol than in acetone (entries 9 and 10 in Table 2).

Table 1 Effect of different bases to the reaction in different conditions

Entry[a]	Solvent	Base	Amount of base/mmol	Yield/%[b]
1	EtOH	K_2CO_3	10	96[c]
2	Acetone	K_2CO_3	10	97
3	Acetone	Et_3N	10	9
4	Acetone	NaOAc	10	38
5	Acetone	K_2CO_3	5	88
6	Acetone	K_2CO_3	20	69
7	DMF	K_2CO_3	10	97
8	CH_3OH	K_2CO_3	10	94[c]
9	THF	K_2CO_3	10	78
10	Toluene	K_2CO_3	10	48

[a]Reaction conditions: 1-butyl-3-methylimidazolidine chloride 5 mmol; Se, 5 mmol; solvent, 5 mL; base 10 mmol; refluxing, 6 h.
[b]Isolated yields.
[c]Refluxing, 3 h.



Scheme 1

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Table 2 Synthesis of 1,3-dialkylimidazole-2-selenones in ethanol or acetone

Entry[a]	R	X	Cmpd	Yield/%[b]	
				Ethanol[c]	Acetone[d]
1[16]	n-Butyl	Cl	**1b**	96	97
2[16]	n-Butyl	BF_4	**1b**	94	90
3[9]	n-Propyl	Br	**2b**	95	96
4[9]	Ethyl	Br	**3b**	91	94
5[16]	n-Hexadecyl	Br	**4b**	97	89
6	2-Bromobenzyl	Br	**5b**	94	96
7	3-Chlorobenzyl	Cl	**6b**	97	94
8[9]	Iso-propyl	Br	**7b**	88	90
9[16]	n-Butyl	I	**1b**	92[e]	37
10[9]	Methyl	I	**8b**	89[e]	33

[a]Reaction conditions: 1,3-dialkylimidazolium salts, 5 mmol; Se, 5 mmol; solvent: ethanol or acetone, 5 mL; K_2CO_3, 10 mmol.
[b]Isolated yields.
Refluxing time [c]3 h; [d]6–8 h; [e]6 h.

A possible mechanism for the reaction is shown in Fig. 1 based on that proposed for the reaction of 1,3-dialkylimidazolium salts and Se.[3–6] The formation of 1-butyl-3-methylimidazole-2-selenone (**1b**) may involve two-steps (see Fig. 1): (1) deprotonation of 1-butyl-3-methylimidazolidine chloride salt **1a** by K_2CO_3 to give the N-heterocyclic carbene intermediate **C** and (2) reaction of intermediate **C** with selenium to produce 1-butyl-3-methylimidazole-2-selenone **1b**.

In summary, we have developed an efficient synthetic method for 1,3-dialkylimidazole-2-selenones from 1,3-dialkylimidazolium salts and selenium in the presence of K_2CO_3 in ethanol or acetone. Further studies regarding the mechanism for the synthesis of 1,3-dialkylimidazole-2-selenones are underway.

Experimental

All melting points were recorded on a WRS-1A melting-point apparatus and are uncorrected. All 1H NMR spectra were recorded on a 400 MHz Bruker AZ 400 spectrometer. Chemical shifts are given as δ value with reference to tetramethylsilane (TMS) as internal standard. Carbon monoxide (99.9%) was dried by Zeolite 5A. Elemental selenium (99.5%) and the reagents were obtained from commercial suppliers without purification prior to use. All operations should be carried out in an efficient fume hood.

Synthesis of 1,3-dialkylimidazole-2-selenones; typical procedure

1-Butyl-3-methylimidazolidine, chloride salt (5 mmol), selenium (5 mmol), potassium carbonate (10 mmol), ethanol or acetone (5 mL) and a magnetic stirring bar were placed in a 50 mL, two-necked flask. Then the reaction mixture was vigorously stirred under reflux for the given times (see Table 2). After the reaction was complete, the resultant mixture was filtered, and the solvent evaporated under reduced pressure. Further purification by column chromatography on silica gel gave the pure product. All the products were characterised by NMR and HRMS.

1-Butyl-3-methyl-1H-imidazole-2(3H)-selenone (**1b**):[16] Yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (t, J = 8 Hz, 3H, CH_3), 1.34–1.44 (m, 2H, CH_2), 1.75–1.86 (m, 2H, CH_2), 3.71 (s, 3H, N–CH_3), 4.13 (t, J = 7.6 Hz, 2H, N–CH_2), 6.88 (br, 1H, J = 2 Hz, CH), 6.90 (br, J = 2 Hz, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.65, 19.70, 29.24, 31.14, 37.05, 49.70, 118.78, 119.92, 154.61 (C=Se). HRMS for $C_8H_{14}N_2Se$: (*m/z*) calcd: 218.0322; found: 218.0317 $[M]^+$.

3-Methyl-1-propyl-1H-imidazole-2(3H)-selenone (**2b**):[9] Yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, J = 8.4 Hz, 3H, CH_3), 1.83 (m, 2H, CH_2), 3.71 (s, 3H, N–CH_3), 4.10 (t, J = 7.2 Hz, 2H, N–CH_2), 6.91 (br, J = 2.4 Hz, 2H, CH), 6.93 (br, J = 2 Hz, 2H, CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.61, 21.99, 36.63, 51.03, 118.39, 119.39, 154.52 (C=Se). HRMS for $C_7H_{12}N_2Se$: (*m/z*) calcd: 204.0166; found: 204.0172 $[M]^+$.

1-Ethyl-3-methyl-1H-imidazole-2(3H)-selenone (**3b**):[9] Yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40 (t, J = 5.6 Hz, 3H, CH_3), 3.71 (s, 3H, N–CH_3), 4.18 (q, J = 7.2 Hz, 2H, N–CH_2), 6.92 (m, 2H, CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.08, 36.58, 44.51, 117.56, 119.62, 154.20 (C=Se). HRMS for $C_6H_{10}N_2Se$: (*m/z*) calcd: 190.0009; found: 190.0000 $[M]^+$.

1-Hexadecyl-3-methyl-1H-imidazole-2(3H)-selenone (**4b**):[16] M.p. 71–72 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 7.2 Hz, 3H, CH_3), 1.25–1.34 (m, 28H, CH_2), 1.80 (m, 2H, CH_2), 3.71 (s, 3H, N–CH_3), 4.11 (t, J = 7.6 Hz, 2H, N–CH_2), 5.93 (s, 1H, CH), 5.98 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.32, 22.89, 26.75, 29.40, 29.56, 29.68, 29.76, 29.88, 32.13, 37.38, 50.36, 119.23, 120.43, 155.67 (C=Se). HRMS for $C_{20}H_{38}N_2Se$: (*m/z*) calcd: 386.2200; found: 386.2201 $[M]^+$.

1-(2-Bromobenzyl)-3-methyl-1H-imidazole-2(3H)-selenone (**5b**): M.p. 110–112 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.73 (s, 3H, N–CH_3), 5.46 (s, 2H, N–CH_2), 6.82 (br, J = 2.4 Hz, 1H, CH), 6.90 (br, J = 2.4 Hz, 1H, CH), 7.19 (m, 2H, 2 × ArH), 7.27 (d, J = 4.4 Hz, 2H, 2 × ArH), 7.58 (d, J = 7.6 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.09, 22.51, 26.53, 29.13, 29.68, 30.96, 31.75, 37.05, 49.98, 118.64, 119.71, 155.33 (C=Se). HRMS for $C_{11}H_{11}N_2BrSe$: (*m/z*) calcd: 329.9271; found: 329.9279 $[M]^+$.

1-(3-Chlorobenzyl)-3-methyl-1H-imidazole-2(3H)-selenone (**6b**): M.p. 97–98 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.70 (s, 3H, N–CH_3), 5.34 (s, 2H, N–CH_2), 6.66 (s, 1H, CH), 6.96 (s, 1H, CH), 7.22–7.27 (m, 3H, 3 × ArH), 7.30 (s, 1H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.77, 37.11, 52.15, 118.43, 120.40, 126.15, 127.85, 128.14, 129.97, 134.29, 137.44, 156.26 (C=Se). HRMS for $C_{11}H_{11}N_2ClSe$: (*m/z*) calcd: 285.9776; found: 285.9753 $[M]^+$.

1-Isopropyl-3-methyl-1H-imidazole-2(3H)-selenone (**7b**):[9] M.p. 109–110 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40 (d, J = 8 Hz, 6H, 2 × CH_3), 3.72 (s, 3H, N–CH_3), 5.20 (m, 1H, N–CH), 6.93 (m, 2H, 2 × CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.52, 30.54, 36.40, 50.39, 114.53, 119.93, 153.35 (C=Se). HRMS for $C_7H_{12}N_2Se$: (*m/z*) calcd: 204.166; found: 204.0169 $[M]^+$.

1,3-Dimethyl-1H-imidazole-2(3H)-selenone (**8b**):[9] M.p. 201–202 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.70 (6H, 2 × CH_3), 6.99 (m, 2H, 2 × CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.21, 119.68, 155.90 (C=Se). HRMS for $C_5H_8N_2Se$: (*m/z*) calcd: 175.9853; found: 175.9853 $[M]^+$.

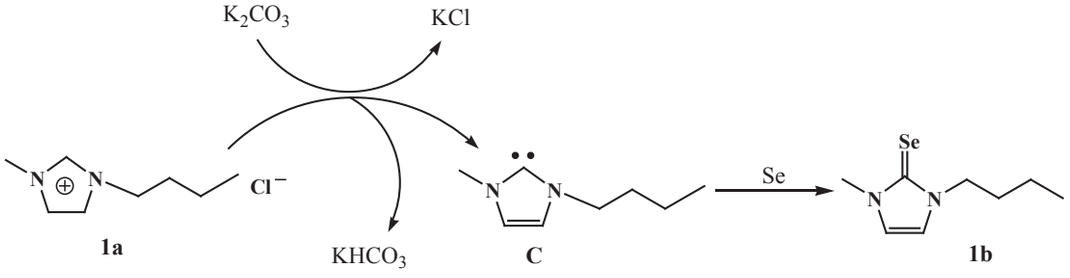

Fig. 1 Proposed pathway to 1,3-dialkylimidazole-2-selenone (**1b**).

We are grateful to the Natural Science Foundation of Henan Province (Project No. 142102310365) and the Natural Science Foundation of Education Department of Henan Province (No.14A150015) and the Doctor Start-up Foundation of Zhoukou Normal University (No. zksybscx201204) for financial support.

Received 1 April 2014; accepted 25 April 2014
Paper 1402564 doi: 10.3184/174751914X14007821182269
Published online: 10 June 2014

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