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Convenient Syntheses of N,N-Dialkylselenoamides and N,N,N',N'-Tetraalkylselenoureas by Treating Terminal *gem*-Dihaloalkanes, Chloroform, or Sodium Trichloroacetate with a Base, Elemental Selenium, and Amines

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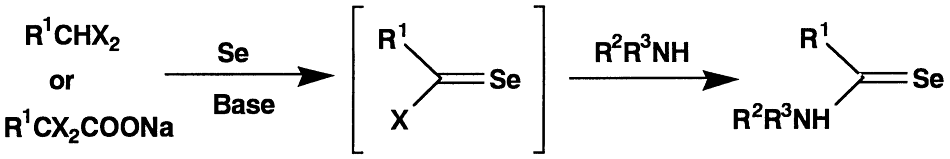
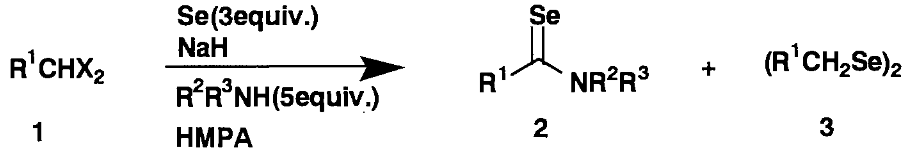
Treatment of terminal *gem*-dihaloalkanes, chloroform, or sodium trichloroacetate with elemental selenium in the presence of NaH and an excess amount of primary or secondary amines gave selenoamides and selenoureas in modest yields.

To date, several methods for the preparation of selenoamides and selenoureas including the treatment of amides and ureas, respectively, with various selenating reagents possessing reactive metal-selenium bonds have been reported.[1-4] However, the synthesis of such selenocarbonyl compounds has often been impeded by the difficulty of the preparation and the treatment of the reagents, and the recent interests in the selenating reagents have been concentrated to elemental selenium itself.[5,6] It was expected that elemental selenium would react with α,α-dihalocarbanions or α-halocarbenes to afford the reactive selenocarbonyl compounds like selenoacyl halides as was the case of the reactions of carbanions or carbenes with elemental selenium.[7-9] In this paper, we wish to describe the novel use of elemental selenium for the convenient syntheses of selenoamides and selenoureas under the reaction conditions conventionally used for the generation of halo- and dihalocarbenes.[10,11]



A procedure for the conversion of terminal *gem*-dihaloalkanes **1**, $CHCl_3$, or sodium trichloroacetate to selenoamides **2** and selenoureas **4** is described below. To a HMPA solution of the substrate was added NaH, amine, and selenium powder, and the reaction mixture was heated for a few hours under an Ar atmosphere. After the usual workup, the products were separated by SiO_2 column chromatography. The treatment with *gem*-dihaloalkanes **1** in such a manner gave **2** and diselenides **3**. On the other hand, the treatment with $CHCl_3$ or sodium trichloroacetate gave selenoureas **4** at a higher reaction temperature and bis(N,N-dialkylselenocarbamoyl) triselenides **6**[12-14] at a lower temperature, respectively. By the reaction from sodium trichloroacetate, N,N,N',N'-tetraalkylureas **5**[15] were also formed in addition to **2** and **6**. The structures of the products were confirmed by identification with those of the reported physical data,[16-18] and the elemental analysis data.[19,20] Table 1 and 2 show the results of the reactions.

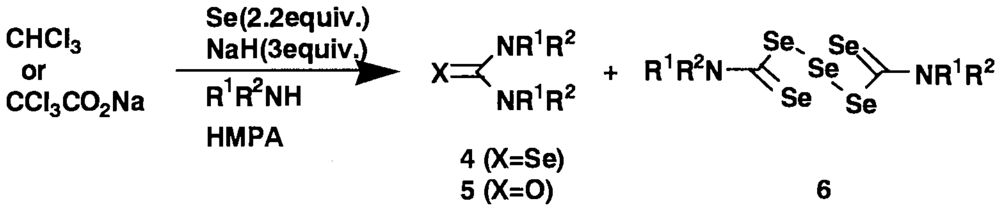
Table 1. Preparation of selenoamides **2**



Substrate		NaH	Amine		Temp	Time	Product	Yield /% a)	
R^1	X	/ equiv.	R^2	R^3	/°C	/h		**2**	**3**
H	Cl	3	Et	Et	120	4	**2a**	40	- b)
H	Br	3	Et	Et	130	3	**2a**	47	- b)
H	I	3	Et	Et	120	3	**2a**	48	- b)
C_6H_5	Cl	4	Et	Et	120	3	**2b**	41	10
C_6H_5	Cl	3	Bu	H	120	3	**2c**	10	- b)
C_6H_5	Cl	3	$-(CH_2)_5-$		130	6	**2d**	30	- b)
p-$NO_2C_6H_4$	Cl	3	Et	Et	120	1	**2e**	31	- b)
p-$CH_3C_6H_4$	Cl	3	Et	Et	130	4	**2f**	12	- b)
C_6H_5CO	Cl	4	Et	Et	r.t.	5	**2g**	80	- b)
CO_2Et	Cl	4	Et	Et	r.t.	4	**2h**	35	- b)

a) Isolated yields. b) Not determined.

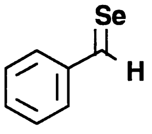
Table 2. Preparation of N,N,N',N'-tetraalkylselenoureas **4**



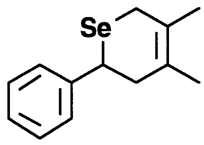
Substrate	Secondary Amine			Temp	Time	Yield /% a)		
	R^1	R^2	equiv.	/°C	/h	**4**	**5**	**6**
CCl_3CO_2Na	Et	Et	10	130	23	65	23	0
CCl_3CO_2Na	Et	Et	2.2	80	0.5	12	trace	34
CCl_3CO_2Na b)	Et	Et	5	r.t.	2	21	- c)	8
CCl_3CO_2Na	Bu	Bu	2.2	80	0.5	22	- c)	35
CCl_3CO_2Na	$-(CH_2)_5-$		2.2	100	1	43	- c)	0
$CHCl_3$ d)	Et	Et	5	130	3	37	0	0
$CHCl_3$	Et	Et	5	r.t.	4	5	0	46

a) Isolated yields. b) The reaction was carried out under ultrasonic irradiation. c) Not determined. d) N,N,-Diethylselenoformamide **2a** was obtained in 13% yield besides **4a**(R^1=R^2=Et).

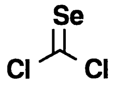
When the reaction of benzal chloride was carried out in the presence of an excess amount of 2,3-dimehtyl-1,3-butadiene, selenapyran derivative **B** was obtained in place of dibenzyl diselenide **3**. This fact clearly showed that the diselenide **3** was formed by the reduction of selenobenzaldehyde **A** that was transiently generated by the nucleophilic attack of the selenide anion species to benzal chloride.



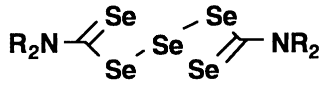
A



B



C



6

Interestingly, the reactions of $CHCl_3$ or sodium trichloroacetate carried out at 80 °C or under ultrasonic irradiation at room temperature afforded triselenides **6** in modest yields, in addition to selenoureas **4**. Furthermore, **6** was treated with amines at 130 °C to give the corresponding selenoureas **4** according to the report of Henriksen.16) These results strongly suggested that triselenides **6** were formed in the first stage of the reaction of some reactive precursors like selenophosgene **C** with the selenide species generated by the reaction of amines with elemental selenium. The formation of N,N-diethyl-selenoformamide (**2a**) by the reaction with $CHCl_3$ in the presene of Et_2NH at higher temperature also suggested the generation of the selenide anion species in the reaction mixture.21) However, the reaction of sodium trichloroacetate with NaH and elemental selenium in the presence of tertiary amines (DBU or Et_3N) in place of secondary amines afforded a trace amount of an unidentified product.

gem-Dihaloalkanes **1** are known to generate α-halocarbenes by the treatment with bases.11) However, in our experiments some doubts arose concerning the mechanisms including the generation of α-halocarbene species because no selenoamides **2** were obtained by the thermal decomposition of 3-chloro-3-phenyldiazirine22) in the presence of elemental selenium and secondary amines. Thus, alternative reaction mechanisms including the nucleophilic attack of α-halocarbanions to selenium and the subsequent conversion of the resulting selenide anion species to selenoacyl halides are postulated in these cases.9)

In conclusion, this work has shown a convenient synthesis of selenoamides and selenoureas by using elemental selenium as the easily treatable selenating reagent. Studies on the mechanisms of these reactions are in progress in our laboratory.

References

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14) Physical data of **6**. **6a**(R^1=R^2=Et): Red needles, mp 135 °C (lit.[13] 136-137 °C). **6b**(R^1=R^2=i-Pr): Red prisms, mp 160-163 °C (lit.[12] 165-167 °C). **6c**(R^1=R^2=Bu): Red needles, mp 37-39 °C (lit.[13] 39-40 °C).

15) N,N,N',N'-Tetraalkylureas **5** were formed by the reaction of amines with CO_2 generated by the decarboxylation of trichloroacetate.

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19) Physical data of **2**. **2a**(R^1=H, R^2=R^3=Et): Pale yellow oil; MS(*m/z*) 165(M^+, bp, ^{80}Se); IR(neat) 2976, 1516 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 1.30(t, J=7.6 Hz, 3H), 1.32(t, J=7.6 Hz, 3H), 3.56(q, J=7.6 Hz, 2H), 3.95(q, J=7.6 Hz, 2H), 10.64(s, 1H). Found: C, 36.41; H, 6.91; N, 8.37%. Calcd for $C_5H_{11}NSe$: C, 36.59; H, 6.76; N, 8.54%. **2b**(R^1=C_6H_5, R^2=R^3=Et): Yellow needles, mp 56.5-57.5 °C(lit.[18] 53.5-54.5 °C). **2c**(R^1=Ph, R^2=Bu, R^3=H): Yellow oil; MS(*m/z*) 241(M^+, bp, ^{80}Se); IR(neat) 3205, 2958, 1531 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 0.95-1.90(m, 7H), 3.76(dt, J=7, 6 Hz, 2H), 7.27-7.74(m, 5H), 8.00-8.26(m, 1H). Found: C, 55.10; H, 6.58; N, 5.73%. Calcd for $C_{11}H_{15}NSe$: C, 55.00; H, 6.29; N, 5.83%. **2d**(R^1=Ph, R^2=R^3=-$CH_2)_5$-): Red prisms, mp 88-89 °C (lit.[17] 89-89.5 °C). **2e**(R^1=4-$NO_2C_6H_4$, R^2=R^3=Et): Orange prisms, mp 143-144 °C; MS(*m/z*) 286(M^+, bp, ^{80}Se); IR(KBr) 2976, 1589, 1519, 1490, 1344, 852 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.19(t, J=7 Hz, 3H), 1.47(t, J=7 Hz, 3H), 3.45(q, J=7 Hz, 2H), 4.26(q, J=7 Hz, 2H), 7.36(d, J=8 Hz, 2H), 8.25(d, J=8 Hz, 2H). Found: C, 46.28; H, 4.80; N, 9.72%. Calcd for $C_{11}H_{14}N_2O_2Se$: C, 46.33; H, 4.95; N, 9.82%. **2f**(R^1=4-$CH_3C_6H_4$, R^2=R^3=Et): Yellow prisms, mp 97-97.5 °C; MS(*m/z*) 255(M^+, 69%, ^{80}Se); IR(KBr) 2977, 1514, 1358, 810 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 1.15(t, J=7 Hz, 3H), 1.44(t, J=7 Hz, 3H), 2.33(s, 3H), 3.46(q, J=7 Hz, 2H), 4.25(q, J=7 Hz, 2H), 7.13(br. s, 4H). Found: C, 56.62; H, 6.77; N, 5.29%. Calcd for $C_{12}H_{17}NSe$: C, 56.69; H, 6.74; N, 5.51%. **2g**(R^1=C_6H_5CO), R^2=R^3=Et): Orange oil; MS(*m/z*) 269(M^+, 75%, ^{80}Se); IR(neat) 2979, 1660, 1596, 1580, 1519, 697 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 1.22(t, J=7 Hz, 3H), 1.46(t, J=7 Hz, 3H), 3.50(q, J=7 Hz, 2H), 4.17(q, J=7 Hz, 2H), 7.20-8.10(m, 5H). Found: C, 53.47; H, 5.63; N, 5.00%. Calcd for $C_{12}H_{15}NOSe$: C, 53.74; H, 5.64; N, 5.22%. **2h**(R^1=CO_2Et, R^2=R^3=Et): Brown oil; MS(*m/z*) 237(M^+, bp, ^{80}Se); IR(neat) 2981, 1725, 1519 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 1.36(t, J=7 Hz, 9H), 3.52(q, J=7 Hz, 2H), 4.01(q, J=7 Hz, 2H), 4.38(q, J=7 Hz, 2H). Found: C, 40.55; H, 6.45; N, 5.70%. Calcd for $C_8H_{15}NO_2Se$: C, 40.69; H, 6.40; N, 5.93%.

20) Physical data of **4**. **4a**(X=Se, R^1=R^2=Et): Yellow oil; MS(*m/z*) 236(M^+, bp, ^{80}Se); IR(neat) 2900, 1630, 1420, 1240, 1108 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 1.20(t, J=6.5 Hz, 12H), 3.60(q, J=6.5 Hz, 8H). Found: C, 45.88; H, 8.87; N, 11.84%. Calcd for $C_9H_{20}N_2Se$: C, 45.95; H, 8.57; N, 11.91%. **4b**(X=Se, R^1=R^2= Bu): Orange oil; MS(*m/z*) 348(M^+, 54%, ^{80}Se); IR(neat) 2958, 2872, 1465, 1204, 1106, 741 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 0.80-1.80(m, 28H), 3.84(t, J=7.5 Hz, 8H). Found: C, 57.33; H, 10.85; N, 8.10%. Calcd for $C_{16}H_{36}N_2Se$: C, 57.29; H, 10.82; N, 8.35%. **4c**(X=Se, R^1=R^2=-$(CH_2)_5$-): Colorless plates, mp 78-79 °C (lit.[16] 79-80 °C).

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