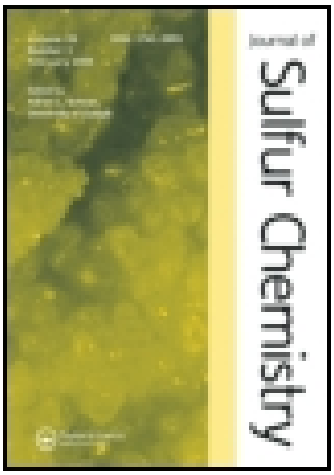

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Synthesis of E,E-bis(chloromethylidene) derivatives of N-organylthiomorpholines and -selenomorpholines and their quaternary salts

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Synthesis of *E*,*E*-bis(chloromethylidene) derivatives of *N*-organylthiomorpholines and -selenomorpholines and their quaternary salts

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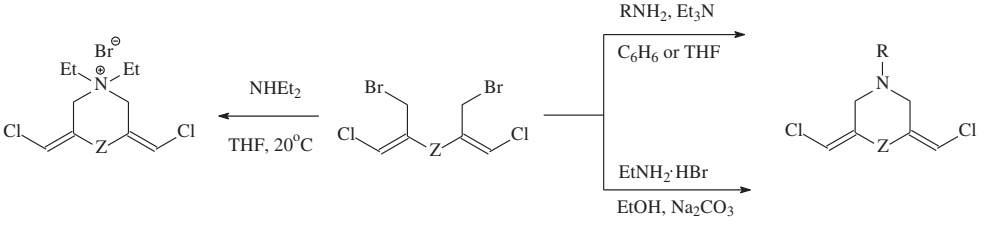
An efficient method for preparation of hitherto unknown *E*,*E*-bis(chloromethylidene) derivatives of *N*-organylthiomorpholines and -selenomorpholines by the reaction of *E*,*E*-bis(3-bromo-1-chloro-1-propen-2-yl) sulfide and selenide with primary amines in benzene or THF as well as with ethylammonium bromide in ethanol in the presence of Na_2CO_3 has been described. Heterocylization of the above sulfide and selenide by reaction with diethylamine in THF affords the unknown *E*,*E*-bis(chloromethylidene) derivatives of heterocyclic quaternary salts-4,4-diethyl-1,4-thiazinan-4-onium and -1,4-selenazinan-4-onium bromides.



Z = S, Se
R = 4-$CH_3C_6H_4$, 4-$CH_3C(O)C_6H_4$, CH_2=$CHCH_2$, $HOCH_2CH_2CH_2$, CH_3CH_2

Keywords: *E*,*E*-bis(3-bromo-1-chloro-1-propen-2-yl) chalcogenides; amines; heterocyclization; *N*-organyl chalcogenomorpholines; 1,4-chalcogenazinan-4-onium bromides

1. Introduction

Recently, we have developed regio- and stereoselective method for high-yield synthesis of hitherto unknown *E*,*E*-bis(3-bromo-1-chloro-1-propen-2-yl) sulfide (**1**) and selenide (**2**) by *anti*-addition of sulfur dichloride or selenium dichloride to propargyl bromide against Markovnikov rule.[1,2] Heterocyclization of chalcogenides **1** and **2** by reaction with sodium sulfide or selenide and

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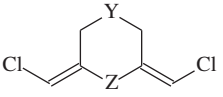


Z	S	S	Se	Se
Y	S	Se	S	Se

Figure 1. Structure of *E*,*E*-bis(chloromethylidene) derivatives of the 1,4-dithiane type heterocycles.

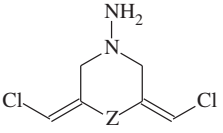


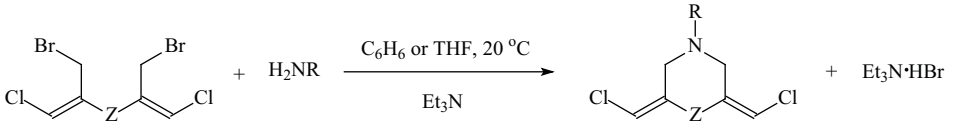
Figure 2. Structure of *E*,*E*-bis(chloromethylidene) derivatives of 4-thio- and 4-selenomorpholinamines.

hydrazine hydrate has led to hitherto unknown *E*,*E*-bis(chloromethylidene) derivatives of the 1,4-dithiane type heterocycles [2] (Figure 1), 4-thio- and 4-selenomorpholinamines [3] (Figure 2). However, bis(chloromethylidene) derivatives of *N*-substituted thio- and selenomorpholine as well as their quaternary salts are unknown. In the literature, there is only one work describing quaternary thiomorpholine salts, bearing the methylidene group in 3-position, which have been prepared by cyclization of $HC{\equiv}CCH_2SCH_2CH_2NRR_1$ ($R = R^1 = Me$, Et, $RR^1 = (CH_2)_5$, $CH_2CH_2OCH_2CH_2$) in H_2O at 80°C followed by neutralization of the product with HI.[4] At the same time *N*-substituted thio- and selenomorpholines as well as their derivatives possess a number of useful properties. Thus, *N*-substituted thiomorpholines, containing aromatic substituents with electron-withdrawing groups in its structure, show nonlinear optical properties.[5] Complexes of 4,4-dialkylthiomorpholinium derivatives and tetracyanoquinodimethane (1 : 2) have been thoroughly investigated as promising organic conductors.[6–10] *N*-Substituted selenomorpholines and their salts are found to inhibit the metabolism of *Escherichia coli* [11] and are more effective for the uptake of selenium by radish than sodium selenite.[12,13] Quaternary ammonium salts of thiomorpholine containing propargyl substituent at the nitrogen atom inhibit the growth of bacteria and fungi,[14] while similar salts with sulfanyl group at the nitrogen atom exert bactericide activity and are active against corrosion.[15] Quaternary thiomorpholinium salts of polyepihalohydrin could be used as flocculating agents, corrosion inhibitors and biocides.[16] So, our interest in the synthesis of novel chalcogenomorpholines such as bis(chloromethylidene) derivatives of *N*-substituted thio- and selenomorpholines capable of further transformation due to the presence of the exocyclic double bonds in their structure is justifiable.

2. Results and discussion

In order to synthesize novel nitrogen, chalcogen-containing heterocycles we have employed the heterocyclization reaction of *E*,*E-bis*(3-bromo-1-chloro-1-propen-2-yl) sulfide (**1**) and selenide (**2**) with primary and secondary amines. Both aliphatic, such as allylamine, 3-aminopropanol and ethylamine as a salt $EtNH_2 \cdot HBr$, and aromatic, such as *p*-toluidine and *p*-aminoacetophenone, have been used as primary amines. Heterocylizations with primary amines are found to easily

proceed at room temperature in benzene or THF and in several hours to afford *N*-R-2(*E*),6(*E*)-bis(chloromethylidene) thiomorpholines (**3a**–**d**) and -selenomorpholines (**4a**–**d**) in high yields (Scheme 1).

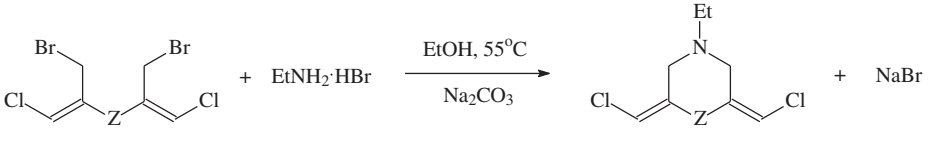


1,2 **3a-d, 4a-d**

N	Z	R	Yield, %
3a	S	4-$CH_3C_6H_4$	95
3b	S	(4-$CH_3C(O)C_6H_4$)	87
3c	S	$CH_2CH{=}CH_2$	97
3d	S	$CH_2CH_2CH_2OH$	95
4a	Se	4-$CH_3C_6H_4$	96
4b	Se	(4-$CH_3C(O)C_6H_4$)	62
4c	Se	$CH_2CH{=}CH_2$	95
4d	Se	$CH_2CH_2CH_2OH$	77

Scheme 1. Preparation of bis(*E*-chloromethylidene) derivatives of *N*-organylthiomorpholines and selenomorpholines by heterocyclization of *E*,*E*-bis(3-bromo-1-chloro-1-propen-2-yl) sulfide and selenide with primary amines.

In the case of ethylammonium bromide, heterocyclization is carried out in alcoholic medium by the generation of ethylamine *in situ* by reaction of Na_2CO_3 with the salt in ethanol (Scheme 2). This procedure also furnishes corresponding *N*-ethylchalcogenomorpholines **3e** and **4e** in up to 87% yields.



1,2 **3e** (87%), **4e** (85%)

Z = S (**1, 3e**), Se (**2, 4e**)

Scheme 2. Preparation of bis(*E*-chloromethylidene) derivatives of *N*-ethylthiomorpholines and -selenomorpholines by heterocyclization of *E*,*E*-bis(3-bromo-1-chloro-1-propen-2-yl) sulfide and selenide with the primary ethylammonium salt.

Structures of heterocyles **3** and **4** have been proved by the ^1H, ^{13}C NMR spectroscopy and mass spectrometry. In the ^1H NMR spectra, apart from the signals of the substituents at nitrogen atom, triplet signals of vinyl protons at 6.13–6.26 ppm range are present which are shifted up-field compared to the signals of bis(*E*-chloromethylidene) substituted thio- and selenomorpholin-4-amines (δ 6.38 and 6.38 ppm, correspondingly [3]), as well as doublet signals of methylene protons in δ 3.69–4.52 ppm range, which up-field or downfield shifts compared to the signals of

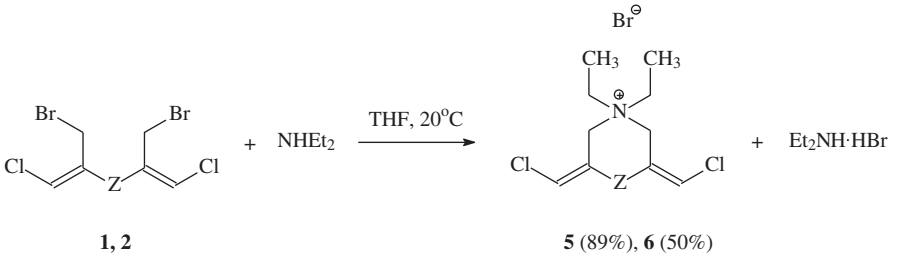
bis(*E*-chloromethylidene) substituted thio- and selenomorpholin-4-amines (δ 3.87 and 3.98 ppm, correspondingly [3]) are influenced to a great extent by the substituent at nitrogen atom. The ^{13}C NMR spectra of the heterocycles **3** and **4** are characterized by doublet–triplet signals of the carbon atoms of =CHCl group at δ 112.4–114.9 ppm, the same way as the proton signals shifted up-field compared to the signals of bis(*E*-chloromethylidene) substituted thio- and selenomorpholin-4-amines (δ 115.5 and 117.2 ppm, correspondingly [3]), as well as multiplet signals of carbon of the CH_2 group in the morpholine ring at δ 50.1–53.2 ppm, which manifest themselves in a stronger field compared to the signals of the CH_2 group of bis(*E*-chloromethylidene) substituted thio- and selenomorpholin-4-amines (δ 57.5 and 58.2 ppm, correspondingly [3]). *E*,*E*-Configuration of the heterocycles **3** and **4** follows from fine structures of the ^{13}C NMR spectra characterized by *trans*-vicinal spin-spin coupling constants between vinyl proton and carbon atom of the CH_2 group ($^3J_{CH}$ 6.6–7.0 Hz).[17] Their values coincide with the values of the constants for both the parent chalcogenides **1** and **2** ($^3J_{CH}$ 7–7.4 Hz [2]) and the 1,4-dithiane type heterocycles ($^3J_{CH}$ 6.7–7.3 Hz [2]) prepared by heterocyclization of the chalcogenides **1** and **2** by reaction with sodium sulfide and selenide. *E*,*E*-Configuration of the 1,4-dithane-type heterocycles was in turn unambiguously proved by the XRD.[2]

Mass spectra of the chalcogenomorpholines **3** and **4**, except for the propanolic derivatives **3d** and **4d**, are characterized by pronounced molecular ions. Further decomposition of these compounds under electron impact depends on substituent at nitrogen atom. In a case of *N*-allylmorpholines **3c** and **3c**, the main processes involve the splitting out of the CH = CH_2 fragment and chlorine atom, while for *N*-aryl-substituted morpholines **3a**, **3b**, **4a** and **4b**, mainly chlorine abstraction occurs. In a case of morpholines **3c** and **4c**, molecular ions are also detected, but the main process is the formation of fragment ions $[M - C_2H_4OH]^+$ and $[M - C_3H_6OH]^+$.

For bifunctional 3-aminopropanol nucleophile, participation in the reaction of both functional groups, amine and alcoholic ones, is possible. But neither generation of sodium 3-aminopropanolate in ethanol under the action of sodium ethanolate nor the application of sodium 3-aminopropanolate preliminary synthesized from 3-aminopropanol and NaOH leads to the formation of the substitution products of bromine atoms in bromomethyl groups of chalcogenides **1** and **2** by the hydroxy-group of 3-aminopropanol both in ethanol and DMSO. In all cases, the only reaction products are chalcogenides **3d** and **4d**.

The reaction of *E*,*E*-bis(3-bromo-1-chloro-1-propen-2-yl) sulfide (**1**) and selenide (**2**) with secondary amine, diethylamine, also follows the heterocyclization path. Even in the presence of a large excess of diethyl amine, substitution of the bromine atoms by amino-group at both bromomethyl groups does not take place. The reaction delivers the heterocycles containing quaternary nitrogen atom, 4,4-diethyl-2(*E*),6(*E*)-bis(*E*-chloromethylidene)-1,4-thiazinan-4-onium bromide (**5**) and 4,4-diethyl-2(*E*),6(*E*)-bis(*E*-chloromethylidene)-1,4-selenazinan-4-onium bromide (**6**). Separation of the heterocycles **5** and **6** and diethylammonium bromide formed in the reaction has been achieved by treatment of the reaction mixture with $NaHCO_3$ solution resulting in the regeneration of the parent diethylamine which further is separated from this mixture to give pure heterocycles **5** or **6** (Scheme 3).

The formation of the heterocycles **5** and **6** was confirmed by the ^1H and ^{13}C NMR spectroscopy, mass spectrometry data as well as elemental analysis. In the ^1H NMR spectra, singlet signals of vinyl and methylene protons of chalcogenomorpholine ring and methylene and methyl protons of the ethyl group in a ratio of 2 : 4 : 4 : 6 are distinctly observed, while the ^{13}C NMR spectra are characterized by doublet–triplet signals of the =CHCl group (δ 124.18 and 122.70 ppm) and triplet–doublet signals of the CH_2 group of the morpholine rings (δ 56.10 and 56.95 ppm). Fine structures of these signals confirm, on one hand, direct bonding of the carbon atom of the =CHCl group to the halogen atom ($^1J_{CH}$ 199–202 [18]) and indicate, on the other hand, retention of the configuration of the parent *E*,*E*-bis(chlorovinyl) chalcogenides **1** and **2** in the heterocycle prepared since the $^3J_{CH}$ values between the carbon atom of the methylene group and vinyl proton of the



1, 2 **5** (89%), **6** (50%)

Z = S (**1, 5**), Se (**2, 6**)

Scheme 3. Preparation of bis(*E*-chloromethyliodene) derivatives of 4,4-diethyl-1,4-thiazinan-4-onium and -1,4-selenazinan-4-onium bromides by heterocylization of *E*,*E*-bis(3-bromo-1-chloro-1-propen-2-yl) sulfide and selenide with diethylamine.

=CHCl group (6 Hz) practically agree with the similar values for chalcogenides **1** and **2** (7 Hz [2]). Mass spectra of the heterocycles **5** and **6** are characterized by lack of the molecular ions and in general coincide with the mass spectra of *N*-ethylchalcogenomorpholines **3e** and **4e**, which is due to thermal decomposition of quaternary ammonium salts accompanied by the release of C_2H_5Br during analysis and generation in the mass spectrometer of the heterocycles **3e** and **4e**.

3. Conclusion

Hitherto unknown *E*,*E*-bis(chloromethylidene) derivatives of *N*-organyl-substituted thio- and selenomorpholines **3** and **4** and their quaternary salts **5** and **6** have been prepared. Heterocycles **3–6** are conceptually the bridged derivatives of *E*,*E*-bis(2-chlorovinyl) sulfide and selenide and could be modified through participation of the chlorine atoms at double bonds in the cross-coupling reactions to form functionally substituted derivatives of thio- and selenomorpholines similar to the modification of *E*,*E*-bis(chloromethylidene)-1,4-dithiane in cross-coupling with phenylacetylene.[19] Judging from the known biological activity in certain derivatives of selenomorpholine,[20–22] including *N*-allylselenomorpholine and *N*-arylselenomorpholines,[13,23] it may be suggested that heterocycles **4** possess potential biological activity as well.

4. Experimental

4.1. *General*

The ^1H (400.13 MHz) and ^{13}C (100.61 MHz) NMR spectra were recorded on a Bruker DPX-400 spectrometer in 5–10% solutions in $CDCl_3$, chemical shifts (δ) are expressed in ppm downfield from hexamethyldisiloxane as an internal standard. Electron ionization mass spectra (EI-MS) were determined on Agilent 5975 at 70 eV. The C, H, N, S analyses were done by Thermo Finnigan EA 1112 elemental analyzer. Se and Cl contents were determined by iodometric titration and by the method of volumetric deposition in the presence of an indicator. Melting points of the compounds were determined with PolyTherm A melting point apparatus are reported uncorrected.

E,*E*-Bis(3-bromo-1-chloro-1-propen-2-yl) sulfide (**1**) and *E*,*E*-bis(3-bromo-1-chloro-1-propen-2-yl) selenide (**2**) were prepared in 90% and 80% yields from propargyl bromide and sulfur dichloride or selenium dichloride, correspondingly, as described earlier.[1,2] Amines (Et_3N, Et_2NH, $CH_2{=}CHCH_2NH_2$, $HOCH_2CH_2CH_2NH_2$) were distilled over powdered potassium

hydroxide or recrystallized from EtOH (4-$CH_3C_6H_4NH_2$, $CH_3C(O)C_6H_4NH_2$, $EtNH_2 \cdot HBr$) prior to use. Benzene was stirred with H_2SO_4, decanted and distilled before use. THF was refluxed over KOH, distilled off and redistilled over sodium metal with the addition of benzophenone.

4.2. *General procedure for the synthesis of N-R-2(E),6(E)-bis(chloromethylidene) thiomorpholines (3a-d)*

A mixture of *E*,*E*-bis(3-bromo-1-chloro-1-propen-2-yl) sulfide (**1**) (2–2.6 mmol), primary amine (2–5.1 mmol) and Et_3N (4–7.6 mmol) in ratio 1 : 1 : 2 (**3a**, **3b**), 1 : 2 : 2 (**3c**) or 1 : 2 : 4 (**3d**) was stirred in benzene (**3a**, **3c**) or THF (**3b**, **3d**) at 20°C (**3a**, **3c**, **3d**) or at reflux (**3b**) 24 h (**3b**, **3d**) or 48 h (**3a**, **3c**).

4.2.1. *N-(4-Methylphenyl)-2(E),6(E)-bis(chloromethylidene) thiomorpholine (**3a**)*

The resulting reaction mixture was diluted with chloroform, the chloroform solution was rinsed with water and dried over K_2CO_3. The solvents were evacuated in vacuo. Yield 619 mg (95%). Brown oil. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 2.25 (s, 3H, CH_3), 4.37 (d, ^4J = 1.3 Hz, 4H, 2 CH_2), 6.08 (t, ^4J = 1.3 Hz, 2H, 2 =CHCl), 6.80 (d, ^3J = 8.4 Hz, 2H, 2 $^{2,6}C_{ar}$H=), 7.07 (d, ^3J = 8.4 Hz, 2H, 2 $^{3,5}C_{ar}$H=). ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 20.49 (q. t, $^1J_{CH}$ = 126.0, $^3J_{CH}$ = 4.2 Hz, CH_3), 50.18 (t. d. t, $^1J_{CH}$ = 141.2, $^3J_{CH}$ = 6.2, $^3J_{CH}$ = 4.4 Hz, CH_2), 112.38 (d. t, $^1J_{CH}$ = 200.0, $^3J_{CH}$ = 4.6 Hz, =CHCl), 115.82 (d. d, $^1J_{CH}$ = 155.9, $^2J_{CH}$ = 5.1 Hz, $^{2,6}C_{ar}$), 130.05 (d. m, $^1J_{CH}$ = 155.5 Hz, $^{3,5}C_{ar}$), 145.80 (s, =C). EI-MS (*m*/*z*, %) (for isotopes ^{14}N, ^{35}Cl): 285 (M^+ 100), 250 ($[M - Cl]^+$ 73), 214 (20), 158 (11), 144 (30), 118 (55), 91 (83), 65 (20). Anal. Calc. for $C_{13}H_{13}NCl_2S$: C, 54.55; H, 4.58; N, 4.89; Cl, 24.77; S, 11.20. Found: C, 54.30; H, 4.90; N, 4.62; Cl, 24.51; S, 11.15%.

4.2.2. *N-(4-acetylphenyl)-2(E),6(E)-bis(chloromethylidene) thiomorpholine (**3b**)*

The resulting reaction mixture was diluted with chloroform, the chloroform solution was rinsed with 5% HCl solution and dried over K_2CO_3. The solvents were evacuated in vacuo. Yield 399 mg (87%), light-brown oil. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 2.51 (s, 3H, CH_3), 4.49 (d, ^3J = 1.3 Hz, 4H, 2 =CCH_2N), 6.15 (t, ^3J = 1.3 Hz, 2H, 2 =CHCl), 6.85 (d, ^3J = 9 Hz, 2H, $^{2,6}C_{ar}$H=), 7.90 (d, ^3J = 9 Hz, 2H, 2 $^{3,5}C_{ar}$H=). ^{13}C NMR (100.61 MHz, $CDCl_3$): 26.18 (q, $^1J_{CH}$ = 127.2 Hz, CH_3), 49.37 (t. d. t, $^1J_{CH}$ = 142, $^3J_{CH}$ = 6.2, $^3J_{CH}$ = 3.9 Hz, CH_2N), 113.26 (d. t, $^1J_{CH}$ = 200, $^3J_{CH}$ = 4.4 Hz, =CHCl), 113.65 (d. d, $^1J_{CH}$ = 158, $^2J_{CH}$ = 5.2 Hz, $^{2,6}C_{ar}$), 128.24 (t, $^2J_{CH}$ = 7, CH_2C=), 130.30 (s, =*C*–C=O), 130.79 (d. d, $^1J_{CH}$ = 160, $^2J_{CH}$ = 5.2 Hz, $^{3,5}C_{ar}$), 151.35–151.80 (m, =CN), 196.30–196.56 (m, C=O). EI-MS (*m*/*z*, %) (for isotopes ^{14}N, ^{35}Cl): 313 (M^+ 98), 298 ($[M - CH_3]^+$ 17), 278 ($[M - Cl]^+$ 100), 192 (24), 149 (22), 132 (65). Anal. Calc. for $C_{14}H_{13}NOCl_2S$: C, 53.51; H, 4.17; N, 4.46; Cl, 22.56; S, 10.20. Found: C, 53.85; H, 4.09; N, 4.67; Cl, 22.75; S, 10.41%.

4.2.3. *N-Allyl-2(E),6(E)-bis(chloromethylidene) thiomorpholine (**3c**)*

The resulting reaction mixture was diluted with chloroform, the chloroform solution was rinsed with water and dried over K_2CO_3. The solvents were evacuated in vacuo and the crude product was further purified by extraction with Et_2O. Yield 592 mg (97%), brown oil. ^{1}H NMR (400.13 MHz, $CDCl_3$): 3.15 (d. t, ^3J = 6.6, ^4J = 1.1 Hz, 2H, CH_2CH=CH_2), 3.69 (d, ^4J = 1.1 Hz, 4H, 2 NCH_2C=), 5.20–5.25 (m, 2H, =CH_2), 5.80–5.87 (m, 1H, =CH), 6.13 (t, ^4J = 1.1 Hz, 2H, =CHCl). ^{13}C NMR (100.61 MHz, $CDCl_3$): 52.35 (t. d. t, $^1J_{CH}$ = 140.4, $^2J_{CH}$ = 5.2, $^3J_{CH}$ = 5.2 Hz, NCH_2), 57.24 (t. m, $^1J_{CH}$ = 128.8 Hz, CH_2CH=CH_2), 113.12 (d. t, $^1J_{CH}$ = 199, $^3J_{CH}$ = 4.8 Hz, =CHCl), 119.05 (d. d. t, $^1J_{CH}$ = 154.8, $^1J_{CH}$ = 158.6, $^3J_{CH}$ = 5.5 Hz, =CH_2), 130.07 (m, =C), 134.31 (d. m, $^1J_{CH}$ = 154.8 Hz,

=CH). EI-MS (*m/z*, %) (for isotopes ^{14}N, ^{35}Cl): 235 (M^+ 64), 208 ([M – $CH{=}CH_2$]$^+$ 15), 200 ([M – Cl]$^+$ 100), 164 (17), 128 (32), 108 (20), 92 (15), 71 (24). Anal. Calc. for $C_9H_{11}NCl_2S$: C, 45.77; H, 4.69; N, 5.93; Cl, 30.02; S, 13.58. Found: C, 45.34; H, 4.63; N, 6.03; Cl, 29.79; S, 13.23%.

4.2.4. *N-(3-Hydroxypropyl)-2(E),6(E)-bis(chloromethylidene) thiomorpholine (**3d**)*

The resulting reaction mixture was diluted with chloroform, the chloroform solution was rinsed with water and dried over K_2CO_3. The solvents were evacuated in vacuo. Yield 480 mg (95%), brown viscous oil. ^1H NMR (400.13 MHz, $CDCl_3$): 1.76 (quint, ^3J = 5.8 Hz, $CH_2CH_2CH_2$), 2.73 (t, ^3J = 6.1 Hz, 2H, NCH_2CH_2), 3.76 (d, ^3J = 1.1 Hz, 4H, 2 $=CCH_2N$), 3.79 (t, 2H, ^3J = 5.3 Hz, $HOCH_2$), 6.16 (t, ^3J = 1.1 Hz, 2H, 2 =CHCl). ^{13}C NMR (100.61 MHz, $CDCl_3$): 28.76 (t, $^1J_{CH}$ = 125.9 Hz, $CH_2CH_2CH_2$), 51.64 (t. t, $^1J_{CH}$ = 133.0, $^2J_{CH}$ = 3.9 Hz, NCH_2CH_2), 52.22 (t. d. t, $^1J_{CH}$ = 139.5, $^3J_{CH}$ = 5.2, $^3J_{CH}$ = 4.8 Hz, $=CCH_2N$), 61.62 (t. t, $^1J_{CH}$ = 141.2, $^2J_{CH}$ = 3.9 Hz, $HOCH_2$), 113.28 (d. t, $^1J_{CH}$ = 199.4, $^3J_{CH}$ = 4.6 Hz, =CHCl), 129.37 (d. t, $^2J_{CH}$ = 4.1, $^2J_{CH}$ = 3.9 Hz, =C). EI-MS (*m/z*, %) (for isotopes ^{14}N, ^{35}Cl): 253 (M^+ 9), 236 ([M – OH]$^+$ 3), 218 ([M – Cl]$^+$ 29), 208 ([M – $(CH_2)_2OH$]$^+$ 100), 194 ([M – $(CH_2)_3OH$]$^+$ 18), 182 (15), 160 (7). Anal. Calc. for $C_9H_{13}NOCl_2S$: C, 42.53; H, 5.16; N, 5.51; Cl, 27.90; S, 12.62. Found: C, 42.33; H, 5.28; N, 5.41; Cl, 27.60; S, 12.91%.

4.3. *General procedure for the synthesis of N-R-2(E),6(E)-bis (chloromethylidene) selenomorpholines (4a–d)*

A mixture of *E*,*E*-bis(3-bromo-1-chloro-1-propen-2-yl) selenide (**2**) (2–7.6 mmol), primary amine (2–9 mmol) and Et_3N (4–19 mmol) in a ratio of 1 : 1 : 2 (**4a**, **4b**) or 1 : 2 : 4 (**4c**, **4d**) was stirred in benzene (**4a**, **4c**, **4d**) or THF (**4b**) at 20°C 48 h in an argon atmosphere.

4.3.1. *N-(4-Methylphenyl)-2(E),6(E)-bis(chloromethylidene) selenomorpholine (**4a**)*

The resulting reaction mixture was diluted with chloroform, the chloroform solution was rinsed with water and dried over K_2CO_3. Yield 640 mg (96%), brown powder, m.p. 75–76°C (hexane). ^1H NMR (400.13 MHz, $CDCl_3$): 2.24 (s, 3H, CH_3), 4.45 (d, ^4J = 1.6 Hz, 4H, 2 CH_2), 6.13 (t, ^4J = 1.6 Hz, 2H, 2 =CHCl), 6.78 (d, ^3J = 8.2 Hz, 2H, 2 $^{3,5}C_{ar}H$=), 7.06 (d, ^3J = 8.2 Hz, 2H, 2 $^{2,6}C_{ar}H$=). ^{13}C NMR (100.61 MHz, $CDCl_3$): 20.52 (q, m, $^1J_{CH}$ = 125.6 Hz, CH_3), 50.88 (t. d. t, $^1J_{CH}$ = 140.9, $^3J_{CH}$ = 7.0, $^3J_{CH}$ = 4.2 Hz, CH_2), 113.30 (d. t, $^1J_{CH}$ = 200.6, $^3J_{CH}$ = 4.9 Hz, =CHCl), 115.36 (d. d, $^1J_{CH}$ =161.3, $^2J_{CH}$ = 5.4 Hz, $^{2,6}C_{ar}$), 127.0.9 (q, $^2J_{CH}$ = 4.0 Hz, =C), 128.75 (d. d, $^2J_{CH}$ = 6.2, $^2J_{CH}$ = 7.3 Hz, =C), 130.14 (d. m, $^1J_{CH}$ = 155.9 Hz, $^{3,5}C_{ar}$). EI-MS (*m/z*, %) (for isotopes ^{80}Se, ^{14}N, ^{35}Cl): 333 (M^+ 72), 298 ([M – Cl]$^+$ 14), 252 (7), 218 (38), 179 (18), 144 (62), 118 (63), 91 (100), 65 (33), 49 (15). Anal. Calc. for $C_{13}H_{13}NCl_2Se$: C, 46.87; H, 3.93; N, 4.20; Cl, 21.29; Se, 23.70. Found: C, 46.65; H, 3.96; N, 3.95; Cl, 21.57; Se, 23.50%.

4.3.2. *N-(4-acetylphenyl)-2(E),6(E)-bis(chloromethylidene) selenomorpholine (**4b**)*

The resulting reaction mixture was diluted with chloroform, the chloroform solution was rinsed with 5% HCl solution and dried over K_2CO_3. The solvents were evacuated in vacuo and the residue was further purified by column chromatography (silicagel, eluent-hexane : chloroform = 1 : 1). Yield 1.712 g (62%), brown viscous oil. ^1H NMR (400.13 MHz, $CDCl_3$): 2.50 (s, 3H, CH_3), 4.52 (d, ^3J = 1.5 Hz, 4H, 2 $=CCH_2N$), 6.18 (t, ^3J = 1.5 Hz, 2H, 2 =CHCl), 6.83 (d, ^3J = 9.1 Hz, 2H, 2 $^{2.6}C_{ar}H$=), 7.89 (d, ^3J = 9.1 Hz, 2H, 2 $^{3,5}C_{ar}H$=). ^{13}C NMR (100.61 MHz, $CDCl_3$): 26.12 (q,

$^{1}J_{CH}$ = 127.1 Hz, CH_3), 50.12 (t. m, $^{1}J_{CH}$ = 141.7 Hz, CH_2N), 113.24 (d. d, $^{1}J_{CH}$ = 158.7, $^{2}J_{CH}$ = 5.0 Hz, $^{2,6}C_{ar}$), 113.86 (d. t, $^{1}J_{CH}$ = 201.2, $^{3}J_{CH}$ = 4.2 Hz, =CHCl), 126.55 (d. t, $^{3}J_{CH}$ = 4.2, $^{2}J_{CH}$ = 4.2 Hz, =*C*–C=O), 127.82 (t, $^{2}J_{CH}$ = 6.5 Hz, *C*H_2C=), 130.60 (d. d, $^{1}J_{CH}$ =159.5, $^{2}J_{CH}$ = 6.9 Hz, $^{3,5}C_{ar}$), 149.90-151.20 (m, =C–N), 196.15-196.40 (m, C=O). EI-MS (*m/z*, %) (for isotopes ^{80}Se, ^{14}N, ^{35}Cl): 361 (M^+ 96), 346 ($[M - CH_3]^+$ 24), 326 ($[M - Cl]^+$ 37), 290 (8), 266 (17), 246 (66), 192 (70), 172 (22), 155 (36), 132 (100), 104 (29), 91 (52). Anal. Calc. for $C_{14}H_{13}NOCl_2Se$: C, 46.56; H, 3.63; N, 3.88; Cl, 19.63; Se, 21.86. Found: C, 46.87; H, 3.95; N, 3.61; Cl, 19.84; Se, 21.72%.

4.3.3. *N-Allyl-2(E),6(E)-bis(chloromethylidene) selenomorpholine (**4c**)*

The resulting reaction mixture was diluted with chloroform, the chloroform solution was rinsed with 5% HCl solution and dried over K_2CO_3. The solvents were evacuated in vacuo and the residue was further purified by extraction with hexane. Yield 600 mg (95%), brown viscous oil. ^{1}H NMR (400.13 MHz, $CDCl_3$): 3.11 (d. t, ^{3}J = 6.5, ^{4}J = 1.2 Hz, 2H, *CH*$_2$CH=CH$_2$), 3.81 (d, ^{4}J = 1.2 Hz, 4H, 2 N*CH*$_2$C=CH), 5.19–5.24 (m, 2H, =CH$_2$), 5.78–5.88 (m, 1H, =CH), 6.21 (t, ^{4}J = 1.2 Hz, 2H, =CHCl). ^{13}C NMR (100.61 MHz, $CDCl_3$): 134.49 (d. m, $^{1}J_{CH}$ = 154.9 Hz, =CH), 125.80 (m, =C), 118.98 (d. d. t, $^{1}J_{CH}$ = 154.6, $^{1}J_{CH}$ = 154.6, $^{3}J_{CH}$ = 5.7 Hz, =CH$_2$), 114.36 (d. t, $^{1}J_{CH}$ = 200, $^{3}J_{CH}$ = 5, $^{3}J_{SeH}$ = 38 Hz, =CHCl), 56.00 (t. m, $^{1}J_{CH}$ = 131.3 Hz, *C*H$_2$CH=CH$_2$), 53.24 (t. d. t, $^{1}J_{CH}$ = 139.5, $^{2}J_{CH}$ = 5.0, $^{3}J_{CH}$ = 5.5 Hz, NCH$_2$). EI-MS (*m/z*, %) (for isotopes ^{80}Se, ^{14}N, ^{35}Cl): 283 (M^+ 100), 256 ($[M - CH{=}CH_2]^+$ 25), 248 ($[M - Cl]^+$ 79), 202 (30), 168 (48), 153 (28), 128 (77), 118 (50), 108 (29), 93 (36). Anal. Calc. for $C_9H_{11}NCl_2Se$: C, 38.19; H, 3.91; N, 4.95; Cl, 25.05; Se, 27.90. Found: C, 38.46; H, 4.20; N, 4.97; Cl, 24.66; Se, 27.88%.

4.3.4. *N-(3-Hydroxypropyl)-2(E),6(E)-bis(chloromethylidene) selenomorpholine (**4d**)*

The resulting reaction mixture was diluted with chloroform, the chloroform solution was rinsed with 5% $NaHCO_3$ solution and dried over K_2CO_3. The solvents were evacuated in vacuo and the residue was further purified by extraction with MeOH. Yield 567 mg (77%), brown viscous oil. ^{1}H NMR (400.13 MHz, $CDCl_3$): 1.76 (quint, ^{3}J = 5.4 Hz, 2H, $CH_2CH_2CH_2$), 2.71 (t, ^{3}J = 6.0 Hz, 2H, N*CH*$_2$CH$_2$), 3.79 (t, ^{3}J = 5.3 Hz, 2H, HOCH$_2$), 3.88 (d, ^{3}J = 0.9 Hz, 4H, 2 =CCH$_2$N), 6.26 (t, ^{3}J = 0.9 Hz, 2H, 2 =CHCl). ^{13}C NMR (100.61 MHz, $CDCl_3$): 28.58 (t, $^{1}J_{CH}$ = 126.0 Hz, CH$_2$*C*H$_2$CH$_2$), 50.91 (t, $^{1}J_{CH}$ =132.9 Hz, N*C*H$_2$CH$_2$), 53.24 (t, $^{2}J_{CH}$ = 138.4 Hz, =C*C*H$_2$N), 62.47 (t. t, $^{1}J_{CH}$ = 142.0, $^{2}J_{CH}$ = 3.7 Hz, HOCH$_2$), 114.87 (d. t, $^{1}J_{CH}$ = 200.9, $^{3}J_{CH}$ = 4.6 Hz, =CHCl), 125.15 (d. t, $^{2}J_{CH}$ = 4.1, $^{2}J_{CH}$ = 3.9 Hz, =C). EI-MS (*m/z*, %) (for isotopes ^{80}Se, ^{14}N, ^{35}Cl): 301 (M^+ 6), 284 ($[M - OH]^+$ 1), 256 ($[M - C_2H_4OH]^+$ 100), 242 ($[M - C_3H_6OH]^+$ 11), 227 (36), 182 (29). Anal. Calc. for $C_9H_{13}NOCl_2Se$: C, 35.90; H, 4.35; N, 4.65; Cl, 23.55; Se, 26.23. Found: C, 36.20; H, 4.52; N, 4.77; Cl, 23.36; Se, 26.32%.

4.4. *General procedure for the synthesis of N-ethyl-2(E),6(E)-bis (chloromethylidene)thiomorpholine- and selenomorpholines (3e, 4e)*

A solution of sulfide **1** or selenide **2** (1.1 mmol), $EtNH_2HBr$ (1.1 mmol) and $NaHCO_3$ (3.3 mmol) in 15 ml EtOH was stirred 10 h at room temperature and 7 h at 50–55°C. The reaction mixture was diluted with H_2O (20 ml), extracted with $CHCl_3$, chloroform extract was rinsed with 15% solution of HCl and the resulting water solution was carefully neutralized with Na_2CO_3, extracted with Et_2O, the ether extract was dried over K_2CO_3.

4.4.1. *N-Ethyl-2(E),6(E)-bis(chloromethylidene) thiomorpholine (**3e**)*

Yield 194 mg (87%), brown oil. ^{1}H NMR (400.13 MHz, $CDCl_3$): 1.14 (t, ^3J = 7.0 Hz, 3H, CH_2CH_3), 2.59 (q, ^3J = 7.2 Hz 2H, CH_2CH_3), 3.71 (d, ^3J = 1.1 Hz, 4H, 2 NCH_2C=CH), 6.13 (t, ^3J = 1.1 Hz, 2H, =CHCl). ^{13}C NMR (100.61 MHz, $CDCl_3$): 12.60 (q. t, $^1J_{CH}$ = 125.9, $^2J_{CH}$ = 3.0 Hz, NCH_2CH_3), 47.85 (t. q, $^1J_{CH}$ = 133.0, $^2J_{CH}$ = 3.8 Hz, NCH_2CH_3), 52.19 (t. d. t, $^1J_{CH}$ = 139.0, $^2J_{CH}$ = 4.8, $^3J_{CH}$ = 4.8 Hz, NCH_2C=), 112.83 (d. t, $^1J_{CH}$ = 199.0, $^3J_{CH}$ = 4.6 Hz, =CHCl), 130.14 (d. t, $^2J_{CH}$ = 3.4, $^2J_{CH}$ = 3.4 Hz, =C). EI-MS (*m*/*z*, %) (for isotopes ^{14}N, ^{35}Cl): 223 (M^+ 44), 208 ([M – CH_3]$^+$ 73), 188 ([M – Cl]$^+$ 100), 173 (5), 155 (12), 152 (16), 131 (16), 116 (35), 96 (79), 82 (13), 71 (40), 56 (36). Anal. Calc. for $C_8H_{11}NCl_2S$: C, 42.87; H, 4.95; N, 6.25; Cl, 31.63; S, 14.31. Found: C, 42.82; H, 4.80; N, 5.97; Cl, 31.73; S, 13.92%.

4.4.2. *N-Ethyl-2(E),6(E)-bis(chloromethylidene) selenomorpholine (**4e**)*

Yield 255 mg (85%), yellow oil. ^{1}H NMR (400.13 MHz, $CDCl_3$): 1.11 (t, ^3J = 7.2 Hz, 3H, CH_2CH_3), 2.54 (q, ^3J = 7.2 Hz, 2H, CH_2CH_3), 3.84 (d, ^3J = 1.1 Hz, 4H, NCH_2C=), 6.20 (t, ^3J = 1.1 Hz, 2H, =CHCl). ^{13}C NMR (100.61 MHz, $CDCl_3$): 12.91 (q. t, $^1J_{CH}$ = 125.9, $^2J_{CH}$ = 3.0 Hz, NCH_2CH_3), 46.60 (t. q, $^1J_{CH}$ = 133.2, $^2J_{CH}$ = 3.8, NCH_2CH_3), 53.16 (t. d. t, $^1J_{CH}$ = 139.1, $^2J_{CH}$ = 5.5, $^3J_{CH}$ = 4.2 Hz, NCH_2C=), 114.35 (d. t, $^1J_{CH}$ = 200.1, $^3J_{CH}$ = 5.0 Hz, =CHCl), 125.90 (d. t, $^2J_{CH}$ = 3.4, $^2J_{CH}$ = 3.4 Hz, =C). EI-MS (*m*/*z*, %) (for isotopes ^{80}Se, ^{14}N, ^{35}Cl): 271 (M^+ 36), 256 ([M – Me]$^+$ 58), 236 ([M – Cl]$^+$ 37), 182 (32), 155 (89), 140 (28), 119 (64), 116 (100), 96 (84), 75 (41), 56 (40). Anal. Calc. for $C_8H_{11}NCl_2Se$: C, 35.45; H, 4.09; N, 5.17; Cl, 26.16; Se, 29.13. Found: C, 35.56; H, 4.17; N, 4.96; Cl, 26.03; Se, 29.35%.

4.5. *General procedure for the synthesis of 4,4-diethyl-2(E),6(E)-bis (chloromethylidene)-1,4-thiazinan-4-onium and -1,4-selenazinan-4-onium bromides (5,6)*

A solution of sulfide **1** or selenide **2** (4.0 mmol) and Et_2NH (10.0 mmol) in 20 ml THF was stirred for 20 h at room temperature. The deposits settled out were filtered off and dissolved in 5% $NaHCO_3$. The resulting solution was evaporated dry in vacuo, the residue was extracted with $CHCl_3$ and the chloroform solution was dried over K_2CO_3.

4.5.1. *4,4-Diethyl-2(E),6(E)-bis (chloromethylidene)-1,4-thiazinan-4-onium bromide (**5**)*

Yield 956 mg (89%), light-brown powder, m.p. 195–200°C with decomp. (EtOH). ^{1}H NMR (400.13 MHz, $CDCl_3$): 1.43 (t, ^3J = 7.2 Hz, 6H, CH_3), 3.72 (q, ^3J = 7.2 Hz, 4H, NCH_2CH_3), 5.17 (s, 4H, NCH_2C=), 6.63 (s, 2H, =CHCl). ^{13}C NMR (100.61 MHz, $CDCl_3$): 7.41 (q, $^1J_{CH}$ = 129.1 Hz, NCH_2CH_3), 53.46 (t, $^1J_{CH}$ = 145.4 Hz, NCH_2CH_3), 56.95 (t. d, $^1J_{CH}$ = 147.8, $^3J_{CH}$ = 5 Hz, =CCH_2N), 121.71 (s, =C), 122.70 (d. t, $^1J_{CH}$ = 199.4, $^3J_{CH}$ = 5 Hz, =CHCl). EI-MS (*m*/*z*, %) (for isotopes ^{14}N, ^{35}Cl): 223 ([M – C_2H_5Br]$^+$ 60), 208 (74), 188 (100), 145 (12), 116 (23.5), 96 (33.5), 71 (38). Anal. Calc. for $C_{10}H_{16}NBrCl_2S$: C, 36.06; H, 4.84; N, 4.20; Br, 23.99; Cl, 21.29; S, 9.63. Found: C, 35.78; H, 4.73; N, 4.35; Br, 23.84; Cl, 21.39; S, 9.88%.

4.5.2. *4,4-Diethyl-2(E),6(E)-bis (chloromethylidene)-1,4-selenazinan-4-onium bromide (**6**)*

Yield 760 mg (50%), light-brown powder, m.p. 194–197°C with decomp. (EtOH). ^{1}H NMR (400.13 MHz, $CDCl_3$): 1.44 (t, ^3J = 7.2 Hz, 6H, CH_3), 3.68 (q, ^3J = 7.2 Hz, 4H, NCH_2CH_3), 5.19 (s, 4H, NCH_2C=), 6.78 (s, 2H, =CHCl). ^{13}C NMR (100.61 MHz, $CDCl_3$): 7.85 (q, $^1J_{CH}$ =

128.5 Hz, NCH_2CH_3), 53.73 (t, $^1J_{CH}$ = 144.8 Hz, NCH_2CH_3), 59.10 (t. d, $^1J_{CH}$ = 145.8, $^3J_{CH}$ = 6 Hz, =CCH_2N), 118.12 (d. t, $^2J_{CH}$ = 5.2, $^2J_{CH}$ = 5.0 Hz, =C), 124.18 (d. t, $^1J_{CH}$ = 202.0, $^3J_{CH}$ = 5 Hz, =CHCl). EI-MS (*m/z*, %) (for isotopes ^{80}Se, ^{14}N, ^{35}Cl): 271 ([M – C_2H_5Br]$^+$ 94), 256 (100), 236 (63), 190 (14), 182 (30), 155 (59), 119 (35), 96 (47), 73 (26), 56 (32). Anal. Calc. for $C_{10}H_{16}NBrCl_2Se$: C, 31.61; H, 4.24; N, 3.69; Br, 21.02; Cl, 18.66; Se, 20.78 Found: C, 31.39; H, 4.12; N, 3.74; Br, 20.90; Cl, 18.50; Se, 20.60%.

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