

A General Two-Step Procedure for the *N*-Alkylation of Selenoamides

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Selenoamides are prepared via *N*-alkylated in a two-step procedure: Benzotriazole, aldehyde and primary selenoamide reacted together to yield an adduct which was then reduced to the *N*-substituted selenoamide by NaBH₄.

Keywords primary selenoamides, benzotriazole, aldehyde, *N*-alkylated selenoamides

Selenoamides are not only useful for the synthesis of selenium-nitrogen heterocycles, such as 1,3-selenazoles,^{1,2} 1,2,4-diaselenazolines³ and 1,3,5-oxaselenazines,⁴ but also synthetically promising because they can be expected to react with various organic or inorganic reagents owing to the high reactivity of their carbon-selenium double bond.^{5,6} However, selenoamides are still little known although they were synthesized one hundred years ago. The application of selenoamides has also been greatly restricted due to the difficulty in their preparation.

Primary selenoamides have been prepared from hydrogen selenide and nitriles,⁷⁻⁹ or an improved method by using nitriles and aluminum selenide in boiling water.^{10,11} There are only a few known methods for the synthesis of *N*-substituted selenoamides: the reaction of phosphorous pentaselenides with amines;¹¹ the reaction of selenoesters with alkylamide magnesium bromides or secondary amides;¹² the addition of secondary amines to alkyneselelenols;¹³ the one-pot reaction from nitriles, metallic selenium, carbon monoxide, water and amines;¹⁴ the four-component coupling reaction of terminal acetylenes, selenium, amines, allylic bromides¹⁵ and the amine group exchange reaction of the intermediate primary selenoamide

with an amine.¹⁶ However, these methods are not convenient and with low yields.

We have reported a convenient synthesis of primary selenoamides by the reaction of corresponding nitriles with sodium hydrogen selenide in ethanol previously.¹⁷ Now we would like to describe a new efficient method for synthesis of *N*-substituted selenoamides from primary selenoamides. When aldehydes were treated with primary selenoamides and benzotriazole in dry toluene for 5—7 h, the adducts **5a—5h** were obtained with the loss of molecule of water. The adducts were then reduced by NaBH₄ in refluxing THF to give the expected *N*-substituted selenoamides **6a—6f**. All adducts were characterized by IR spectra, NMR spectra, MS and elemental analysis.

The reaction probably involves the formation of a hydroxymethylbenzotriazole intermediate (**3**) which subsequently reacts with the amide (Scheme 1). Details were given in Table 1. The result shows that various aliphatic aldehydes can easily react with selenoamides (**4**) and benzotriazole to form adducts **5** which are reduced to *N*-alkylated selenoamides in good yields. Aromatic aldehydes have also been treated with selenoamides and benzotriazole, but the yields of the corresponding **6** were very low.

In summary, a new and convenient method for the synthesis of *N*-alkylated selenoamides was developed. The reaction described in this paper was carried out under neutral conditions. Moreover, the method has other advantages such as mild reaction conditions, simple procedures and easily available starting materials.

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Scheme 1

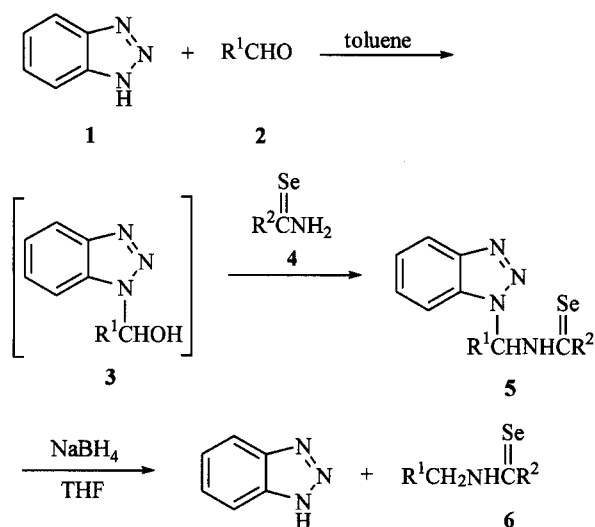


Table 1 Preparation of N-alkylated selenoamides

Entry	R ¹	R ²	Time (h)	Product	Isolated yield (%)
1	<i>n</i> -C ₃ H ₇	<i>m</i> -CH ₃ C ₆ H ₄	15	5a	30
2	<i>n</i> -C ₈ H ₁₇	C ₆ H ₅	4	5b^a	60
3	<i>n</i> -C ₈ H ₁₇	<i>m</i> -CH ₃ C ₆ H ₄	7	5c	60
4	<i>n</i> -C ₈ H ₁₇	<i>p</i> -CH ₃ C ₆ H ₄	16	5d	70
5	<i>n</i> -C ₉ H ₁₉	<i>m</i> -CH ₃ C ₆ H ₄	14	5e	50
6	<i>n</i> -C ₉ H ₁₉	<i>p</i> -CH ₃ C ₆ H ₄	30	5f	65
7	<i>n</i> -C ₃ H ₇	C ₆ H ₅	18	5g	36
8	<i>n</i> -C ₉ H ₁₉	C ₆ H ₅	10	5h	49
9	<i>n</i> -C ₃ H ₇	C ₆ H ₅	2	6a	98
10	<i>n</i> -C ₈ H ₁₇	C ₆ H ₅	2	6b	96
11	<i>n</i> -C ₈ H ₁₇	<i>m</i> -CH ₃ C ₆ H ₄	2	6c	98
12	<i>n</i> -C ₉ H ₁₉	C ₆ H ₅	2	6d	97
13	<i>n</i> -C ₉ H ₁₉	<i>m</i> -CH ₃ C ₆ H ₄	2	6e	98

^aThe structure of **5b** was further determined by ¹³C NMR run on a FX-90Q spectrometer.

Experimental

All reactions were conducted under a nitrogen atmosphere. IR spectra were recorded on a PE-683 spectrometer in KBr with absorption in cm⁻¹. ¹H NMR spectra were obtained on a Bruker AC-80 spectrometer in CDCl₃ with TMS as internal standard. MS were recorded on an HP 5989B MS spectrometer. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer.

General procedure for preparation of **5**

Under a nitrogen atmosphere, a mixture of benzotriazole (3 mmol), benzaldehyde (3 mmol) and selenobenzamide (3 mmol) in dry toluene (30 mL) was refluxed for 15 h. Then toluene was removed and the residue was dissolved in dichloromethane. The solution was washed subsequently with water (40 mL × 3) and 10% Na₂CO₃ (20 mL), and dried over MgSO₄. Then the solvent was evaporated and the residue was purified by preparative TLC on silica gel [cyclohexane-ethyl ether (2:1) as the eluent] to give pure adduct **5**.

5a M.p. 91–93 °C (cyclohexane); ¹H NMR δ: 0.87–1.07 (m, 3H), 1.22–1.74 (m, 4H), 2.26 (s, 3H), 2.36–2.62 (m, 2H), 7.00–7.88 (m, 9H), 9.14 (d, *J* = 9 Hz, 1H); IR ν: 3195, 1621 cm⁻¹; MS (70 eV) *m/z* (%): 372 (M⁺, 2.81), 253 (15.63), 224 (43.71), 184 (35.49), 119 (43.42), 118 (100), 104 (68.98), 91 (90.47). Anal. calcd for C₁₈H₂₀N₄Se: C 58.23, H 5.43, N 15.09; found C 58.48, H 5.54, N 14.99.

5b M.p. 124–126 °C (cyclohexane); ¹H NMR δ: 0.82–0.99 (m, 3H), 1.18–1.67 (m, 14H), 2.45–2.84 (m, 3H), 7.17–8.03 (m, 10H), 9.26 (d, *J* = 9 Hz, 1H); ¹³C NMR (CDCl₃) δ: 206.0, 145.5, 144.3, 133.4, 131.8, 129.3, 128.2, 127.2, 124.6, 119.7, 110.8, 70.87, 34.4, 31.8, 29.2, 29.1, 25.1, 22.7, 14.1; IR ν: 3195, 1603 cm⁻¹; MS (70 eV) *m/z* (%): 428 (M⁺, 0.57), 387 (0.96), 309 (16.18), 210 (86.04), 169 (40.48), 119 (46.51), 104 (100), 77 (48.32). Anal. calcd for C₂₂H₂₈N₄Se: C 61.83, H 6.60, N 13.11; found C 62.04, H 6.67, N, 12.97.

5c M.p. 99–101 °C (cyclohexane); ¹H NMR δ: 0.82–0.94 (m, 3H), 1.22–2.89 (m, 14H), 2.26 (s, 3H), 2.48–2.64 (m, 2H), 7.00–7.92 (m, 9H), 9.39 (d, *J* = 9 Hz, 1H); IR ν: 3192, 1620 cm⁻¹; MS (70 eV) *m/z* (%): 442 (M⁺, 0.99), 323 (15.84), 242 (33.66), 224 (100), 183 (36.63), 119 (73.27), 118 (88.12), 91 (86.14). Anal. calcd for C₂₃H₃₀N₄Se: C 62.58, H 6.85, N 12.69; found C 62.80, H 7.02, N 12.53.

5d M.p. 132–134 °C (cyclohexane); ¹H NMR δ: 0.82–0.92 (m, 3H), 1.24–1.73 (m, 14H), 2.31 (s, 3H), 2.49–2.67 (m, 2H), 7.08–7.98 (m, 9H), 9.24 (d, *J* = 9 Hz, 1H); IR ν: 3190, 1620 cm⁻¹; MS (70 eV) *m/z* (%): 323 (0.93), 260

(6.44), 183 (1.56), 119 (100), 91 (35.49). Anal. calcd for $C_{23}H_{30}N_4Se$: C 62.58, H 6.85, N 12.69; found C 62.81, H 6.97, N 12.57.

5e M.p. 132—133 °C (cyclohexane); 1H NMR δ : 0.73—0.92 (m, 3H), 1.16—1.68 (m, 16H), 2.12 (s, 3H), 2.44—2.59 (m, 2H), 6.97—7.85 (m, 9H), 9.14 (d, $J = 8.5$ Hz, 1H); IR ν : 3197, 1620 cm^{-1} ; MS (70 eV) m/z (%): 456 (M^+ , 0.55), 428 (0.67), 337 (14.51), 256 (28.12), 224 (90.70), 183 (34.52), 119 (45.89), 118 (69.91), 104 (24.65), 91 (67.30). Anal. calcd for $C_{24}H_{32}N_4Se$: C 63.29, H 7.08, N 12.30; found C 63.38, H 7.21, N 12.12.

5f M.p. 126—127 °C (cyclohexane); 1H NMR δ : 0.89—1.00 (m, 3H), 1.25—1.84 (m, 16H), 2.31 (s, 3H), 2.50—2.77 (m, 2H), 7.02—8.01 (m, 9H), 9.78 (d, $J = 9$ Hz, 1H); IR ν : 3193, 1620 cm^{-1} ; MS (70 eV) m/z (%): 337 (3.22), 274 (5.23), 224 (19.29), 183 (6.64), 119 (100), 91 (44.26). Anal. calcd for $C_{24}H_{32}N_4Se$: C 63.29, H 7.08, N 12.30; found C 63.46, H 7.23, N 12.48.

5g M.p. 146—148 °C (cyclohexane); 1H NMR δ : 0.85—1.10 (m, 3H), 1.26—1.68 (m, 4H), 2.33—2.68 (m, 2H), 7.24—8.01 (m, 10H), 9.25 (d, $J = 9$ Hz, 1H); IR ν : 3200, 1604 cm^{-1} ; MS (70 eV) m/z (%): 358 (M^+ , 1.32), 301 (1.20), 239 (8.36), 210 (20.42), 119 (22.64), 104 (100), 77 (69.14). Anal. calcd for $C_{17}H_{18}N_4Se$: C 57.15, H 5.07, N 15.68; found C 57.29, H 4.99, N 15.26.

5h M.p. 114—116 °C (cyclohexane); 1H NMR δ : 0.82—0.97 (m, 3H), 1.19—1.82 (m, 16H), 2.40—2.85 (m, 2H), 7.16—7.99 (m, 10H), 9.16 (d, $J = 9$ Hz, 1H); IR ν : 3195, 1605 cm^{-1} ; MS (70 eV) m/z (%): 323 (17.38), 242 (24.13), 210 (100), 169 (37.22), 119 (47.03), 104 (74.56), 77 (37.64). Anal. calcd for $C_{23}H_{30}N_4Se$: C 62.58, H 6.85, N 12.69; found C 62.47, H 6.90, N 12.57.

General procedure for preparation of **6**

Adduct **5** (1 mmol) was dissolved in dry THF (30 mL). Solid sodium borohydride (1.2 mmol) was added to the stirred solution. The solution was refluxed for 2 h under N_2 . Then the reaction mixture was washed with 10% Na_2CO_3 (20 mL) and water (20 mL \times 2), dried over $MgSO_4$ and concentrated. The residue was purified by preparative TLC on silica gel [cyclohexane-ethyl ether

(2.5:1) as the eluent] to give pure product **6**.

6a Oil; ^{13}C 1H NMR δ : 0.84—0.97 (m, 3H), 1.20—1.90 (m, 4H), 3.53—3.85 (m, 2H), 6.70—7.70 (m, 5H), 8.40 (brs, 1H); IR ν : 3180, 1530 cm^{-1} ; MS (70 eV) m/z (%): 239 (M^+ , 20.07), 169 (25.06), 104 (100), 77 (63.09). Anal. calcd for $C_{11}H_{15}NSe$: C 55.00, H 6.29, N 5.83; found C 55.08, H 6.35, N 5.90.

6b Oil; 1H NMR δ : 0.80—0.97 (m, 3H), 1.30—1.92 (m, 14H), 3.63—3.94 (m, 2H), 7.29—7.79 (m, 5H), 8.15 (brs, 1H); IR ν : 3210, 1540 cm^{-1} ; MS (70 eV) m/z (%): 309 (M^+ , 16.76), 230 (44.33), 169 (28.53), 104 (100), 77 (30.82). Anal. calcd for $C_{16}H_{25}NSe$: C 69.92, H 8.12, N 4.51; found C 69.99, H 8.23, N 4.32.

6c M.p. 43—44 °C (cyclohexane); 1H NMR δ : 0.74—0.89 (m, 3H), 1.17—2.17 (m, 14H), 2.26 (s, 3H), 3.40—3.76 (m, 2H), 7.01—7.43 (m, 4H), 8.30 (brs, 1H); IR ν : 3215, 1535 cm^{-1} ; MS (70 eV) m/z (%): 323 (M^+ , 13.65), 244 (38.45), 183 (28.95), 118 (100), 91 (31.75). Anal. calcd for $C_{17}H_{27}NSe$: C 62.95, H 8.39, N 4.32; found C 63.11, H 8.46, N 4.23.

6d M.p. 33—34 °C (cyclohexane); 1H NMR δ : 0.79—0.93 (m, 3H), 1.23—1.73 (m, 16H), 3.63—3.98 (m, 2H), 7.23—7.80 (m, 5H), 8.10 (brs, 1H); IR ν : 3210, 1540 cm^{-1} ; MS (70 eV) m/z (%): 323 (M^+ , 13.63), 244 (43.79), 169 (27.72), 104 (100), 77 (28.43). Anal. calcd for $C_{17}H_{27}NSe$: C 62.95, H 8.39, N 4.32; found C 63.13, H 8.50, N 4.25.

6e M.p. 40—41 °C (cyclohexane); 1H NMR δ : 0.66—0.92 (m, 3H), 1.56—2.27 (m, 16H), 2.32 (s, 3H), 3.36—3.66 (m, 2H), 6.90—7.33 (m, 5H), 8.01 (br, 1H); IR ν : 3210, 1540 cm^{-1} ; MS (70 eV) m/z (%): 337 (M^+ , 13.6), 258 (40.91), 183 (27.05), 118 (100), 91 (25.53). Anal. calcd for $C_{18}H_{29}NSe$: C 63.89, H 8.64, N 4.14; found C 64.02, H 8.78, N 4.06.

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