Thermal Ring Expansion of 2-Azidoselenochromenes: First Synthetic Examples of 1,3-Benzoselenazepines[1)]

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The thermolysis of 2-azido-2-*tert*-butyl-2*H*-selenochromenes (2a, b), which were easily obtained by the reaction of the corresponding 1-benzoselenopyrylium salts (1) with sodium azide, resulted in a ring expansion to give the novel stable 1,3-benzoselenazepines (5a, b) with denitrogenation in good yields.

Key words 1,3-benzoselenazepine; 2-azido-2-*tert*-butyl-2*H*-selenochromene; ring expansion; 1-benzoselenopyrylium salt

Benzothiazepines,[2—6)] fully conjugated seven-membered heterocycles containing both the heteroatoms of sulfur and nitrogen, have received much attention from the synthetic, theoretical, and reactive points of view. In contrast, there are only a limited number of reports on the synthesis of their selenium and tellurium analogues, the selenazepine and tellurazepine ring systems; dibenzo[*b*,*f*][1,4]-selenazepines[7,8)] and -tellurazepines[9)] have been prepared by the thermal or photochemical rearrangements of the 9-azidoselenoxanthenes and 9-azidotelluroxanthenes, respectively. However, no monocyclic and benzene ring-fused selenazepines have yet been reported to the best of our knowledge. Recently, we have succeeded in the construction of the first benzotellurazepine ring system, the 1,5-benzotellurazepinines.[10,11)] Furthermore, we have focused attention on the syntheses and reactions of the telluro-[12—17)] and selenopyrylium salts,[18—21)] six-membered heterocyclic cations containing a tellurium or selunium element.

Since Le Roux and coworkers[22,23)] discovered the conversion of pyrylium salts into 1,3-oxazepines through azidopyran intermediates 25 years ago, several thermal and photo rearrangements of the azide compounds, prepared from pyrylium salts and relatives with sodium azide, have been reported for the purpose of synthesizing seven-membered heterocycles.[24—27)] Among them, neither the monocyclic selenazepines nor benzoselenazepines were prepared by any method including the above ring expansion access from the azide compounds. In this paper, we describe the first isolation of stable selenazepines, 2-*tert*-butyl-1,3-benzoselenazepines, using the thermal ring expansion of 2-azidoselenochromenes, which are readily obtained from 1-benzoselenopyrylium salts.[19,21)]

The reaction of 1-benzoselenopyrylium salts (**1**) with NaN_3 is shown in Chart 1. 2-*tert*-Butyl-1-benzoselenopyrylium tetrafluoroborate (**1a**)[19)] and 2-*tert*-butyl-4-phenyl-1-benzoselenopyrylium tetrafluoroborate (**1b**)[21)] were treated with 4.0 eq of sodium azide in anhydrous CH_3CN at room temperature to give the 2-azido-2-*tert*-butyl-2*H*-selenochromene (**2a**) and 2-azido-2-*tert*-butyl-4-phenyl-2*H*-selenochromene (**2b**) in 95% and 85% yields, respectively, in spite of the steric hindrance of the *tert*-butyl group at the C-2 position. Similarly, 2-azido-2*H*-selenochromene (**2c**) was obtained from the parent selenopyryrylium salt (**1c**)[19)] in 90% yield. During this azidation of selenopyrylium salts (**1**), the preparation of 2-azido derivatives with any other substituents at the C-2 or -4 position failed. For example, the treatment of the 4-ethyl-1-benzoselenopyrylium salts (**1d**,[21)] **e**[21)]) with sodium azide resulted in δ-hydrogen elimination of the methylene carbon of the ethyl group to afford the (*Z*)-ethyleneselenochromenes (**3d**, **e**) in 91% and 90% yield, respectively. The stereochemistry of the olefin moiety of **3** was determined by nuclear Overhauser enhancement (NOE) measurement. The NOE was observed between the 4′-H and the aromatic 5-H in the 400-MHz ^{1}H-NMR spectra of **3d**. Thus the olefin moiety was determined to have (*Z*)-stereochemistry. A similar reaction of the 2-phenylselenopyrylium salt (**1f**) with sodium azide gave 4-azido-2-phenyl-4*H*-selenochromene (**4**) in 94% yield as the sole product; no 2-azido-2-phenyl-2*H*-selenochromene was produced.

Next, we examined the thermolysis of the 2-azidoselenochromenes obtained. Thermolysis of the 2-azido-2-*tert*-butylselenochromenes (**2a**, **b**) at 100 °C in refluxing dioxane resulted in a ring expansion with denitrogenation to give the desired stable 2-*tert*-butyl-1,3-benzoselenazepines (**5a**, **b**) in 65% and 69% yields, respectively. A plausible mechanism for the formation of **5** is outlined in Chart 2. Thermal decomposition of the azides (**6**) probably involves the assisted elimination of nitrogen to form azirine intermediates (**7**), which leads to the corresponding selenazepines (**5**). However, unsubstituted 1,3-benzoselenazepine, the ring-expanded prod-

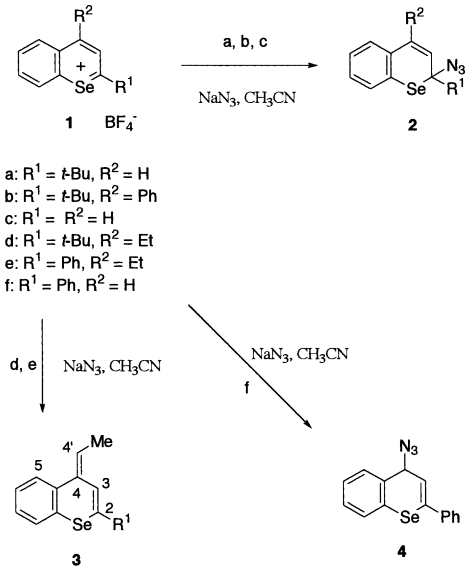

Chart 1

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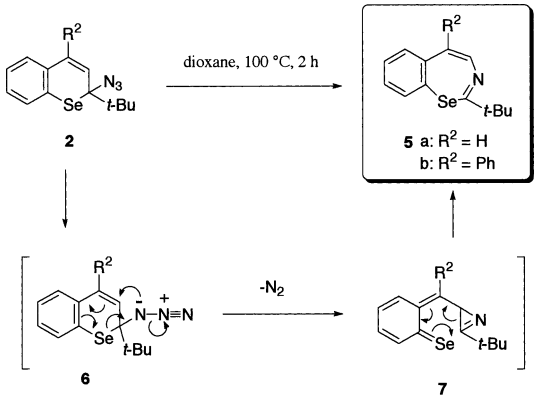

Chart 2

uct from (**2c**), could not be obtained. It is well known that thiepines,[28] thiazepines,[29] and selenepines[30] are thermally unstable due to the easy exclusion of sulfur or selenium, but the monocyclic[28—30] or benzene ring-fused[31,32] thiepines, selenepines, and tellurepines can be isolated when introducing a bulky substituent such as the *tert*-butyl group at the C-2 and/or C-7 position. The unsubstituted selenazepine could not be isolated, probably because of its thermal instability. The 1,3-benzoselenazepines (**5a**, **b**) can be stored below 0°C for several months. Photolysis of the 2-azidoselenochromenes (**2a**—**c**) in benzene resulted in decomposition to give a complex mixture. In addition, the thermal reaction of 4-azido-2-phenylselenochromene (**4**) under similar conditions decomposed without affording any products. Neither the azidotellurochromenes nor the benzotellurazepines could be obtained by the reaction of 1-benzoteluropyrylium salts with sodium azide under the conditions employed.

In conclusion, the first synthesis and isolation of the elusive 1,3-benzoselenazepines were achieved using the thermal ring expansion of 2-azidoselenochromenes prepared by the reaction of 1-benzoselenopyrylium salts with sodium azide.

Experimental

Melting points were measured on a Yanagimoto micro melting point hot-stage apparatus and are uncorrected. IR spectra were determined with a Hitachi 270-30 spectrometer. Mass spectra (MS) and high-resolution-MS were recorded on a JEOL JMS-DX300 instrument. NMR spectra were determined with a JEOL EX-90A (90 MHz) or JEOL JNM-GSX 400 (400 MHz) spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard. Microanalyses were performed in the Microanalytical Laboratory of this faculty.

Treatment of Selenopyrylium Salts (1) with NaN_3 To a suspended mixture of selenopyrylium salt (**1**, 2 mmol) in acetonitrile (40 ml) was added NaN_3 (520 mg, 8 mmol) all in one portion at 0 °C. The reaction mixture was stirred at room temperature for 30 min and poured into ice-water. The aqueous layer was extracted with dichloromethane (50 ml×3). The organic layer was washed with brine (50 ml×2), dried over magnesium sulfate, and evaporated. Products (**2a**—**c**, **4**) were obtained in a nearly pure form and decomposed during the attempted purification with silica gel chromatography. The compounds (**3d**, **e**) could be chromatographed on silica gel.

2-Azido-2-*tert*-butyl-2*H*-selenochromene (**2a**): Yield: 95%, mp 92—93 °C (from CH_2Cl_2–hexane). IR (KBr) ν 2108 cm^{-1}. ^{1}H-NMR (90 MHz) δ: 1.11 (9H, s, *t*-Bu), 5.65 (1H, d, J=10.9 Hz, 3-H), 6.81 (1H, d, J=10.9 Hz, 4-H), 7.06—7.45 (4H, m, Ph-H). EI-MS *m/z* (relative intensity): 293 (M^+, 5), 251 (100), 249 (50), 208 (23), 182 (62), 180 (31). EI-HR-MS *m/z* M^+ Calcd for $C_{13}H_{15}N_3{}^{80}Se$: 293.0432. Found 293.0432. *Anal.* Calcd for $C_{13}H_{15}N_3{}^{80}Se$: C, 53.43; H, 5.17; N, 14.38. Found: C, 53.27; H, 5.10; N, 14.39.

2-Azido-2-*tert*-butyl-4-phenyl-2*H*-selenochromene (**2b**): Yield: 85%, pale yellow oil. IR (neat) ν 2104 cm^{-1}. ^{1}H-NMR (90 MHz) δ: 1.16 (9H, s, *t*-Bu), 5.78 (1H, s, 3-H), 7.00—7.56 (9H, m, Ph-H). EI-MS *m/z* (relative intensity): 327 (M^+-42, 40), 325 (22), 259 (100), 178 (27). FAB-HR-MS *m/z* M^+-N_3 Calcd for $C_{19}H_{19}{}^{80}Se$: 327.0653. Found 327.0659.

2-Azido-2*H*-selenochromene (**2c**): Yield: 90%, yellow oil. IR (neat) ν 2100 cm^{-1}. ^{1}H-NMR (90 MHz) δ: 5.06 (1H, d, J=6.4 Hz, 2-H), 5.87 (1H, dd, J=6.4, 10.5 Hz, 3-H), 6.87 (1H, d, J=10.5 Hz, 4-H), 7.17—7.45 (4H, m, Ph-H). EI-MS *m/z* (relative intensity): 237 (M^+, 21), 195 (55), 182 (100), 180 (48). EI-HR-MS *m/z* M^+ Calcd for $C_9H_7N_3{}^{80}Se$: 236.9805. Found 236.9803.

(*E*)-2-*tert*-Butyl-4-ethylidene-4*H*-selenochromene (**3d**): Yield: 91%, yellow oil. ^{1}H-NMR (90 MHz) δ: 1.28 (9H, s, *t*-Bu), 1.81 (3H, d, J=7.0 Hz, 4′-Me), 5.87 (1H, q, J=7.0 Hz, 4′-H), 6.61 (1H, s, 3-H), 6.86—7.47 (4H, m, Ph-H). EI-MS *m/z* (relative intensity): 278 (M^+, 100), 276 (50), 225 (40), 223 (25). EI-HR-MS *m/z* M^+ Calcd for $C_{15}H_{18}{}^{80}Se$: 278.0574. Found 278.0574.

(*E*)-4-Ethylidene-2-phenyl-4*H*-selenochromene (**3e**): Yield: 90%, yellow oil. ^{1}H-NMR (90 MHz) δ: 1.87 (3H, d, J=7.0 Hz, 4′-Me), 6.03 (1H, q, J=7.0 Hz, 4′-H), 7.03 (1H, s, 3-H), 7.10—7.61 (9H, m, Ph-H). EI-MS *m/z* (relative intensity): 298 (M^+, 100), 271 (25), 269 (24), 217 (37), 215 (34). EI-HR-MS *m/z* M^+ Calcd for $C_{17}H_{14}{}^{80}Se$: 298.0261. Found 298.0258.

4-Azido-2-phenyl-4*H*-selenochromene (**4**): Yield: 94%, yellow oil. IR (neat) ν 2104 cm^{-1}. ^{1}H-NMR (90 MHz) δ: 5.19 (1H, d, J=6.0 Hz, 4-H), 6.51 (1H, d, J=6.0 Hz, 3-H), 7.23—7.56 (9H, m, Ph-H). EI-MS *m/z* (relative intensity): 313 (M^+, 3), 286 (21), 271 (100), 269 (65), 191 (80), 182 (38). EI-HR-MS *m/z* M^+ Calcd for $C_{15}H_{11}N_3{}^{80}Se$: 313.0119. Found 313.0081.

2-*tert*-Butyl-1,3-benzoselenazepine (5a) A solution of **2a** (293 mg, 1 mmol) in dioxane (10 ml) was heated at 100 °C with stirring under an argon atmosphere for 1 h. The solvent was evaporated and the resulting residue was purified by silica gel chromatography (*n*-hexane/CH_2Cl_2, 10/1) to give **5a**. Yield: 65%, pale yellow prisms, mp 45—48 °C (acetone–hexane). ^{1}H-NMR (400 MHz) δ: 1.17 (9H, s, *t*-Bu), 6.83 (1H, d, J=12.8 Hz, 5-H), 7.10 (1H, d, J=12.8 Hz, 4-H), Ph-H [7.23—7.33 (3H, m), 7.58 (1H, d, J=7.3 Hz)]. ^{13}C-NMR (100 MHz) δ: 28.82 (q), 41.77 (s), 128.78 (d), 129.05 (d), 129.79 (d), 132.42 (d), 133.05 (d), 135.73 (s), 139.66 (s), 141.09 (d), 187.87 (s). EI-MS *m/z* (relative intensity): 265 (M^+, 44), 263 (23), 182 (100), 180 (62). EI-HR-MS *m/z* M^+ Calcd for $C_{13}H_{15}N^{80}Se$: 265.0370. Found 265.0359.

2-*tert*-Butyl-5-phenyl-1,3-benzoselenazepine (5b) The title compound **5b** was prepared from **2b** in a similar manner to that described for **5a**. Yield: 69%, yellow oil. ^{1}H-NMR (400 MHz) δ: 1.22 (9H, s, *t*-Bu), 7.14 (1H, s, 4-H), Ph-H [7.01 (1H, d, J=7.7 Hz), 7.24—7.36 (7H, m), 7.75 (1H, d, J=7.7 Hz)]. ^{13}C-NMR (100 MHz) δ: 28.94 (q), 42.03 (s), 128.39 (d), 128.58 (d), 128.65 (d), 128.84 (d), 129.43 (d), 130.42 (d), 130.93 (d), 133.83 (d), 137.86 (s), 141.57 (s), 142.93 (s), 152.09 (s), 188.26 (s). EI-MS *m/z* (relative intensity): 341 (M^+, 19), 285 (10), 258 (100), 256 (54). EI-HR-MS *m/z* M^+ Calcd for $C_{19}H_{19}N^{80}Se$: 341.0684. Found 341.0677.

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References and Notes

1) This paper constitutes Part 23 in the "Studies on Tellurium-Containing Heterocycles," Part. 22; ref. 11.
2) Chimirri A., Gitto R., Grasso S., Monforte A. M., Zappala M., "Advances in Heterocyclic Chemistry: Annelated 1,5-Benzotiazepines," Vol. 63, ed. by Katritzky A. R., Academic Press, London, 1995, pp. 61—101.
3) Bohle M., Liebscher J., "Advances in Heterocyclic Chemistry: Ring Contraction of Heterocycles by Sulfur Extrusion," Vol. 65, ed. by Katritzky A. R., Academic Press, London, 1996, pp. 39—92.
4) Wunsch K.-H., Ehlers A., *Z. Chem.*, **10**, 361—370 (1970).
5) Murata I., *Phosphorus Sulfur Silicon Relat. Elem.*, **43**, 243—259 (1989).
6) Levai A., *J. Heterocyclic Chem.*, **37**, 199—214 (2000).
7) Le Roux J.-P., Desbene P.-L., Seguin, M., *Tetrahedron Lett.*, **36**, 3141—3144 (1976).
8) Desbene P.-L., Jehanno N., *J. Heterocycl. Chem.*, **21**, 1321—1327 (1984).
9) Ladatko A. A., Sadekov I. D., Minkin V. I., *Khim. Geterotsikl. Soedin.*, **1987**, 279 [*Chem. Abstr.*, **107**, 198270*p* (1987)].
10) Sashida H., *Heterocycles*, **48**, 631—634 (1998).
11) Sashida H., Satoh H., *Chem. Pharm. Bull.*, **52**, 413—417 (2004).
12) Sashida H., Ohyanagi K., *J. Chem. Soc. Perkin Trans. 1*, **1998**, 2123—2124 (1998).
13) Sashida H., Ohyanagi K., Minoura M., Akiba K.-Y., *J. Chem. Soc. Perkin Trans. 1*, **2002**, 606—612 (2002).

14) Sashida H., Ohyanagi K., *Chem. Pharm. Bull.*, **52**, 57—62 (2004).
15) Sashida H., Yoshida M., *Heterocycles*, **57**, 649—656 (2002).
16) Sashida H., Satoh H., Ohyanagi K., *Heterocycles*, **63**, 309—317 (2004).
17) Sashida H., Minamida H., *J. Chem. Soc. Perkin Trans. 1*, **1999**, 1665—1670 (1999).
18) Sashida H., Ohyanagi K., *Heterocycles*, **51**, 17—20 (1999).
19) Sashida H., Minamida H., *J. Chem. Res.* (*S*), **2000**, 569—571 (2000).
20) Sashida H., Minamida H., Yamamoto K., *J. Chem. Res.* (*S*), **2000**, 572—575 (2000).
21) Sashida H., Yoshida M., Minamida H., Teranishi M., *J. Heterocyclic Chem.*, **39**, 405—409 (2002).
22) Le Roux J.-P., Cherton J.-C., Desbene P.-L., *Compt. Rend. Ser. C*, **278**, 1389—1392 (1974).
23) Le Roux J.-P., Cherton J.-C., Desbene P.-L., *Compt. Rend. Ser. C*, **280**, 37—39 (1975).
24) Toda T., Takase T., Mukai T., Suzuki Y., *Heterocycles*, **11**, 331—336 (1978).
25) Suzuki Y., *Nippon Kagakukaishi*, **1980**, 604—608 (1980).
26) Le Roux J.-P., Cherton J.-C., Desbene P.-L., *J. Heterocyclic Chem.*, **18**, 847—849 (1981).
27) Desbene P.-L., Cherton J.-C., *Tetrahedron*, **40**, 3567—3577 (1984).
28) Nishio K., Yano S., Kohashi Y., Yamamoto K., Murata I., *J. Am. Chem. Soc.*, **101**, 5059—5060 (1979).
29) Yamamoto K., Yamazaki S., Osedo H., Murata I., *Angew. Chem. Int. Ed. Engl.*, **25**, 635—637 (1986).
30) Hori H., Yamazaki S., Yamamoto K., Murata I., *Angew. Chem. Int. Ed. Engl.*, **29**, 424—425 (1990).
31) Sashida H., Ito K., Tsuchiya T., *J. Chem. Soc. Chem. Commun.*, **1993**, 1493—1494 (1993).
32) Sashida H., Ito K., Tsuchiya T., *Chem. Pharm. Bull.*, **43**, 19—25 (1995).