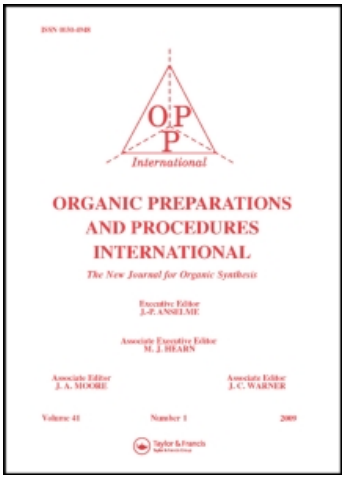

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SYNTHESIS OF 3-SELENA-7-AZABICYCLO[3.3.1]NONANES AND CERTAIN DERIVATIVES

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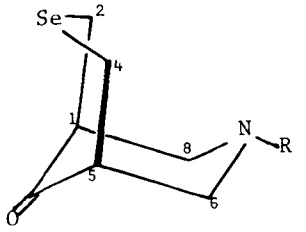
Intriguing aspects of the stereochemical ramifications[1,2] and anti-arrhythmic action[3,4] of 3,7-diheterabicyclo[3.3.1]nonanes have appeared recently in the literature. In view of the biological activity found with the sulfur derivatives,[4] we report herein the first examples of selenium analogues. Ketones 1 and 2 and selenanone (3)[5] were key synthons utilized for the preparation of 4-6, the title compounds. A conformational analysis



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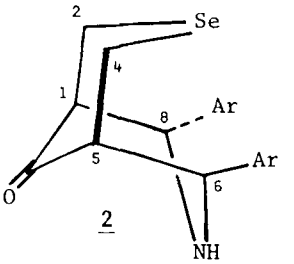

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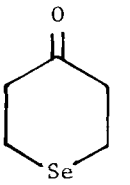

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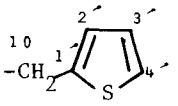
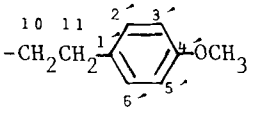
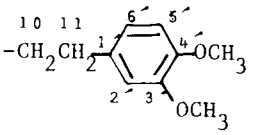
a. 

b. 

c. 

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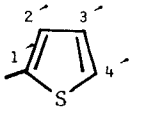
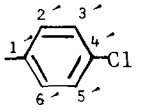
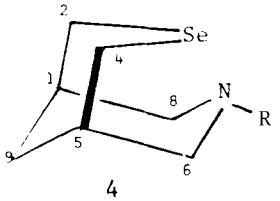
a. 

b. 

was performed on these systems in terms of the spectral data (IR, ^{1}H, ^{13}C, ^{15}N, and ^{77}Se NMR analysis) obtained. The basic overall conversion of ketone 3 to 1 and 2, which in turn were then converted to 4-6, involved a Mannich type condensation followed by a Wolff-Kishner reduction of the carbonyl groups. The corresponding amines were then treated with a 60%



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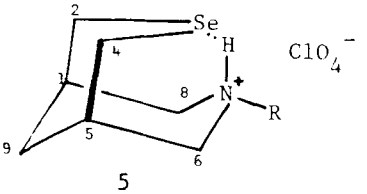

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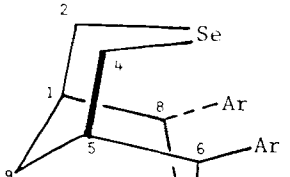

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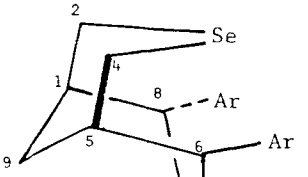

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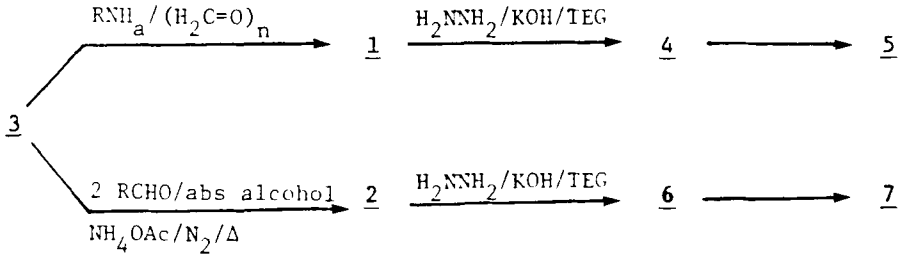
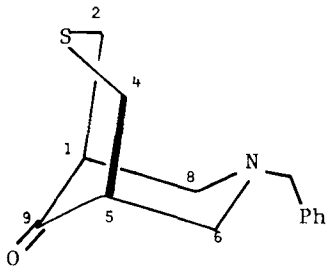
solution of perchloric acid to give salts 5 or 7 as shown in the scheme below. The salts proved easiest to purify in contrast to the ketones and amines which gave excellent spectral data but could not be freed of trace contaminants which led to slightly inferior elemental analyses. The reactions to form ketones 1 and 2 gave yields which ranged from modest to



very good but the mixtures were dark and apparently some competitive processes were in operation.[2,6] The yields of the amines were quite fine and conversions to the perchlorates were presumably quantitative.

Absorption for the C=O group in the infrared occurred in the range of 1710-1730 cm^{-1} for ketones 1a-c and 2a,b. The perchlorates displayed bands near 3400 cm^{-1} for the N-H stretch and a band near 1100 cm^{-1} for the perchlorate ion.[7] A band near 610 cm^{-1} appeared in the salts 5 and 7 and may be due to a C-Se stretch[8] but this is not confirmed.

All proton NMR spectra were quite complex due to high signal density in most regions. However, the ^{13}C NMR signals were informative and, except for the signals for carbon α to selenium, the ^{13}C chemical shifts were very similar to those found in the sulfur analogues.[1,4] The average shifts for C(2,4) in 1 and 5 were 24.9 and 29.1 ppm, respectively, while the sulfur counterparts 8 and 9 and relatives thereof[1] *averaged* 34.6 and 30.5 ppm, respectively. Thus the selenium appears to be less electronegative than sulfur and the alpha carbons are less deshielded. In view of the close



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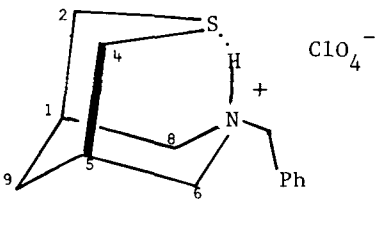

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similarity of chemical shifts of the ^{13}C resonances, we conclude that the chair-boat conformers for 1, 2, 6, and 7 are reasonable as are the chair-chair forms for 4 and 5.[9]

The use of ^{15}N and in particular ^{77}Se NMR resonances to identify the stereochemistry in 3,7-diheterabicyclo[3.3.1]nonanes is quite rare.[1-5,10] The presence of the thiophene ring causes an additional downfield shift for both the ^{15}N and ^{77}Se resonances in all systems. In the ketones, the ^{15}N signals ranged from 35.16 to 40.31 ppm in 1a-c and at 62.84 and 67.09 ppm

in 2a,b. In the salts, the range was from 48.03 to 58.54 ppm for 5a-c and at 62.39 and 57.67 ppm for 7a,b. For comparison, N-benzylpiperidone has a signal at 49.1 ppm [from $NH_3(\ell)$] while N-ethylpiperidine has a signal reported at 50.8 ppm.[11] The increased shielding for the ^{15}N signal in ketones 1a-c compared to the signal for N benzylpiperidone is likely due to the nitrogen atom being in a chair conformation in a biased system and with a γ-shielding effect operating via interaction with the axial C(1,2) and C(4,5) bonds.[11,12] The ^{15}N signals for ketones 2a,b is reminiscent of that found in the sulfur relatives.[4] The protonated amines 5 and 7 were expected to be considerably deshielded[4,11] although no model systems with a selenium atom were available in the literature.

The ^{77}Se shifts were novel and appeared [relative to $(H_3C)_2Se$] in the range of 77.00 to 86.28 ppm for ketones 1a-c. In sharp contast the signals for ketones 2a,b appeared at 30.60 and 26.67 ppm, respectively. This dramatic *upfield* shift must, in our opinion, surely arise from a γ-shielding effect from the C(1,8) and C(5,6) bonds and possibly from some influence from the aryl rings at C(6,8). Again there is no precedent in any selenium models. In salts 5 and 7 the results were even more striking. The chair-chair system 5a had a signal at 189.41 ppm while 5b and 5c had shifts near 88 ppm. In the bicyclic systems 7, 7a had a ^{77}Se signal at 5.11 ppm while 7b showed a signal at 2.25 ppm. This enormous *upfield* shift may be due to loss of H-bonding to the Se atom. Thus, the effect of C(1,8) and C(5,6) axial bonds cannot be fully assessed in terms of enhancement to the shift. This field is ripe for development.

EXPERIMENTAL SECTION

All reactions were performed under nitrogen and in a good hood. Residues from the reactions were destroyed by adding bleach. All effuents from the reactions were trapped via the use of alcoholic KOH. *CAUTION: GLOVES MUST BE WORN AT ALL TIMES IN HANDLING SELENIUM COMPOUNDS AND ALL SHOULD BE*

CONSIDERED POTENTIALLY TOXIC. No danger was encountered when the above technique was applied and no odors could be detected. All melting points were taken in a Thomas-Hoover apparatus and are uncorrected. IR spectra were gathered on a Perkin-Elmer 681 as KBr pellets or filsm. All ^{1}H, ^{15}N, and ^{77}Se spectra were recorded on a Varian XL-300 unit operating at 299.99, 30.41, and 57.22 MHz, respectively. All ^{13}C spectra were obtained on an XL-100(15) or an XL-300 unit at 25.20 or 75.4 MHz, respectively. Chemical shifts were measured in ppm downfield for ^{13}C (from TMS), for ^{15}N [from $NH_3(\ell)$ using $^{15}NH_4NO_3$ as an external reference], and for ^{77}Se [from $(H_3C)_2Se$ (0 ppm) using $(C_6H_5Se)_2$ (481.0 ppm) as the external, secondary reference]. Chemical shifts for ^{1}H were measured in δ values (from TMS). Elemental analyses were performed by Galbraith Labs, Knoxville, TN.

7-(2-Thiophene)methyl-3-selena-7-azabicyclo[3.3.1]nonan-9-one (**1a**).- To a solution of 2-aminomethylthiophene (1.39 g, 12.3 mmol) and of glacial acetic acid (1.10 g, 18.3 mmol) in methanol (60mL) was added paraformaldehyde (3.0 g, 100 mmol), and the resulting mixture was heated to reflux. Then ketone **3** (1.00 g, 6.13 mmol) was added and boiling was continued for 5 hrs. After the resulting red solution had been cooled to room temperature, the methanol was evaporated to a red oil. Partitioning the oil between water and ether (100 mL:30 mL) gave an ether portion which was discarded. The aqueous layer was made basic (NaOH, 1.5 g, 37.5 mmol) and the resultant yellow suspension was extracted (ether, 5 x 40 mL). The combined extracts were washed (H_2O, 2 x 30 mL) and dried (K_2CO_3). Evaporation gave a brown oil which was digested in boiling petroleum ether (bp 60-71°C) (3 x 100 mL). Evaporation gave ketone **1a** as a colorless viscous oil (1.72 g, 47%). IR (film): 1710 cm^{-1} (C=O); ^{1}H NMR ($DCCl_3$): δ 2.60-2.74 [m 4 H, H(2,4)], 3.02-3.18 [m, 4 H, H(1,5), H(6,8)ax], 3.27 [dd, 2 H, H(6,8)eq, J = 11.7 Hz, 3.4 Hz], 3.75 [s, 2 H, H(10)], 6.80-7.30 [m, 3 H, ArH]; ^{13}C NMR ($DCCl_3$): ppm 24.8 [C(2,4)], 46.0 [C(1,5)], 55.6 [C(10)], 58.5 [C(6,8)], 124.9 [C(4')], 125.5 [C(2')], 126.1 [C(3')], 141.4 [C(1')], 212.9 [C(9)]; ^{15}N NMR ($DCCl_3$): ppm 40.31 [N(7)]; ^{77}Se NMR ($DCCl_3$): ppm 86.28 [Se(3)]. Ketone **1a** proved

difficult to purify further and was converted to 5a.

7-p-Methoxyphenethyl-3-selena-7-azabicyclo[3.3.1]nonan-9-one (1b).- To a solution made of p-methoxyphenethylamine (0.93 g, 6.16 mmol) and glacial acetic acid (0.50 g, 8.33 mmol) in methanol (40 mL) was added paraformaldehyde (1.50 g, 50.0 mmol), and the resultant solution was heated to reflux. Ketone 3 (1.00 g, 6.13 mmol) was added in one portion and boiling was continued for 4 hrs. Evaporation of the methanol gave a red viscous oil which was dissolved in water (150 mL) and made basic by addition of KOH (85%, 1.0 g, 15.2 mmol). The resulting yellow suspension was extracted (ether, 5 x 40 mL) and the combined extracts were washed (H_2O, 30 mL) and dried (K_2CO_3). Evaporation of the ether gave 1b (0.72 g, 35%) as a light yellow oil. IR (neat) 1723 cm^{-1} (C=O); ^1H NMR ($DCCl_3$): δ 2.50-2.80 [m, 8 H, H(1,2,4,5,11)], 2.96-3.14 [m, 6 H, H(6,8,10)], 3.71 [s, 3 H, OCH_3], 6.72-6.90 [m, 2 H, H(3', 5')], 7.00-716 [m, 2 H, H(2', 6')]; ^{13}C NMR ($DCCl_3$): ppm 24.6 [C(2,4)], 32.0 [C(11)], 45.4 [C(1,5)], 54.2 [C(OCH_3)], 57.8 [C(10)], 58.2 [C(6,8)], 112.8 [C(3', 5')], 128.5 [C(2', 6')], 130.9 [C(1')], 156.9 [C(4')], 212.5 [C(9)]; ^{15}N NMR ($DCCl_3$): ppm 35.43 [N(7)]; ^{77}Se ($DCCl_3$): ppm 78.81 [Se(3)]. Ketone 1b proved very difficult to purify to a satisfactory elemental analysis and was converted to 5b.

7-(3,4-Dimethoxy)phenethyl-3-selena-7-azabicyclo[3.3.1]nonan-9-one (1c).- To a solution of 3,4-dimethyoxyphenethylamine (2.23 g, 12.3 mmol) and glacial acetic acid (1.0 g, 16.6 mmol) in methanol (60 mL) was added paraformaldehyde (3.0 g, 100 mmol), and the resulting solution was heated to a boil Ketone 3 (2.00 g, 12.3 mmol) was added and boiling was continued for 4 hrs. The resultant brown solution was evaporated to a brown oil which was added to water (150 mL). The mixture was extracted (ether, 4 x 50 mL) and the combined extracts were washed (H_2O, 30 mL) and dried (K_2CO_3). Evaporation gave a dark brown oil which, after digestion with petroleum ether (bp 60-71°C) and followed by evaporation, gave 1c as a pale yellow

oil (1.4 g, 31%), IR (film) 1730 cm^{-1} (C=O); ^{1}H NMR ($DCCl_3$): δ 2.60-2.80 [m, 8 H, H(1,2,4,5,11)], 3.00-3.20 [m, 6 H, H(6,8,10)], 3.80 [s, 3 H, OCH_3)], 3.84 [s, 3 H, OCH_3)], 7.70-7.90 [m, 3 H, ArH)]; ^{13}C NMR ($DCCl_3$): ppm 25.4 [C(2,4)], 33.2 [C(11)], 46.2 [C(1,5)], 55.7 [both OCH_3], 58.6 [C(10)], 59.1 [C(6,8)], 111.3, 112.0, 120.5, 132.8 [C(1')], 141.2, 148.7, 213.8 [C(9)]; ^{14}N NMR ($DCCl_3$) ppm 35.16 [N(7)]; ^{77}Se NMR ($DCCl_3$): ppm 77.00 [Se(3)]. Since **1c** proved very difficult to purify for a satisfactory analysis, it was converted to **5c**. Attempts to distill **1c** gave decomposition.

6,8-Di(2,-thiophene)-3-selena-7-azabicyclo[3.3.1]nonan-9-one (**2a**).- To a solution of 2-thiophenecarboxaldehyde (1.38 g, 12.3 mmol) and dry ammonium acetate (0.094 g, 12.3 mmol) in absolute alcohol (20 mL) heated to boiling was added freshly sublimed ketone **3** (1.00 g, 6.13 mmol) in absolute alcohol (15 mL). Boiling was continued for 10 min with ethanol being added to maintain volume. The colorless solution turned yellow and the flask was stoppered and allowed to cool and stand for 3 days. A yellow solid formed and was filtered from the dark red solution. The solid was dissolved in benzene (100 mL) and the solution was treated with decolorizing charcoal. Filtration followed by evaporation gave a light brown solid which was recrystallized (methanol) to give 0.40 g (18%) of ketone **2a** as a light yellow solid. Mp 155-161°C (dec); IR (KBr) 3260 cm^{-1} (N-H), 1723 (C=O); ^{1}H NMR δ 2.16 [b s, 1 H, H(7)], 2.80 [m 4 H, H(1,5) and H(2,4) ax], 3.57 [d, 2 H, H(2,4)eq, J = 10.0 Hz], 5.32 [d, 2 H, H(6,8), J = 4.0 Hz], 6.90-7.40 [m, 6 H, ArH]; ^{13}C NMR ($DCCl_3$): ppm 29.3 [C(2,4)], 54.6 [C(1,5)], 59.1 [C(6.8)], 123.7, 124.8, 126.3 [C(2', 3', 4')], 147.0 [C (1')], 212.5 [C(9); ^{15}N NMR ($DCCl_3$): ppm 67.09 [N(7)]; ^{77}Se NMR ($DCCl_3$): ppm 30.60 [Se(3)]. Again **1c** proved difficult to gain a satisfactory elemental analysis and was converted directly to amine **6a**.

6,8-Di(4-chlorophenyl)-3-selena-7-azabicyclo[3.3.1]nonan-9-one (2b).- To a solution of ammonium acetate (0.94 g, 12.3 mmol) and p-chlorobenzaldehyde (1.73 g, 12.3 mmol) in absolute alcohol (20 mL) heated to boiling was added freshly sublimed ketone 3 (1.00 g, 6.13 mmol) in absolute alcohol (15 mL). The new solution was boiled for 10 min with alcohol being added to keep a constant volume (the solution turned yellow). The solution was stoppered and allowed to stand for 3 days at room temp (the solution turned reddish-brown and a yellow solid formed). The liquid was decanted the solid was dissolved in bezene (100 mL). The final solution was treated with decolorizing charcoal and filtered. Evaporation of the benzene gave a light brown solid which was recrystallized (absolute ethanol) to give 2b as a light tan solid (0.33 g, 13%). Mp 219-220°C (dec); IR (KBr) 3280 cm^{-1} (N-H), 1722 (C=0); ^{1}H NMR ($DCCl_3$): δ 1.70 [b s, 1 H, H(7)], 2.69 [m, 4 H, H(1,5) and H(2,4)ax], 3.56 (d, 2 H, H(2,4)eq, J = 10.2 Hz)], 4.99 [d, 2 H, H(6,8), J = 4.1 Hz], 7.30-7.40 [M, 8 H, ArH]; ^{13}C NMR ($DCCl_3$): ppm 29.0 [C(2,4)], 53.9 [C(1,5)], 63.4 [C(6,8)], 128.2 [C(2', 6') or C(3'5')], 128.8 [C(3', 5') or C(2', 6')], 133.7 [C(4')], 142.5 [C(1')], 213.4 [C(9)]; ^{15}N NMR ($DCCl_3$): ppm 62.84 [N(7)]; ^{77}Se NMR ($DCCl_3$): ppm 26.67 [Se(3)]. Ketone 2b proved exceedingly difficult to obtain in pure form to give a satisfactory elemental analysis and was converted to 6b.

7-(2-Thiophene)methyl-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (5a).- Ketone 1a (1.0 g, 3.33 mmol) and anhydrous hydrazine (95%, 2.0 g, 5.94 mmol) were dissolved in triethylene glycol (TEG, 40 mL) in a jacketed flask equipped for distillation. Pellet KOH (85%, 3.0 g, 45.5 mmol) was added all at once and the resulting mixture was stirred and heated (140-145°C) by boiling xylene in the jacket of the flask. After 4 hrs, the reaction mixture was cooled to room temp and poured into cool water (150 mL). The resulting suspension was extracted (ether, 5 x 40 mL) and the

combined extracts were dried (K_2CO_3). This solution of 4a was filtered and 60% $HClO_4$ (1.0 g, 6.0 mmol) was added dropwise and slowly caused an orange solid to precipitate. The filtered solid was recrystallized (isopropyl alcohol, decolorizing charcoal) twice to give 5a, (0.88 g, 68%) as white needles. Mp 141.0-141.5°C; ^{1}H NMR (DMSO-d_6) δ 1.74 [d, 1 H, H(9), J = 13.6 Hz], 1.86 [d, 1 H, H(9), J = 13.6 Hz], 2.43 [b s, 2 H, H(1,5)], 2.64 [d, 2 H, H(2,4)ax, J = 12.0 Hz], 3.19 [d, 2 H, H(2,4)eq, J = 11.3 Hz], 3.35 [m, 2 H, H(6,8)ax], 3.62 d, 2 H, H(6,8)eq, J = 12.7 Hz], 4.53 [d, 2 H, H(10), J = 5.3 Hz], 7.17 [dd, 1 H, H(3'), J = 5.1 Hz, 3.7 Hz], 7.36 [d, 1 H, H(2'), J = 3.3 Hz], 7.75 [d, 1 H, H(4'), J = 5.1 Hz], 9.24 [b s, 1 H, H(7)]; ^{13}C NMR (DMSO-d_6) ppm 21.9 [t, C(2,4)], 25.3 [d, C(1,5)], 28.6 [C(9)], 54.9 [t, C(10)], 56.1 [t, C(6,8)], 127.2 [d, C(4')], 129.3 [d, C(2')], 130.5 [s, C(1')], 131.8 [C(3')]; ^{15}N NMR (DMSO-d_6) ppm 58.54 [N (7)]; ^{77}Se NMR (DMSO-d_6) ppm 189.41 [se(3)].

Anal. Calcd: for $C_{12}H_{18}ClNO_4Se$: C, 37.27; H, 4.69; N, 3.62; Se, 20.42.
Found: C, 37.20; H, 4.76; N, 3.60; Se, 20.10.

7-p-Methoxyphenethyl-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (5b).- The same equipment as in 5a was used and was charged with ketone 1b (0.65 g, 1.92 mmol), hydrazine (95%, 1.00 g, 29.7 mmol) and KOH (85%, 3.0 g, 45.5 mmol) in TEG (25 mL). The suspension was stirred at 140-145°C (boiling xylene in the jacket of the flask) for 3 hrs during which a small amount of H_2O and excess hydrazine distilled from the system. After cooling to room temp, the reaction mixture was diluted (H_2O, 100 mL) and then extracted (ether, 5 x 40 mL). The combined extracts were dried (K_2CO_3) overnight and were then treated slowly with 60% perchloric acid (0.5 g, 3.0 mmol). An orange precipitate formed and was filtered and recrystallized (abs ethanol) with the aid of decolorizing charcoal to give 5b as white needles (0.58 g, 71%). Mp 208.5-209.0°C: ^{1}H NMR (DMSO-

d_6) δ 1.73 [b s, 1 H, H(9), J = 14 Hz], 1.90 [b d, 1 H, H(9), J = 14 Hz] 2.42 [b s 2 H, H(1,5)] 2.65 [d, 2 H, H(2,4)ax, J = 12 Hz], 3.02 [t, 2 H, H(11), J = 7 Hz], 3.22 [d, 2 H, H(2,4)eq, J = 12 Hz], 3.30 [m, 2 H, H(10)], 3.36 [d, 2 H, H(6,8), J = 12 Hz], 3.76 [s, 3 H, OCH_3], 3.86 [d, 2 H, H(6,8)eq, J = 12 Hz], 6.97 [d, 2 H, H(3', 5'), J = 9 Hz], 7.32 [d, 2 H, H(2', 6'), J = 9 Hz], 8.92 [b s, 1 H, H(7)]; ^{13}C NMR (DMSO-d_6) ppm 21.9 [5, C(2,4)], 25.3 [d, C(1,5)], 28.5 [t, C(9) or C(11)], 28.9 [t, C(11) or C(9)], 55.0 [q, OCH_3], 56.7 [t, C(6,8)], 58.9 [C(t, C(10)], 114.0 [C(3', 5')], 127.7 [s, C(1')], 129.6 [d, C(2', 6')], 158.1 [s, C(4')]; ^{15}N NMR (DMSO-d_6) ppm 48.10 [N(7)]; ^{77}Se (DMSO-d_6) ppm 88.64 [Se(3)].

Anal. Calcd. for $C_{16}H_{24}ClNO_4Se$: C, 45.24; H, 5.69; N, 3.30; Se, 18.59.
Found: C, 45.42; H, 5.80; N, 3.30; Se, 18.46.

7-(3,4-Dimethoxy)phenethyl-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (5c).- In the same equipment as described for 1a and 1b, ketone 3 (1.10 g, 3.00 mmol), hydrazine (95%, 2.00 g, 5.94 mmol), and KOH (85%, 3.0 g, 45.5 mmol) were dissolved in TEG (40 mL). After 4 hrs of stirring at 140-145°C, the brown reaction mixture was cooled and poured into cool water (150 mL). The suspension was extracted (ether, 4 x 50 mL) and the extracts were dried (K_2CO_3). Perchloric acid (60%, 1.0 g, 6.0 mmol) was added very slowly and a white precipitate formed at once but rapidly turned orange. The solid was filtered off and recrystallized twice (abs ethanol, decolorizing charcoal) to give 5c as a white crystalline solid (0.92 g, 68%). Mp 162-163°C; ^1H NMR (DMSO-d_6) δ 1.74 [d, 1 H, H(9), J = 13 Hz], 1.92 [d, 1 H, H(9), J = 13 Hz], 2.42 [b s, 2 H, H(1,5)], 2.65 [d, 2 H, H(2,4)ax, J = 12 Hz], 3.02 [5, 2 H, H(11)], 3.22 [d, 2 H, H(2,4)eq, J = 12 Hz], 3.36 [m 4 H, H(10) and H(6,8) ax],

3.76 [s, 3 H, OC$\underline{H}_3$], 3.80 [s, 3 H, OC$\underline{H}_3$], 3.87 [d, 2 H, H(6,8)eq, J = 12 Hz], 6.88-7.02 [m, 3 H, Ar$\underline{H}$], 8.88 [b s, 1 H, H(7)]; ^{13}C NMR (DMSO-$\underline{d}_6$) ppm 22.0 [C(2,4)], 25.3 [C(1,4)], 28.5 [C(11) or C(9)], 29.4 [C(9) or C(11)], 55.4 [O$\underline{C}H_3$], 55.5 [O$\underline{C}H_3$], 56.7 [C(6,8)], 58.9 [C(10)], 112.0, 112.3, 120.6, 128.3 [C(1')], 147.7 [C(3)] or C(4')], 148.8 [C(3') or C(4')]; ^{15}N NMR (DMSO-$\underline{d}_6$) ppm 48.03 [N(7)]; ^{77}Se (DMSO-$\underline{d}_6$) ppm 88.35 [Se(3)].

Anal. Calcd. for $C_{17}H_{26}ClNO_6Se$: C, 44.90; H, 5.76; N, 3.08.
Found: C, 44.86; H, 5.86; N, 3.04.

6,8-Di(2-thiophene)-3-selena-7-azabicyclo[3.3.1]nonane (**6a**).- Ketone 2a (1.00 g, 2.71 mmol) and hydrazine (95%, 1.0 g, 30 mmol) were dissolved in TEG and placed in the jacketed flask as described previously. By boiling H_2O in the jacket, the reaction mixture was heated to a temp of 100°C for 2 hrs. At this time, KOH (85%, 2.0 g, 30 mmol) was added all at once and the water was replaced by xylene in the jacket. Stirring was initiated and heating at 140-145°C was continued for 5 hrs. After cooling to room temp, the mixture was poured into ice-cold H_2O (200 mL) and a precipitate formed. The mixture was allowed to stand overnight and was then filtered. The solid filtrate was taken up in boiling benzene and treated with charcoal. Evaporation of the benzene gave a residue which was recrystallized (95% ethanol) to give 6a as a light tan solid (0.64 g, 76%). Mp 183-136°C (dec); IR (KBr) 3270 cm^{-1} (N-H); ^{1}H NMR ($DCCl_3$): δ 1.28 [d, 1 H, H(9), J = 13 Hz], 1.78 [b s, 1 H, H(7)], 2.18 [b s, 2 H, H(1,5)], 2.32 [d, 2 H, H(2,4)ax, J = 12 Hz], 2.50 [m, 1 H, H(9)], 3.20 [dd, 2 H, H(2,4) eq, J = 12 Hz, 2 Hz], 4.79 [d, 2 H, H(6,8), J = 4 Hz], 6.96 [dd, 2 H, Ar$\underline{H}$], 7.01 [d,

2 H, ArH], 7.21 [d, 2 H, ArH]; ^{13}C NMR ($DCCl_3$): ppm 25.0 [C(2,4)], 25.8 [C(9)], 34.6 [C(1,4)], 57.1 [C(6,8)], 122.2 [C(4')], 122.6 [C(2')], 126.1 [C(3')], 150.7 [C(1')]: ^{15}N NMR ($DCCl_3$): ppm 60.10 [N(7)]; ^{77}Se NMR ($DCCl_3$): ppm 4.05 [Se(3)]. Amine **6a** proved difficult to purify to the extent a satisfactory elemental analysis could be obtained and it was converted directly to **7a**.

6,8-Di(4-chlorophenyl)-3-selena-7-azabicyclo[3.3.1]nonane (**6b**).- Ketone **2b** (2.00 g, 4.71 mmol), hydrazine (95%, 2.0 g, 60 mmol), and TEG were placed in a system with a jacketed flask as described earlier. Water was boiled in the jacket of the flask for 3 hrs and the contents were stirred. Pellet KOH (85%, 5.0 g, 76 mmol) was added at once and xylene replaced the water in the jacket. After 4 hrs at 140-145°C, the resulting mixture was cooled to 60-70°C and poured into water (100 mL) and a cream-colored solid formed. The solid was filtered, washed (H_2O, 200 mL), and recrystallized twice (abs alcohol and decolorizing charcoal) to give **6b** as a light tan solid (0.91 g, 47%). Mp 179-180°C (dec); IR (KBr) 3260 cm^{-1} (N-H); ^1H NMR ($DCCl_3$): δ 1.30 [d, 1 H, H(9), J = 12 Hz], 1.74 [b s, 1 H, H(7)], 2.04 [b s, 2 H, H(1,5)], 2.28 [b d, 2 H, H(2,4)ax, J = 12 Hz], 2.48 [m, 1 H, H(9)], 3.17 [dd, 2 H, H(2,4)eq, J = 12 Hz, 4 Hz], 4.43 [d, 2 H, H(6,8), J = 5 Hz], 7.26-7.50 [m, 8 H, ArH]; ^{13}C NMR ($DCCl_3$): ppm 25.1 [C(2,4)], 26.9 [C(9)], 33.8 [C(1,5)], 60.9 [C(6,8)], 127.9, 128.6, 132.6 [C(4')], 145.7 [C(1')]; ^{15}N NMR ($DCCl_3$): ppm 55.37 [N(7)]; ^{77}Se NMR ($DCCl_3$): ppm -0.79 [Se(3)]. This amine proved difficult to obtain a sample to give satisfactory elemental analysis and was converted to salt **7b**.

6,8-Di(2-thiophene)-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (**7a**).- To a solution of **6a** (0.5 g, 1.4 mmol) in benzene (200 mL) and isopropyl alcohol (10 mL) was added dropwise 60% $HClO_4$ (0.5 g, 3.0 mmol) which caused a white precipitate to form. The solid turned light yellow

quickly and was then filtered. Two recrystallizations (isopropyl alcohol, decolorizing charcoal) gave **7a** as white needles (0.4 g, 63%). Mp 285°C (dec); ^{1}H NMR (DMSO-d_6) δ 1.78 [d, 1 H, H(9), J = 14 Hz], 2.36 [d, 2 H, H(3,4)ax, J = 14 Hz], 2.44 [m, 1 H, H(9)], 2.66 [b s, 2 H, H(1,5)], 3.19 [dd, 2 H, H(2,4)eq, J = 12 Hz, 3 Hz], 5.07 [m, 2 H, H(6,8)], 7.16 [dd, 2 H, H(3')], 7.43 [3, 2 H, H(2')], 7.69 [dd, 2 H, H(4')], 9.36 [b s, 1 H, H(7)], 9.61 [b s, 1 H, H(7)]; ^{13}C NMR (DMSO-d_6) ppm 23.5 [C(2,4)], 26.2 [C(9)], 32.5 [C(1,4)], 56.1 [C(6,8)], 127.3 [C(2')] or C(4')], 127.6 [C(4') or C(2')], 129.2 [C(3')], 138.9 [C(1')]; ^{15}N NMR (DMSO-d_6) ppm 62.39 [N(7)]; ^{77}Se NMR (DMSO-d_6) ppm 5.11 [Se(3)].

Anal. Calcd. for $C_{15}H_{18}ClNO_4S_2Se$: C, 39.61; H, 3.99; N, 3.08; S, 14.10 Se, 17.36.

Found: C, 39.81; H, 3.97; N, 3.10; Se, 14.35; Se, 17.18.

6,8-Di(2-chlorophenyl)-3-selena-7-azabicyclo[3.3.1]nonane Hydroperchlorate (**7b**).- Amine **6b** (1.00 g, 2.43 mmol) was dissolved in ether (200 mL) and $HClO_4$ (60%, 1.0 g, 6.0 mmol) was added slowly with vigorous swirling. The mixture was allowed to stand for 24 hrs with occasional swirling. A yellow-orange solid formed and was filtered and recrystallized twice (abs alcohol, decolorizing charcoal) to give **7b** as a white powder (0.46 g, 37%). Mp 272-274°C (dec); ^{1}H NMR (DMSO-d_6) δ 1.77 [d, 1 H, H(9), J = 12 Hz], 2.36 [d, 2 H, H(2,4)ax, J = 10.8 Hz], 2.53 [m, 2 H, H(1,5)], 3.14 [d, 2 H, H(2,4)eq, J = 10.5 Hz], 3.38 [b s, 1 H, H(9)], 4.76 [b s, 2 H, H(6,8)], 7.50-7.75 [m, 8 H, ArH], 8.77 [b s, 1 H, H(7)], 9.59 [b s, 1 H, H(7)]; ^{13}C NMR (DMSO-d_6) ppm 23.5 [C(2,4)], 26.5 [C(9)], 31.1 [C(1,5)], 60.6 [C(6,8)], 128.5, 130.9, 133.8 [C(4')], 136.1 [C(1')]; ^{15}N NMR (DMSO-d_6) ppm 57.67 [N(7)]; ^{77}Se (DMSO-d_6) ppm 2.25 [Se(3)].

Anal. Calcd. for $C_{19}H_{20}Cl_3NO_4Se$: C, 44.60; H, 3.94; N, 2.47.

Found: C, 44.53; H, 3.84; N, 2.74.

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