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CONVERSION OF OLEFINS INTO FIVE-MEMBERED NITROGEN HETEROCYCLES BY RADICAL CYCLIZATION

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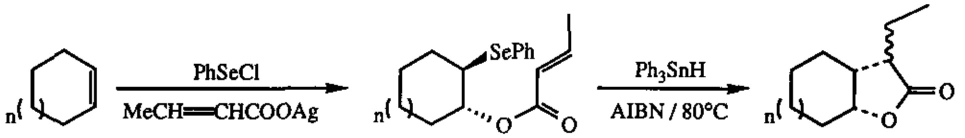
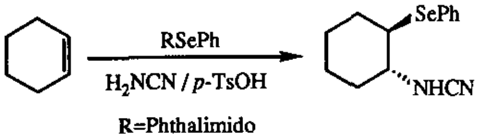
This paper is dedicated to Professor Sir Derek Barton, F.R.S. on the occasion of his seventieth birthday.

Abstract — 2-(Phenylseleno)alkyl cyanamides, available in one step from olefins, according to a known procedure, are easily alkylated on nitrogen by allylic and propargylic halides. The products undergo radical cyclization in the presence of a stannane to produce five-membered nitrogen heterocycles by an *exo trigonal* or exo *digonal* pathway. The method can be used to make spiro heterocycles and bicyclic compounds with *cis* ring-fusion geometry.

Nitrogen heterocycles are a large and significant class of organic compounds and there is, therefore, sustained interest in the development of new preparative methods for this area. We report here a procedure for converting olefins into five-membered nitrogen heterocycles and we have illustrated the method by preparing several octahydroindoles and one azaspirodecane. The approach is an extension of our earlier method for the preparation of γ-lactones.[1] That process involves ionic addition of a benzeneseleno group and an α,β-unsaturated carboxylate unit to the termini of a double bond followed by radical cyclization (see equation 1) in the presence of a stannane. The cyclization is under the influence of stereoelectronic control and occurs by the *exo* pathway. In order to use this approach for the preparation of nitrogen heterocycles[2,3] a method is required to convert olefins into β-aza selenides[4,5] and this has recently become possible, in an appropriate manner, through the finding[4] that *N*-(phenylseleno)phthalimide reacts with olefins in the



Eq. 1

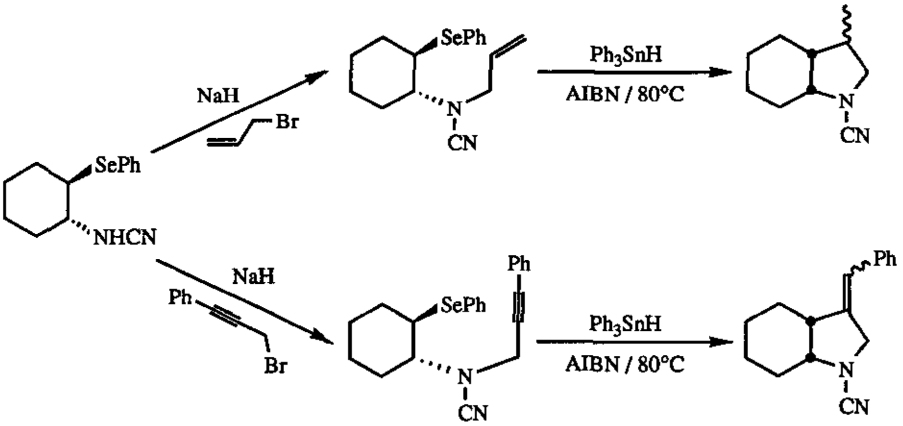


Eq. 2

presence of cyanamide according to the stoichiometry of equation 2. The resulting 2-(phenylseleno)alkyl cyanamides are ideally suited for attachment of an unsaturated alkyl chain on the amino nitrogen and, in practice, this was readily achieved by deprotonation and alkylation with an allylic or propargylic bromide (Scheme 1 and Table 1). In this way the disubstituted cyanamides shown in Table 1 were readily assembled.

The initial addition of the benzeneseleno group and the nitrogen function across the double bond is sometimes highly regioselective with unsymmetrical olefins, but this was not the case with methylenecyclohexane. In all of our examples the alkylation step worked smoothly, and, for the radical cyclization, we used our usual technique[6] of adding dilute benzene solutions of triphenyltin hydride and AIBN to a refluxing solution of the substrate in the same solvent. It is known that methodology based on stannane reductions is not usually compatible with the presence of free N-H bonds.[7] This problem does not arise in the present method because an inherent feature is that the cyano group serves not only to facilitate attachment of the unsaturated chain but also to protect the nitrogen during subsequent operations. A variety of methods is then available for deprotection.[8] As expected,[9] all of the bicyclic compounds are produced with *cis* ring-fusion. The yields in all steps of the sequence are generally good and we encountered a problem only with compound **14**. Attempts to carry out the radical cyclization with this material were not successful. We did obtain some spectroscopic evidence (^{1}H nmr) for production of the desired azaspirodecane **15** but, surprisingly, we were unable to obtain the compound pure.

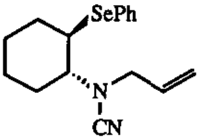
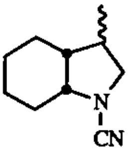
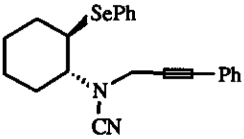
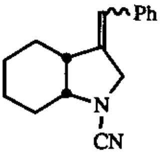
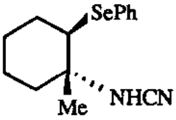
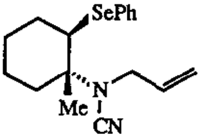
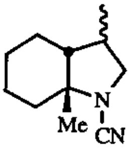
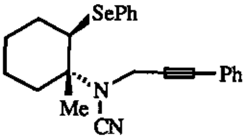
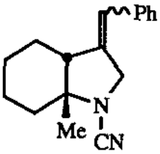
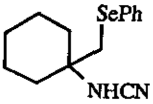
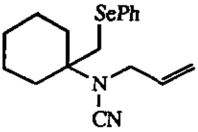
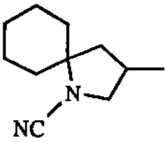
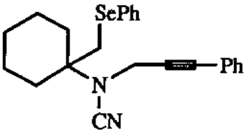
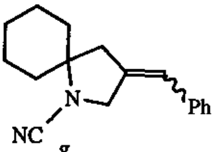
Scheme 1



EXPERIMENTAL

Unless otherwise stated, the following particulars apply. Experiments were carried out under argon purified by passage through a column (35 x 42 cm) of R 311 catalyst (Chemical Dynamics Corp., South Plainfield, NJ) and then dried through a similar column of Drierite. Glassware was dried in an oven for at least 2 h (115°C), cooled in a desiccator, assembled quickly and sealed with rubber septa (where applicable). Inlet and exit needles were passed through the septa on the apparatus and argon was

Table 1[a]

Starting material	Alkylation Product	Cyclization Product
 1[b] (80%)	 2 (91%)	 3[c] (97%)
	 4 (85%)	 5[c] (87%)
 6[d] (82%)	 7 (93%)	 8[c] (95%)
	 9 (74%)	 10[c] (85%)
 11[e] (67%)	 12 (79%)	 13 (66%)
	 14[f] (61%)	 15[g]

Footnotes to Table 1

[a] Yields refer to pure isolated compounds. [b] From cyclohexene. [c] Two isomers. [d] From 1-methylcyclohexene. [e] From methylenecyclohexane. Compound **11** was formed together with the isomer [[1-(phenylseleno)cyclohexyl]methyl]cyanamide **11'**. Yield refers to mixture of **11** and **11'**. [**11**:**11'**::92:8]. [f] Yield based on amount of **11** in starting mixture of **11** and **11'**. [g] We were unable to obtain this compound pure.

purged through the system. The exit needle was removed after a few minutes and the apparatus was kept under a slight static pressure of argon. Solvents were distilled for chromatography. Dry tetrahydrofuran was distilled from sodium-benzophenone ketyl; benzene was distilled from sodium; dichloromethane and hexane were distilled from calcium hydride. Azobisisobutyronitrile (AIBN, Eastman) was stored at 0°C and used without further purification. Products were isolated from solution by concentration under water pump vacuum at *ca.* 30°C using a rotatory evaporator. Commercial silica (Merck 60F-254) thin layer chromatography plates were used. Silica gel for flash chromatography was Merck type 60 (230-400 mesh). Combustion analyses were performed in the microanalytical laboratories of the University of Alberta. Infrared spectra were recorded on a Perkin-Elmer 297 spectrophotometer or a Nicolet 7000 FT-IR instrument. Nmr spectra were recorded on a Bruker WH-300 instrument. The following abbreviations are used in the text: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Mass spectra were recorded on an A.E.I. MS 50 mass spectrometer at an ionizing potential of 70 eV.

***Trans*-[2-(Phenylseleno)cyclohexyl]cyanamide 1**[4]

N-(Phenylseleno)phthalimide (1.741 g, 5.77 mmol) in dry dichloromethane (5 ml) was added over 1 h in the dark to a magnetically stirred solution of cyclohexene (0.364 g, 4.43 mmol), freshly distilled [80°C, oil pump vacuum] cyanamide, (3.725 g, 51 mmol) and anhydrous *p*-toluenesulphonic acid[10] (0.763 g, 4.43 mmol) in dry dichloromethane (60 ml). Stirring at room temp was continued for 24 h and the mixture was then filtered and evaporated. Chromatography of the residue over silica gel (5 x 15 cm) using 5:1 hexane-ethyl acetate yielded **1** (0.992 g, 80%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-ir ($CHCl_3$, cast) 3207, 3072, 3052, 2939, 2856, 2218, 1477, 1447, 1437, 1022, 742, 691 cm^{-1}; ^1H nmr ($CDCl_3$, 300 MHz) δ 1.13-1.53 (m, 4 H), 1.55-1.70 (m, 1 H), 1.71-1.82 (m, 1 H), 2.11-2.28 (m, 2 H), 2.78-2.96 (m, 2 H), 4.87 (broad s, 1 H), 7.21-7.38 (m, 3 H) 7.52-7.68 (m, 2 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 24.04, 26.29, 31.63, 33.41, 48.54, 57.08, 114.59, 125.90, 128.42, 129.12, 136.08; exact mass, m/z calcd for $C_{13}H_{16}N_2Se$ 280.0479, found 280.0478.

***Trans*-[2-(Phenylseleno)cyclohexyl](2-propenyl)cyanamide 2**

Trans-[2-(Phenylseleno)cyclohexyl]cyanamide **1** (0.356 g, 1.27 mmol) in dry THF (1 ml) and 3-bromo-1-propene (0.192 g, 1.59 mmol) in THF (1 ml) were injected into a stirred suspension of sodium hydride (0.056 g, 60% in oil, 1.71 mmol) in THF (10 ml). Stirring at room temperature was continued overnight and the solvent was then evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) using 9:1 hexane-ethyl acetate and Kugelrohr distillation (90°C, 0.005 mm) of appropriate fractions gave **2** (0.372 g, 91%) as a homogeneous (TLC, silica, 9:1 hexane-ethyl acetate), slightly yellowish oil: FT-ir ($CHCl_3$, cast) 3062, 3042, 2954, 2843, 2204, 1476, 1443, 1437, 738, 689 cm^{-1}; ^1H nmr ($CDCl_3$, 300 MHz) δ 1.11-1.35 (m, 2 H), 1.41-1.66 (m, 3 H), 1.77-1.87 (m, 1 H), 2.00-2.20 (m, 2 H), 2.75 (dt, J = 4.25, 11.25 Hz, 1 H), 3.24 (dt, J = 4.25, 11.25 Hz, 1 H), 3.70 (d, J = 6.5 Hz, 2 H), 5.27-5.38 (m, 2 H), 5.86 (dddd, J = 6.5, 6.5, 10.0, 17.0 Hz, 1 H), 7.21-7.37 (m, 3 H), 7.55-7.66 (m, 2 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 24.77, 26.17, 31.80, 34.28, 46.15, 54.37, 63.58, 115.77, 120.35, 127.61, 128.00, 129.00, 131.67, 135.62; exact mass, m/z calcd for $C_{16}H_{20}N_2Se$ 320.0792, found 320.0783. Anal. Calcd for $C_{16}H_{20}N_2Se$: C, 60.19; H, 6.31; N, 8.77. Found: C, 60.41; H, 6.47; N, 8.62.

General procedure for radical cyclization

Oven-dried apparatus and anhydrous solvents were used. A 100-ml round-bottomed flask containing a Teflon-coated magnetic stirring bar and equipped with a reflux condenser fitted with a rubber septum was purged with argon and immersed in an oil bath preheated to 80°C. A benzene solution of the substrate (0.01-0.02 M) was injected into the flask and then benzene solutions of triphenyltin hydride (1.1-1.25 equivalent, 0.7-0.1 M) and of azobisisobutyronitrile (AIBN) (Eastman, 0.05 equivalent, 0.003 M) were added simultaneously by double syringe pump over a period of 12-15 h. Refluxing was continued for an arbitrary period of 3 h after the end of the addition and the solvent was then evaporated. The residue was processed as described for the individual examples.

(3aα,7aα)-3-Methyloctahydro-1*H*-indole-1-carbonitrile 3

The general procedure for radical cyclization was followed using cyanamide **2** (0.120 g, 0.38 mmol) in benzene (50 ml), triphenyltin hydride (0.164 g, 0.47 mmol) in benzene (10 ml) and AIBN (10 mg, 0.07 mmol) in benzene (10 ml). After evaporation of the reaction mixture, flash chromatography of the residue over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate and Kugelrohr distillation (49-51°C, 0.1 mm) yielded **3** [as a mixture of two isomers in a ratio of 61:39 (^{1}H nmr)] (0.06 g, 97%) as an apparently homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), colorless oil: FT-ir ($CHCl_3$, cast) 2924, 2840, 2205 cm^{-1}; ^{1}H nmr ($CDCl_3$, 300 MHz) δ 0.88-1.95 [m, 11.5 H, including doublets at δ 0.95 (J = 7 Hz) and at δ 1.02 (J = 7 Hz) in a ratio of 61:39, respectively], 2.04-2.13 (m, 1 H), 2.25-2.42 (m, 0.5 H), 3.01 (dd, J = 5.5, 9 Hz), 3.14 (dd, J = 9, 10.5 Hz), 3.50 (t, J = 9 Hz), 3.64-3.72 (m), [the signals between 3.01 and 3.72 δ together correspond to 3 H]; ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 11.96, 17.63, 19.97, 21.45, 21.53, 22.38, 23.91, 25.69, 25.85, 27.19, 35.33, 36.52, 40.80, 44.20, 54.37, 56.02, 59.52, 61.20, 116.96, 117.09; exact mass, m/z calcd for $C_{10}H_{16}N_2$ 164.1314, found 164.1314. Anal. calcd for $C_{10}H_{16}N_2$: C 73.13; H, 9.82; N, 17.06. Found: C, 73.01; H, 9.71; N, 17.10.

Trans-(3-Phenyl-2-propynyl)[2-(phenylseleno)cyclohexyl]cyanamide 4

The procedure employed for the allylation of **1** was followed using **1** (0.435 g, 1.55 mmol) in THF (1 ml), 3-bromo-1-propynylbenzene (0.378 g, 1.94 mmol) in THF (1 ml), sodium hydride (0.068 g, 60% in oil, 1.74 mmol) in THF (15 ml) and a reaction time of 3 h. Flash chromatography of the crude product over silica gel (5 x 15 cm) using 5:1 hexane-ethyl acetate gave **4** (0.435 g, 85%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-ir ($CHCl_3$, cast) 3045, 2926, 2846, 2209, 1483, 1467, 1434, 1129, 751, 739 cm^{-1}; ^{1}H nmr ($CDCl_3$, 300 MHz) δ 1.13-1.37 (m, 2 H), 1.42-1.71 (m, 3 H), 1.78-1.88 (m, 1 H), 2.12-2.29 (m, 2 H), 2.99 (dt, J = 4.2, 11.15 Hz, 1 H), 3.25 (dt, J = 4.2, 11.25 Hz, 1 H), 4.15 (s, 2 H), 7.23-7.38 (m, 6 H), 7.42-7.48 (m, 2 H), 7.62-7.68 (m, 2 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 24.79, 26.19, 31.77, 34.23, 42.33, 46.16, 63.82, 82.07, 86.65, 115.18, 121.99, 127.63, 128.12, 128.39, 128.86, 129.08, 131.81, 135.92; exact mass, m/z calcd for $C_{22}H_{22}N_2Se$ 394.0948, found 394.0939. Anal. Calcd for $C_{22}H_{22}N_2Se$: C, 67.19; H, 5.64; N, 7.12. Found: C,66.85; H, 5.79; N, 6.69.

(3aα,7aα)-Octahydro-3-(phenylmethylene)-1*H*-indole-1-carbonitrile 5

The general procedure for radical cyclization was followed using cyanamide **4** (0.183 g, 0.47 mmol) in benzene (50 ml), triphenyltin hydride (0.204 g, 0.58 mmol) in benzene (10 ml) and AIBN (10 mg, 0.07 mmol) in benzene (10 ml). After evaporation of the reaction mixture, flash chromatography of the residue over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate yielded **5** [as a mixture of two isomers in a ratio of 60:40 (^{1}H nmr)] (0.97 g, 87%) as an apparently homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-ir ($CHCl_3$, cast) 2927, 2849, 2208, 1447 cm^{-1}; ^{1}H nmr ($CDCl_3$, 300 MHz) δ 1.21-2.22 (m, 8 H), 2.67-2.77 (m), 2.85-2.96 (m), [both signals together correspond to 1 H and are in a ratio of 40:60, respectively], 3.59-3.70 (m, 1 H), 4.03-4.47 (m, 2 H), 6.28 (broad s), 6.31 (broad s), [both signals together correspond to 1 H and are in a ratio of 60:40, respectively], 7.12-7.40 (m, 5 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 19.62, 20.76, 22.91, 24.12, 25.27, 25.79, 26.23, 27.29, 40.18, 44.61, 51.92, 54.47, 59.67, 60.84, 116.46, 122.59, 122.83, 127.26, 127.97, 128.10, 128.67, 136.50, 139.18, 140.21; exact mass, m/z calcd for $C_{16}H_{18}N_2$ 238.1470, found 238.1470. The two isomers were separated by preparative HPLC [Hewlett Packard column of Si-100, 7μm; 100 x 4.6 mm; 1:13 hexane-ethyl acetate; flow rate 2 ml/min]. The major isomer has: ^{1}H nmr ($CDCl_3$, 300 MHz) (characteristic peaks only) δ 2.67-2.76 (m, 1 H), 3.65 (q, J = 7.25 Hz, 1 H), 4.27 (dd, J = 2.2, 14 Hz, 1 H), 4.44 (dm, J = 14 Hz, 1 H), 6.44 (broad s, 1 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 20.74, 22.88, 25.76, 27.27, 44.59, 51.90, 59.65, 116.52, 122.57, 127.20, 128.07, 128.65, 136.39, 139.15; exact mass, m/z calcd for $C_{16}H_{18}N_2$ 238.1470, found 238.1465. The minor isomer has: ^{1}H nmr ($CDCl_3$, 300 MHz) (characteristic peaks only) δ 2.18 (dm, J = 14 Hz, 1 H), 2.86-2.95 (m, 1 H), 3.59-3.65 (m, 1 H), 4.08 (dd, J = 1.5, 13.5 Hz, 1 H), 4.40 (dm, J = 13.5, 1 H), 6.31 (broad s, 1 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 19.60, 24.10, 25.25, 26.21, 40.15, 54.45, 60.82, 116.44, 122.81, 127.24, 127.95, 128.61, 136.48, 140.18; exact mass, m/z calcd for $C_{16}H_{18}N_2$ 238.1470, found 238.1461.

Trans-[1-Methyl-2-(phenylseleno)cyclohexyl]cyanamide 6[4]

The procedure employed for **1** was followed using 1-methylcyclohexene (0.220 g, 2.20 mmol), cyanamide (1.863 g, 44.36 mmol) and anhydrous *p*-toluenesulphonic acid[10] (0.382 g, 2.20 mmol) in dichloromethane (60 ml), and *N*-(phenylseleno)phthalimide (0.871 g, 2.88 mmol) in dichloromethane (5 ml). Flash chromatography of the crude product over silica gel (2.5 x 15 cm) using 5:1 hexane-ethyl acetate gave **6** (0.534 g, 82%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-ir (CHCl3, cast) 3193, 2936, 2210, 1473, 1437, 1390, 1189, 1019, 739, 691 cm^{-1}; ^{1}H nmr ($CDCl_3$, 300 MHz) δ 1.16-1.53 (m, 5 H), 1.60-1.84 (m, 4 H), 1.92-2.02 (m, 1 H), 2.08-2.19 (m, 1 H), 3.19 (dd, J = 4, 12 Hz, 1 H) 4.57 (broad s, 1 H), 7.23-7.43 (m, 3 H), 7.55-7.65 (m, 2 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 21.47, 22.22, 26.42, 32.31, 37.29, 55.83, 58.64, 113.78, 127.92, 128.82, 129.26, 134.71; exact mass, m/z calcd for $C_{14}H_{18}N_2Se$, 294.0635, found 294.0640.

Trans-[1-Methyl-2-(phenylseleno)cyclohexyl](2-propenyl)cyanamide 7

The procedure employed for **2** was followed using **6** (0.50 g, 1.71 mmol) in THF (1 ml), 3-bromo-1-propene (0.261 g, 2.13 mmol) in THF (1 ml), and sodium hydride (0.085 g, 60% in oil, 2.13 mmol) in THF (20 ml). Flash chromatography of the crude product over silica gel (5 x 15 cm) using 5:1 hexane-ethyl acetate and Kugelrohr distillation (99°C, 0.05 mm) gave **7** (0.532 g, 93%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate) oil: FT-ir ($CHCl_3$, cast) 3072, 3052, 2931, 2854, 2202, 1476, 1437, 1383, 1153, 1115, 1023, 927, 740, 693 cm^{-1}; ^1H nmr ($CDCl_3$, 300 MHz) δ 1.16-1.32 (m, 1 H), 1.36-1.53 (m, 4 H, including singlet at δ 1.41), 1.60-1.87 (m, 5 H), 2.03-2.14 (m, 1 H), 3.44 (dd, J = 4.5, 10.5 Hz, 1 H), 3.50-3.66 (m, 2 H), 5.24-5.36 (m, 2 H), 5.85 (dddd, J = 6.5, 6.5, 10.0, 17.0 Hz, 1 H), 7.22-7.32 (m, 3 H), 7.60-7.78 (m, 2 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 20.02, 22.31, 25.54, 31.60, 36.45, 48.35, 51.87, 62.40, 115.99, 119.58, 127.79, 128.93, 129.07, 132.32, 135.10; exact mass, m/z calcd for $C_{17}H_{22}N_2Se$ 334.0948, found 334.0950. Anal. Calcd for $C_{17}H_{22}N_2Se$: C, 61.26; H, 6.65; N, 8.40. Found: C, 61.30; H, 6.55; N, 8.41.

(3aα,7aα)-3,7-Dimethyloctahydro-1*H*-indole-1-carbonitrile 8

The general procedure for radical cyclization was followed using cyanamide **7** (0.437 g, 1.30 mmol) in benzene (50 ml), triphenyltin hydride (0.574 g, 1.64 mmol) in benzene (10 ml) and AIBN (15 mg, 0.10 mmol) in benzene (10 ml). After evaporation of the reaction mixture, flash chromatography of the residue over silica gel (2.5 x 15 cm) using 5:1 hexane-ethyl acetate and Kugelrohr distillation (65°C, 0.05 mm) yielded **8** [as a mixture of two isomers in a ratio of 60:40 (^1H nmr)] (0.221 g, 95%) as an apparently homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), colorless oil: FT-ir ($CHCl_3$, cast) 2932, 2860, 2202 cm^{-1}; ^1H nmr (CD_3COOD, 300 MHz) δ 0.95 (d, J = 6.5 Hz), 1.01 (d, J = 6.5 Hz), [both signals together correspond to 3 H], 1.08-1.83 (m, 11 H, including two singlets at δ 1.26 and δ 1.38), 1.93-2.06 (m, 1 H), 2.27-2.46 (m), 2.65-2.81 (m), [both signals together correspond to 1 H and are in a ratio of 40:60, respectively], 3.05 (t, J = 9.5 Hz), 3.15 (t, J = 9.9 Hz), [both signals together correspond to 1 H and are in a ratio of 40:60, respectively], 3.54 (t, J = 9 Hz), 3.64 (t, J = 8.75 Hz), [both signals together correspond to 1 H and are in a ratio of 60:40, respectively]; ^{13}C nmr (CD_3COOD, 75.5 MHz) δ 12.50, 16.17, 21.03, 22.24, 23.23, 23.38, 23.60, 23.95, 24.93, 27.74, 33.81, 34.60, 34.65, 34.88, 46.64, 51.71, 54.57, 56.22, 65.82, 66.67, 116.66, 116.93; exact mass, m/z calcd for $C_{11}H_{18}N_2$ 178.1470, found 178.1472. Anal. Calcd for $C_{11}H_{18}N_2$: C, 74.11; H, 10.18; N, 15.71. Found: C, 74.34; H, 10.19; N, 15.71.

Trans-[1-Methyl-2-(phenylseleno)cyclohexyl](3-phenyl-2-propynyl)cyanamide 9

The procedure employed for **4** was followed using **6** (0.144 g, 0.49 mmol) in THF (1 ml), 3-bromo-1-propynylbenzene (0.120 g, 0.61 mmol) in THF (1 ml), and sodium hydride (0.022 g, 60% in oil, 0.61 mmol) in THF (15 ml). Flash chromatography of the crude product over silica gel (2.5 x 15 cm) using 5:1 hexane-ethyl acetate gave **9**

(0.149 g, 74%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-ir ($CHCl_3$, cast) 2937, 2205, 1490, 1437, 1382, 757, 742, 691 cm^{-1}; ^1H nmr ($CDCl_3$, 300 MHz) δ 1.19-1.34 (m, 1 H), 1.37-1.56 (m, 4 H, including singlet at δ 1.49), 1.59-2.15 (m, 6 H), 3.48 (dd, J = 4, 10.5 Hz, 1 H), 4.04 (d, J = 4.75 Hz, 2 H), 7.22-7.34 (m, 6 H), 7.37-7.46 (m, 2 H), 7.60-7.68 (m, 2 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 19.89, 22.40, 25.55, 31.63, 36.54, 37.29, 51.76, 63.19, 83.27, 86.35, 115.62, 122.12, 127.92, 128.30, 128.70, 128.90, 129.17, 131.70, 135.21; exact mass, m/z calcd for $C_{23}H_{24}N_2Se$ 408.1105, found 408.1142. Anal. Calcd for $C_{23}H_{24}N_2Se$: C,67.81; H, 5.94; N, 6.88. Found: C, 67.61; H, 5.73; N,6.68.

(3aα,7aα)-7a-Methyloctahydro-3-(phenylmethylene)-1*H*-indole-1-carbonitrile 10

The general procedure for radical cyclization was followed using cyanamide **9** (0.080 g, 0.20 mmol) in benzene (50 ml), triphenyltin hydride (0.086 g, 0.25 mmol) in benzene (10 ml) and AIBN (5 mg, 0.04 mmol) in benzene (10 ml). After evaporation of the solvent, flash chromatography of the residue over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate yielded **10** [as a mixture of two isomers in a ratio of 63:37 (^1H nmr)] (0.42 g, 85%) as an apparently homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-ir ($CHCl_3$, cast) 2939, 2859, 2205, 1448, 1324, 736, 695 cm^{-1}; ^1H nmr ($CDCl_3$, 300 MHz) δ 1.12-2.17 (m, 11 H, including two singlets at δ 1.15 and δ 1.33), 2.40-2.47 (m), 2.63-2.70 (m), [both signals together correspond to 1 H], 4.06 (dd, J = 1.5, 13.75 Hz, 1 H), 4.28-4.43 (m) [both signals together correspond to 2 H], 6.32-6.36 (bq, J = 2.25 Hz), 6.38 (broad s), [both signals together correspond to 1 H], 7.14-7.40 (m, 5 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 21.27, 22.06, 22.33, 23.49, 24.21, 26.50, 26.69, 27.45, 32.38, 32.69, 46.01, 50.24, 51.03, 53.13, 63.58, 65.22, 122.72, 123.52, 127.17, 127.96, 128.12, 128.36, 128.62, 128.69, 136.48, 136.48, 136.61, 138.72, 140.19; exact mass, m/z calcd for $C_{17}H_{20}N_2$ 252.1626, found 252.1626. One isomer was obtained by preparative HPLC [Hewlett Packard column of Si-100, 7μm; 100 x 4.6 mm; 1:13 hexane-ethyl acetate; flow rate 2 ml/min], and had ^1H nmr ($CDCl_3$, 300 MHz) δ 1.25-1.39 (m, 4 H, including singlet at δ 1.33), 1.43-1.65 (m, 4 H), 1.65-1.83 (m, 3 H), 2.45 (bt, J = 6 Hz, 1 H), 4.35 (m, J = 12.3, 2 H), 6.31-6.36 (m, 1 H), 7.12-7.20 (m, 2 H), 7.20-7.28 (m, 1 H), 7.32-7.40 (m, 2 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 22.04, 22.30, 24.27, 26.86, 32.36, 50.23, 51.01, 63.56, 115.60, 122.71, 127.14, 128.10, 128.67, 136.44, 138.70; exact mass, m/z calcd for $C_{17}H_{20}N_2$ 252.1626, found 252.1627.

[1-[(Phenylseleno)methyl]cyclohexyl]cyanamide 11[4] and [[1-(phenylseleno)-cyclohexyl]methyl]cyanamide 11'[4]

The procedure employed for **1** was followed using 1-methylcyclohexene (0.263 g, 2.74 mmol), cyanamide (2.300 g, 54.76 mmol) and anhydrous *p*-toluenesulphonic acid[10] (0.420 g, 2.74 mmol) in dichloromethane (50 ml), and *N*-(phenylseleno)phthalimide (1.075 g, 3.56 mmol) in dichloromethane (5 ml). Flash chromatography of the crude product over silica gel (2.5 x 15 cm) using 5:1 hexane-ethyl acetate yielded **11** and **11'** (0.542 g, 67%) as an apparently homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil which was a mixture of **11** and **11'** in a ratio[11] of *ca.* 92:8 (^{13}C nmr): FT-ir ($CHCl_3$, cast) 3194, 2953, 2859, 2209, 1477, 1447, 730, 691 cm^{-1}; ^{1}H nmr (DMSO-d$_6$, 300 MHz) (signals for major isomer only) δ 1.25-1.75 (m, 10 H), 3.08 (s, 2 H), 6.90 (broad s, 1 H), 7.15-7.64 (m, 5 H); ^{13}C nmr (CDCl$_3$, 75.5 MHz) (signals for major isomer only) δ 21.57, 24.96, 34.71, 41.00, 57.73, 113.76, 127.38, 129.26, 129.95, 133.10; exact mass, m/z calcd for $C_{14}H_{19}N_2Se$, 294.0636, found 294.0635.

[1-[(Phenylseleno)methyl]cyclohexyl](2-propenyl)cyanamide 12

The procedure employed for **2** was followed using a mixture of the isomeric cyanamides **11** and **11'** [*ca.* 92% **11** (^{13}C nmr)] (0.114 g, 0.39 mmol) in THF (1 ml), 3-bromo-1-propene (0.06 g, 0.50 mmol) in THF (1 ml), and sodium hydride (0.020 g, 60% in oil, 0.50 mmol) in THF (10 ml). Flash chromatography of the crude product over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate and Kugelrohr distillation (107°C, 0.07 mm) gave **12** (0.102 g, 79%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-ir (CHCl$_3$, cast) 2937, 2856, 2202, 1477, 1435, 926, 735, 692 cm^{-1}; ^{1}H nmr (CDCl$_3$, 300 MHz) δ 1.22-1.36 (m, 1 H), 1.45-1.70(m, 7 H), 1.85-1.96 (m, 2 H), 3.12 (s, 2 H), 3.46(dt, J = 1.25, 6.65 Hz, 2 H), 5.23 (dq, J = 1.25, 5.0 Hz, 1 H), 5.29 (q, J = 1.4 Hz, 1 H), 5.83 (ddt, J = 4.13, 9.65, 17.2 Hz, 1 H), 7.22-7.29 (m, 3 H), 7.54-7.62 (m, 2 H); ^{13}C nmr (CDCl$_3$, 75.5 MHz) δ 21.74, 25.07, 33.87, 38.54, 47.98, 61.03, 116.04, 120.28, 127.38, 129.23, 130.32, 131,89, 133.38; exact mass, m/z calcd for $C_{17}H_{22}N_2Se$ 334.0942, found 334.0951. Anal. Calcd for $C_{17}H_{22}N_2Se$: C, 61.26; H, 6.65; N, 8.40. Found: C, 61.30; H, 6.62; N, 8.35.

3-Methyl-1-azaspiro[4.5]decane-1-carbonitrile 13

The general procedure for radical cyclization was followed using cyanamide **12** (0.130 g, 0.34 mmol) in benzene (50 ml), triphenyltin hydride (0.177 g, 0.51 mmol) in benzene (10 ml) and AIBN (5 mg, 0.04 mmol) in benzene (10 ml). After evaporation of the solvent, flash chromatography of the residue over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate and Kugelrohr distillation (50°C, 0.07 mm) yielded **13** (0.046 g, 66%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), colorless oil: FT-ir (CHCl$_3$, cast) 2931, 2850, 2202 cm^{-1}; ^{1}H nmr (CDCl$_3$, 300 MHz) δ 1.05 (d, J = 6.75 Hz, 3 H), 1.08-1.40 (m, 4 H), 1.49-1.68 (m, 4 H), 1.70-1.84 (m, 3 H), 2.15 (dd, J = 7, 12 Hz, 1 H), 2.20-2.42 (m, 1 H), 3.01 (t, J = 9.5 Hz, 1 H), 3.54 (t, J = 8 Hz, 1 H); ^{13}C nmr (CDCl$_3$, 75.5 MHz) δ 17.26, 23.92, 24.26, 24.93, 31.91, 35.27, 37.68, 42.65, 56.36, 66.55, 115.97; exact mass, m/z calcd for $C_{11}H_{18}N_2$ 178.1470, found 178.1471. Anal. Calcd for $C_{11}H_{18}N_2$: C, 74.11; H, 10.18; N, 15.71. Found: C, 74.05; H, 10.32; N, 15.93.

(3-Phenyl-2-propynyl)[1-[(phenylseleno)methyl]cyclohexyl]cyanamide 14

The procedure employed for the cyanamide **4** was followed using a mixture of the isomeric cyanamides **11** and **11'** [in a ratio of 66:34, respectively (^{1}H nmr)] (0.831 g, 2.83 mmol) in THF (2 ml), 3-bromo-1-propynylbenzene (0.689 g, 3.53 mmol) in THF (1 ml) and sodium hydride (0.124 g, 60% in oil, 3.10 mmol) in THF (20 ml). Flash chromatography of the crude product over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate gave **14** and (3-phenyl-2-propynyl)[[1-(phenylseleno)cyclohexyl]-methyl]cyanamide (0.977 g, 84%). The two isomers were separated by flash chromatography over silica gel (2.5 x 15 cm) using 14:1 hexane-ethyl acetate. The major isomer **14** (0.471 g, 62%, calculated by using the ratio of **11** and **11'** in the starting material) was obtained as a homogeneous (TLC, silica 5:1 hexane-ethyl acetate) white powder and had: FT-ir ($CHCl_3$, cast) 2933, 2857, 2204, 1490, 1477, 1442, 1437, 757, 739, 691 cm^{-1}; ^1H nmr ($CDCl_3$, 300 MHz) δ 1.20-1.36 (m, 1 H), 1.45-1.77 (m, 7 H), 1.98 (bd, J = 9 Hz, 2 H), 3.29 (s, 2 H), 3.95 (s, 2 H), 7.20-7.37 (m, 6 H), 7.37-7.47 (m, 2 H), 7.53-7.62 (m, 2 H); ^{13}C nmr ($CDCl_3$, 75.5 MHz) δ 21.79, 25.04, 33.66, 36.91, 38.48, 61.94, 83.01, 86.60, 115.85, 122.08, 127.40, 128.34, 128.76, 129.25, 130.45, 131.81, 133.34; exact mass, m/z calcd for $C_{23}H_{24}N_2Se$ 408.1105, found 408.1126. Anal. Calcd for $C_{23}H_{24}N_2Se$: C, 67.81; H, 5.94; N,6.88; Found: C, 66.92; H, 6.04; N, 6.65. The minor product (0.237 g, 61%, calculated by using the ratio of **11** and **11'** in the starting material) was obtained as a yellowish oil and had: ^1H nmr ($CDCl_3$, 300 MHz) δ 1.17-1.36 (m, 1 H), 1.51-1.76 (m, 7 H), 1.82-1.96 (m, 2 H), 3.36 (s, 2 H), 4.20 (s, 2 H), 7.24-7.40 (m, 6 H), 7.40-7.48 (m, 2 H), 7.62-7.67 (m, 2 H).

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11. Our impression is that the ratio is sensitive to the quality of the *N*-(phenylseleno)phthalimide: with pure material a high ratio of 92:8 is obtained.

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