Novel construction of 5-methylenepyrrol-2-ones by intramolecular cyclization of selenium-stabilized alkynyl amides

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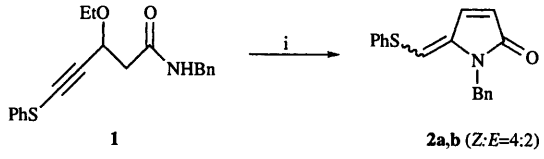
(*Z*)-5-(Phenylselenomethylene)pyrrol-2-ones 18–22 have been obtained in good yields from the cyclization of ω-seleno-substituted alkynyl amides 11–15 with Bu^{t}OK–18-crown-6.

Alkynyl chalcogenides are synthetic intermediates of great potential,[1] although, the fundamental character of these compounds has still to be elucidated. Recently, Funk *et al.* reported that alkynyl sulfides are good electrophiles for stabilized carbanions,[2] and treatment of ω-sulfone-substituted alkynyl sulfides with BuLi–THF–HMPA gave 2-(alkylthiomethylene)carbocycles by carbometallation. We have also allowed ω-sulfur-substituted alkynes to react with intramolecular amides (Scheme 1). A preliminary result showed that ω-phenylsulfur-



1 **2a,b** (*Z*:*E*=4:2)

Scheme 1 *Reagents:* i, Bu^{t}OK–Bu^{t}OH, RT, 30 min

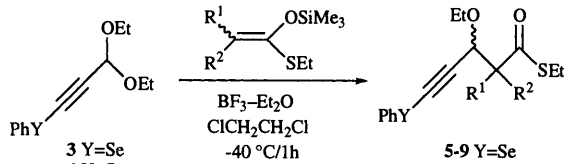
substituted alkynyl amides **1** treated with Bu^{t}OK–Bu^{t}OH gave the 5-(phenylthiomethylene)pyrrol-2-one **2a** (37%) accompanied by the isomer **2b** (20%). Thus, amide-anion cyclization stabilized by a sulfur atom afforded 5-methylenepyrrol-2-ones with no stereoselectivity. 5-Methylenepyrrol-2-ones are useful in the synthesis of compounds with biologically important functions such as vitamins, co-factors and light-absorbing pigments such as the tetrapyrrole pigment bilirubin, the prosthetic groups of biliproteins such as phytochrome and heme (the red pigment of blood).[3]

Most cyclizations with nitrogen nucleophiles involving alkynes have utilized Pd^{II}[4] or Ag^{I}[5] catalysts. Recently, Jacobi *et al.* reported a convenient synthesis of dihydro derivatives by Bu_4NF- or $LiAl(NHBn)_4$-catalysed ring closure of acetylenic amides,[6] although 3,4-unsaturated derivatives could not be synthesized by this method. The stereoselective synthesis of 5-methylenepyrrol-2-ones simply, without Pd^{II} or Ag^{I}, would be useful for the preparation of phytochromes and hemes. Such a synthesis is described here and involves intramolecular amidometallation of an alkynyl amide stabilized by a selenium atom with subsequent dehydroalkoxylation.

We first examined the preparation of the *S*-ethyl 3-ethoxy-5-(phenylchalcogeno)pent-4-ynethioates **5–10** by our previously reported method, an α-site selective reaction of γ-chalcogen-substituted prop-2-ynyl cations with *S*-ethyl *O*-silyl enol ethers (Table 1).[7] These thioesters were treated with amines to give the alkynyl amides **1** and **11–17** in moderate yields (see Table 2).

The alkynyl amide **11** reacted with Bu^{t}OK–Bu^{t}OH in the presence of 18-crown-6 to give 5-(phenylselenomethylene)pyrrol-2-one **18a** (63%) and **18b** (7%), respectively. Assignment of structure to the pyrrolone **18a** was established on

Table 1 Syntheses of ω-chalcogen-substituted alkynyl thioesters



3 Y=Se
4 Y=S

5-9 Y=Se
10 Y=S

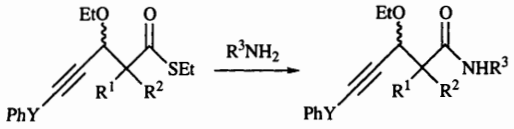
		Silyl enol ether		
Entry	Y	R^1	R^2	Product (% yield)
1	Se	H	H	**5** (90)
2	Se	Me	Me	**6** (73)
3	Se	H	Me	**7** (65)
4	Se	H	Ph	**8** (73)
5	Se	H	Pr^i	**9** (72)
6	S	H	H	**10** (45)

the basis of IR and ^1H and ^{13}C NMR spectroscopic results and elemental analysis. IR spectroscopy showed the presence of an amide function at ν/cm^{-1} 1660. The ^1H NMR spectrum exhibited a pair of doublets at δ 6.19 (J 6 Hz) and 6.90 (J 6 Hz) arising from 3- and 4-H, and a broad singlet at δ 6.32 characteristic of an *exo*-methylene proton. The stereostructure of the isomer **18a** was determined as *Z* by differential NOE experiments. Irradiation of the *exo*-methylene proton of **18a** increased the intensity of the 4-H and not the *N*-benzyl H signal. Irradiation of **18b** increased the intensities of the *N*-benzyl H signal, not that of 4-H.

The cyclization of **12** gave (*Z*)-5-(phenylselenomethylene)pyrrol-2-one **19**, exclusively (Table 3, entry 2); the *N*-*p*-methoxyphenyl amide **13** also gave the (*Z*)-pyrrol-2-one **20**. 2,2-Dimethylalkynyl amide **14** gave 3,3-dimethyl-4-ethoxypyrrolidin-2-one **21** (91%). This result supports the suggestion that, initially, the amide anion attacks regioselectively at the alkynyl carbon. 5-(Phenylchalcogenomethylene)pyrrolones are likely to be formed by the same mechanism as operates in the intramolecular cyclization of α-lithio sulfones to alkynyl sulfides, since cyclization of allenyl amides gives 6-*endo*-mode products.[8] The 2-methyl derivative **15** also gave 3-methylpyrrol-2-one **22a**, accompanied by the *E*-isomer **22b** (entry 5); however, the 3-phenyl derivatives **23** and **24** were obtained as *E*- and *Z*-isomeric mixtures (entries 6 and 7). This result shows that the aromatic substituent at the 3-position of the pyrrolones **23** and **24** stabilises the carbanion in the isomerisation of the conjugated system under basic conditions.

Ricci *et al.* reported that pyrrol-2-ones easily reacted with $TMSNEt_2$–TMSCl to give trimethylsilyloxypyrroles, which

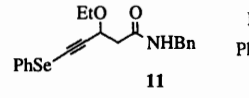
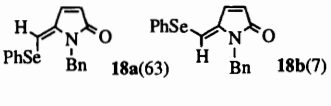
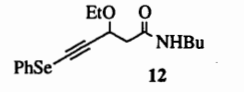
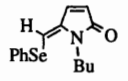
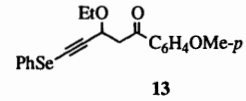
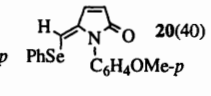
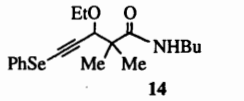
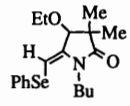
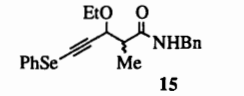
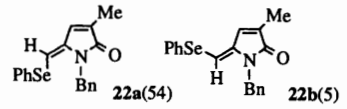
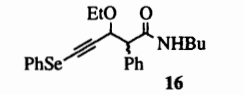
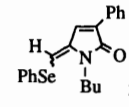
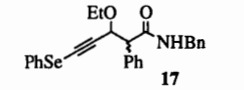
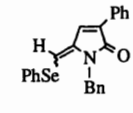
Table 2 Syntheses of ω-chalcogen-substituted alkynyl amides



Entry	Y	R^1	R^2	Amine* R^3	Product (% yield)
1	Se	H	H	Bn	**11** (67)
2	Se	H	H	Bu	**12** (68)
3	Se	H	H	*p*-$MeOC_6H_4$	**13** (44)
4	Se	Me	Me	Bu	**14** (66)
5	Se	H	Me	Bn	**15** (64)
6	Se	H	Ph	Bu	**16** (32)
7	Se	H	Ph	Bn	**17** (54)
8	Se	H	Pr^i	Bu	—
9	S	H	H	Bn	**1** (72)

* Bn = CH_2Ph.

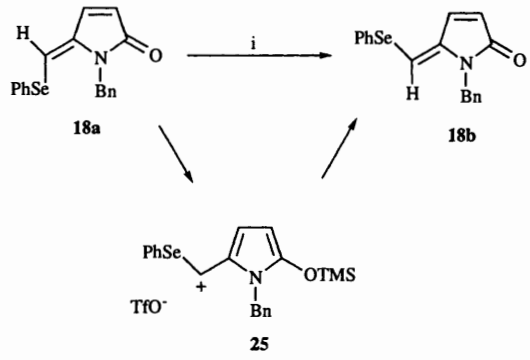
Table 3 Cyclization of ω-chalcogen-substituted alkynyl amides*

Entry	ω-Chalcogen-substituted alkynyl amide	Products (%yields)
1	 **11**	 **18a**(63) **18b**(7)
2	 **12**	 **19**(72)
3	 **13**	 **20**(40)
4	 **14**	 **21**(91)
5	 **15**	 **22a**(54) **22b**(5)
6	 **16**	 **23**(78)
7	 **17**	 **24**(87)

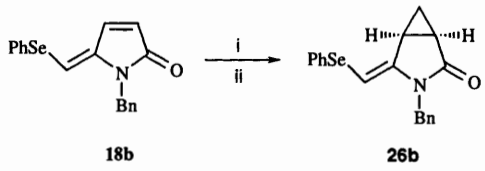
* Bn = CH_2Ph.

underwent nucleophilic addition with ketones, lactones and enones in the presence of Lewis acid to give 5-methylenepyrrolones and 1,4-addition products.[9] These results led us to examine the nucleophilic addition of 5-(phenylselenomethylene)pyrrolone **18a** and allylsilane. However, the addition products could not be obtained and isomerization of the *E*- and *Z*-alkenyl groups of the pyrrolones was observed under acidic conditions such as TMSOTf or TfOH or BF_3–Et_2O (see Scheme 2). This result showed that the reaction intermediate is the α-selenocarbenium ion **25**.

We also examined the cycloaddition of pyrrol-2-one **18b** and diazomethane to give, regioselectively, pyrazoles the subsequent denitrogenation of which gave cyclopropane derivatives **26b** in good yield. The pyrrolone cyclopropane derivatives are important intermediates for a synthesis of cyclopropane amino acids.[10]



Scheme 2 *Reagents:* i, TMSOTf or TfOH or BF_3–Et_2O



Scheme 3 *Reagents:* i, CH_2N_2; ii, *hv*

Experimental

Mps were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. IR spectra of solids (KBr) and liquids (film) were recorded on a JASCO IRA-100 spectrophotometer. ^1H NMR spectra were obtained for solution in $CDCl_3$ on a JEOL GX-270 (270 MHz) or a JEOL EX-400 (400 MHz) spectrometer with tetramethylsilane as an internal standard, unless otherwise indicated. ^{13}C NMR spectra and NOE were run on a JEOL EX-400 spectrometer. *J* Values are given in Hz. Mass spectra were obtained using a JEOL JMS-D 300 spectrometer with a direct-insertion probe at 70 eV. All exact mass determination was obtained on the JMA 2000 on-line system.

Preparation of alkynethioates 5–10

General procedure. BF_3·Et_2O (2.42 g, 14.2 mmol) was added dropwise to a $ClCH_2CH_2Cl$ (10 cm^3) solution of 3,3-diethoxy-1-phenylselenoprop-1-yne **3** (2.0 g, 7.1 mmol) and the appropriate ethylthio(trimethylsilyloxy)ethylene (1.8 g, 10.5 mmol) under an Ar atmosphere at −40 °C. The reaction mixture was stirred for 1 h after which it was poured into water (100 cm^3). The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layer and extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with AcOEt–hexane (1:20) to give *S*-ethyl 3-ethoxy-5-phenylselenopent-4-ynethioate **5** (2.18 g, 90%) as a yellow oil.

***S*-Ethyl 3-ethoxy-5-phenylselenopent-4-ynethioate 5.** ν_{max}/cm^{-1} 2160 (acetylene) and 1680 (CO); δ_H(400 MHz; $CDCl_3$) 1.21 (3 H, t, *J* 7, Me), 1.25 (3 H, t, *J* 7, Me), 2.90 (2 H, dq, *J* 1 and 7, CH_2S), 2.93 (1 H, dd, *J* 5 and 15, 2-H), 3.07 (1 H, dd, *J* 8 and 15, 2-H), 3.46–3.54 (1 H, m, OCH_2), 3.77–3.85 (1 H, m, OCH_2), 4.75 (1 H, dd, *J* 5 and 8, 3-H), 7.23–7.33 (3 H, m, ArH) and 7.50 (2 H, dd, *J* 1 and 2, ArH); δ_C(100 MHz; $CDCl_3$) 14.57 (q), 14.89 (q), 23.43 (t), 49.62 (t), 64.69 (t), 66.41 (d), 101.40 (s), 127.10 (d), 128.21 (s), 128.99 (d), 129.47 (d) and 195.49 (s) (Found: M^+, 342.0200. $C_{15}H_{18}O_2SSe$ requires *M*, 342.0193).

***S*-Ethyl 2,2-dimethyl-3-ethoxy-5-phenylselenopent-4-ynethioate 6.** ν_{max}/cm^{-1} 2170 (acetylene) and 1670 (CO); δ_H(400 MHz; $CDCl_3$) 1.17 (3 H, t, *J* 7, Me), 1.28 (3 H, t, *J* 7, Me), 1.28 (3 H, s, Me), 1.38 (3 H, s, Me), 2.86 (2 H, q, *J* 7, CH_2S), 3.42–3.46 (1 H, m, CH_2O), 3.78–3.82 (1 H, m, CH_2O), 7.26–7.33 (3 H, m, ArH) and 7.51 (2 H, d, *J* 8, ArH); δ_C(100 MHz; $CDCl_3$) 14.55 (q), 14.84 (q), 19.47 (q), 23.01 (s), 23.16 (q), 54.16 (t), 65.39 (t), 65.67

(s), 76.69 (d), 100.74 (s), 127.09 (d), 128.52 (s), 129.01 (d), 129.49 (d) and 204.34 (s) (Found: C, 55.45; H, 6.16. $C_{17}H_{22}O_2SSe$ requires C, 55.28; H, 6.00%).

***S*-Ethyl 3-ethoxy-2-methyl-5-phenylselenopent-5-ynethioate 7.** ν_{max}/cm^{-1} 2180 (acetylene) and 1690 (CO); δ_H(400 MHz; $CDCl_3$) 1.18 (t, *J* 7, Me), 1.21 (t, *J* 7, Me), 1.22 (t, *J* 7, Me), 1.25 (t, *J* 7, Me), 1.29 (d, *J* 7, Me), 1.34 (d, *J* 7, Me), 2.83–3.01 (m, SCH_2 and 2-H), 3.42–3.52 (m, OCH_2), 3.77–3.85 (m, OCH_2), 4.50 (d, *J* 3, 3-H), 4.52 (d, *J* 6, 3-H), 7.23–7.33 (m, ArH) and 7.50–7.52 (m, ArH); δ_C(100 MHz; $CDCl_3$) 13.33 (q), 14.58 (q), 14.61 (q), 14.65 (q), 14.89 (q), 23.28 (t), 53.07 (d), 53.40 (d), 64.79 (t), 65.00 (t), 66.81 (s), 67.10 (s), 71.21 (d), 72.38 (d), 100.84 (s), 101.19 (s), 127.07 (d), 127.16 (d), 128.42 (s), 129.04 (d), 129.46 (d), 129.53 (d), 200.24 (s) and 200.75 (s) (Found: C, 54.02; H, 5.67. $C_{16}H_{20}O_2SSe$ requires C, 54.08; H, 5.67%).

***S*-Ethyl 3-ethoxy-2-phenyl-5-phenylselenopent-5-ynethioate 8.** ν_{max}/cm^{-1} 2180 (acetylene) and 1690 (CO); δ_H(400 MHz; $CDCl_3$) 1.07 (t, *J* 7, Me), 1.16 (t, *J* 7, Me), 1.20 (t, *J* 7, Me), 1.21 (t, *J* 7, Me), 2.75–2.94 (m, CH_2S), 3.33–3.42 (m, OCH_2), 3.49–3.61 (m, OCH_2), 3.70–3.91 (m, OCH_2), 4.08 (d, *J* 10, benzyl H), 4.10 (d, *J* 8, benzyl H), 4.92 (d, *J* 8, CHO), 4.98 (d, *J* 10, CHO) and 7.08–7.45 (m, ArH); δ_C(100 MHz; $CDCl_3$) 14.35 (q), 14.37 (q), 14.74 (q), 14.92 (q), 23.69 (t), 23.74 (t), 64.69 (d), 64.75 (d), 64.90 (t), 65.30 (t), 67.10 (s × 2), 71.01 (d), 72.10 (d), 100.58 (s), 101.27 (s), 126.90 (d), 127.89 (d), 128.04 (d), 128.23 (s), 128.36 (d), 128.66 (d), 128.75 (d), 128.80 (d), 128.82 (d), 129.37 (d), 129.41 (d), 129.43 (d), 134.49 (s), 134.71 (s), 197.55 (s) and 197.62 (s) (Found: C, 60.63; H, 5.30. $C_{21}H_{22}O_2SSe$ requires C, 60.43; H, 5.31%).

***S*-Ethyl 3-ethoxy-2-isopropyl-5-phenylselenopent-4-ynethioate 9.** ν_{max}/cm^{-1} 2180 (acetylene) and 1680 (CO); δ_H(400 MHz; $CDCl_3$) 0.97 (d, *J* 7, Me), 0.98 (d, *J* 7, Me), 1.04 (d, *J* 7, Me), 1.06 (d, *J* 7, Me), 1.17 (t, *J* 7, Me), 1.21 (t, *J* 7, Me), 1.22 (t, *J*, 7 Me), 1.25 (t, *J* 7, Me), 2.23–2.29 (m, C*H*Me_2), 2.83–2.92 (m, SCH_2 and COCH), 3.43–3.52 (m, OCH_2), 3.78–3.87 (m, OCH_2), 4.51 (d, *J* 8, OCH), 4.58 (d, *J* 10, OCH), 7.22–7.33 (m, ArH) and 7.50–7.55 (m, ArH); δ_C(100 MHz; $CDCl_3$) 14.67 (q), 14.74 (q), 14.89 (q), 14.98 (q), 18.18 (q), 19.04 (q), 21.16 (q), 21.69 (q), 23.52 (q), 23.59 (q), 28.11 (d), 28.40 (d), 63.70 (d), 64.25 (d), 64.58 (t), 65.07 (t), 66.99 (s), 67.21 (s), 69.49 (d), 70.92 (d), 101.15 (s), 101.19 (s), 126.94 (d), 127.18 (d), 128.38 (s), 128.62 (s), 128.95 (d), 129.04 (d), 129.42 (d), 129.53 (d), 198.94 (s) and 199.05 (s) (Found: C, 56.19; H, 6.40. $C_{18}H_{24}O_2SSe$ requires C, 56.39; H, 6.31%).

***S*-Ethyl 3-ethoxy-5-phenylthiopent-4-ynethioate 10.** ν_{max}/cm^{-1} 2170 (acetylene) and 1640 (CO); δ_H(400 MHz; $CDCl_3$) 1.21 (3 H, q, *J* 7, Me), 1.24 (3 H, q, *J* 7, Me), 2.90 (2 H, br q, *J* 7, SCH_2), 2.94 (1 H, dd, *J* 5 and 15, CH_2CO), 3.09 (1 H, dd, *J* 5 and 15, CH_2CO), 3.46–3.53 (1 H, m, OCH_2), 3.77–3.85 (1 H, m, OCH_2), 4.76 (1 H, dd, *J* 5 and 8, 3-H), 7.20–7.25 (1 H, m, ArH), 7.30–7.34 (2 H, m, ArH) and 7.38–7.41 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 14.53 (q), 14.86 (q), 23.40 (t), 49.48 (t), 64.64 (t), 66.27 (d), 73.01 (s), 96.59 (s), 126.14 (d), 126.52 (d), 129.16 (d), 133.84 (s) and 195.36 (s) (Found: M^+, 294.0748. $C_{15}H_{18}O_2S_2$ requires *M*, 294.0735).

Preparation of the alkynyl amides 1 and 11–17

General procedure. A dry benzene (10 cm^3) solution of the alkynethioate **5** (6.04 g, 17.7 mmol) and benzylamine (3.79 g, 35.4 mmol) was stirred for 2 days at room temperature and then evaporated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with AcOEt–hexane (1 : 2) to give *N*-benzyl-3-ethoxy-5-phenylselenopent-4-ynamide **11** (4.6 g, 67%) as a yellow oil.

***N*-Benzyl-3-ethoxy-5-phenylselenopent-4-ynamide 11.** ν_{max}/cm^{-1} 3300 (NH), 2150 (acetylene) and 1640 (CO); δ_H(400 MHz; $CDCl_3$) 1.17 (3 H, t, *J* 7, Me), 2.72 (2 H, d, *J* 6, CH_2), 3.46–3.50 (1 H, m, OCH_2), 3.83–3.87 (1 H, m, OCH_2), 4.45 (2 H, m, OCH_2), 4.66 (1 H, t, *J* 6, CHO), 6.57 (1 H, br s, NH), 7.24–7.31 (8 H, m, ArH) and 7.48 (2 H, br d, *J* 6, ArH); δ_C(100 MHz; $CDCl_3$) 14.91 (q), 43.02 (t), 43.42 (t), 64.89 (t), 66.76 (s), 67.09 (d), 101.29 (s), 127.20 (d), 127.29 (d), 127.46 (d), 128.08 (s), 128.57 (d), 129.01 (d), 129.54 (d), 138.10 (s) and 169.15 (s) (Found: M^+, 387.0721. $C_{20}H_{21}NO_2Se$ requires *M*, 387.0737).

***N*-Butyl-3-ethoxy-5-phenylselenopent-4-ynamide 12.** ν_{max}/cm^{-1} 3300 (NH), 2170 (acetylene) and 1640 (CO); δ_H(400 MHz; $CDCl_3$) 0.90 (3 H, t, *J* 7, Me), 1.23 (3 H, t, *J* 7, Me), 1.28–1.54 (4 H, m, alkyl H), 2.66 (2 H, d, *J* 6, CH_2O), 3.24 (2 H, br q, *J* 6, 4-CH_2), 3.44–3.57 (1 H, m, CH_2O), 3.82–3.93 (1 H, m, CH_2O), 4.63 (1 H, t, *J* 6, CHO), 6.24 (1 H, br s, NH), 7.15–7.35 (3 H, m, ArH) and 7.48–7.57 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 13.73 (q), 15.03 (q), 20.01 (t), 31.53 (t), 39.16 (t), 43.12 (t), 64.92 (t), 66.59 (s), 67.19 (d), 101.44 (s), 127.13 (d), 128.16 (s), 129.02 (d), 129.57 (d) and 169.16 (s) (Found: C, 57.82; H, 6.74; N, 4.05. $C_{17}H_{23}NO_2Se$ requires C, 57.97; H, 6.58; N, 3.98%).

***N*-*p*-Methoxyphenyl-3-ethoxy-5-phenylselenopent-4-ynamide 13.** ν_{max}/cm^{-1} 3300 (NH), 2160 (acetylene) and 1660 (CO); δ_H(400 MHz; $CDCl_3$) 1.26 (3 H, t, *J* 7, Me), 2.82 (2 H, d, *J* 6, CH_2CO), 3.50–3.56 (1 H, m, CH_2O), 3.74 (3 H, s, OMe), 3.87–3.92 (1 H, m, CH_2O), 4.70 (1 H, t, *J* 6, CHO), 6.81 (1 H, t, *J* 9, ArH), 7.20–7.22 (3 H, m, ArH), 7.39 (2 H, d, *J* 9, ArH), 7.39–7.46 (2 H, m, ArH), 8.40 (1 H, br s, NH); δ_C(100 MHz; $CDCl_3$) 15.09 (q), 43.62 (t), 55.41 (q), 65.00 (t), 67.06 (d), 101.13 (s), 114.04 (d), 121.73 (d), 127.19 (d), 128.02 (s), 128.95 (d), 129.55 (d), 131.09 (s), 156.27 (s) and 167.50 (s) (Found: C, 59.64; H, 5.25; N, 3.53. $C_{21}H_{23}NO_3Se$ requires C, 59.70; H, 5.26; N, 3.48%).

***N*-Butyl-2,2-dimethyl-3-ethoxy-5-phenylselenopent-4-ynamide 14.** ν_{max}/cm^{-1} 3360 (NH), 2170 (acetylene) and 1650 (CO); δ_H(400 MHz; $CDCl_3$) 0.89 (3 H, t, *J* 7, Me), 1.23 (3 H, t, *J* 7, Me), 1.27 (3 H, s, Me), 1.30 (3 H, s, Me), 1.25–1.37 (2 H, m, alkyl H), 1.41–1.48 (2 H, m, alkyl H), 3.23 (2 H, q, *J* 7, NCH_2), 3.44–3.51 (1 H, m, OCH_2), 3.86–3.92 (1 H, m, OCH_2), 4.27 (1 H, s, 3-H), 6.59 (1 H, br s, NH), 7.23–7.33 (3 H, m, ArH) and 7.48–7.50 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 13.69 (q), 14.88 (q), 19.96 (t), 21.42 (q), 23.60 (q), 31.46 (t), 39.00 (t), 46.81 (s), 65.39 (t), 66.72 (s), 76.60 (d), 100.67 (s), 127.04 (d), 128.32 (s), 128.88 (d), 129.45 (d) and 174.99 (s). A M^+ peak at *m*/*z* 381 was too small to be measured exactly.

***N*-Benzyl-3-ethoxy-2-methyl-5-phenylselenopent-4-ynamide 15.** ν_{max}/cm^{-1} 3360 (NH), 2160 (acetylene) and 1650 (CO); δ_H(400 MHz; $CDCl_3$) 1.13 (t, *J* 7, Me), 1.14 (t, *J* 7, Me), 1.26 (d, *J* 7, Me), 1.29 (d, *J* 7, Me), 2.57–2.63 (m, CHMe), 2.63–2.73 (m, CHMe), 3.39–3.46 (m, OCH_2), 3.77–3.84 (m, OCH_2), 4.27–4.54 (m, 3-H and NCH_2), 6.72 (br t, *J* 5, NH), 6.91 (br s, NH), 7.18–7.29 (m, ArH) and 7.46–7.49 (m, ArH); δ_C(100 MHz; $CDCl_3$) 13.10 (q), 14.46 (q), 14.75 (q), 43.02 (t), 43.08 (t), 45.53 (d), 46.53 (d), 64.67 (d), 65.00 (t), 66.61 (s), 67.02 (s), 71.97 (d), 72.59 (d), 100.50 (s), 101.29 (s), 126.91 (d), 126.96 (d), 127.16 (d), 127.22 (d), 128.24 (d), 128.30 (d), 128.77 (d), 129.34 (d), 138.21 (s), 138.27 (s), 172.39 (s) and 173.20 (s) (Found: C, 63.03; H, 5.93; N, 3.58. $C_{21}H_{23}NO_2Se$ requires C, 63.00; H, 5.79; N, 3.50%).

***N*-Butyl-3-ethoxy-2-phenyl-5-phenylselenopent-4-ynamide 16.** White needles, mp 121–122 °C; ν_{max}/cm^{-1} 3300 (NH), 2180 (acetylene) and 1640 (CO); δ_H(400 MHz; $CDCl_3$) 0.86 (3 H, t, *J* 7, Me), 1.21 (3 H, t, *J* 7, Me), 1.25–1.33 (2 H, m, alkyl H), 1.39–1.46 (2 H, m, alkyl H), 3.12–3.19 (1 H, m, NCH_2), 3.21–3.32 (1 H, m, NCH_2), 3.52–3.59 (1 H, m, OCH_2), 3.63 (1 H, d, *J* 9, benzyl H), 3.84–3.91 (1 H, m, OCH_2), 4.93 (1 H, d, *J* 9, 3-H), 6.29 (1 H, br s, NH), 7.12–7.31 (8 H, m, ArH), 7.41–7.43 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 13.61 (q), 14.97 (q), 19.81 (t), 31.46 (t), 39.31 (t), 58.64 (d), 65.46 (t), 66.45 (s), 72.34 (d), 101.14 (s), 126.76 (d), 127.82 (d), 128.39 (d), 128.61 (d), 128.66 (d), 128.70 (d), 129.34 (d) and 170.43 (s) (Found: C, 64.21; H, 6.43; N, 3.37. $C_{23}H_{27}NO_2Se$ requires C, 64.48; H, 6.35; N, 3.27%).

***N*-Benzyl-3-ethoxy-2-phenyl-5-phenylselenopent-4-ynamide 17.** White needles, mp 137–140 °C; ν_{max}/cm^{-1} 3260 (NH), 2160 (acetylene) and 1630 (CO); δ_H(400 MHz; $CDCl_3$) 1.20 (3 H, t, *J*

7, Me), 3.54–3.57 (1 H, m, NCH_2), 3.67 (1 H, d, *J* 9, 2-H), 3.84–3.89 (1 H, m, NCH_2), 4.27 (1 H, dd, *J* 6 and 15, OCH_2), 4.55 (1 H, dd, *J* 6 and 15, OCH_2), 4.96 (1 H, d, *J* 9, 3-H), 6.31 (1 H, br s, NH), 7.15–7.31 (8 H, m, ArH) and 7.42–7.51 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 15.03 (q), 43.53 (t), 58.80 (d), 65.54 (t), 66.97 (s), 72.44 (d), 101.02 (s), 126.86 (d), 127.25 (d), 127.39 (d), 127.80 (d), 128.27 (s), 128.51 (d), 128.80 (d), 129.42 (d), 135.72 (s), 138.17 (s) and 170.63 (s) (Found: C, 67.41; H, 5.36; N, 3.10. $C_{26}H_{25}NO_2Se$ requires C, 67.53; H, 5.45; N, 3.03%).

***N*-Benzyl-3-ethoxy-5-phenylthiopent-4-ynamide 1.** ν_{max}/cm^{-1} 3300 (NH), 2190 (acetylene) and 1650 (CO); δ_H(400 MHz; $CDCl_3$) 1.17 (3 H, t, *J* 7, Me), 2.71 (2 H, d, *J* 6, NCH_2), 3.42–3.53 (1 H, m, OCH_2), 3.78–3.89 (1 H, m, OCH_2), 4.36–4.48 (2 H, m, $COCH_2$), 4.67 (1 H, t, *J* 6, CHO), 6.69 (1 H, br s, NH) and 7.18–7.40 (10 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 14.90 (q), 42.88 (t), 43.36 (t), 64.86 (t), 66.98 (d), 73.24 (s), 96.60 (s), 126.15 (d), 126.62 (d), 127.24 (d), 127.41 (d), 128.52 (d), 129.22 (d), 132.02 (s), 138.05 (s) and 169.12 (s) (Found: M^+, 339.1293. $C_{20}H_{21}NO_2S$ requires *M*, 339.1297).

Reactions of alkynyl amides with Bu^{t}OK

General procedure. Bu^{t}OK (0.13 g, 1.0 mmol) and 18-crown-6 ether (10 mg, 0.04 mmol) were added to a solution of the alkynyl amide (0.5 mmol) in Bu^{t}OH (1 cm^3) at room temperature and the reaction mixture was stirred for 30 min. It was then poured into water (100 cm^3) and the organic layer was separated. The aqueous layer was extracted with diethyl ether and the combined organic layer and extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt–hexane (1:10) to give the pyrrolones **18–24** (see Table 3).

(*Z*)-*N*-Benzyl-5-phenylselenomethylenepyrrol-2-one 18a. Pale yellow prisms, mp 88–89 °C; ν_{max}/cm^{-1} 1660 (CO); δ_H(400 MHz; $CDCl_3$) 5.18 (2 H, s, benzyl H), 6.19 (1 H, d, *J* 6, olefinic H), 6.32 (1 H, s, olefinic H), 6.90 (1 H, d, *J* 6, olefinic H), 7.18–7.22 (2 H, m, ArH), 7.24–7.33 (6 H, m, ArH) and 7.41–7.43 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 43.99 (t), 110.89 (d), 121.13 (d), 126.56 (d), 127.42 (d), 128.55 (d), 128.79 (d), 129.78 (d), 130.62 (s), 132.94 (d), 137.66 (s), 137.97 (d), 140.04 (s) and 172.04 (s) (Found: C, 63.38; H, 4.44; N, 4.09. $C_{18}H_{15}NOSe$ requires C, 63.53; H, 4.44; N, 4.12%).

(*E*)-*N*-Benzyl-5-phenylselenomethylenepyrrol-2-one 18b. Pale yellow prisms, mp 49–50 °C; ν_{max}/cm^{-1} 1660 (CO); δ_H(400 MHz; $CDCl_3$) 4.87 (2 H, s, benzyl H), 6.28 (1 H, br s, olefinic H), 6.32 (1 H, dd, *J* 2 and 6, olefinic H), 7.11–7.33 (10 H, m, ArH) and 7.43 (1 H, d, *J* 6, olefinic H); δ_C(100 MHz; $CDCl_3$) 42.83 (t), 104.32 (d), 124.98 (d), 126.97 (d), 127.08 (d), 127.41 (d), 128.75 (d), 129.37 (d), 130.38 (d), 132.73 (s), 134.69 (d), 136.90 (s), 143.40 (s) and 170.26 (s) (Found: C, 63.67; H, 4.38; N, 4.18. $C_{18}H_{15}NOSe$ requires C, 63.53; H, 4.44; N, 4.12%).

(*Z*)-*N*-Butyl-5-phenylselenomethylenepyrrol-2-one 19. Pale yellow needles, mp 77–78 °C; ν_{max}/cm^{-1} 1660 (CO); δ_H(400 MHz; $CDCl_3$) 0.98 (3 H, t, *J* 7, Me), 1.39–1.44 (2 H, m, alkyl H), 1.65–1.73 (2 H, m, alkyl H), 3.85 (2 H, t, *J* 7, NCH_2), 6.09 (1 H, d, *J* 6, olefinic H), 6.29 (1 H, s, olefinic H), 6.81 (1 H, d, *J* 6, olefinic H), 7.36–7.38 (3 H, m, ArH) and 7.59–7.61 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 13.82 (q), 19.98 (t), 32.60 (t), 40.66 (t), 109.28 (d), 121.07 (d), 128.37 (d), 129.63 (d), 130.29 (s), 132.71 (d), 137.09 (d), 140.06 (s) and 171.55 (s) (Found: C, 58.56; H, 5.62; N, 4.63. $C_{15}H_{17}NOSe$ requires C, 58.83; H, 5.59; N, 4.57%).

(*Z*)-*N*-*p*-Methoxyphenyl-5-phenylselenomethylenepyrrol-2-one 20. Pale yellow needles, mp 154–155 °C (decomp.); ν_{max}/cm^{-1} 1680 (CO); δ_H(400 MHz; $CDCl_3$) 3.87 (3 H, s, OMe), 6.21 (1 H, d, *J* 5, olefinic H), 6.41 (1 H, s, olefinic H), 6.95 (1 H, d, *J* 5, olefinic H), 7.01 (2 H, d, *J* 9, ArH), 7.29 (2 H, d, *J* 9, ArH), 7.26–7.31 (3 H, m, ArH) and 7.44–7.47 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 55.52 (q), 112.89 (d), 114.63 (d), 120.76 (d), 126.70 (s), 128.24 (d), 129.48 (d), 130.87 (d), 131.53 (s), 132.72 (d), 136.69 (d), 138.81 (s), 160.17 (s) and 171.62 (s) (Found: C, 60.55; H, 4.29; N, 4.02. $C_{18}H_{15}NO_2Se$: C, 60.68; H, 4.24; N, 3.93%).

(*Z*)-*N*-Butyl-3,3-dimethyl-4-ethoxy-5-phenylselenomethylenepyrrolidin-2-one 21. Pale yellow oil, ν_{max}/cm^{-1} 1730 (CO); δ_H(400 MHz; $CDCl_3$) 0.91 (3 H, t, *J* 7, Me), 1.14 (3 H, s, Me), 1.21 (3 H, s, Me), 1.22 (3 H, t, *J* 7, Me), 1.25–1.37 (2 H, m, alkyl H), 1.53–1.60 (2 H, m, alkyl H), 3.52–3.60 (1 H, m, NCH_2), 3.64–3.71 (1 H, m, NCH_2), 3.76–3.80 (2 H, m, OCH_2), 3.91 (1 H, s, OCH), 5.68 (1 H, s, olefinic H), 7.23–7.31 (3 H, m, ArH) and 7.47 (2 H, br d, *J* 7, ArH); δ_C(100 MHz; $CDCl_3$) 13.78 (q), 15.23 (q), 17.86 (q), 19.58 (t), 30.53 (q), 40.72 (t), 44.56 (s), 66.03 (t), 85.71 (d), 89.62 (d), 126.80 (d), 129.29 (d), 130.64 (d), 132.23 (s), 142.60 (s) and 179.78 (s) (Found: M^+, 381.1222. $C_{19}H_{27}NO_2Se$ requires *M*, 381.1207).

(*Z*)-*N*-Benzyl-3-methyl-5-phenylselenomethylenepyrrol-2-one 22a. Pale yellow oil, ν_{max}/cm^{-1} 1700 (CO); δ_H(400 MHz; $CDCl_3$) 2.01 (3 H, d, *J* 1, Me), 5.20 (2 H, s, benzyl H), 6.13 (1 H, s, olefinic H), 6.59 (1 H, d, *J* 1, olefinic H), 7.12–7.33 (8 H, m, ArH) and 7.41 (2 H, dd, *J* 2 and 7, ArH); δ_C(100 MHz; $CDCl_3$) 10.75 (q), 44.13 (t), 106.31 (d), 126.44 (d), 127.01 (d), 128.02 (d), 128.51 (d), 129.46 (d), 130.65 (s), 130.83 (s), 132.41 (d), 132.48 (d), 137.64 (s), 139.34 (s) and 172.33 (s) (Found: M^+, 355.0486. $C_{19}H_{17}NOSe$ requires *M*, 355.0475).

(*E*)-*N*-Benzyl-3-methyl-5-phenylselenomethylenepyrrol-2-one 22b. Pale yellow oil, ν_{max}/cm^{-1} 1680 (CO); δ_H(400 MHz; $CDCl_3$) 2.06 (3 H, s, Me), 4.88 (2 H, s, benzyl H), 6.14 (1 H, s, olefinic H) and 7.11–7.34 (10 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 11.23 (q), 43.17 (t), 100.61 (d), 126.80 (d), 127.02 (d), 127.37 (d), 128.72 (d), 129.08 (d), 129.30 (d), 130.09 (d), 134.96 (d), 137.08 (s), 143.29 (s) and 170.08 (s) (Found: M^+, 355.0462. $C_{19}H_{17}NOSe$ requires *M*, 355.0475).

(*Z*)- and (*E*)-*N*-Butyl-3-phenyl-5-phenylselenomethylenepyrrol-2-one 23a and 23b. Pale yellow oil, **22a** and **22b** (3.7:2.1). The *E*- and *Z*-isomer ratio was determined from the NCH_2 intensities; ν_{max}/cm^{-1} 1680 (CO); δ_H(400 MHz; $CDCl_3$) 0.94 (t, *J* 7, b-Me), 0.99 (t, *J* 7, a-Me), 1.34–1.49 (m, alkyl H), 1.58–1.77 (m, alkyl H), 3.71 (t, *J* 7, b-NCH_2), 3.93 (t, *J* 7, a-NCH_2), 6.34 (s, a-olefinic H), 6.43 (s, b-olefinic H), 6.97 (s, a-olefinic H), 7.25–7.49 (m, ArH), 7.59–7.63 (m, ArH), 7.95 (br d, *J* 7, a-ArH) and 7.98 (br d, *J* 7, ArH); δ_C(100 MHz; $CDCl_3$) 13.78 (b-q), 13.87 (a-q), 20.09 (a- and b-q), 31.01 (b-q), 32.60 (a-t), 39.14 (b-t), 40.97 (a-t), 101.85 (b-d), 108.58 (a-d), 126.25 (d), 127.04 (d), 127.37 (d), 127.46 (d), 128.35 (d), 128.44 (d), 128.50 (d), 129.03 (d), 129.49 (d), 129.67 (d), 129.72 (d), 130.62 (s), 130.71 (s), 131.11 (d), 131.37 (s), 132.65 (d), 134.53 (s), 139.02 (s), 142.91 (s), 169.06 (s) and 170.07 (s) (Found: M^+, 383.0781. $C_{21}H_{21}NOSe$ requires *M*, 383.0788).

(*Z*)- and (*E*)-*N*-Benzyl-3-phenyl-5-phenylselenomethylenepyrrol-2-one 24a and 24b. Pale yellow oil **23a** and **23b** (1.0:1.4), The *E*- and *Z*-isomer ratio was determined from the intensities of the benzyl H; ν_{max}/cm^{-1} 1680 (CO); δ_H(400 MHz; $CDCl_3$) 4.96 (s, b-benzyl H), 5.27 (s, a-benzyl H), 6.32 (s, b-olefinic H), 6.37 (s, a-olefinic H), 7.08 (s, a-olefinic H), 7.15–7.47 (m, ArH), 7.59 (s, b-olefinic H), 7.96–7.99 (m, a-ArH) and 8.02–8.04 (m, b-ArH); δ_C(100 MHz; $CDCl_3$) 43.09 (b-t), 44.11 (a-t), 103.47 (b-d), 109.71 (a-d), 126.52 (d), 126.70 (d), 127.03 (d), 127.10 (d), 127.19 (d), 127.43 (d), 127.50 (d), 128.25 (d), 128.58 (d), 128.62 (d), 128.77 (d), 129.39 (d), 129.55 (d), 130.19 (s), 130.34 (d), 131.07 (s), 131.25 (s), 132.64 (d), 134.40 (s), 136.98 (s), 137.49 (s), 138.81 (s), 142.37 (s), 169.04 (s) and 170.33 (s) (Found: M^+, 417.0644. $C_{24}H_{19}NOSe$ requires *M*, 417.0632).

(*Z*)-*N*-Benzyl-5-phenylthiomethylenepyrrol-2-one 2a. Colourless needles, mp 83–84 °C, ν_{max}/cm^{-1} 1660 (CO); δ_H(400 MHz; $CDCl_3$) 5.23 (2 H, s, benzyl H), 6.04 (1 H, s, olefinic H), 6.20 (1 H, d, *J* 6, olefinic H), 6.90 (1 H, d, *J* 6, olefinic H) and 7.20–7.32 (10 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 44.22 (t), 113.17 (d), 120.99 (d), 126.99 (d), 127.07 (d), 128.02 (d), 128.46 (d), 129.37 (d), 130.30 (d), 137.47 (s), 137.76 (s), 137.82 (d) and 171.56 (s) (Found: C, 73.75; H, 5.17; N, 4.85. $C_{18}H_{15}NOS$ requires C, 73.69; H, 5.15; N, 4.77%).

(*E*)-*N*-Benzyl-5-phenylthiomethylenepyrrol-2-one 2b. Pale yellow oil, ν_{max}/cm^{-1} 1690 (CO); δ_H(400 MHz; $CDCl_3$) 4.90 (2 H, s, benzyl H), 5.98 (1 H, br s, olefinic H), 6.31 (1 H, dd, *J* 1 and 6, olefinic H), 7.00 (1 H, d, *J* 6, olefinic H), 7.19–7.34 (9 H, m, ArH) and 7.49 (1 H, d, *J* 6, ArH); δ_C(100 MHz; $CDCl_3$) 42.93 (t), 107.96 (d), 124.38 (d), 126.63 (d), 126.98 (d), 127.48 (d), 127.82 (d), 128.81 (d), 129.14 (d), 133.18 (d), 136.88 (s), 141.96 (s) and 170.03 (s) (Found: M^+, 293.0884. $C_{18}H_{15}NOSe$ requires *M*, 293.0875).

Isomerization of the (*Z*)-pyrrol-2-one 18a to the (*E*)-isomer 18b
Trifluoromethanesulfonic acid (45 mg, 0.3 mmol) was added dropwise to a CH_2Cl_2 (1 cm^3) solution of (*Z*)-pyrrol-2-one **18a** (50 mg, 0.15 mmol) under an Ar atmosphere at 0 °C and the mixture was stirred for 30 min. It was then poured into sat. aq. $NaHCO_3$ (100 cm^3). The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layer and extracts were dried ($MgSO_4$) and evaporated under reduced pressure and the residue was crystallized from hexane to give the (*E*)-pyrrolone **18b** (50 mg, quant.) as pale yellow prisms. The reactions of **18a** with TMSOTf or BF_3·Et_2O were also handled as described above.

Cyclopropanation of the pyrrol-2-one 18b
A diethyl ether (5 cm^3) solution of diazomethane [11] [generated *in situ* from *N*-methylnitrosourea (0.5 g, 4.9 mmol) and 50% KOH] was added to a diethyl ether (2 cm^3) solution of **18b** (0.52 g, 1.5 mmol) at 0 °C and the reaction mixture was stirred for 1 h. The yellow crystals which formed were filtered off and washed with a small amount of diethyl ether to give the almost pure pyrazole; this was used without further purification because of its instability. A dry CH_3CN (20 cm^3) solution of the pyrazole was irradiated using Padwa's method [12] for 4 h after which it was evaporated under reduced pressure. The mixture was purified by TLC on silica gel eluting with AcOEt–hexane (1 : 10) to give (1*R**,3*S**)-(*E*)-*N*-benzyl-4-(phenylselenomethylene)-3-azabicyclo[3.1.0]hexan-2-one **26b** (0.3 g, 57%) as a yellow oil; ν_{max}/cm^{-1} 1730 and 1630 (NCO); δ_H(400 MHz; $CDCl_3$) 0.88–0.93 (1 H, m, 6-H), 1.26–1.34 (1 H, m, 6-H), 2.28–2.35 (1 H, m, 1-H), 2.82–2.88 (1 H, m, 5-H), 4.65 (2 H, s, benzyl H), 5.56 (1 H, d, *J* 1, olefinic H) and 7.06–7.36 (10 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 17.10 (t), 18.25 (d), 20.03 (d), 43.41 (t), 87.05 (d), 125.87 (d), 127.19 (d), 127.50 (d), 128.71 (d), 128.80 (d), 129.02 (s), 132.80 (s), 135.95 (s) and 149.12 (s) (Found: M^+, 355.0480. $C_{19}H_{17}NOSe$ requires *M*, 355.0476).

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Paper 6/00091F
Received 4*th January* 1996
Accepted 5*th March* 1996