A Novel Synthesis of Pyrrolizidine Alkaloids by Means of an Intramolecular Carbenoid Displacement (ICD) Reaction[1]

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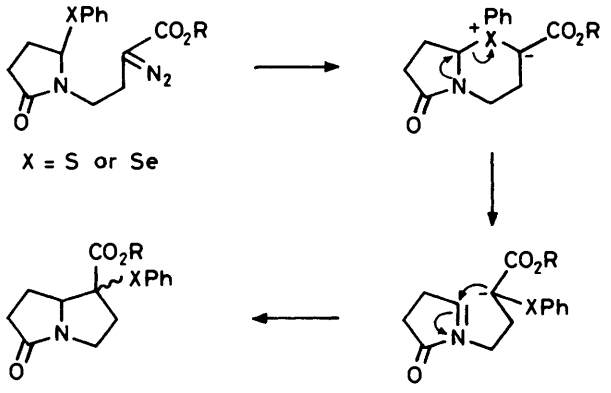
The pyrrolizidine alkaloids, (±)-trachelanthamidine, (±)-isoretronecanol, and (±)-supinidine were synthesized by using an intramolecular carbenoid displacement (ICD) reaction of the diazo-sulphide or the diazo-selenide derivatives as a key step.

Pyrrolizidine alkaloids,[2] a large class of natural products, are popular synthetic targets, because they exhibit attractive physiological activity and also provide further opportunities to develop new synthetic methods and strategies for five-membered nitrogen heterocycles.

Recently, we have been engaged in the development[3,4] of a novel carbon–carbon bond formation reaction at the α-position to the nitrogen in lactams and have found that a carbenoid displacement[5] would be an efficient and convenient method for this purpose. This strategy seemed to be applicable to the synthesis of natural products, and we here describe a novel synthesis of the pyrrolizidine alkaloids (±)-trachelanthamidine, (±)-isoretronecanol, and (±)-supinidine by this method.

The synthesis involves a site-specific carbon–carbon bond formation reaction at the α-position to the nitrogen to form the 1-azabicyclo[3.3.0]octane system, which arises from the preferential participation of carbenoid with the electron sufficient atoms such as sulphur or selenium, probably *via* the ylide intermediate as shown in Scheme 1. Furthermore the synthesis of natural products with a variety of functionalities can be accomplished by manipulation of the organosulphur or organoselenium groups.[6]



Scheme 1.

Thus, succinimide (**1**) was treated with ethyl 4-bromobutyrate in the presence of sodium hydride to give the ester (**2**) in 78.9% yield. Reduction of the imide group of compound (**2**) with sodium borohydride[7] in ethanol at 0 °C, followed by acidification of the resulting mixture with ethanolic hydrogen chloride afforded the ethoxypyrrolidinone (**3**), treatment of which with thiophenol[8] in the presence of toluene-*p*-sulphonic acid furnished the sulphide derivative (**4**) in 72.9% yield from (**2**). The selenide (**5**) was prepared in 55.9% yield from (**2**) by Hart's procedure.[9]

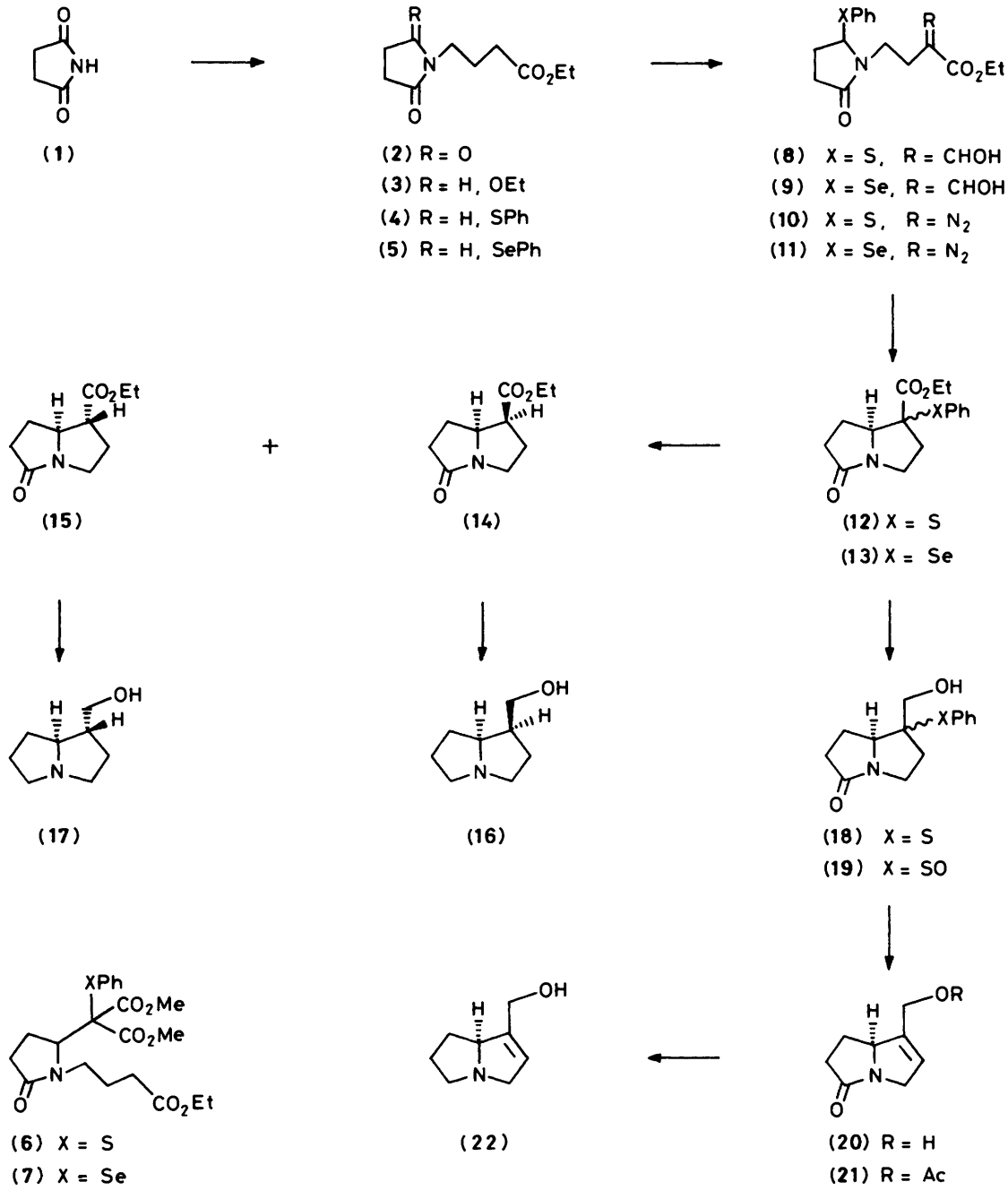
First, the intermolecular carbenoid displacement reaction of (**4**) and (**5**) was carried out using dimethyl α-diazomalonate as a carbenoid precursor to investigate the possibility of formation of a new carbon–carbon bond at the desired position. Heating the diazo-compound with compound (**4**) in the presence of a catalytic amount of rhodium acetate in benzene afforded the triester (**6**) in 83.6% yield. Similarly the treatment of the selenide (**5**) with the diazo-compound gave the triester (**7**) in 68.8% yield.

Since both the sulphide (**4**) and the selenide (**5**) were found to be effective to carbenoid displacement, the compounds (**10**) and (**11**) were subjected to the ICD reaction. The desired diazo-compounds (**10**) and (**11**) were prepared[9] from compounds (**4**) and (**5**) by formylation with ethyl formate in the presence of sodium hydride or lithium hexamethyldisilazide, followed by treatment of the formyl compounds [(**8**) and (**9**)] with toluene-*p*-sulphonyl azide in 65.8% and 26.2% yields respectively. The ICD reaction of (**10**) in refluxing dry benzene in the presence of a catalytic amount of rhodium acetate for 15 min gave the desired bicyclic compound as an inseparable diastereoisomeric mixture (**12**) in 55.2% yield. Conversion of the sulphide group of (**12**) to hydrogen was achieved by reductive elimination with Raney-nickel in refluxing ethanol to furnish the esters (**14**) and (**15**) in 40.2% and 38.2% yields, respectively. The spectral data of these compounds (**14**) and (**15**) were identical with those reported.[10] Since compounds (**14**) and (**15**) have already been converted[10] into (±)-isoretronecanol (**16**) and (±)-trachelanthamidine (**17**) respectively, this synthesis constitutes their formal synthesis. Furthermore, the ICD reaction of (**11**) afforded the bicyclic compound (**13**), in 36.4% yield, which in turn gave the esters (**14**) and (**15**) in 48.9% and 37.6% yields, respectively on reductive elimination of the selenide group by treatment with tributyltin hydride and azoisobutyronitrile in refluxing benzene.

It is known[2] that necine bases must contain a 1,2-didehydro system in their molecules to exhibit physiological activity, and the sulphide (**12**) was, therefore, subjected to the oxidative elimination. Thus, the reduction of the sulphide (**12**) with lithium aluminium hydride in ether at 0 °C furnished the alcohol (**18**), in 78.5% yield. Oxidation of compound (**18**) with *m*-chloroperbenzoic acid in dichloromethane at ambient temperature, followed by thermal elimination of the sulphoxide (**19**) by refluxing in toluene for 45 min gave the allyl alcohol (**20**), acetylation of which with acetic anhydride provided compound (**21**) in 44.5% yield from (**19**). Since the acetate (**21**) was also converted into (±)-supinidine (**22**) by Hart,[11] this constitutes its formal synthesis.

Experimental

I.r. spectra were obtained with a Hitachi 260-10 spectrophotometer, n.m.r. spectra with JEOL PMX-60 and JEOL JNM FX-100 instruments (tetramethylsilane as an internal reference), and mass spectra with a JEOL JMS D-300 spectrometer. M.p.s were determined with a Yanagimoto micro apparatus and are uncorrected.



Scheme 2.

1-(3-*Ethoxycarbonylpropyl*)*pyrrolidine*-2,5-*dione* (**2**).—Sodium hydride (5.8 g) (60% dispersion in mineral oil) was added to a stirred solution of succinimide (11.9 g) in dry dimethylformamide at 0 °C. The mixture was stirred for 30 min, ethyl 4-bromobutyrate (23.6 g) was added, and the resulting mixture further stirred overnight at ambient temperature. The mixture was poured into water and extracted with benzene. The extract was washed with water and aqueous sodium chloride, dried (Na_2SO_4), and evaporated to give an oil. Chromatography on silica gel with benzene–ethyl acetate (95:5 v/v) as eluant afforded compound (**2**) (20.19 g, 78.9%) as a colourless oil (Found: C, 56.1; H, 7.2; N, 6.4. $C_{10}H_{15}NO_4$ requires C, 56.3; H, 7.1; N, 6.55%); $\nu_{max.}(CHCl_3)$ 1 700 cm^{-1} (CO); δ_H(60 MHz; CCl_4) 1.23 (3 H, t, *J* 7 Hz, Me), 1.60—2.42 (4 H, m, CH_2 × 2), 2.61 (4 H, s, CH_2 × 2), 3.44 (2 H, t, *J* 6.5 Hz, NCH_2), and 4.03 (2 H, q, *J* 7 Hz, OCH_2); *m/z* 213 (M^+).

5-*Ethoxy*-1-(3-*ethoxycarbonylpropyl*)*pyrrolidin*-2-*one* (**3**).—Sodium borohydride (1.56 g) at 0 °C was added to a stirred solution of the imide (**2**) (2.94 g) in anhydrous ethanol (70 ml) and the mixture stirred for 2 h at the same temperature, while the pH of the solution was maintained at 8—9 by frequent addition of ethanolic hydrogen chloride. The mixture was acidified with ethanolic hydrogen chloride to pH 3, and the resulting mixture stirred for a further 15 min at 0 °C, then basified with 1% ethanolic potassium hydroxide solution to pH 9. The reaction mixture was poured into water and extracted with chloroform. The organic layer was washed with water,

dried (Na_2SO_4), and the solvent evaporated to afford the title compound (**3**) as a colourless oil, $\nu_{max.}$($CHCl_3$) 1 685 and 1 720 cm^{-1} (CO); δ_H(60 MHz; CCl_4) 1.18 (3 H, t, *J* 7 Hz, Me), 1.24 (3 H, t, *J* 7 Hz, Me), 1.49—2.63 (8 H, m, CH_2 × 4), 2.80—3.72 (4 H, m, NCH_2 and OCH_2), 4.02 (2 H, q, *J* 7 Hz, OCH_2), and 4.87 (1 H, br d, *J* 4 Hz, CH); *m/z* 244 (M^+ + 1). This material was dissolved in thiophenol (15 g), toluene-*p*-sulphonic acid monohydrate (100 mg) was added, and the resulting mixture was stirred for 15 min at room temperature then partitioned between 1M aqueous sodium hydroxide (150 ml) and dichloromethane (150 ml). The aqueous layer was extracted with dichloromethane (150 ml), and the combined organic layers dried (Na_2SO_4), and evaporated to give a white turbid oil, which was subjected to column chromatography on silica gel. Elution with benzene–ethyl acetate (9:1 v/v) afforded compound (**4**) (3.09 g, 72.9%) as a colourless oil (Found: C, 62.6; H, 6.95; N, 4.6. $C_{16}H_{21}NO_3S$ requires C, 62.5; H, 6.9; N, 4.55%); $\nu_{max.}$($CHCl_3$) 1 680 and 1 720 cm^{-1} (CO); δ_H(60 MHz; CCl_4) 1.22 (3 H, t, *J* 7 Hz, Me), 1.47—2.68 (8 H, m, CH_2 × 4), 2.98—3.79 (2 H, m, NCH_2), 4.14 (2 H, q, *J* 7 Hz, OCH_2), 4.93 (1 H, dd, *J* 6.5 Hz and 2.5 Hz, CH), and 7.30 (5 H, br s, ArH); *m/z* 308 (M^+ + 1).

Intermolecular Reaction of the Sulphide (**4**) *with Dimethyl Diazomalonate*.—A solution of the sulphide (**4**) (536 mg) in dry benzene (20 ml) containing a catalytic amount of rhodium acetate was heated under reflux, and a solution of dimethyl diazomalonate (551 mg) in dry benzene (10 ml) was added dropwise to the refluxing solution. The mixture was stirred further for 2 h at the same temperature, the solvent was evaporated, and the residue subjected to chromatography on silica gel. Elution with benzene–ethyl acetate (8:2 v/v) afforded compound (**6**) (639 mg, 83.6%) as a colourless oil, $\nu_{max.}$($CHCl_3$) 1 680 and 1 725 cm^{-1} (CO); δ_H(60 MHz; CCl_4) 1.23 (3 H, t, *J* 7 Hz, Me), 3.58 and 3.65 (each 3 H, s, OMe × 2), 4.10 (2 H, q, *J* 7 Hz, OCH_2), 4.35—4.67 (1 H, br s, CH), and 7.25—7.80 (5 H, m, ArH) (Found: M^+, 437.1495). $C_{21}H_{27}NO_7S$ requires *M*, 437.1507).

1-(3-*Ethoxycarbonyl*-3-*hydroxymethylenepropyl*)-5-*phenylthiopyrrolidin*-2-*one* (**8**).—Sodium hydride (383 mg) (60% dispersion in mineral oil) at 0 °C was added to a stirred solution of the sulphide (**4**) (1.94 g) and ethyl formate (0.8 ml) in dry benzene (5 ml), and the resulting mixture was stirred overnight at ambient temperature. The mixture was poured into water, washed with benzene, and the aqueous layer acidified with 10% aqueous hydrochloric acid and extracted with ethyl acetate. The extract was dried (Na_2SO_4), and the solvent evaporated to give an oil, which was subjected to chromatography on silica gel. Elution with chloroform gave compound (**8**) (1.53 g, 72.3%) as a pale brown oil, $\nu_{max.}$($CHCl_3$) 1 670 (CO) and 3 250 cm^{-1} (OH); δ_H(60 MHz; $CDCl_3$) 1.23 (3 H, t, *J* 7 Hz, Me), 1.50—2.77 (6 H, m, CH_2 × 3), 3.12—3.88 (2 H, m, NCH_2), 4.10 (2 H, q, *J* 7 Hz, OCH_2), 4.96—5.21 (1 H, m, CH), 7.27 (5 H, s, ArH), and 9.29 (1 H, br s, formyl H); *m/z* 226 (M^+ − 109).

1-(3-*Diazo*-3-*ethoxycarbonylpropyl*)-5-*phenylthiopyrrolidin*-2-*one* (**10**).—A solution of compound (**8**) (2.63 g) and triethylamine (2.2 ml) in dichloromethane (15 ml) was cooled at −15 °C, and toluene-*p*-sulphonyl azide (1.8 g) added to the cooled mixture with stirring. The mixture was stirred for 2 h at the same temperature, a solution of potassium hydroxide (0.5 g) in water (1 ml) was added, and the resulting two phase mixture stirred for a further 15 min at room temperature. The organic layer was separated, washed with water, dried (Na_2SO_4), and evaporated to give an oil. Chromatography on silica gel with chloroform as eluant afforded the diazo-compound (**10**) (2.38 g, 91.0%) as a yellow oil, $\nu_{max.}$($CHCl_3$) 1 685 (CO) and 2 100 cm^{-1} (N_2); δ_H(60 MHz; CCl_4) 1.24 (3 H, t, *J* 7 Hz, Me), 1.50—2.68 (6 H, m, CH_2 × 3), 3.08—3.92 (2 H, m, NCH_2), 4.15 (2 H, q, *J* 7 Hz, OCH_2), 4.92 (1 H, dd, *J* 6.5 Hz and 2.5 Hz, CH), and 7.31 (5 H, s, ArH).

6-*Ethoxycarbonyl*-6-*phenylthio*-1-*azabicyclo*[3.3.0]*octan*-2-*one* (**12**).—A catalytic amount of rhodium acetate was added to a refluxing solution of the diazo-compound (**10**) (2.19 g) in dry benzene (200 ml) and the mixture heated for 15 min. The solution was cooled, the solvent evaporated, and the residue subjected to chromatography on silica gel, with benzene–ethyl acetate (8:2 v/v) as eluant to afford an inseparable mixture of the two diastereoisomers (**12**) (1.11 g, 55.2%) as a colourless oil (Found: C, 62.7; H, 6.25; N, 4.3. $C_{16}H_{19}NO_3S$ requires C, 62.95; H, 6.25; N, 4.6%); $\nu_{max.}$($CHCl_3$) 1 680 and 1 720 cm^{-1} (CO); δ_H(60 MHz; CCl_4) 1.20 (3 H, t, *J* 7 Hz, Me), 1.62—2.74 (6 H, m, CH_2 × 3), 2.85—3.83 (3 H, m, NCH_2 + CH), 4.07 (2 H, q, *J* 7 Hz, OCH_2), and 7.28 (5 H, br s, ArH); *m/z* 305 (M^+).

rel-(5S,6S)- *and* rel-(5S,6R)-6-*Ethoxycarbonyl*-1-*azabicyclo*[3.3.0]*octan*-2-*one* [(**14**) *and* (**15**)] *from the Sulphide* (**12**).—A suspension of Raney-nickel (W-2) (3 g) in ethanol (30 ml) was added to a stirred solution of the sulphide (**12**) (228 mg) in anhydrous ethanol (10 ml), and the mixture heated under reflux for 9 h with stirring. After being cooled, the mixture was filtered, and the filtrate concentrated to give an oil. Chromatography on silica gel with benzene–ethyl acetate (6:4 v/v) as eluant afforded (**14**) (59 mg, 40.2%) as a colourless oil, and further elution with the same solvent yielded (**15**) (56 mg, 38.2%) as a colourless oil. The spectral data of these compounds were identical with those from previous reports.[10]

6-*Hydroxymethyl*-6-*phenylthio*-1-*azabicyclo*[3.3.0]*octan*-2-*one* (**18**).—Lithium aluminium hydride (104 mg) was added to a stirred solution of the ester (**12**) (1.11 g) in anhydrous ether (50 ml) at 0 °C and stirring was continued for 2 h at the same temperature. Aqueous sodium hydroxide (10%) was added dropwise until the aluminium compound had entirely precipitated. The mixture was filtered and the filtrate evaporated to give an oil, which was subjected to chromatography on silica gel. Elution with ethyl acetate afforded a mixture of two diastereoisomers (**18**) (754 mg, 78.5%) as a pale yellow oil, $\nu_{max.}$($CHCl_3$) 1 670 (CO) and 3 370 cm^{-1} (OH); δ_H(60 MHz; $CDCl_3$) 1.42—2.82 (6 H, m, CH_2 × 3), 2.82—3.40 (2 H, m, NCH_2), 3.42—3.93 (2 H, m, OCH_2), 3.98—4.75 (2 H, m, CH + OH), and 7.29 (5 H, br s, ArH) (Found: M^+ + 1, 264.1052. $C_{14}H_{18}NO_2S$ requires *M* + 1, 264.1057).

6-*Hydroxymethyl*-6-*phenylsulphinyl*-1-*azabicyclo*[3.3.0]-*octan*-2-*one* (**19**).—*m*-Chloroperbenzoic acid (80%; 618 mg) in dichloromethane solution (5 ml) was added to a stirred two phase solution of the alcohol (**18**) (754 mg) in dichloromethane (5 ml) and saturated aqueous sodium hydrogen carbonate (5 ml) at room temperature. After being stirred for 40 min, the mixture was poured into water, extracted with dichloromethane and the extract washed with aqueous sodium hydrogen carbonate and aqueous sodium chloride, and dried (Na_2SO_4). Evaporation of the solvent yielded a residue, which was subjected to chromatography on silica gel with ethyl acetate–methanol (99:1 v/v) as eluant to afford a mixture of diastereoisomers of the sulphoxide (**19**) as a colourless oil, $\nu_{max.}$($CHCl_3$) 1 680 (CO) and 3 400 cm^{-1} (OH); δ_H(60 MHz; $CDCl_3$) 1.56—1.93 (2 H, m), 2.12—3.88 (8 H, m), 4.09—5.02 (2 H, m), and 7.55 (5 H, s, ArH); *m/z* 280 (M^+ + 1).

6-*Acetoxymethyl*-1-*azabicyclo*[3.3.0]*oct*-6-*en*-2-*one* (**21**).—A solution of the sulphoxide (**19**) (519 mg) in toluene (10 ml) was refluxed for 45 min. The solvent was evaporated to leave the

residue, which was dissolved in dichloromethane (7 ml) containing acetic anhydride (0.4 ml), triethylamine (0.4 ml), and a catalytic amount of 4-dimethylaminopyridine at room temperature. The resulting mixture was stirred for 2 h, then diluted with dichloromethane, washed with water, aqueous sodium hydrogen carbonate, and water, dried (Na_2SO_4), and evaporated to give an oil. Chromatography on silica gel with ethyl acetate–benzene (8:2 v/v) as eluant afforded the acetate (**21**) (148 mg, 44.5%) as a colourless oil, the spectral data of which were identical with those previously reported.[11]

1-(3-*Ethoxycarbonylpropyl*)-5-*phenylselenopyrrolidin*-2-*one* (**5**).—Sodium borohydride (8.8 g) was added to a stirred solution of the imide (**2**) (18.7 g) in anhydrous ethanol (200 ml) at 0 °C. The resulting mixture was stirred for 2 h at the same temperature and then poured into water and extracted with chloroform. The extract was dried (Na_2SO_4) and evaporated to give 1-(3-ethoxycarbonylpropyl)-5-hydroxypyrrolidin-2-one (14.0 g, 74.2%) as a colourless oil. Toluene-*p*-sulphonic acid (10 mg) and benzeneselenol (730 mg) was added to the ketone (1.0 g) at room temperature and the mixture stirred for 3 h. Chromatography on silica gel with benzene–ethyl acetate (8:2 v/v) as eluant afforded the selenide (**5**) (920 mg, 55.9%) as a yellow oil, $\nu_{max.}(CHCl_3)$ 1 680 and 1 720 cm^{-1} (CO); δ_H(60 MHz; CCl_4) 1.26 (3 H, t, *J* 7 Hz, Me), 1.52—2.85 (8 H, m, $CH_2 \times 4$), 2.94—3.86 (2 H, m, NCH_2), 4.13 (2 H, q, *J* 7 Hz, OCH_2), 5.15 (1 H, dd, *J* 6 Hz and 2.5 Hz, CH), and 7.20—7.83 (5 H, m, ArH); *m/z* 198 ($M^+ - 156$).

Intermolecular Reaction of the Selenide (**5**) *with Dimethyl Diazomalonate*.—Dimethyldiazomalonate (310 mg) in dry benzene (10 ml) was added dropwise with stirring to a refluxing solution of the selenide (**5**) (300 mg) in dry benzene (20 ml) containing a catalytic amount of rhodium acetate. After being refluxed for 1 h, the solvent was evaporated and the residue subjected to chromatography on silica gel. Elution with benzene–ethyl acetate (8:2 v/v) afforded compound (**7**) (282 mg, 68.8%) as a pale yellow oil (Found: C, 51.7; H, 5.75; N, 2.9. $C_{21}H_{27}NO_7Se$ requires C, 52.05; H, 5.6; N, 2.9%); $\nu_{max.}(CHCl_3)$ 1 680 and 1 720 cm^{-1} (CO); δ_H 1.24 (3 H, t, *J* 7 Hz, Me), 3.67 and 3.77 (each 3 H, s, OMe × 2), 4.12 (2 H, q, *J* 7 Hz, OCH_2), and 7.48—7.92 (5 H, m, ArH); *m/z* 485 ($M^+ + 1$).

1-(3-*Ethoxycarbonyl*-3-*hydroxymethylenepropyl*)-5-*phenylselenopyrrolidin*-2-*one* (**9**).—Butyl-lithium in hexane (1.57M; 1.8 ml) was added to a stirred solution of hexamethyldisilazane (0.75 ml) in anhydrous tetrahydrofuran (THF) (5 ml) at −78 °C. The mixture was stirred for 15 min, a solution of the selenide (**5**) (500 mg) in anhydrous THF (10 ml) was added, and the resulting mixture stirred for a further 30 min at the same temperature. Ethyl formate (0.2 ml) was added and the reaction temperature gradually warmed to room temperature. Stirring was continued for a further 4 h then the mixture was poured into water and washed with benzene. The aqueous layer was acidified with 10% aqueous hydrochloric acid and extracted with ethyl acetate. The extract was dried (Na_2SO_4), the solvent evaporated, and the residue subjected to chromatography on silica gel with benzene–ethyl acetate (7:3 v/v) as eluant to afford (**9**) (183 mg, 34.0%) as a yellow oil, $\nu_{max.}(CHCl_3)$ 1 670 cm^{-1} (CO); δ_H(60 MHz; CCl_4) 1.25 (3 H, t, *J* 7 Hz, Me), 4.10 (2 H, q, *J* 7 Hz, OCH_2), 4.91—5.42 (1 H, m, CH), 7.25—7.76 (5 H, m, ArH), and 9.65, 11.27, and 11.50 (total 1 H, each s, formyl H).

1-(3-*Diazo*-3-*ethoxycarbonylpropyl*)-5-*phenylselenopyrrolidin*-2-*one* (**11**).—A stirred solution of (**9**) (941 mg) and triethylamine (0.45 ml) in dichloromethane (20 ml) was cooled at −15 °C, toluene-*p*-sulphonyl azide (631 mg) was added, and the resulting mixture stirred for a further 2 h at the same temperature. The solvent was evaporated and the residue subjected to chromatography on silica gel with hexane–ethyl acetate (7:3 v/v) as eluant to give the diazo-compound (**11**) (719 mg, 76.9%) as a yellow oil, $\nu_{max.}(CHCl_3)$ 1 680 (CO) and 2 100 cm^{-1} (N_2); δ_H(60 MHz; CCl_4) 1.26 (3 H, t, *J* 7 Hz, Me), 1.57—2.66 (6 H, m, $CH_2 \times 3$), 3.08—3.97 (2 H, m, NCH_2), 4.22 (2 H, q, *J* 7 Hz, OCH_2), 5.18 (1 H, dd, *J* 6.5 Hz and 2.5 Hz, CH), and 7.29—7.86 (5 H, m, ArH).

6-*Ethoxycarbonyl*-6-*phenylseleno*-1-*azabicyclo*[3.3.0]*octan*-2-*one* (**13**).—A catalytic amount of rhodium acetate was added to a stirred solution of the diazo-compound (**11**) (273 mg) in refluxing dry benzene (10 ml) and dry dichloromethane (10 ml). The solution was refluxed for 10 min, the solvent was evaporated, and the residue subjected to chromatography on silica gel. Elution with benzene–ethyl acetate (8:2 v/v) afforded compound (**13**) (92 mg, 36.4%) as a colourless oil, $\nu_{max.}(CHCl_3)$ 1 670 cm^{-1} (CO); δ_H(60 MHz; CCl_4) 1.28 (3 H, t, *J* 7 Hz, Me), 4.20 (2 H, q, *J* 7 Hz, OCH_2), and 7.22—8.03 (5 H, m, ArH); *m/z* 353 ($M^+ + 1$).

rel-(5S,6S)- *and* rel-(5S,6R)-6-*Ethoxycarbonyl*-1-*azabicyclo*[3.3.0]*octan*-2-*one* [(**14**) *and* (**15**)] *from the Selenide* (**13**).—A solution of tributyltin hydride (117 mg) in dry benzene (10 ml) was added dropwise to a stirred solution of the selenide (**13**) (95 mg) in dry benzene (10 ml) containing a catalytic amount of azoisobutyronitrile under reflux. The mixture was stirred for 2 h at the same temperature, the solvent was evaporated, and the residue subjected to chromatography on silica gel. Elution with benzene–ethyl acetate (6:4 v/v) afforded compound (**14**) (26 mg, 48.9%) as a colourless oil, and further elution with the same solvent yielded (**15**) (20 mg, 37.6%) as a colourless oil. These products had i.r. and n.m.r. spectra and t.l.c. behaviour identical with authentic samples.

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