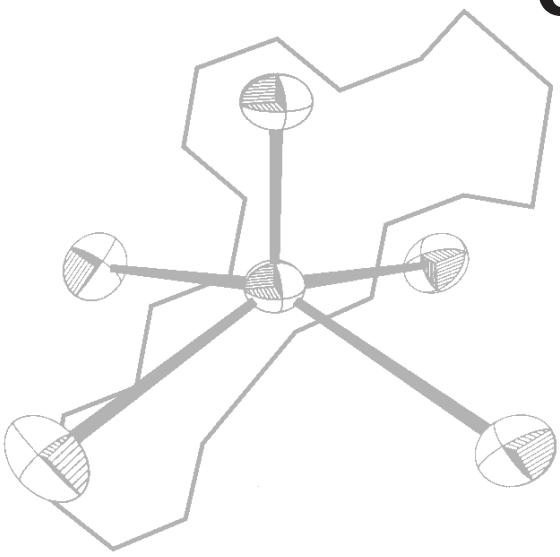
CSIRO PUBLISHING

Australian Journal of Chemistry



Volume 53, 2000

A journal for the publication of original research
in all branches of chemistry and chemical technology

www.publish.csiro.au/journals/ajc

All enquiries and manuscripts should be directed to
The Managing Editor
Australian Journal of Chemistry
CSIRO PUBLISHING
PO Box 1139 (150 Oxford St)
Collingwood Telephone: 61 3 9662 7630
Vic. 3066 Facsimile: 61 3 9662 7611
Australia Email: john.zdysiewicz@publish.csiro.au

Published by **CSIRO** PUBLISHING
for CSIRO and
the Australian Academy of Science

Aust. J. Chem., 2000, **53**, 123–129

The Reactions of *N*-Substituted 2-(Dimethylallyl)aniline Compounds with Phenylselanyl Halides

Matthew A. Cooper,[A] *Craig L. Francis,*[A] *Jeffrey W. Holman,*[A] *Bruno Kasum,*[A] *Thomas Taverner,*[A] *Edward R. T. Tiekink*[A] *and A. David Ward*[A,B]

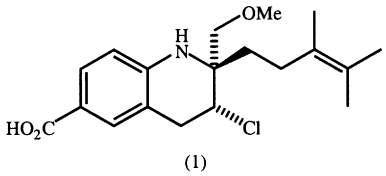
[A] Department of Chemistry, The University of Adelaide, Adelaide, S.A. 5005.
[B] Author to whom inquiries should be addressed (david.ward@adelaide.edu.au).

Cyclization of the carbamate of 2-(dimethylallyl)aniline with phenylselanyl chloride (benzeneselenenyl chloride) gave a 1 : 1 mixture of a dihydroindole and a tetrahydroquinoline. With phenylselanyl bromide only the dihydroindole was obtained. Addition of methanol to the silica used in the procedure trapped the reaction at the non-cyclized stage forming a 3-methoxy-3-methyl-2-(phenylselanyl)butyl side chain. The sulfonamide of 2-(dimethylallyl)aniline only formed the dihydroindole with phenylselanyl chloride. The corresponding trifluoroacetamide derivative did not form any cyclized product under the same conditions. The dihydroindole could be converted into the corresponding alkene by oxidative removal of the phenylseleno group. 4-Ethoxycarbonyl-2-(3,3-dimethylallyl)aniline cyclized with mercuric nitrate to give, after a reductive workup, a 2,2-dimethyltetrahydroquinoline. The X-ray crystal structures of ethyl *N*-{2-[3-methoxy-3-methyl-2-(phenylselanyl)butyl]phenyl}carbamate and 2-[1-methyl-1-(phenylselanyl)ethyl]-1-[(4-methylphenyl)sulfonyl]indoline are reported.

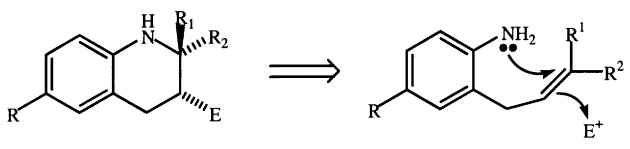
Keywords. Synthesis; X-ray crystallography; phenylselanyl halide; virantmycin; cyclization.

Introduction

We have been investigating synthetic approaches to the novel antibiotic virantmycin (1)[1–3] for some time. While other groups[4–11] have focused on the total synthesis of virantmycin we have been investigating general routes to structural analogues of virantmycin for use in structure–activity relationships. One of our methodologies involves the electrophile-initiated cyclization of 2-(3,3-disubstituted allyl)aniline systems (Scheme 1).[12–15]



(1)



Scheme 1

Our early results on model compounds in this area of electrophile-initiated cyclization have been reported.[12–15] While simple model compounds underwent iodine-initiated cyclization to produce iodotetrahydroquinolines, compounds which had larger allylic substituents either failed to produce any cyclized product or formed only very small amounts of these desired products. Reactions involving mercuric salts were unsuccessful in producing substituted tetrahydroquinolines but gave non-substituted products after a reductive workup. We have recently reported our results using a copper-catalysed cyclization process to form 2,2-disubstituted 1,2-dihydroquinolines.[16] We now report the results obtained from the use of selenium-containing reagents as the electrophilic species for the cyclization process.

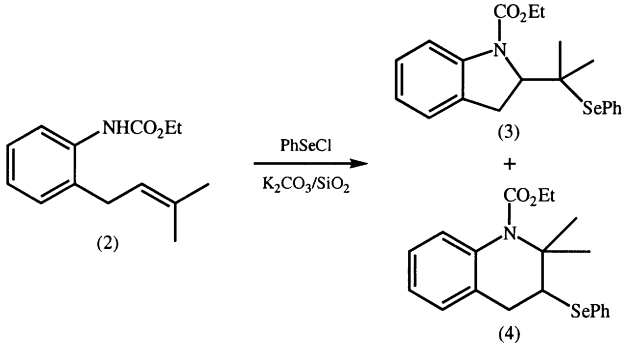
Results and Discussion

Treatment of the carbamate (2)[17] with 1 equiv. of phenylselanyl chloride, dry silica gel and anhydrous potassium carbonate in dichloromethane at –78° for 15 min and then at room temperature for 3 days produced a 1 : 1 mixture of the dihydroindole (3) and the tetrahydroquinoline (4) which could not be separated by chromatography (Scheme 2). A cleaner reaction product was obtained by using chloroform as the solvent rather than the more usual dichloromethane.[17,18] It was also found that higher yields of product were obtained when the selenium reagent was added at low temperature and the reaction mixture subsequently allowed to warm to room temperature than when the reagent was added at ambient temperature. This competition between *endo* and *exo* cyclization processes has also been observed by Clive.[17]

Manuscript received 6 September 1999 10.1071/CH99109 0004-9425/00/020123

When the carbamate (2) was treated with phenylselanyl chloride, dry silica gel and anhydrous potassium carbonate in chloroform at –78° for 30 min, then at room temperature for 6 days, the only product observed was the dihydroindole (3). Reaction of (2) with phenylselanyl bromide, dry silica gel and anhydrous potassium carbonate in dichloromethane at –78° for 30 min then at room temperature for 6 days also gave only the dihydroindole (3).

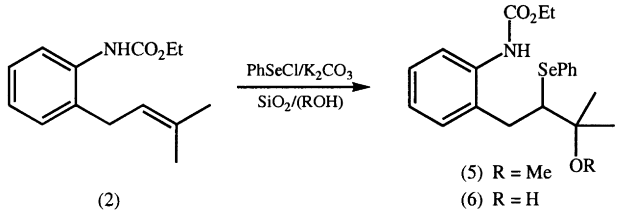
^{1}H n.m.r. analysis revealed that the signal from the C 2 hydrogen of (3) appeared as a doublet of doublets at δ 4.6 and that the two methyl resonances are widely spaced at δ 1.42 and 1.02. The methyl resonances of (4) are much more closely spaced, appearing at δ 1.80 and 1.67.



Scheme 2

A mixture of dihydroindole (3) and tetrahydroquinoline (4) in chloroform was refluxed overnight in the presence of potassium carbonate and silica gel. No change in the ratio of the two heterocycles was observed.

Treatment of the carbamate (2) with phenylselanyl chloride, anhydrous potassium carbonate and silica gel containing pre-absorbed methanol in dichloromethane afforded (Scheme 3) the methoxy selenide (5), the structure of which was confirmed by X-ray crystallography (Fig. 1). An analogous reaction using dry silica gel, but with a small amount of added water present, gave a mixture of starting alkene and products that could not be separated by chromatography. Mass spectroscopic and n.m.r. data were inconclusive as to whether the non-alkene-containing components of this mixture were the alcohol (6) and/or either of the possible cyclized products.



Scheme 3

It was of interest to see whether the selenides (3) and (4) could be converted (Scheme 4) into their chloro-substituted derivatives by using our previously established methodology.[18,19] However, reaction of the selenide mixture with tetrabutylammonium chloride and chlorine at either room temperature or –22° gave a complex mixture of products,

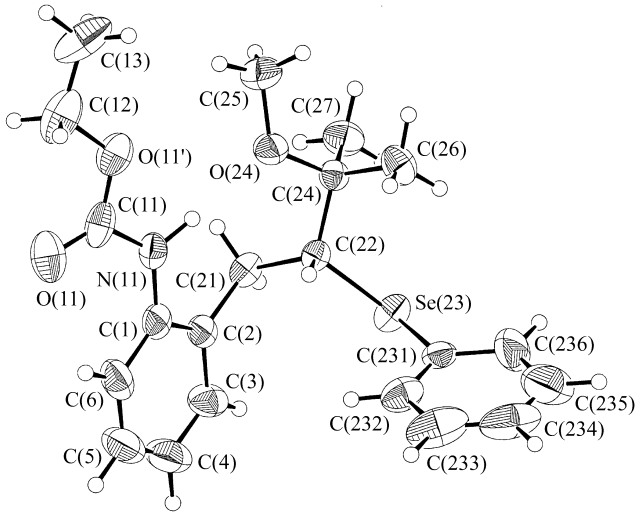
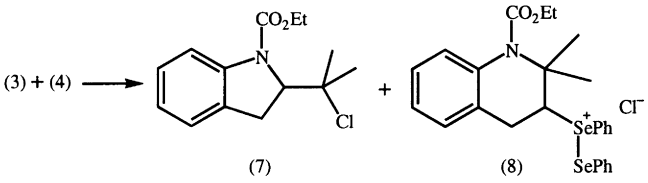


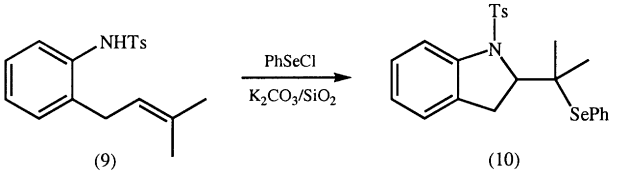
Fig. 1. Molecular structure and crystallographic numbering scheme for (5).

from which it was possible to isolate the chlorodihydroindole (7) by chromatography. Reaction of selenides (3) and (4) with phenylselanyl chloride at either room temperature or –78° also gave a mixture of products, from which it was possible to isolate, by h.p.l.c., the chloride (7) and a solid which rapidly decomposed. The ^{1}H n.m.r. spectrum of this solid indicated the presence of 14 aromatic hydrogens and this and the mass spectrum were consistent with the solid being the selenonium salt (8) although no molecular ion was observed. When the reaction was followed by h.p.l.c., it was seen that the salt (8) decomposed to a complex mixture of products rather than form the corresponding chloride.



Scheme 4

The effect of the *para*-toluenesulfonamide protecting group on the selenium-induced cyclization reaction was also studied (Scheme 5). Treatment of the sulfonamide (9) with phenylselanyl chloride, dry silica gel and anhydrous potassium carbonate at room temperature for 64 h gave only the dihydroindole (10), the structure of which was confirmed by X-ray crystallography (Fig. 2).



Scheme 5

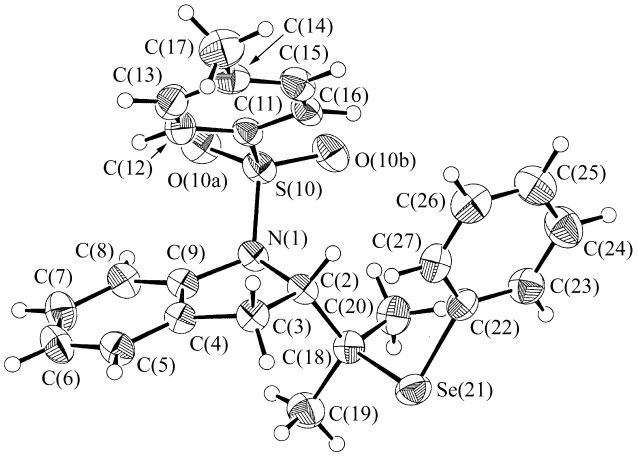
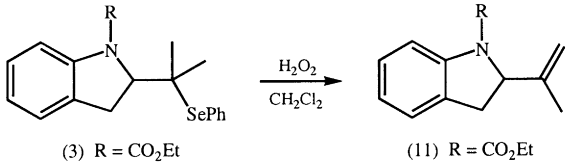


Fig. 2. Molecular structure and crystallographic numbering scheme for (10).

The ^{1}H n.m.r. spectrum of (10) was markedly different from that of the ethyl carbamate analogue (3). Whereas the benzylic hydrogens of (3) appear as a multiplet centred at δ 3.37, the two benzylic hydrogens of (10) have quite different chemical shifts with one centred at δ 2.36 and the other at δ 3.15. The C 2 hydrogen of (3) appears at δ 4.62; the same hydrogen is found at δ 4.03 in the spectrum of (10). The carbamate group of (3) is planar and this would require the two methyl groups of the side chain at C 2 to align themselves so that they are directed away from the carbamate group. This leaves the selenium atom nearest to the carbamate group and positions the attached phenyl ring away from any ring hydrogen. In the case of (10) the nitrogen of the sulfonamido group is pyramidal, not trigonal planar, and the methyl groups of the side chain can occupy the space beneath the indole ring system with the sulfonyl portion above. This places the phenyl of the phenylselenide group in a shielding position to the C 2 hydrogen. The structure of (10) (Fig. 2) shows the proximity of this phenyl ring to the C 2 hydrogen. It also shows that the aromatic ring of the arylsulfonyl system is sufficiently close to one of the benzylic hydrogens to make them magnetically non-equivalent.

Since the selenides (3) and (10) could be prepared cleanly and in high yield, it was of interest to determine if they could be further manipulated to remove the seleno moiety.[20] By using a two-phase dichloromethane/hydrogen peroxide system at room temperature, the selenides (3) and (10) were converted cleanly, via the corresponding selenoxide, into the alkenes (11) and (12) respectively (Scheme 6). Compounds such as (11) and (12) are of potential synthetic interest as the isoprenoid unit inherent in these molecules occurs widely in natural products.



(3) R = CO_2Et
(10) R = Ts

(11) R = CO_2Et
(12) R = Ts

Scheme 6

The methyl carbamate analogue of (2) and the sulfonamide (9) have been cyclized to a dihydroquinoline[21] and a dihydroindole[22] system respectively, by using palladium catalysts.

Treatment of the trifluoroacetamide (13)[13] with phenylselanyl chloride, dry silica gel[17] and anhydrous potassium carbonate in dichloromethane produced no cyclized material after 4 days reaction time but it was possible to isolate the hydroxy selenide (15) from the reaction product in low yield by chromatography (Scheme 7). This compound may arise from displacement of the chloro group of (14) on silica.

In our previous paper,[13] we reported that organomercury acetates, formed by treatment of the corresponding allylanilines with mercuric acetate, could not be converted into the desired 3-halotetrahydroquinolines in spite of numerous attempts with a variety of conditions (Scheme 8). However, reductive workup with alkaline sodium borohydride provided non-functionalized tetrahydroquinolines in high yield.[13]

The allylanilino ester (18) (prepared as shown in Scheme 9) was treated with 3 equiv. of mercuric acetate, followed by reductive workup to form the tetrahydroquinoline (19). This sequence shows that the mercury(II)-induced cyclization is tolerant of an electron-withdrawing substituent.

Attempts to functionalize the heterocyclic ring at the 3-position, using an amidomercuration/oxidative demercuration procedure[23] on both the carbamate (2) and 2-allylaniline, were unsuccessful. Attempted conversion of the intermediate organomercury derivative from 2-allylaniline into the bromide using potassium bromide resulted in the immediate precipitation of mercury and recovery of the allylaniline.

Experimental

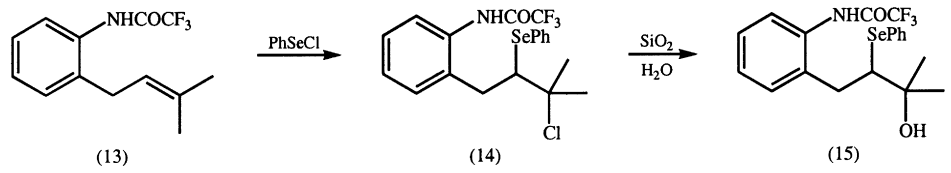
General experimental conditions have been described previously.[15] N.m.r. spectra were determined in (D)chloroform solution. High-performance liquid chromatography (h.p.l.c.) was carried out with a Waters 501 solvent delivery system and a U6K injector with a Waters 481 absorbance detector. Analyses were performed by using a Waters Z-module with a Waters Radial-PAK™ C_{18} reverse-phase cartridge (10 cm by 8 mm), with a gradient of methanol/water as eluent.

Ethyl N-*[2-(3-Methylbut-2-enyl)phenyl]carbamate (2)*

Ethyl chloroformate (1.08 g, 9.9 mmol) was added dropwise over 5 min to an emulsified mixture of 2-allylaniline[17] (2.75 g, 17 mmol) in water (10 ml) at 0°. The mixture was stirred vigorously for 10 min, and then a solution of sodium hydroxide (0.8 g, 20 mmol) in water (5 ml) was added, immediately followed by more ethyl chloroformate (1.08 g, 9.9 mmol). The resulting mixture was stirred at 0° for a further 2 h and extracted with dichloromethane (2×30 ml). The organic extracts were dried (Na_2SO_4) and evaporated and the residue was distilled to give the carbamate (2)[17] (3.56 g, 90%) as a light brown oil, b.p. 120°/0.1 mm (lit.[17] 120°/0.1 mm). ν_{max} (film) 3325, 1715, 1585, 1510, 1220 cm^{-1}. ^{1}H n.m.r. δ 1.28, t, *J* 7 Hz, CH_2; 1.78, s, $(CH_3)_2$; 3.32, d, *J* 7.2 Hz, $ArCH_2$; 4.20, q, *J* 7.1 Hz, CO_2CH_2; 5.20, t, *J* 6.5 Hz, C=C–H; 6.72, s, NH; 6.80–7.78, m, ArH. Mass spectrum *m/z* 233 (M).

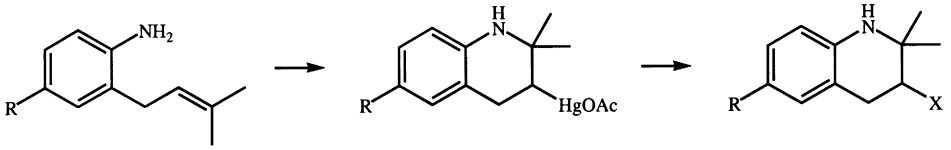
Ethyl 2-[1-Methyl-1-(phenylselanyl)ethyl]indoline-1-carboxylate (3) and Ethyl 2,2-Dimethyl-3-(phenylselanyl)-1,2,3,4-tetrahydroquinoline-1-carboxylate (4)

A solution of phenylselanyl chloride (170 mg, 0.87 mmol) in dry dichloromethane (6 ml) was added dropwise to a stirred mixture of the carbamate (2) (200 mg, 0.85 mmol), anhydrous potassium carbonate (1.18 g, 8.5 mmol) and silica gel (Merck 60, 230–400 mesh, oven-dried,

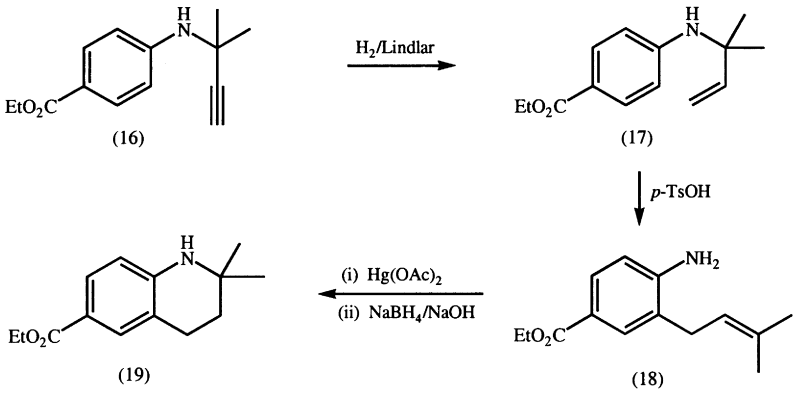


(13) (14) (15)

Scheme 7



Scheme 8



(16) (17) (18) (19)

Scheme 9

400 mg) in dry dichloromethane (5 ml) at –78° under an atmosphere of nitrogen. The mixture was stirred at this temperature for a further 15 min and then at room temperature in darkness for 74 h. The solution was then filtered through Celite, the Celite washed with ethyl acetate (10 ml) and the solvent evaporated to give a light yellow oil which was purified by chromatography (ethyl acetate/hexane; 1 : 9) to give a chromatographically homogeneous product consisting of a mixture of the selenides[17] (3) and (4) (0.302 g, 91%) in the ratio 1 : 1 (Found *m/z*, 389.0882. Calc. for $C_{20}H_{23}NO_2{}^{80}Se$: *m/z*, 389.0894). ν_{max} (CCl_4) 1715, 1600, 1590 cm^{-1}. ^1H n.m.r. δ [for (3)] 1.02, s, CH_3; 1.2, t, *J* 7.2 Hz, $CH_2C\mathbf{H}_3$; 1.42, s, CH_3; 3.37, br d, *J* 7.8 Hz, $ArCH_2$; 4.15, q, *J* 7.2 Hz, $C\mathbf{H}_2CH_3$; 4.62, dd, *J* 3.3, 7.8 Hz, NCH; 6.75–7.80, m, ArH. ^1H n.m.r. δ [for (4)] 1.25, t, *J* 7 Hz, $CH_2C\mathbf{H}_3$; 1.67, s, CH_3; 1.80, s, CH_3; 2.91–3.30, m, $C\mathbf{H}_2C\mathbf{H}$(SePh); 4.2, q, *J* 7 Hz, $C\mathbf{H}_2CH_3$; 6.75–7.80, m, ArH. Mass spectrum *m/z* 389 (M).

Ethyl N-*{2-[3-Methoxy-3-methyl-2-(phenylselanyl)butyl]phenyl}-carbamate (5)*

Using a similar procedure to that described above but with silica gel to which a few drops of methanol had been added gave, after chromatography, a fraction which was crystallized from hexane to give the *carbamate* (5) as white crystals, m.p. 83–85°, whose structure was confirmed by X-ray structure analysis. ν_{max} ($CHCl_3$) 3320, 1730 cm^{-1}. ^1H n.m.r. δ 1.29 and 1.33, both s, CH_3; 1.31, overlapping t, $CH_2C\mathbf{H}_3$; 2.61, dd, J_{AB} 14, $J_{A,C}$ 9.5 Hz, H_A of methylene; 2.85, d, J_{AC} 9.5, J_{BC} 0 Hz, CHSe; 3.37, s, OMe; 3.47, d, J_{AB} 14, J_{BC} 0 Hz, H_B of methylene; 4.20, overlapping q, $OC\mathbf{H}_2CH_3$; 6.97–7.14 and 7.25–7.37, both Ar. ^{13}C n.m.r. δ 14.58, 19.05, 24.00, 31.55, 33.90, 50.28, 60.41, 60.43, 127.30, 127.40, 128.95, 130.92, 133.82. Some aromatic carbon signals and the carbonyl signal were not observed.

Reaction of (2) with Phenylselanyl Chloride and Wet Silica Gel

Using the procedure described above but with silica gel to which a few drops of water had been added, gave, after chromatography, a fraction that appeared to be mainly a mixture of several carbamates and the starting alkene. ^1H n.m.r. for the carbamates showed overlapping signals at δ 1.2, $CH_2C\mathbf{H}_3$; 1.3 and 1.4, CH_3; 2.9 and 3.2, both m, 2H; 4.1, q and m, $OC\mathbf{H}_2CH_3$ and 1H; 6.8–7.4, m, ArH. The mass spectrum showed a peak at *m/z* 250 (M+H) which indicated the presence of (6) in the mixture.

Ethyl 2-[1-Methyl-1-(phenylselanyl)ethyl]indoline-1-carboxylate (3)

A solution of phenylselanyl bromide (147 mg, 0.56 mmol) in dry dichloromethane (6 ml) was added to a rapidly stirred mixture of the carbamate (2) (100 mg, 0.43 mmol), anhydrous potassium carbonate (590 mg, 4.3 mmol) and silica gel (Merck 230–400 mesh, oven-dried, 300 mg) in dry dichloromethane (5 ml) at –78° under an atmosphere of nitrogen. The mixture was stirred at this temperature for 30 min, at room temperature in darkness for 6 days, and then filtered through Celite. The Celite was washed with ethyl acetate (10 ml), the combined organic phases were evaporated and the residue was purified by reverse-phase h.p.l.c. (water/methanol; 20 : 80) to give the selenide (3)[17] (120 mg, 72%) as a colourless oil (Found: C, 61.3; H, 5.9; N, 3.6%; *m/z*, 389.0891. Calc. for $C_{20}H_{23}NO_2{}^{80}Se$: C, 61.7; H, 6.0; N, 3.6%; *m/z*, 389.0894). ν_{max} (film) 1700, 1600, 1480, 1270 cm^{-1}. ^1H n.m.r. δ 1.02, s, CH_3; 1.2, t, *J* 7.2 Hz, $CH_2C\mathbf{H}_3$; 1.42, s, CH_3; 3.37, br d, *J* 7.8 Hz, $ArCH_2$; 4.15, q, *J* 7.2 Hz, $C\mathbf{H}_2CH_3$; 4.62, dd, *J* 3.3, 7.8 Hz, NCH; 6.75–7.80, m, ArH. Mass spectrum *m/z* 389 (M, 4%), 232 (100).

Reactions of the Selenides (3) and (4)

(i) *With chlorine and tetrabutylammonium chloride at room temperature*. Chlorine in carbon tetrachloride (1.8 M, 0.3 ml, 0.56 mmol) was added to a stirred solution of the selenides (3) and (4) (210 mg, 0.5 mmol) in dry acetonitrile (10 ml). Tetrabutylammonium chloride (140 mg, 0.5 mmol) was then added. The mixture was stirred at room temperature for 40 h, then quenched by the addition of hydrogen peroxide (28%, 0.3 ml, 2.5 mmol). The mixture was extracted with dichloromethane (2×10 ml) and the solvent evaporated to give a yellow oil. Chromatography (ethyl acetate/hexane) gave *ethyl 2-(1-chloro-1-methylethyl)indoline-1-carboxylate* (7) as a light yellow oil (40 mg, 30%) (Found: *m/z*, 267.1036. $C_{14}H_{18}ClNO_2$ requires *m/z*, 267.1026). ν_{max} (film) 1700, 1600, 1270 cm^{-1}. ^1H n.m.r. δ 1.24, s, $(CH_3)_2$; 1.25, t, *J* 9 Hz, $CH_2C\mathbf{H}_3$; 3.28, d, J_{BX} 9 Hz, $ArCH_A\mathbf{H}_B$; 3.35, d, J_{AX} 4 Hz, $ArC\mathbf{H}_AH_B$; 4.25, q, *J* 7 Hz, $C\mathbf{H}_2CH_3$; 4.75, dd, J_{AX} 4, J_{BX} 9 Hz, CHN; 7.1–7.6, m, ArH. Mass spectrum *m/z* 267 (M, 3%), 232 (28), 190 (74), 118 (100). Further elution with ethyl acetate gave a complex mixture of products.

(ii) *With chlorine and tetrabutylammonium chloride at –23°*. The reaction was carried out as above except that the mixture was stirred at –23° for 30 min, then warmed to room temperature and the crude product purified by preparative reverse-phase h.p.l.c. (methanol/water gradient). This yielded the chloride (7) (50 mg, 30%) (spectroscopic data as above).

(iii) *With phenylselanyl chloride at room temperature*. Phenylselanyl chloride (80 mg, 0.40 mmol) in dry dichloromethane (6 ml) was added to a stirred mixture of the selenides (3) and (4) (150 mg, 0.38 mmol) and silica gel (Merck 60, 230–400 mesh, 1.0 g) in dry dichloromethane (20 ml) at room temperature under an atmosphere of nitrogen. The mixture was stirred at room temperature for 8 h, and then filtered through Celite. The Celite was washed with ethyl acetate and the combined filtrate concentrated to give a yellow oil. Chromatography (ethyl acetate/hexane) gave the chloride (7) (51 mg, 50%) as a yellow oil (spectroscopic data as above).

(iv) *With phenylselanyl chloride at –78°*. The reaction was carried out as above except that the mixture was stirred at –78° for 1 h, and then allowed to warm to room temperature over 30 min. Preparative reverse-phase h.p.l.c. (water/methanol; 30 : 70) gave the chloride (7) (52 mg, 51%) as a yellow oil and the selenonium salt (8) (40 mg, 39%) as an unstable, white solid. ^1H n.m.r. δ 1.25, t, *J* 7 Hz, $CH_2C\mathbf{H}_3$; 1.67, s, CH_3; 1.80, s, CH_3; 2.91–3.30, m, $C\mathbf{H}_2C\mathbf{H}$(SePh); 4.2, q, *J* 7 Hz, $C\mathbf{H}_2CH_3$; 6.75–7.80, m, ArH. F.a.b. mass spectrum *m/z* 389 (M – SePh).

4-Methylphenyl N-*[2-(3-Methylbut-2-enyl)phenyl]sulfamate (9)*

Tosyl chloride (1.78 g, 9.3 mmol) was added to a stirred mixture of 2-allylaniline[17] (1 g, 6.2 mmol) in dry pyridine (10 ml) under an atmosphere of nitrogen. The mixture was stirred at room temperature for 48 h, diluted with ethyl acetate, washed with dilute hydrochloric acid (1 M, 2×40 ml), and then with saturated sodium bicarbonate solution (2×30 ml). The organic phase was dried and evaporated and the residue purified by chromatography (hexane) to give a fraction which on crystallization from dichloromethane/hexane gave the *sulfonamide* (9) (1.71 g, 87%) as white crystals, m.p. 75–77°, b.p. 121–124°/0.02 mm (Found: C, 68.2; H, 6.6; N, 4.4. $C_{18}H_{21}NO_2S$ requires C, 68.5; H, 6.7; N, 4.4%). ν_{max} (CCl_4) 3280, 1660, 1600, 1495, 1335, 1160 cm^{-1}. ^1H n.m.r. δ 1.63, s, CH_3; 1.68, s, CH_3; 2.29, s, $PhCH_3$; 3.00, br d, *J* 7 Hz, $PhCH_2$; 4.94, t, *J* 7 Hz, C=C–H; 7.36 and 7.58, d, *J* 9 Hz, ArH. Mass spectrum *m/z* 315 (M, 2%), 201 (100), 173 (39), 161 (30), 156 (45).

2-[1-Methyl-1-(phenylselanyl)ethyl]-1-[(4-methylphenyl)sulfonyl]indoline (10)

Phenylselanyl chloride (98 mg, 0.51 mmol) in dry dichloromethane (6 ml) was added dropwise to a stirred mixture of the sulfonamide (9) (157 mg, 0.5 mmol), potassium carbonate (600 mg, 5 mmol) and silica gel (Merck 60, 230–400 mesh, oven-dried, 300 mg) in dry dichloromethane (10 ml) at –78° under an atmosphere of nitrogen. The mixture was stirred at –78° for 15 min, and then at room temperature in darkness for 64 h. The mixture was filtered through Celite, the Celite washed with ethyl acetate (20 ml) and the solvent evaporated to give a yellow oil. Chromatography (ethyl acetate/hexane) gave a white solid which was recrystallized from dichloromethane/hexane to give the *selenide* (10) (183 mg, 78%) as translucent crystals, m.p. 122–122.5° (Found: C, 61.2; H, 5.2; N, 3.0. $C_{24}H_{25}NO_2SSe$ requires C, 61.3; H, 5.4; N, 3.0%). ν_{max} (CCl_4) 1600, 1490, 1360, 1170 cm^{-1}. ^1H n.m.r. δ 0.97, s, CH_3; 1.70, s, CH_3; 2.33, s, $ArCH_3$; 2.36, dd, J_{AX} 8.7, J_{BX} 16.5 Hz, CHN; 3.15, d, J_{BX} 16.5 Hz, $ArCH_A\mathbf{H}_B$; 4.03, d, J_{AX} 8.7 Hz, $ArC\mathbf{H}_AH_B$; 6.98–7.48, m, C_6H_4 and C_6H_5Se; 7.37 and 7.60, d, *J* 6.9 Hz, $C_6H_4SO_2$. Mass spectrum *m/z* 471 (M, 5%), 314 (23), 272 (65), 91 (100).

2-Isopropenyl-1-[(4-methylphenyl)sulfonyl]indoline (12)

A mixture of the selenide (10) (230 mg, 0.5 mmol) and hydrogen peroxide (28%, 5.4 g, 60 mmol) in dichloromethane (30 ml) was stirred at room temperature for 4 h. The mixture was washed with water, the organic phase dried (Na_2SO_4) and evaporated to give a white solid which was recrystallized from dichloromethane/hexane to give the *alkene* (12) (118 mg, 76%) as white needles, m.p. 107–107.5° (Found: C, 69.0; H, 6.3; N, 4.6%; *m/z*, 313.1147. $C_{18}H_{19}NO_2S$ requires C, 69.0; H, 6.1; N, 4.5%; *m/z*, 313.1139). ν_{max} (CCl_4) 1655, 1600, 1580, 1360 cm^{-1}. ^1H n.m.r. δ 1.66, s, CH_3; 2.33, s, $ArCH_3$; 2.62, dd, J_{AX} 3.9, J_{AB} 16.2 Hz, $Ar\mathbf{H}_AH_B$; 2.91, dd, J_{BX} 10.2, J_{AB} 16.2 Hz, $ArCH_A\mathbf{H}_B$; 4.55, dd, J_{AX} 3.9, J_{BX} 10.2 Hz, CHN; 4.76 and 4.97, both s, $C=CH_2$; 6.9, m, ArH; 7.10 and 7.50, d, *J* 8.4 Hz, $C_6H_4SO_2$; 7.60, d, *J* 7.8 Hz, ArH. Mass spectrum *m/z* 313 (M, 100%), 272 (21), 158 (73).

Ethyl 2-Isopropenylindoline-1-carboxylate (11)

In a similar manner to that described above the carbamate (3) was converted into the alkene (11) which was isolated as a colourless oil, b.p. 150°/0.4 mm. The n.m.r. spectrum indicated that the material, while largely the required alkene (11), was not pure (Found: *m/z*, 231.1251. Calc. for $C_{14}H_{17}NO_2$: *m/z*, 231.1255). ^1H n.m.r. [for (11)] δ 1.27, t, *J* 7 Hz, $OCH_2C\mathbf{H}_3$; 1.67, d, *J* 1 Hz, $CH_3C=C$; 2.52–3.48, m, CH_2, CHN; 4.25, q, *J* 7 Hz, OCH_2; 4.78, br d, *J* 2.4 Hz, $C=CH_2$; 6.92–7.35, m, ArH.

2,2,2-Trifluoro-N-*{2-[3-hydroxy-3-methyl-2-(phenylselanyl)butyl]phenyl}acetamide (15)*

Phenylselanyl chloride (191 mg, 1 mmol) in dry dichloromethane (6 ml) was added to a stirred mixture of the trifluoroacetamide (13)[13] (257 mg, 1 mmol), silica gel (Merck 60, 230–400 mesh, oven-dried, 500 mg) and anhydrous potassium carbonate (1.2 g, 10 mmol) in dry dichloromethane (10 ml) at –78° under an atmosphere of nitrogen. The mixture was stirred at –78° for 20 min, and then at room temperature in darkness for 4 days. The mixture was filtered through Celite, the Celite washed with ethyl acetate (20 ml), and the filtrate evaporated to give a yellow oil which was flash-chromatographed on silica gel. Elution with ethyl acetate/hexane gave the *hydroxy selenide* (15) (90 mg, 21%) as a light yellow oil (Found: *m/z*, 432.0675. $C_{19}H_{20}F_3NO_2{}^{80}Se$ requires M+H, 432.0689). ν_{max} (film) 3380, 3360, 1720, 1590, 1160 cm^{-1}. ^1H n.m.r. δ 1.40, s, CH_3; 1.44, s, CH_3; 2.37, s, OH; 2.88, dd, J_{AX} 14.7, J_{BX} 9.9 Hz, CH_XSe; 3.05, dd, J_{BX} 9.9, J_{AB} 2.7 Hz, $ArCH_A\mathbf{H}_B$; 3.40, dd, J_{AX} 14.7, J_{AB} 2.7 Hz, $ArC\mathbf{H}_AH_B$; 6.9–7.3, m, ArH; 7.82, d, *J* 8.1 Hz, ArH; 9.33, s, NH. Mass spectrum *m/z* 432 (M+H, 12%), 373 (100), 335 (14).

Attempted Amidomercuration/Oxidative Demercuration of Carbamate (2)

Mercuric nitrate (0.376 g, 1.1 mmol) was added to a stirred mixture of the carbamate (2) (0.173 g, 0.74 mmol), sodium bicarbonate (62 mg, 0.74 mmol) and dry acetonitrile (10 ml) under an atmosphere of nitrogen and the resulting mixture stirred at room temperature for 1 h. Saturated, aqueous potassium bromide solution (5 ml) was added and the mixture stirred for a further 2 h. The mixture was extracted with ethyl acetate (30 ml) and the organic phase dried and evaporated. The residue was dissolved in dimethylformamide (5 ml) and added dropwise to a mixture of sodium borohydride (28 mg, 0.74 mmol) and dimethylformamide (6 ml) through which oxygen had been bubbled for 20 min. Sulfuric acid (0.05 M, 20 ml) was added and the mixture shaken and extracted with dichloromethane (2×20 ml). The combined organic layers were dried and evaporated to return the starting carbamate (2) in nearly quantitative yield.

Attempted Amidomercuration/Oxidative Demercuration of 2-Allylaniline

2-Allylaniline (0.17 g, 1.13 mmol) in acetone (1 ml) was added to a stirred suspension of mercuric acetate (1.05 g, 3.3 mmol) in acetone (4 ml) and water (1 ml) and the resulting mixture stirred at room temperature for 10 min. Sodium borohydride (0.13 g, 3.51 mmol) in acetone (1 ml) was slowly added whilst oxygen gas was bubbled through the mixture. After stirring for 1 min, the mixture was filtered, diluted with water (5 ml) and extracted with dichloromethane. The combined organic phases were dried and evaporated to give a complex product mixture.

Ethyl 4-[(1,1-Dimethylallyl)amino]benzoate (17)

A mixture of the alkyne[16] (16) (507 mg), Lindlar catalyst (0.149 mg) and quinoline (100 mg) in ethyl acetate (15 ml) was stirred under hydrogen for 10 min. The solution was filtered and the filtrate evaporated to give an off-white solid which was recrystallized from dichloromethane/hexane to give the *alkene* (17) (464 mg, 91%), m.p. 102.5–104° (Found: C, 71.9; H, 8.0; N, 6.1. $C_{14}H_{19}NO_2$ requires C, 72.1; H, 8.2; N, 6.0%). ν_{max} (Nujol) 3310, 1680, 1600, 1510 cm^{-1}. ^1H n.m.r. δ 1.35, t, *J* 7.5 Hz, CH_3; 1.45, s, $(CH_3)_2$; 4.25, s, NH; 4.35, q, *J* 7.5 Hz, CH_2; 5.2, dd, J_{trans} 17, J_{gem} 1 Hz, C=$CH_A\mathbf{H}_B$; 5.3, dd, J_{cis} 10, J_{gem} 1 Hz, C=C$\mathbf{H}_A$$H_B$; 6.05, dd, J_{cis} 10, J_{trans} 17 Hz, C$\mathbf{H}$=CH_2; 6.8, d, *J* 9 Hz, ArH; 7.9, d, *J* 9 Hz, ArH. Mass spectrum *m/z* 233 (M, 88%), 218 (100), 206 (51), 188 (34).

Ethyl 4-Amino-3-(3-methylbut-2-enyl)benzoate (18)

A mixture of the alkene (17) (1.5 g, 6.5 mmol), *p*-toluenesulfonic acid (200 mg), acetonitrile (200 ml) and water (50 ml) was stirred at 65° for 16 h. The cooled solution was extracted with ethyl acetate (2×50 ml), dried (Na_2SO_4), the solvent evaporated and the residue flash-chromatographed on silica gel. Elution with ethyl acetate/hexane) gave the *allylaniline* (18) (1.36 g, 91%) as a light brown oil (Found: *m/z*, 233.1416. $C_{14}H_{19}NO_2$ requires *m/z*, 233.1416). ν_{max} 3445, 3300, 1690, 1615, 1600, 1500 cm^{-1}. ^1H n.m.r. δ 1.29, t, *J* 6.0 Hz, CH_3; 1.69, br s, $(CH_3)_2$; 3.16, d, *J* 6.9 Hz, $ArCH_2$; 4.21, s, NH_2; 4.25, q, *J* 6.0 Hz, CH_2; 5.17, m, C=C–H; 6.56, dd, *J* 7.5, 0.9 Hz, ArH; 7.67, m, ArH. Mass spectrum *m/z* 233 (M, 100%), 218 (26), 178 (71), 160 (40).

Ethyl 2,2-Dimethyl-1,2,3,4-tetrahydroquinoline-6-carboxylate (19)

A mixture of the alkene (18) (96 mg, 0.41 mmol), mercuric acetate (400 mg, 1.26 mmol), acetone (4 ml) and water (1 ml) was vigorously stirred at room temperature for 10 min. Sodium borohydride (65 mg, 1.72 mmol) in aqueous sodium hydroxide solution (10%, 1 ml) was then added dropwise, the solution diluted with water (5 ml) and the resultant mixture extracted with dichloromethane (2×10 ml). The organic extracts were dried (Na_2SO_4) and evaporated to give a brown oil that was purified by flash chromatography (ethyl acetate/hexane; 1 : 9) to give the *ester* (19) as a white solid (73 mg) after crystallization from hexane, m.p. 87–88° (Found: C, 72.0; H, 8.5; N, 5.9%; *m/z*, 233.1420. $C_{14}H_{19}NO_2$ requires C, 72.1; H, 8.2; N, 6.0%; *m/z*, 233.1416). ν_{max} (Nujol) 3376, 1679, 1604, 1512 cm^{-1}. ^1H n.m.r. δ 1.23, s, $(CH_3)_2$; 1.35, t, *J* 6.9 Hz, CH_3; 1.70, t, *J* 6.5 Hz, CH_2; 2.79, t, *J* 6.5 Hz, CH_2; 4.13, br s, NH; 4.30, q, *J* 6.9 Hz, OCH_2; 6.38, d, *J* 8.1 Hz, ArH; 7.66, m, ArH; 7.70, br s, ArH. Mass spectrum *m/z* 233 (M, 51%), 218 (100), 190 (29).

Crystallography

Intensity data were measured for transparent crystals of (5) and (10) (0.08×0.48×0.57 mm^3 for (5) and 0.40×0.40×0.40 mm^3 for (10)) at room temperature on a Rigaku AFC6R diffractometer for (5) and an Enraf–Nonius CAD diffractometer for (10), each fitted with graphite

Table 1. Crystallographic data for (5) and (10)

	(5)	(10)
Formula	$C_{21}H_{27}NO_3Se$	$C_{24}H_{25}NO_2SSe$
M	420.4	470.5
Crystal system	monoclinic	monoclinic
Space group	$P2_1/n$	$P2_1/n$
a (Å)	10.262(2)	10.121(2)
b (Å)	13.611(5)	12.368(3)
c (Å)	14.760(4)	18.031(6)
β (deg)	101.26(2)	97.40(2)
V (Å^3)	2022.1(9)	2238.3(9)
Z	4	4
D_c (g cm^{-3})	1.381	1.396
F (000)	872	968
μ (cm^{-1})	18.77	17.91
No. unique reflns meas.	4898	3833
θ_{max} (deg)	27.9	25.0
No. reflns used	2025	2263
R	0.044	0.043
g	0.00002	0.0001
R_w	0.036	0.054
ρ_{max} (e Å^{-3})	0.39	0.67

Table 2. Fractional atomic coordinates for (5)

Atom	*x*	*y*	*z*
Se(23)	0.18657(4)	0.27799(3)	0.52271(3)
O(11)	0.8245(3)	0.0996(2)	0.4423(2)
O(11′)	0.8107(2)	0.0953(2)	0.5920(2)
O(24)	0.5341(2)	0.1558(2)	0.6632(2)
N(11)	0.6334(3)	0.1341(2)	0.4909(2)
C(1)	0.5425(4)	0.1495(2)	0.4066(3)
C(2)	0.4088(4)	0.1455(2)	0.4081(3)
C(3)	0.3181(4)	0.1626(3)	0.3263(3)
C(4)	0.3627(6)	0.1816(3)	0.2474(3)
C(5)	0.4936(6)	0.1838(4)	0.2466(3)
C(6)	0.5850(4)	0.1687(3)	0.3246(3)
C(11)	0.7635(4)	0.1097(3)	0.5017(4)
C(12)	0.9461(4)	0.0633(3)	0.6160(4)
C(13)	0.9756(4)	0.0430(3)	0.7151(4)
C(21)	0.3592(3)	0.1251(2)	0.4952(2)
C(22)	0.3613(3)	0.2167(2)	0.5563(2)
C(24)	0.4031(3)	0.1956(2)	0.6594(2)
C(25)	0.5995(4)	0.1116(3)	0.7460(3)
C(26)	0.4139(3)	0.2888(3)	0.7143(2)
C(27)	0.3117(4)	0.1218(3)	0.6931(2)
C(231)	0.2322(4)	0.4130(3)	0.5151(3)
C(232)	0.3124(4)	0.4413(3)	0.4593(3)
C(233)	0.3382(5)	0.5394(4)	0.4503(4)
C(234)	0.2797(8)	0.6062(4)	0.4966(4)
C(235)	0.1979(9)	0.5784(5)	0.5495(4)
C(236)	0.1729(6)	0.4805(4)	0.5604(3)

Table 3. Fractional atomic coordinates for (10)

Atom	*x*	*y*	*z*
Se(21)	0.20238(3)	0.33969(3)	0.16655(2)
S(10)	0.65808(7)	0.15622(6)	0.10580(4)
O(10a)	0.7194(2)	0.0858(2)	0.0577(1)
O(10b)	0.6460(2)	0.1246(2)	0.1803(1)
N(1)	0.5047(2)	0.1793(2)	0.0643(1)
C(2)	0.4293(2)	0.2667(2)	0.0992(1)
C(3)	0.4159(3)	0.3581(2)	0.0408(2)
C(4)	0.4411(2)	0.3031(2)	–0.0307(1)
C(5)	0.4211(3)	0.3387(2)	–0.1032(2)
C(6)	0.4507(3)	0.2697(3)	–0.1594(2)
C(7)	0.4968(3)	0.1667(3)	–0.1431(2)
C(8)	0.5179(3)	0.1304(2)	–0.0705(2)
C(9)	0.4914(2)	0.2006(2)	–0.0150(1)
C(11)	0.7410(2)	0.2813(2)	0.1093(1)
C(12)	0.7862(3)	0.3232(2)	0.0464(2)
C(13)	0.8470(3)	0.4238(3)	0.0491(2)
C(14)	0.8660(3)	0.4815(2)	0.1159(2)
C(15)	0.8191(3)	0.4386(2)	0.1780(2)
C(16)	0.7572(3)	0.3395(2)	0.1758(1)
C(17)	0.9355(3)	0.5898(3)	0.1198(2)
C(18)	0.2974(3)	0.2204(2)	0.1205(1)
C(19)	0.2016(3)	0.1838(3)	0.0529(2)
C(20)	0.3230(3)	0.1284(2)	0.1760(2)
C(22)	0.3351(3)	0.3787(2)	0.2487(2)
C(23)	0.3323(3)	0.3329(3)	0.3178(2)
C(24)	0.4243(4)	0.3628(3)	0.3774(2)
C(25)	0.5205(4)	0.4373(3)	0.3675(2)
C(26)	0.5239(3)	0.4823(2)	0.2986(2)
C(27)	0.4311(3)	0.4547(2)	0.2397(2)

monochromatized Mo Kα radiation, λ 0.7107 Å. The ω : 2θ scan technique was employed to measure data which were corrected for Lorentz and polarization effects[24] and for (5), for absorption by using an empirical procedure.[25] The structures were solved by direct methods[26] and refined by a full-matrix least-squares procedure based on *F*.[24] Hydrogen atoms were included in each model at their calculated positions and non-hydrogen atoms were refined with anisotropic displacement parameters. After the inclusion of a weighting scheme of the form $w = 1/[\sigma^2(F)+g|F|^2]$, each refinement was continued until convergence using reflections with $I \geq 3.0\sigma(I)$. Crystal data and refinement details are collected in Table 1 and fractional atomic coordinates are listed in Tables 2 and 3; the numbering schemes employed are shown in Figs 1 and 2 which were drawn with ORTEP at the 35% probability level.[27] Evidence of some dynamic disorder in (5) can be seen in the shapes/sizes of the thermal ellipsoids in Fig. 1. Crystallographic Information Files (CIFs) and listings of structure factors for the structures have been deposited with the Australian Journal of Chemistry, P.O. Box 1139, Collingwood, Vic. 3066, and are available until 31 December 2005.

Acknowledgments

M.A.C. acknowledges an Australian Postgraduate Research Award (priority), C.L.F. acknowledges an Australian Postgraduate Research Award and T.T. acknowledges a University of Adelaide Summer Research Scholarship. We thank the Australian Research Council for support of the crystallographic facility.

References

[1] Omura, S., Nakagawa, A., Hashimoto, H., Oiwa, R., Iwai, Y., Hirano, A., Shibukawa, N., and Kojima, Y., *J. Antibiot.*, 1980, **33**, 1395.
[2] Omura, S., and Nakagawa, A., *Tetrahedron Lett*., 1981, **22**, 2199.
[3] Nakagawa, A., Iwai, Y., Hashimoto, H., Miyazaki, N., Oiwa, R., Takahashi, Y., Hirano, A., Shibukawa, N., Kojima, Y., and Omura, S., *J. Antibiot.*, 1981, **34**, 1408.
[4] Hill, M. L., and Raphael, R. A., *Tetrahedron Lett*., 1986, **27**, 1293.
[5] Hill, M. L., and Raphael, R. A., *Tetrahedron*, 1990, **46**, 4587.
[6] Morimoto, Y., Oda, K., Shirahama, H., Matsumoto, T., and Omura, S., *Chem. Lett*., 1988, 909.
[7] Morimoto, Y., Matsuda, F., and Shirahama, H., *Tetrahedron Lett.*, 1990, **31**, 6031.
[8] Morimoto, Y., Matsuda, F., and Shirahama, H., *Synlett*, 1991, 201.
[9] Pearce, C. M., and Sanders, J. K. M., *J. Chem. Soc*., *Perkin Trans. 1*, 1990, 409.
[10] Morimoto, Y., Matsuda, F., and Shirahama, H., *Tetrahedron*, 1996, **52**, 10609.
[11] Morimoto, Y., and Shirahama, H., *Tetrahedron*, 1996, **52**, 10631.
[12] Raner, K. D., Skelton, B. W., Ward, A. D., and White, A. H., *Aust. J. Chem*., 1990, **43**, 609.
[13] Raner, K. D., and Ward, A. D., *Aust. J. Chem*., 1991, **44**, 1749.
[14] De Silva, A. N., Francis, C. L., and Ward, A. D., *Aust. J. Chem*., 1993, **46**, 1657.
[15] Francis, C. L., and Ward, A. D., *Aust. J. Chem*., 1994, **47**, 2109.
[16] Williamson, N. M., March, D. R., and Ward, A. D., *Tetrahedron Lett*., 1995, **36**, 7721.
[17] Clive, D. L. J., Farina, V., Singh, A., Wong, C. K., Kiel, W. A., and Menchen, S. M., *J. Org. Chem*., 1980, **45**, 2120.
[18] Morella, A. M., and Ward, A. D., *Tetrahedron Lett*., 1984, **25**, 1197.
[19] Morella, A. M., and Ward, A. D., *Aust. J. Chem*., 1995, **48**, 445.
[20] Paulmier, C., 'Selenium Reagents and Intermediates in Organic Synthesis' (Pergamon Press: Oxford 1986).
[21] Hegedus, L. S., Allen, G. F., Bozell, J. J., and Waterman, E. L., *J. Am. Chem. Soc*., 1978, **100**, 5800.
[22] Larock, R. C., Hightower, T. R., Hasvold, L. A., and Peterson, K. P., *J. Org. Chem*., 1996, **61**, 3584.
[23] Harding, K. E., Marman, T. H., and Nam, D., *Tetrahedron*, 1988, **44**, 5605.
[24] teXsan: Structure Analysis Software, Molecular Structure Corporation, Texas, U.S.A.
[25] Walker, N., and Stuart, D., *Acta Crystallogr*., *Sect. A*, 1983, **39**, 158.
[26] Sheldrick, G. M., SHELXS86, Program for the Automatic Solution of Crystal Sructure, University of Göttingen, Göttingen, Germany, 1986.
[27] Johnson, C. K., ORTEP, Report ORNL-5138, Oak Ridge National Laboratory, TN, U.S.A., 1976.