Synthesis of *dl*-Guinesines and Related Compounds

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Received January 23, 1990

Guinesines **A**, **B** and **C** were synthesized starting from 1,3-bis(benzylthio)-2-propanone and *N*-methyl-2,2-diethoxypyrrolidine.

J. Heterocyclic Chem., **27**, 1361 (1990).

Insecticidal alkaloid guinesine **A**, **B** and **C** were isolated from the bark of a shrub tree in Brazil, *Cassipourea guianensis* (Rhizophoraceae). They have been proposed to be stereoisomers of 4-hydroxy-3-(1-methylpyrrolidin-2-yl)-1,2-dithiolane by Kato *et al.* [1] and also they reported that guinesines have insecticidal activity. It is interesting that guinesines and nereistoxin, 4-dimethylamino-1,2-dithiolane [2], have the 1,2-dithiolane ring with a tertiary amino group and show similar biological activities. The similarity of the chemical structure and the biological activity of guinesines as those of nereistoxin in spite of difference in their origins attracted our attention as key compounds for novel pesticides. Therefore, we synthesized guinesines and its dimethyl amino congener to study the stereochemistry of natural guinesines and to test for pesticides.

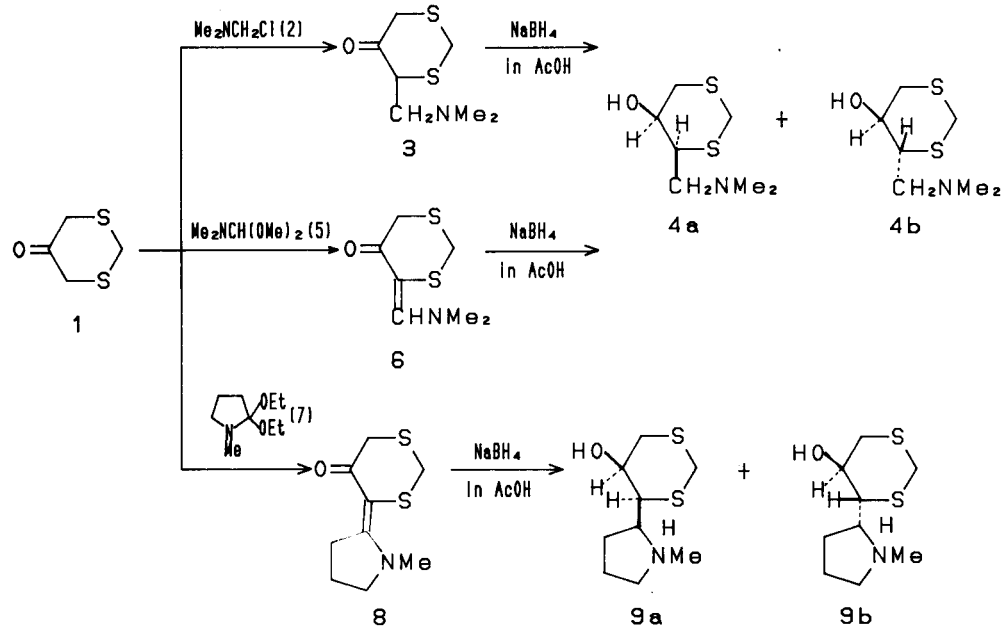
This report describes a method of synthesizing guinesines and its dimethylamino analogues and the identification of the stereochemistry of synthetic guinesines as well as that of natural guinesines, and also describes the insecticidal activity of guinesines and its derivatives against rice stem borers (*Chilo suppressalis*) and two-spotted spider mites (*Tetranychus urticae*).

In the basic strategy for the synthesis of guinesine, the dithiolane and amine parts were prepared, and then the two parts were coupled. The strategy was tested using simpler systems (Scheme 1). With condensation of 1,3-dithian-5-one (**1**) [3] as a precursor of 1,2-dithiolane with Eschen moser's salt **2** [4] as an amino methyl precursor in acetonitrile at room temperature, C–C bond formation took place smoothly and afforded the condensation product **3**. The reduction of **3** with sodium borohydride in methanol afforded many products. However, the reduction with sodium borohydride in acetic acid gave a mixture of *cis* and *trans* amino alcohols **4** in good yield. Also, condensation of **1** with commercially available 1,1-dimethoxytrimethylamine (**5**) on refluxing in toluene for 1 hour gave the enaminoketone **6** [5] in 78% yield. Enaminoketone **6** was reduced with sodium borohydride (excess) in acetic acid [6] to give a mixture of *cis*- and *trans*-isomers of amino alcohol **4** in an 84:16 ratio with a combined yield of 76%. The isomers were separated by column chromatography and identified by their spectral data. In the ^{1}H nmr spectra, the coupling constant ($J_{4,5}$) of **4a** is 2.1 Hz and that of **4b** is 9.3 Hz. This result indicated that the relationship of 4-H and 5-H of **4a** is axial-equatorial and that of **4b** is axial-axial [7], and hence **4a** and **4b** are *cis*-isomer and *trans*-isomer respectively. Instead of using 1,1-dimethoxytrimethylamine (**5**), *N*-methyl-2,2-diethoxypyrrolidine (**7**) [8] was adopted. Condensation of **1** with **7** gave enaminoketone **8** in 66% yield, which was then reduced with sodium borohydride in acetic acid to afford a mixture of *cis*- and *trans*-isomers of amino alcohols **9** in 75:25 ratio with a combined yield of 60%. Thus, the conditions for the C–C bond formation were obtained.

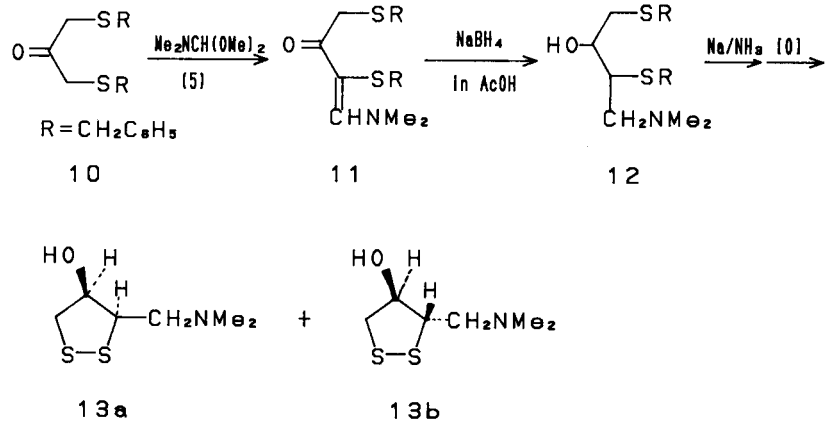
For the second step, we looked for the generation of dithiols from the amino alcohols. Condensation of 1,3-bis(benzylthio)-2-propanone (**10**) [9] as the precursor of the 1,2-dithiolane with 1,1-dimethoxytrimethylamine (**5**) on refluxing in toluene for 1 hour gave the enaminoketone **11** in 76% yield. Enaminoketone **11** was reduced with sodium borohydride in acetic acid to give amino alcohol **12** as a mixture of *syn*- and *anti*-isomers in 57% yield, which without further isolation was used for the next step. Deprotection of mixture **12** with sodium/ammonia and oxidative cyclization gave a mixture of **13a** and **13b** in 82:18 ratio with a combined yield of 62% (Scheme 2). The isomers were separated by column chromatography and identified by their nmr spectra. Thus we established the conditions for the formation of dithiolane.

Using these conditions, *dl*-guinesines were similarly prepared from **10** (Scheme 3). Condensation of **10** with *N*-methyl-2,2-diethoxypyrrolidine **7** gave compound **14** in 66% yield, which was then reduced with sodium borohydride in acetic acid to afford amino alcohol **16** as a mixture of diastereoisomers in 56% yield, which without further isolation was used for the next step. The deprotection of **16** with sodium/ammonia and oxidative cyclization gave a diastereomeric mixture of guinesines **17**. On chromatographic separation of the reaction mixture, the *trans*-isomer

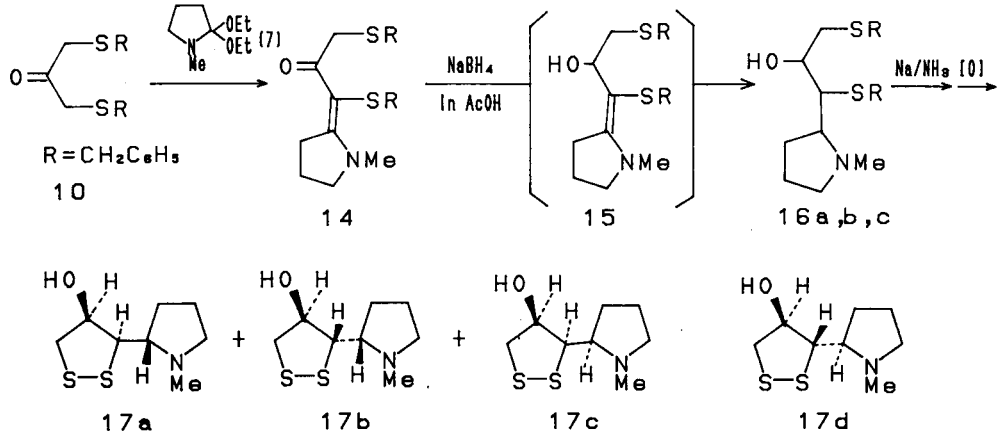
Scheme 1

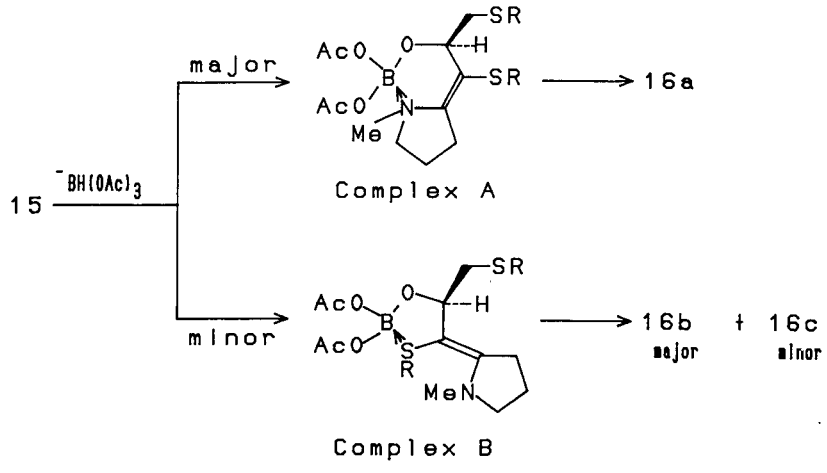


Scheme 2

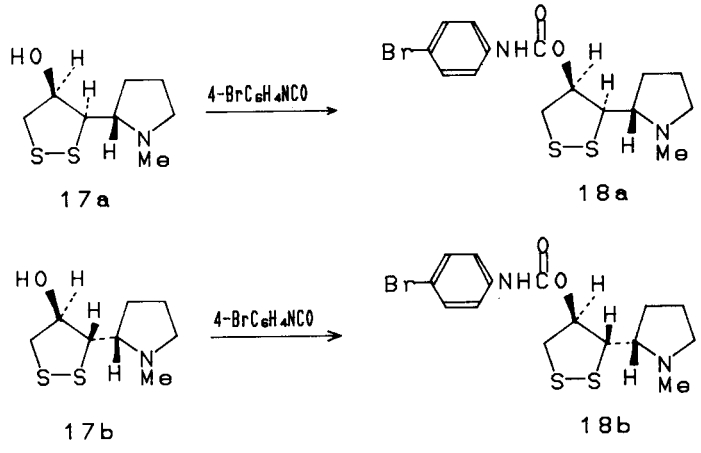


Scheme 3





Scheme 4



was isolated from the fast eluting fraction. A mixture of *cis*-isomers **17a** and **17b** was obtained from the slow eluting fraction. On bromobenzoylation followed by chromatographic separation, bromobenzoates of each *cis*-isomer **17a** and **17b** were separated in the pure state. The ratio of the three isomers 3,4-*cis*-3,2'-*threo*, 3,4-*trans*-3,2'-*erythro* and 3,4-*cis*-3,2'-*erythro* was 65:23:12 with a combined yield of 52%.

From the diastereomeric composition in the order of **17a** > **17b** > **17c**, a self-consistent rationale for the course of these reactions is proposed as follows. This reaction occurred due to the intervention of a three-step transition process between **14** to **16** as depicted in Scheme 3. First was the partial reduction of the enaminone **14** into the enaminol **15**, then came the formation of complexes **A** and **B** [10] between the enaminol **15** and the reagent triacetoxy borohydride anion ($BH(OAc)_3^-$) as shown in Scheme 4, and finally came the reduction of the double bond of the complexes **A** and **B** from the less hindered α-side to afford 3,4-*cis*-3,2'-*threo* **16c** and 3,4-*trans*-3,2'-*erythro* **16a**, respectively, as the major products. Reduction of the complex **B** from the hindered β-side afforded 3,4-*cis*-3,2'-*erythro* **16b** as a minor product. Since pyrrolidine is stronger base than sulfide, complex **A** might be more stable and abundant than complex **B**. Thus the rationale allowed us to explain the diastereomeric composition of the product in the order of **17a** > **17b** > **17c** satisfactorily.

Support for this explanation can be found in the literature. For preferred reduction of the carbonyl over the C=C double bond as assumed from **14** to **16**, Johnson *et al.* [11] reported that the reduction $\alpha\beta$-unsaturated ketones with sodium borohydride affords more $\alpha\beta$-unsaturated alcohols as the steric hindrance around the C=C double bond increases. For the formation from complexes **A** and **B**, there are precedent examples of borane complexes formed with alcohols, amines and sulfides. No detectable formation of 3,4-*trans*-3,2'-*threo* isomer **16d** which might be generated from complex **A** by the β-side reduction has been ascribed to the steric hindrance. Since the double bond of complex **A** is almost buried inside the ring consisting of 2-C, O, N and B, in contrast to the double bond of complex **B** which is located outside the corre-

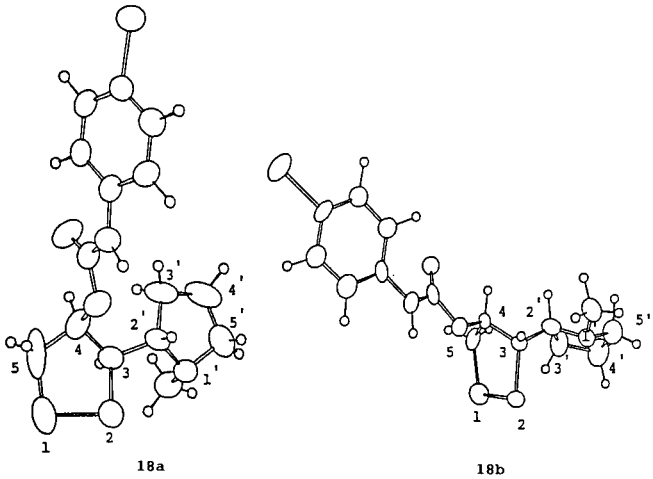
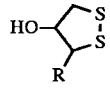


Figure 1. Molecular structure of 3-(1-methylpyrrolidin-2-yl)-4-(*p*-promophenylcarbamoyloxy)-1,2-dithiolanes **18a** and **18b** derived from **17a** and **17b** by single-crystal X-ray analysis.

Table 1

Biological Activities of 1,2-Dithiolane Derivatives



Compound No.	R	RSB Mortality % 50 μg/g	TSM Deceased % 500 ppm
13a	Me_2NCH_2	100	30
13b	Me_2NCH_2	100	100
17a		100	100
17b		100	100

RSB: Rice stem borers, topical application. TSM: Two-spotted spider mites, sprayed on the kidney bean plant seedling.

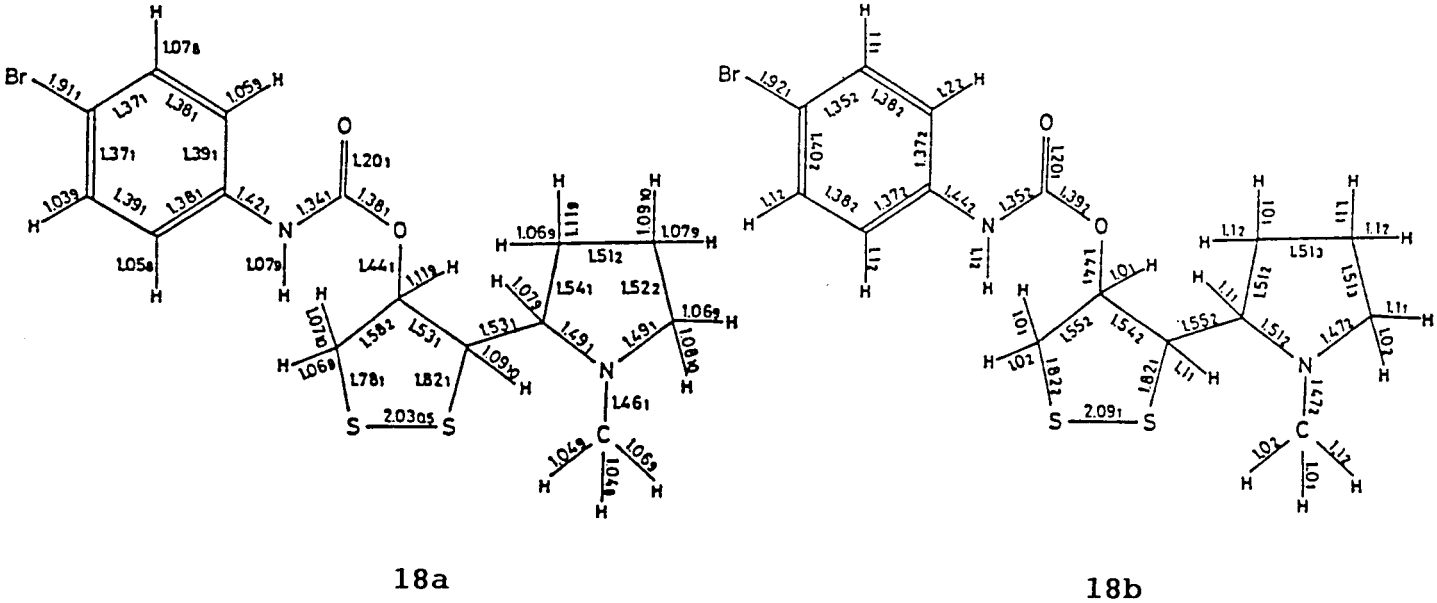


Figure 2. Bond Lengths (Å) in Compound **18**.

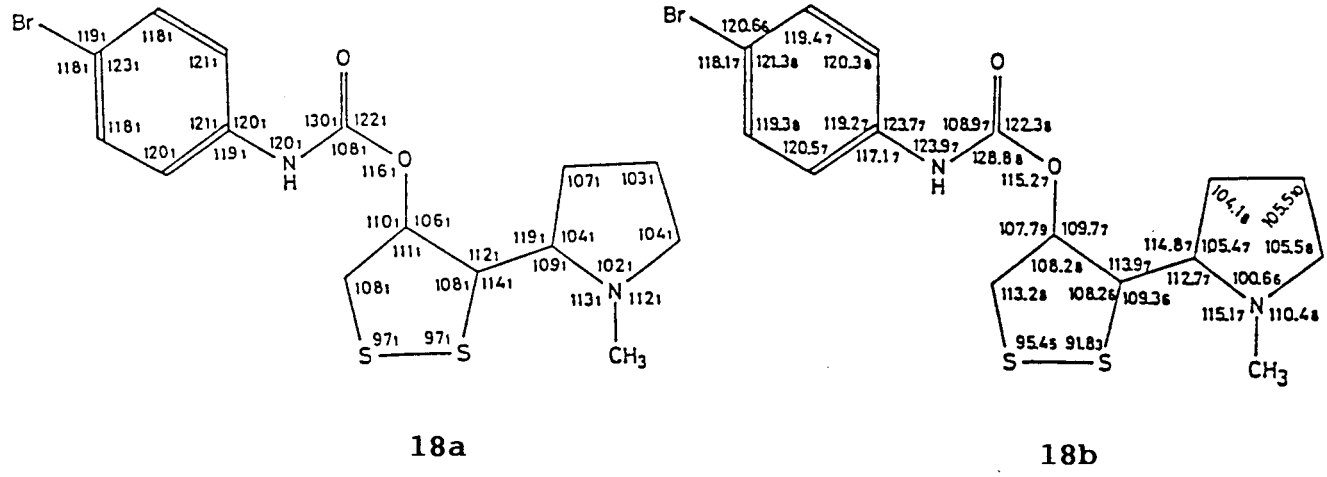


Figure 3. Bond Angles (°) in Compound **18**.

sponding ring, the steric hindrance of the former double bond is expected to be far greater than the latter.

The relative stereochemistry of **17a** and **17b** was established by ^{1}H nmr analysis and single crystal X-ray analysis of *p*-bromophenylcarbamates **18** of **17a** and **17b** [12] (Figures 1, 2 and 3). The ^{1}H nmr, ^{13}C nmr, mass and ir spectral of synthetic compound **17a**, **17b** and **17c** agree with those of guinesine **B**, **A** and **C**, respectively. The biological results are shown in Table 1. These synthetic guinesines and the dimethylaminomethyl analogue showed potent insecticidal activity against rice stem borers and two-spotted spider mites. The detailed structure-activity relationships will be reported elsewhere.

EXPERIMENTAL

The ^{1}H nmr spectra were recorded on a Varian EM-390 (90 MHz) and JOEL G-400 (400 MHz) spectrometer and the ^{13}C nmr were recorded on Varian NCG-XL 400 (400 MHz). All melting points are uncorrected.

Dimethylaminomethyl Chloride (**2**).

A solution of *N,N,N',N'*-tetramethyldiaminomethane (102.2 g, 1.0 mole) in diethyl ether (300 ml) was added dropwise a solution of acetyl chloride (86.4 g, 1.1 moles) in diethyl ether (100 ml) at room temperature and stirred for 2 hours at room temperature. White precipitate was corrected by filtration, washed with ether and dried to give 88.9 g (95%) of **2**.

4-Dimethylaminomethyl-1,3-dithiane-5-one Hydrogen Chloride (**3**).

To acetonitrile (100 ml) were added **1** (6.7 g, 0.05 mole) and dimethylaminomethyl chloride (4.7 g, 0.05 mole). The mixture was stirred for 20 hours at room temperature. The precipitate was filtered and washed with cooled acetonitrile to give **3** (9.7 g, 86%), mp 103-104°; ^{1}H nmr (DMSO-d_6): δ 1.1 (d, 3H, J = 6 Hz).

Anal. Calcd. for $C_7H_{14}NOS_2Cl$: C, 36.91; H, 6.19; N, 6.15. Found: C, 37.02; H, 6.20; N, 6.01.

4-Dimethylaminomethylene-1,3-dithian-5-one (**6**).

A solution of **1** (6.7 g, 0.05 mole) in toluene (50 ml) was added dropwise dimethylformamide dimethylacetal (7.2 g, 0.06 mole) under vigorous stirring at room temperature. The mixture was stirred at 100° for 1 hour. The reaction mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (ethyl acetate) to give **6** (7.4 g, 78%) as a yellow precipitate, mp 72-73°; ^{1}H nmr (deuteriochloroform): δ 3.2 (s, 6H, NMe_2), 7.65 (s, 1H, =CH), 3.65 (s, 2H, $COCH_2$), 3.4 (s, 2H, SCH_2).

Anal. Calcd. for $C_7H_{11}NOS_2$: C, 44.42; H, 5.86; N, 7.40. Found: C, 44.35; H, 5.79; N, 7.35.

4-Dimethylaminomethyl-5-hydroxy-1,3-dithianes **4a** and **4b**.

Sodium borohydride (3.8 g, 0.1 mole) was stirred with glacial acetic acid (50 ml) under a nitrogen atmosphere for 12 hours, the enaminoketone **6** (6.8 g, 0.03 mole) was then added, and the solution was stirred at room temperature for 24 hours. Concentrated hydrochloric acid (4 ml) was added, and the solution was stirred for 1 hour, poured onto ice, and made basic with 50% aqueous sodium hydroxide. The mixture was thoroughly extracted with chloroform, and organic phase was dried (magnesium sulfate) and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (chloroform/ethyl alcohol = 10/1) to give *cis*-isomer **4a** (4.2 g, 64%) and *trans*-isomer **4b** (0.8 g, 12%).

Compound **4a** was obtained as an oil (oxalate mp 164-165°); ^{1}H nmr 400 MHz (deuteriochloroform): δ 2.948 (t, 2H, 6-H), 4.023 (ddd, 1H, 5-H, J = 5.9, 3.4 and 2.1 Hz), 3.203 (ddd, 1H, 4-H, J = 8.5, 6.5 and 2.1 Hz), 2.081 (dd, 1H, 7a-H, J = 12.9 and 6.5 Hz), 2.516 (dd, 1H, 7b-H, J = 12.9 and 6.5 Hz), 3.671 (d, 1H, 2a-H, J = 14.2 Hz), 3.519 (d, 1H, 2b-H, J = 14.2 Hz), 2.306 (s, 6H, NMe_2), $J_{4,5}$ = 2.1 Hz; ^{13}C nmr (chloroform): 28.9 (t, 6-C), 63.1 (d, 5-C), 43.9 (d, 4-C), 60.9 (t, CH_2N), 35.1 (t, 2-C), 45.3 (q, NMe).

Anal. Calcd. for $C_7H_{15}NOS_2$: C, 43.49; H, 7.82; N, 7.24. Found: C, 43.52; H, 7.74; N, 7.19.

Compounds **4b** had mp 89-90° (oxalate mp 162-163°); ^{1}H nmr 400 MHz (deuteriochloroform): δ 2.852 (ddd, 1H, 6-H, J = 13.8, 3.4 and 2.1 Hz), 2.670 (dd, 1H, 6-H, J = 13.8 and 10.1 Hz), 3.88 (ddd, 1H, 5-H, J = 10.3, 9.3 and 3.5 Hz), 2.978 (ddd, 2H, 4-H, J = 11.7, 9.3 and 2.7 Hz), 2.755 (t, 1H, 7a-H, J = 11.8 and 11.8 Hz), 2.329 (dd, 1H, 7b-H, J = 12.5 and 2.9 Hz), 3.959 (d, 1H, 2a-H, J = 14.1 Hz), 3.383 (dd, 1H, 2b-H, J = 14.1 and 2.1 Hz), 2.363 (6H, s, NMe_2), $J_{4,5}$ = 9.3 Hz; ^{13}C nmr (chloroform): 31.2 (t, 6-C), 74.4 (d, 5-C), 43.3 (d, 4-C), 63.5 (t, CH_2N), 35.3 (t, 2-C), 45.1 (q, NMe).

Anal. Calcd. for $C_7H_{15}NOS_2$: C, 43.49; H, 7.82; N, 7.24. Found: C, 43.44; H, 7.87; N, 7.27.

N-Methyl-2,2-diethoxypyrrolidine (**7**).

N-methylpyrrolidin-2-one (50 g, 0.5 mole) and dimethyl sulfate (64 g, 0.5 mole) were mixed at room temperature, and stirred for 2 hours at 60° to give *N*-methylpyrrolidin-2-one dimethyl sulfate adduct. To a solution of ethanol (250 ml containing 12.3 g of sodium) was added dropwise dimethyl sulfate adduct (114 g) under vigorous stirring at room temperature. The mixture was stirred at 60° for 4 hours. The reaction mixture was concentrated under reduced pressure. The crude product was purified by distillation to give **7** (58.3 g, 50%), bp 55-58°/10 mm Hg (lit [8] 59-60°/11 mm Hg).

4-(1-Methylpyrrolidin-2-ylidene)-1,3-dithian-5-one (**8**).

A solution of **1** (5.2 g, 0.039 mole) in toluene (50 ml) was added dropwise *N*-methyl-2,2-diethoxypyrrolidine (**7**, 6.7 g, 0.04 mole) under vigorous stirring at room temperature. The mixture was stirred at 100° for 1 hour. The reaction mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (ethyl acetate) to give **8** (5.5 g, 66%) as yellow crystals, mp 90-91°; ^{1}H nmr (deuteriochloroform): δ 1.7-2.3 (m, 4H), 3.0-3.7 (m, 2H), 2.82 (s, 3H, NMe), 3.45 (s, 2H), 3.70 (s, 2H, $COCH_2$).

Anal. Calcd. for $C_9H_{13}NOS_2$: C, 50.20; H, 6.08; N, 6.52. Found: C, 50.18; H, 5.98; N, 6.49.

5-Hydroxy-4-(1-methylpyrrolidin-2-yl)-1,3-dithianes **9a** and **9b**.

Sodium borohydride (3.8 g, 0.1 mole) was added to glacial acetic acid (50 ml) and stirred under a nitrogen atmosphere for 12 hours, **8** (7.7 g, 0.02 mole) was then added, and the solution was stirred at room temperature for 24 hours. Concentrated hydro-

chloric acid (4 ml) was added, and the solution was stirred for 1 hour, poured onto ice, and made basic with 50% aqueous sodium hydroxide. The mixture was thoroughly extracted with chloroform, and organic phase was dried (magnesium sulfate) and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (chloroform/ethyl alcohol = 10/1) to give *cis*-isomer **9a**, (2.0 g, 45%) and *trans*-isomer **9b**, (0.7 g, 15%) as oils.

Compound **9a**.

Anal. Calcd. for $C_9H_{17}NOS_2$: C, 49.28; H, 7.81; N, 6.39. Found: C, 49.22; H, 7.80; N, 6.31.

Compound **9b**·Oxalate.

Anal. Calcd. for $C_{11}H_{19}NO_5S_2$: C, 42.70; H, 6.19; N, 4.53. Found: C, 42.32; H, 6.01; N, 4.31.

2,4-Bis(benzylthio)-1-dimethylamino-3-oxo-1-butene (**11**).

In a similar manner as described for **6**, reaction of **10** (9.1 g, 0.03 mole) with dimethylformamido dimethylacetal (**5**, 3.9 g, 0.03 mole) gave the title compound. The crude product was purified by silica gel column chromatography (ethyl acetate) to give **11** (8.0 g, 76%) as an oil; ^{1}H nmr (deuteriochloroform): δ 3.00 (s, 6H, NMe_2), 3.53 (s, 2H, CH_2), 3.62 (s, 2H, SCH_2), 3.75 (s, 2H, $COCH_2$), 7.89 (s, 1H, =CH), 7.3 (m, 10H, phenyl protons).

Anal. Calcd. for $C_{20}H_{23}NOS_2$: C, 67.19; H, 6.48; N, 3.92. Found: C, 67.55; H, 6.47; N, 3.69.

N,N-Dimethyl-2,4-bis(benzylthio)-3-hydroxybutylamine (**12**).

In a similar manner as described for **4**, reduction of **11** (7.2 g, 0.02 mole) with sodium borohydride gave the title compound. The crude product was purified by silica gel column chlomatography (chloroform/ethyl alcohol = 10/1) to give **12** (4.1 g, 57%) as an oil; ^{1}H nmr (deuteriochloroform): δ 2.14 (s, 6H, NMe_2), 2.2-3.0 (m, 5H), 5.0 (s, 1H, OH), 7.1-7.5 (m, 10H, phenyl protons).

Anal. Calcd. for $C_{20}H_{27}NOS_2$: C, 66.44; H, 7.53; N, 3.87. Found: C, 66.33; H, 7.50; N, 3.95.

3-Dimethylaminomethyl-4-hydroxy-1,2-dithiolanes **13a** and **13b**.

A solution of **12** (9.7 g, 0.025 mole) in ammonia (100 ml) was added sodium (2.9 g, 0.13 mole) at −60° and stirred for 2 hours at −60° and at −30° for 4 hours. After completion of the reaction, ammonia was removed, and added ethanol (10 ml) and water (100 ml). Water solution was neutralized by addition of concentrated hydrochloric acid and added 10% aqueous ferric chloride (1 ml) and air was bubbled into the mixture for 3 hours. The mixture was thoroughly extracted with chloroform, and the organic phase was dried (magnesium sulfate) and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (chloroform/ethyl alcohol = 10/1) to give **13a** (*cis*-isomer, 2.7 g, 51%) and **13b** (*trans*-isomer, 0.6 g, 11%).

Compound **13a** was obtained as an oil; ^{1}H nmr (deuteriochloroform): δ 2.64 (dd, 1H, 6a-H, J = 12.7 and 6.9 Hz), 2.98 (dd, 1H, 6b-H, J = 12.7 and 9.0 Hz), 3.17 (dd, 1H, 5a-H, J = 11.1 and 4.3 Hz), 3.36 (dd, 1H, 5a-H, J = 11.1 and 4.3 Hz), 3.68 (ddd, 1H, 3-H, J = 4.5 Hz), $J_{3,4}$ = 4.5 Hz), 2.32 (s, 6H, NMe).

Compound **13b** was obtained as an oil; ^{1}H nmr (deuteriochloroform): δ 2.35-2.75 (m, 2H, CH_2N, J = 7.6 and 8.2 Hz), 3.03-3.37 (m, 2H, 5-H, J = 4.4 and 4.6 Hz), 3.46-3.7 (m, 1H, 3-H, J = 4.2 and 8.2 Hz), 4.51 (m, 1H, 4-H, J = 4.2 and 4.4 Hz), $J_{3,4}$ = 4.2 Hz), 2.30 (s, 6H, NMe).

The oxalate of **13a** had mp 126-128°; ^{1}H nmr (DMSO-d_6): δ 2.68 (s, 6H, NMe_2), 3.07 (dd, 1H, 2'-H, J = 11.5 and 3.5 Hz), 3.15 (dd, 1H, J = 13.4 and 8.1 Hz), 3.35 (dd, 1H, J = 11.5 and 4.9 Hz), 3.38 (dd, 1H, J = 13.4 and 5.4 Hz), 3.87 (ddd, 1H, J = 8.1, 5.4 and 4.4 Hz), 4.72 (q, 1H, J = 4.4 Hz).

Anal. Calcd. for $C_8H_{15}NO_5S_2$: C, 35.68; H, 5.61; N, 5.20. Found: C, 35.44; H, 5.38; N, 5.21.

The oxalate of **13b** had mp 164-166°; ^{1}H nmr (DMSO-d_6): δ 2.64 (s, 6H, NMe_2), 2.97 (dd, 1H, J = 12.9 and 8.7 Hz), 3.06 (dd, 1H, J = 11.6 and 4.0 Hz), 3.14 (dd, 1H, J = 12.9 and 5.9 Hz), 3.30 (dd, 1H, J = 11.6 and 5 Hz), 3.72 (ddd, 1H, J = 8.7, 5.9 and 3.2 Hz), 4.47 (q, 1H, J = 3.8 Hz).

Anal. Calcd. for $C_8H_{15}NO_5S_2$: C, 35.68; H, 5.61; N, 5.20. Found: C, 35.32; H, 5.58; N, 5.02.

1-Methyl-2-[1,3-bis(benzylthio)-2-oxopropylidene]pyrrolidine (**14**).

In a similar manner as described for **8**, condensation of **10** (6.1 g, 0.02 mole) with 1-methyl-2,2-diethoxypyrrolidine (**7**, 7.0 g, 0.04 mole) gave the title compound. The crude product was purified by silica gel column chromatography (ethyl acetate) to give **14** (6.1 g, 66%) as an oil; ^{1}H nmr (deuteriochloroform): δ 1.13 (m, 2H), 2.85 (m, 2H), 2.98 (s, 3H, Me), 3.45 (m, 2H, CH_2), 3.59 (s, 2H, SCH_2), 3.65 (s, 2H, SCH_2), 3.75 (s, 2H, $COCH_2$), 7.3 (m, 10H, phenyl protons).

Anal. Calcd. for $C_{22}H_{25}NOS_2$: C, 68.89; H, 6.57; N, 3.65. Found: C, 68.74; H, 6.38; N, 3.51.

1-Methyl-2-[1,3-bis(benzylthio)-2-hydroxypropyl]pyrrolidine (**16**).

In a similar manner as described for **9**, reduction of **14** (7.7 g, 0.02 mole) with sodium borohydride gave the title compound. The crude product was purified by silica gel column chromatography (chloroform/ethyl alcohol = 10/1) to give **16** (4.4 g, 56%) as an oil; ^{1}H nmr (deuteriochloroform): δ 2.14 (s, 3H, NMe), 2.2-3.0 (m, 5H), 5.0 (s, 1H, OH), 7.1-7.5 (m, 10H, phenyl protons).

Anal. Calcd. for $C_{22}H_{29}NOS_2$: C, 68.17; H, 7.54; N, 3.61. Found: C, 67.89; H, 7.38; N, 3.49.

4-Hydroxy-3-(1-methylpyrrolidin-2-yl)-1,2-dithiolanes **17a**, **17b** and **17c**.

In a similar manner as described for **13**, deprotection of **16** (9.7 g, 0.025 mole) with sodium/ammonia and oxidative cyclization gave the title compounds. The crude product was purified by silica gel column chromatography (chloroform/ethyl alcohol = 10/1) to give **17** (2.7 g, 52%) as oils.

Compound **17a** was obtained as an oil in 34% yield; ^{1}H nmr (deuteriochloroform): δ 2.93 (q, 1H, 2'-H), 2.17 (m, 2H, 3'-H_2), 1.83 (m, 2H, 4'-H_2), 2.39 (m, 1H, 5'a-H), 3.14 (m, 1H, 5'b-H), 2.47 (s, 3H, NMe), 3.64 (dd, 1H, 3-H, J = 4.2 and 7.4 Hz), 3.21 (dd, 1H, 5a-H, J = 11.0 and 3.0 Hz), 3.31 (dd, 1H, 5b-H, J = 4.0 Hz), 4.77 (m, 1H, 4-H).

17a·Oxalate.

Anal. Calcd. for $C_{10}H_{17}NO_5S_2$: C, 68.17; H, 7.54; N, 3.61. Found: C, 68.14; H, 7.38; N, 3.51.

Compound **17b** was obtained as an oil in 12% yield; ^{1}H nmr (deuteriochloroform): δ 2.86 (m, 1H, 2'-H), 1.96 (m, 2H, 3'-H_2), 1.84 (m, 2H, 4'-H_2), 2.30 (m, 1H, 5'a-H), 3.15 (m, 1H, 5'b-H), 2.44 (s, 3H, NMe), 3.85 (dd, 1H, 5a-H, J = 4.5 and 7.8 Hz) 3.13 (dd, 1H, 5b-H, J = 6.2 Hz), 4.45 (m, 1H, 4-H).

17b·Oxalate.

Anal. Calcd. for $C_{10}H_{17}NO_5S_2$: C, 68.17; H, 7.54; N, 3.61.

Found: C, 67.95; H, 7.18; N, 3.44.

Compound **17c** was obtained as an oil in 6.2% yield; ^{1}H nmr (deuteriochloroform): δ 1.84 (m, 4H, 3-H and 4-H), 2.35 (m, 1H, 5'a-H), 2.85 (m, 1H, 2'-H), 2.44 (s, 3H, NMe), 3.08 (m, 1H, 5'b-H), 3.19 (dd, 1H, J = 11.5 and 5 Hz), 3.29 (dd, 1H, J = 11.5 and 4.8 Hz), 3.52 (dd, 1H, J = 5 and 7.2 Hz), 4.46 (1H, q, J = 5 Hz, 4-H).

17c·Oxalate.

Anal. Calcd. for $C_{10}H_{17}NO_5S_2$: C, 68.17; H, 7.54; N, 3.61. Found: C, 68.24; H, 7.35; N, 3.46.

4-[*O*-{*N*-(*p*-bromophenyl)carbamoyl}]oxy-3-(1-methylpyrrolidin-2-yl)-1,2-dithiolanes **18a** and **18b**.

Compound **17a** (0.25 g, 0.05 mole) was dissolved in toluene (200 ml). *p*-Bromophenyl isocyanate (0.25 g, 0.16 mole) and triethylamine (0.1 g, 0.16 mole) were added to solution under vigorous stirring at 60°. The mixture was stirred at 60° for 0.5 hour. The reaction mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (ethyl acetate) to give **18a** (0.25 g, 51%) as a yellow powder mp 136-137°; ^{1}H nmr (deuteriochloroform): δ 1.8 and 2.09 (m, 4H, 3'-H and 4'-H), 2.32 (m, 1H, 5'a-H), 3.14 (ddd, 1H, 5'b-H, J = 10.3, 6.6 and 3.6 Hz), 2.53 (s, 3H, NMe), 2.882 (m, 1H, 2'-H), 3.42 (dd, 1H, 5a-H, J = 12.6 and 2.0 Hz), 3.506 (dd, 1H, 5b-H, J = 12.6 and 4.5 Hz), 3.673 (1H, dd, 3-H, J = 9.3 and 3.7 Hz), 5.755 (dt, 1H, 4-H, J = 4.2, 1.7 and 4.2 Hz), 7.091 (bs, 1H, NH), 7.31 and 7.433 (d-like, 4H, phenyl protons, J = 8.8 and 9.0 Hz); ^{13}C nmr (chloroform): 23.69 (4'-C), 31.29 (3'-C), 43.33 (NMe), 44.24 (5-C), 57.18 (5'-C), 65.2 (3-C), 67.63 (2'-C), 78.17 (4-C), 152.21 (CO).

Anal. Calcd. for $C_{15}H_{19}BrN_2O_2S_2$: C, 44.67; H, 4.75; N, 6.95. Found: C, 44.65; H, 4.78; N, 6.85.

In a similar procedure as described for **18a**, **18b** was obtained in 53% yield, mp 149-150°; ^{1}H nmr (deuteriochloroform): δ 1.89 and 1.76 (m, 4H, 3'-H and 4'-H), 2.262 (q-like, 1H, 5'a-H, J = 8.7 Hz), 3.083 (ddd, 1H, 5'b-H, J = 9.3, 7.1 and 2.3 Hz), 2.405 (s, 3H, NMe), 2.892 (d-like, 1H, 2'-H, J = 7.8 and 4.6 Hz), 3.283 (dd, 1H, 5a-H, J = 12.9 and 4.46 Hz), 3.331 (dd, 1H, 5b-H, J = 12.9 and 2.4 Hz), 4.059 (dd, 1H, 3-H, J = 4.5 and 3.3 Hz), 5.447 (dt, 1H, 4-H, J = 4.2, 2.9 and 4.2 Hz), 6.869 (bs, 1H, NH), 7.279 and 7.423 (d-like, 4H, phenyl protons, J = 8.8 Hz); ^{13}C nmr (chloroform): 22.8 (4'-C), 26.62 (3'-C), 40.42 (NMe), 46.13 (5-C), 57.22 (5'-C), 64.01 (3-C), 65.89 (2'-C), 81.12 (4-C), 152.43 (CO).

Anal. Calcd. for $C_{15}H_{19}BrN_2O_2S_2$: C, 44.67; H, 4.75; N, 6.95. Found: C, 44.73; H, 4.69; N, 7.10.

Acknowledgements.

We thank Dr. Kazuhide Kamiya and Mr. Yoshikazu Wada for analysis of X-ray crystallography and Dr. Yasuo Sato for insecticidal test.

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[12] Crystallographic data have been deposited at the Cambridge Crystallographic Data Center. Crystal data for **18a**: monoclinic; space group $P2_1/a$; a = 11.031(3), b = 16.813(4), c = 9.482(3) Å; β = 100.24(3)°; V = 1730.7(8) Å^3; Z = 4; D_x = 1.50 g.cm^{-3}. The intensity measurements were performed for $3° \leq 7\theta \leq 50°$ with Mokα radiation. The structure was solved by direct methods (MULTAN) and refined to give R = 0.076 for 2141 observed reflections $F_o \geq 2\sigma(F_o)$. For **18b**: triclinic; space group P1; a = 13.351(4), b = 6.441(2), c = 10.382(5) Å; α = 89.43(4), β = 105.76(3), γ = 92.75(3)°; V = 858.2(6) Å^3; Z = 2; D_x = 1.56 g.cm^{-3} $3° \leq 2\theta \leq 50°$ (MoKα); R = 0.096; 1735 [$F_o \geq 2\sigma(F_o)$].