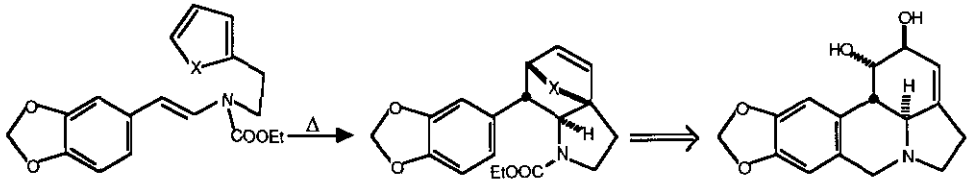
PREPARATION OF *N*-ALKADIENYL *N*-*E*-2-ARYLETHENYLCARBAMATES VIA SULFOXIDE ELIMINATION IN A SYNTHETIC APPROACH TO LYCORINE[1,2]

Michael E. Jung* and Steven J. Miller

Department of Chemistry and Biochemistry, University of California, Los Angeles, CA 90024, USA

Abstract - *N*-*E*-2-Arylethenylcarbamates have been prepared in good yields from *N*-[2-(phenylthio)-2-arylethyl]carbamates via sulfoxide elimination towards nitrogen.

The *Amaryllidaceae* alkaloid lycorine **1** has often been used as a target molecule to test new methods of synthesis.[3,4] Several years ago we envisioned an approach to lycorine that would utilize an intramolecular Diels-Alder reaction of the *N*-(3,5-hexadienyl)-*N*-*E*-(2-arylethenyl)carbamate **2a** or the analogous *N*-[2-(2-furyl)ethyl]carbamate **2b** to afford the adducts **3ab** in which the *E*-geometry of the arylethenylcarbamates would guarantee the required trans stereochemistry of the two hydrogens of the eventual ring juncture. Either of these two intermediates would then be well set up for conversion into lycorine **1** by relatively straightforward and precedented chemistry. The desired substrates **2ab** could be prepared by any of

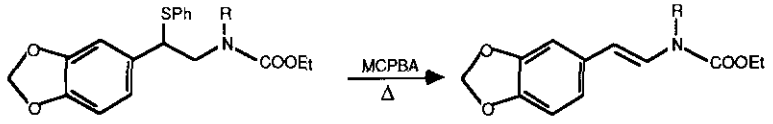


2a X = H_2
2b X = O

3a X = H_2
3b X = O

1

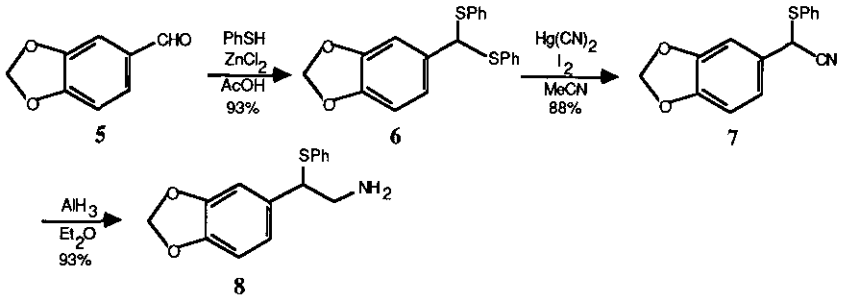
several routes but we chose to investigate the thermal [2,3] elimination of the sulfoxide derived from the sulfide **4** by oxidation. One would predict that the transition state of the [2,3] sulfoxide elimination leading to the *E*-isomer would be greatly favored over that leading to the *Z*-isomer and thus one would expect to obtain mainly the desired stereoisomers **2ab** in this process. Results from other laboratories[4de,5] on similar versions of both of these key steps prompt us to report our results here in detail.



4 **2ab**

We decided to begin our synthesis with the inexpensive, commercially available starting material piperonal **5** rather than other more functionalized systems such as homopiperonal. Although the desired 2-phenylthio-2-arylethylamine **8** could be prepared by addition of thiophenol to the nitrostyrene (derived from condensation of nitromethane with **5**) followed by reduction,[6] the somewhat lower overall yields prompted us to seek alternative routes. The followed route to **8** proved the

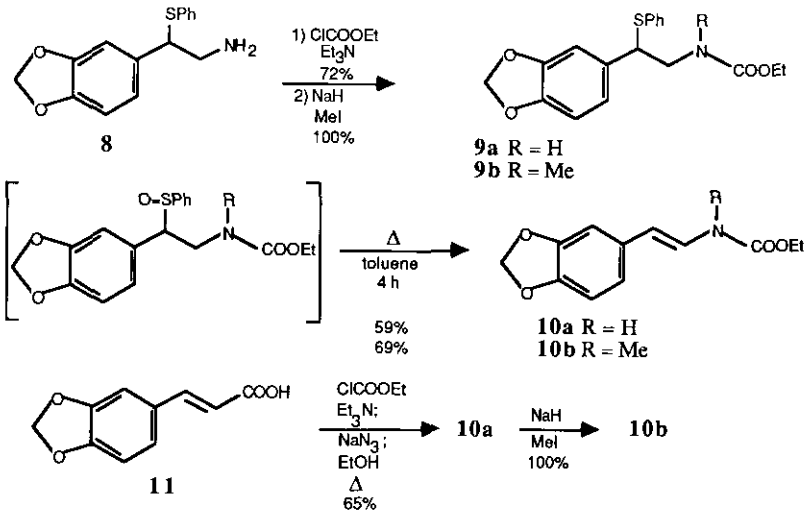
most successful in our hands. The dithioacetal of piperonal **6**[7] was easily prepared from piperonal **5** in 93% yield. Treatment of **6** with one equivalent of mercuric cyanide and one equivalent of iodine in dry acetonitrile afforded the α-thiophenylarylacetonitrile **7**[8] in 88% yield.[9] While several hydride reducing agents (e.g., lithium aluminum hydride, sodium borohydride-cobalt dichloride, borane-tetrahydrofuran) failed to cleanly reduce the nitrile to the amine, treatment with



5 **6** **7** **8**

aluminum hydride in diethyl ether at room temperature gave the desired amine **8**[5] in 93% yield. Thus amine **8** was available from piperonal **5** in three easy steps in 76% overall yield.

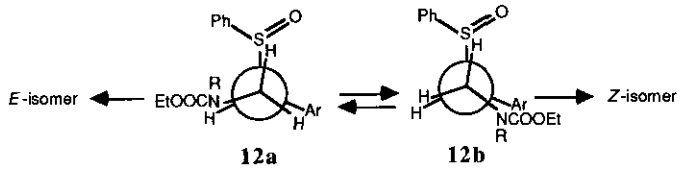
Conversion of this 2-thiophenyl-2-arylethylamine **8** into the desired *E*-stereoisomers of 2-arylethenylcarbamates was first tested in simpler cases as follows. Formation of the carbamate **9a** proceeded under normal conditions in 72% yield. Methylation of the anion of this carbamate (sodium hydride, methyl iodide) produced the *N*-methyl analogue **9b** in quantitative yield. Treatment of these 2-thiophenylethylcarbamates **9ab** with *m*-chloroperbenzoic acid in methylene chloride furnished the corresponding sulfoxides which were not purified but rather directly thermolyzed in refluxing toluene for 4 h to give, after chromatographic purification, the desired *E*-isomers of the 2-arylethenylcarbamates **10ab** in yields of 59% and 69% respectively. None of the undesired *Z*-isomers were isolated. Authentic samples of these *E*-2-arylethenylcarbamates



8 **9a** R = H **9b** R = Me **10a** R = H **10b** R = Me **11** **10a** **10b**

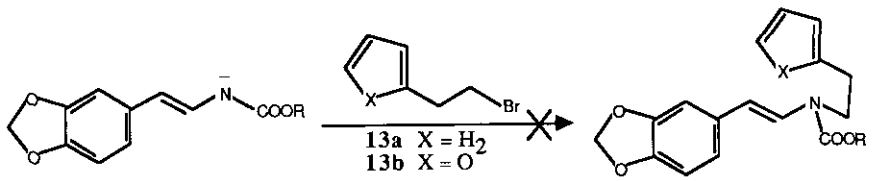
10ab were prepared by a modified Curtius rearrangement[10] of *E*-1,3-benzodioxolepropenoic acid **11**[11] to give **10a** in 65% yield which on alkylation afforded the *N*-methyl compound **10b** in quantitative yield.[12] The coupling constants for the vinyl

protons of these carbamates were 15 Hz, thereby indicating that the elimination was stereoselective for the *E*-isomers. Presumably the sulfoxide elimination prefers to take place via conformation **12a** rather than conformation **12b** on account of the considerable steric interaction present in the latter due to the eclipsing interaction of the aryl and substituted amino group. Having shown that this thermal elimination process produced the desired *E*-isomers in simple cases, we turned our attention to the preparation of the more functionalized derivatives needed for the synthesis of lycorine.

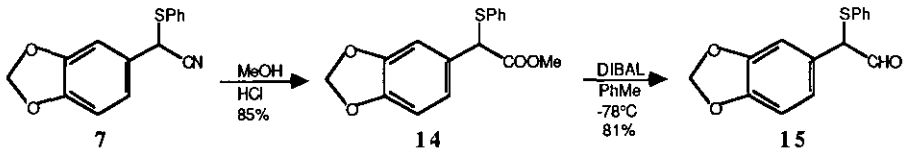


12a **12b**

The most direct route to **2ab** based on the above results would involve alkylation of the anion of the carbamate **10b** with the bromides **13ab**. Unfortunately these alkylations did not proceed well in our hands under a variety of conditions and only small amounts (5-10%) of alkylation could be obtained. We therefore turned to an alternative route to these compounds, in which the N-substituent would be present before sulfoxide elimination. Of the various potential procedures for preparing the

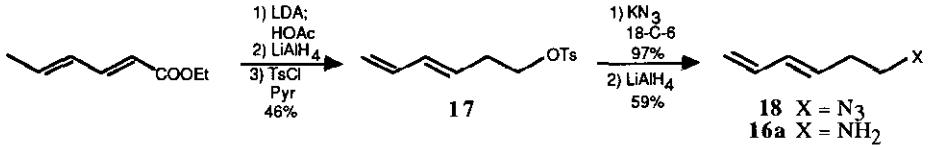


desired thiophenyl amines **19ab** we chose a reductive amination process, which required the aldehyde **15** and the two amines **16ab**. The aldehyde was easily prepared as follows. Treatment of the nitrile **7** with methanolic hydrogen chloride gave the methyl ester **14** which was cleanly reduced with diisobutylaluminum hydride to the aldehyde **15** in 69% overall yield for the two steps. This route was preferable to other simpler methods due to higher yields. For example, treatment of 5-(phenylthio)methyl-1,3-benzodioxole with *n*-butyllithium followed by trapping of the anion with ethyl formate afforded **15**



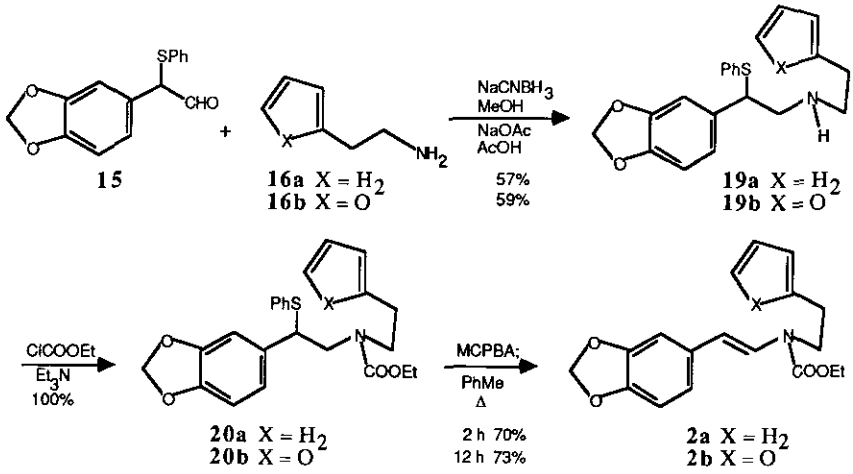
7 **14** **15**

in only 30% yield. 2-(2-Furyl)ethylamine **16b** was prepared by the known two-step route from furfural in 30% overall yield.[14] *E*-1-Amino-3,5-hexadiene **16a** was prepared from the known[15] tosylate **17** (available from ethyl sorbate in three steps in 46% yield)[16,17] by treatment with potassium azide and 18-crown-6 to give the azide **18** (97% crude yield) which was then reduced with lithium aluminum hydride.



17 **18** X = N_3 **16a** X = NH_2

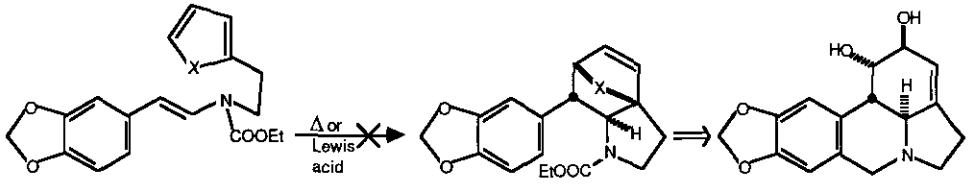
With the components **15** and **16ab** in hand, we pursued the reductive amination to give **19ab**. Initial attempts using sodium cyanoborohydride with hydrochloric acid as the proton source led predominately to reduction of the aldehyde to the corresponding arylethanol. However, use of acetic acid with a sodium acetate buffer in methanol afforded the desired furylethylamine **19b** in 59% yield. For **19a** it was better to form the imine by adding two equivalents of **16a** to the aldehyde **15** in methanol with acetic acid/sodium acetate in the presence of sodium sulfate to absorb the water produced. Sodium cyanoborohydride was then added to this preformed imine to furnish the hexadienylamine **19a** in 57% yield. Treatment of the amines with ethyl chloroformate and triethylamine led to the formation of the carbamates **20ab** in quantitative yield. These carbamates could be isolated, but it generally proved more efficient to carry the crude carbamates through to the subsequent oxidation and thermolysis reactions. Treatment of **20ab** with *m*-chloroperbenzoic acid produced the sulfoxides which were not purified but rather directly thermolyzed in refluxing toluene to give the desired ethyl *N*-alkadienyl-*N*-*E*-(2-arylethenyl)carbamates **2ab** in yields of 70% and 73%, respectively, after column chromatography on silica gel. Again, the coupling constants of the styrenyl protons were 15 Hz, again indicating that the *E*-stereoisomers have been produced stereoselectively. Thus this method seems to be reasonably general for the production of functionalized *E*-2-arylethenyl-carbamates such as **10ab** and **2ab**.



With the Diels-Alder substrates **2ab** in hand, we now turned our attention to efforts to induce the required Diels-Alder cycloadditions of these systems. The hexadienylcarbamate **2a** was heated in refluxing mesitylene (165°C) in the presence of catalytic hydroquinone for 60 h with the result that while some starting carbamate **2a** was recovered, extensive decomposition appeared to have occurred, and no other product could be isolated. Other attempts to effect this Diels-Alder reaction focused on flash vacuum pyrolysis. Carbamate **2a** could be distilled through a 4 inch horizontal quartz column packed with quartz chips and heated to 600°C under vacuum, resulting in a 67% recovery of **2a** again with no other isolable product. Alternatively, a solution of the carbamate **2a** in toluene could be passed through a 6 inch vertical column under vacuum and packed with quartz chips. In this case, various temperatures were used. When the column was heated to 400°C, the material recovered was almost completely the starting carbamate. At 500°C, the proton nmr of the pyrolysate showed both starting carbamate and some additional signals. Purification of the major fractions in this case led to isolation of the starting material,

as well as a second major fraction. This fraction, however, no longer possessed the characteristic proton nmr patterns for the piperonyl moiety although the butadiene pattern was intact. Clearly the product could not have been the desired Diels-Alder product **3a.** Finally, use of the vertical column at 600°C resulted in complete decomposition of the carbamate **2a** with recovery of a tarry residue almost completely devoid of proton nmr signals. Attempts to effect the Diels-Alder reaction of **2a** were then abandoned.

The Diels-Alder reaction of the 2-furylethylcarbamate **2b** expected to be somewhat less straightforward. This reaction would undoubtedly be complicated by the tendency of furan Diels-Alder reactions to be reversible, so that simply going to higher temperatures would probably not be effective in obtaining the Diels-Alder product **3b**. Nonetheless, the carbamate **2b** was heated in refluxing mesitylene (165°C) for 60 h in the presence of catalytic hydroquinone, resulting in recovery of the starting carbamate. It could also be distilled through a 4 inch horizontal quartz tube packed with quartz chips and heated to 600°C under vacuum, with an 87% recovery of the starting material. Finally, passing a toluene solution of the carbamate **2b** through a vertical packed column at 600°C under vacuum resulted in complete destruction of the carbamate, again with recovery of a tarry residue similar to that described above for the hexadienyl case.

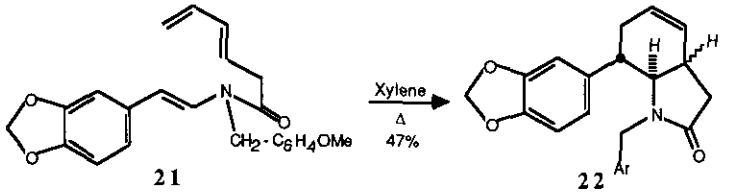


2a X = H_2
2b X = O

3a X = H_2
3b X = O

1

Other techniques for accelerating Diels-Alder reactions were also tried with **2ab**, completely without success. The use of polar solvents, mild acidic material such as silica gel, strongly Lewis acidic compounds such as ethylaluminum dichloride (catalytic and stoichiometric), and radical-cation catalysis using tris-(*p*-bromophenyl)amminium pentachlorostibnate failed to produce any of the desired cycloadducts **3ab**. With the failure of these substances to undergo cycloadditions, we abandoned this route as a synthetic approach to lycorine. It is important to point out that minor modifications of the above route have produced an elegant synthesis of lycorine. Completely independent and concurrent with our work, Martin and Tu prepared the analogous *N*-(*p*-methoxybenzyl)enamide **21** which cyclized in refluxing xylene to give the desired cycloadduct **22** in 47% yield as a 1.4:1 mixture of isomers.[4e] The cis-fused isomer was then converted into an intermediate in a previous lycorine synthesis in only three steps. Thus the two differences of having an amide tether group rather than an amino tether and an



21 **22**

N-arylmethyl group rather than the carbamate allow the cycloaddition to occur. We are unable to offer any explanation (conformational, electronic, steric, or a mixture) for why these two similar systems behave so differently in cycloadditions.

EXPERIMENTAL

Melting points were determined on an electrothermal melting point apparatus and are uncorrected. Infrared spectra (ir) were recorded on a Perkin-Elmer Model 137B or 710B spectrophotometer in chloroform solution or as a neat film, as indicated. Proton nmr spectra, unless otherwise indicated, were measured on a Bruker WP-200 spectrometer. Proton nmr spectra indicated as 60 MHz spectra were determined on a Varian T-60 spectrometer. All were determined in deuteriochloroform solution and are reported in parts per million downfield from internal tetramethylsilane (note: s, d, t, q, m, b refer to singlet, doublet, triplet, quartet, multiplet, and broad, respectively). Mass spectra (ms) were recorded on an AEI MS-9 spectrometer. Data reported are the m/z values for the most abundant peaks and are not a complete tabulation. For column chromatography, Merck silica gel 60 (70-230 mesh) was used as adsorbent. For preparative layer chromatography, Merck silica gel 60 PF-254 was used. Analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan. All reagents and solvents were purified and distilled according to standard methods.

5-(Bisphenylthio)methyl-1,3-benzodioxole, **6**.

Piperonal **5** (30 g; 0.2 mol) was suspended in glacial acetic acid (250 ml) and zinc chloride (20 g; 0.148 mol) and benzenethiol (41 ml; 0.4 mol) was added. The mixture was stirred at 60°C under nitrogen for 3 h. After cooling to room temperature, the mixture was poured into 1 liter of saturated aq. K_2CO_3. This was extracted with 3 x 500 ml of diethyl ether. The combined extracts were washed with 200 ml of saturated aq. $NaHCO_3$ and brine, and dried over Na_2SO_4. Evaporation of the solvent gave 69.6 g of crude dithioacetal **6**. Recrystallization from cyclohexane/petroleum ether yielded 65.45 g (0.186 mol; 93%) of pure dithioacetal **6**, mp 49.5-50°C. ^{1}H Nmr: δ 7.40 - 7.20 (10H, m), 6.97 (1H, d, J = 2 Hz), 6.77 (1H, dd, J = 7.8, 2 Hz), 6.65 (1H, d, J = 7.8 Hz), 5.94 (2H, s), 5.35 (1H, s). Ir ($CHCl_3$): 3080, 3000, 2900, 1580, 1505, 1490, 1440, 1250, 1040, 930 cm^{-1}. Ms (*m/z*): 243 (M^+-SPh, base). Anal. Calcd for $C_{20}H_{16}O_2S_2$: C, 68.15; H, 4.58. Found:- C, 68.15; H, 4.63.

α-Phenylthio-1,3-benzodioxole-5-acetonitrile, **7**.

Mercuric cyanide (7.2 g; 28.4 mmol) and iodine (7.2 g; 28.4 mmol) were added to a solution of the dithioacetal **6** (10 g; 28.4 mmol) in dry acetonitrile (20 ml) and the mixture was stirred at 55°C under nitrogen for 20 min. After cooling to room temperature, the mercuric iodide was removed by filtration and washed with acetonitrile. The combined acetonitrile fractions were evaporated and the residue was taken up in 100 ml of carbon tetrachloride. 1 M Aqueous $Na_2S_2O_3$ (100 ml) was added and the mixture was stirred at room temperature to discharge the color. This was then diluted with water and extracted with 2 x 250 ml of chloroform. The combined chloroform extracts were washed with 50 ml of saturated aq. $NaHCO_3$, dried over Na_2SO_4, and evaporated. The residue was crystallized from benzene/ligroine to give 6.75 g (25.1 mmol; 88.4%) of nitrile **7**. The nitrile could be recrystallized from petroleum ether to give the pure nitrile **7**, mp 83-83.5°C. ^{1}H Nmr: δ 7.55 - 7.30 (5H, m), 6.86 (1H, d, J = 1.5 Hz), 6.79 (1H, dd, J = 8, 1.5 Hz), 6.73 (1H, dd, J = 8 Hz), 5.99 (2H, s), 4.88 (1H, s). Ir ($CHCl_3$): 3000, 2230, 1505, 1490, 1450, 1255, 1240, 1040, 940 cm^{-1}. Ms (*m/z*): 269 (M^+), 160 (M^+-SPh, base). Anal. Calcd for $C_{15}H_{11}NO_2S$: C, 66.90; H, 4.12. Found: C, 67.05; H, 4.12.

α-Phenylthio-1,3-benzodioxole-5-ethanamine, **8**.

A solution of lithium aluminum hydride in diethyl ether (125 ml; 0.5 M; 62.5 mmol) was cooled to 0°C under nitrogen andsulfuric acid (1.7 ml; 31.25 mmol) was added carefully. The mixture was stirred at 0°C for 30 min to complete formation of aluminum hydride. A solution of the nitrile **7** (9 g; 33.5 mmol) in diethyl ether (200 ml) was added dropwise. The mixture was stirred at room temperature under nitrogen for 4 h after the addition was completed. The reaction was quenched by careful addition of water followed by 10% aq. NaOH, and stirring at room temperature for 1 h. The mixture was diluted with water and the amine was extracted with 3 x 150 ml of diethyl ether. The combined extracts were washed with 50 ml of brine, dried over Na_2SO_4, and evaporated to give 8.85 g of the free amine **8** as an oil. This was taken up in ether, and the hydrochloric salt was precipitated by bubbling a gentle stream of hydrochloric acid through the solution. Collection of the salt gave 9.5 g (31.1 mmol; 92.9%) of amine hydrochloride. The salt could be recrystallized from ethanol to give the pure amine hydrochloride, mp 189-190°C. Lit.[6] mp 185-187°C. The amine **8** regenerated from the purified salt exhibited the following spectral properties. ^{1}H Nmr: δ 7.40 - 7.20 (5H, m), 6.84 (1H, s), 6.71 (2H, s), 5.94 (2H, s), 4.08 (1H, t, J = 6.84 Hz), 3.07 (2H, d, J = 6.84 Hz), 1.33 (2H, s). Ir ($CHCl_3$): 3500, 2950, 1505, 1490, 1435, 1235, 1030, 915 cm^{-1}.

Ethyl 2-(1,3-benzodioxol-5-yl)-2-phenylthioethylcarbamate, **9a**.

To a solution of the amine **8** (1.38 g; 5.29 mmol) in diethyl ether (50 ml) was added triethylamine (3 ml; 21.26 mmol), and the mixture was cooled to 0°C under nitrogen. Ethyl chloroformate (0.6 ml; 6.34 mmol) was added slowly and the mixture was stirred at 0°C for 1 h. The mixture was diluted with 50 ml of diethyl ether and washed with 25 ml of water, dilute aq. hydrochloric acid, and saturated aq. $NaHCO_3$, and dried over Na_2SO_4. Recrystallization from methanol gave 1.32 g (3.83 mmol; 72.3%) of pure carbamate **9a**, mp 84-85°C. ^{1}H Nmr: δ 7.40 - 7.20 (5H, m), 6.81 (1H, s), 6.71 (2H, s), 5.95 (2H, s), 4.28 (1H, bt, J = 7.3 Hz), 4.08 (2H, q, J = 7.3 Hz), 3.70 - 3.40 (2H, m), 1.20 (3H, t, J = 7.3 Hz). Ir ($CHCl_3$): 3425, 2975, 1720, 1505, 1490, 1450, 1250, 1050, 940 cm^{-1}.

Ethyl [2-(1,3-benzodioxol-5-yl)-2-phenylthioethyl]methylcarbamate, **9b**.

To a suspension of sodium hydride (48 mg; 50% in oil; 1 mmol) in tetrahydrofuran (THF) (10 ml), a solution of the carbamate **9a** (345 mg; 1 mmol) in THF (20 ml) was added dropwise with stirring. The mixture was stirred at room temperature under nitrogen for 2 h. Methyl iodide (0.1 ml; 1.5 mmol) in THF (20 ml) was added slowly and the mixture was stirred at room temperature under nitrogen overnight. The mixture was diluted with 20 ml of water and extracted with 3 x 50 ml of chloroform. The combined extracts were washed with 50 ml of brine, dried over Na_2SO_4, and evaporated to give 371.5 mg (1.03 mmol; 100%) of crude carbamate **9b** as an oil. The crude nmr showed that complete alkylation had taken place, and the product was not purified further. ^{1}H Nmr (60 MHz): δ 7.42 - 7.00 (5H, m), 6.82 (1H, bs), 6.67 (2H, bs), 5.83 (2H, s), 4.38 (1H, m), 4.03 (2H, q, J = 7 Hz), 3.55 (2H, m), 2.67 (3H, s), 1.18 (3H, t, J = 7 Hz). Ir ($CHCl_3$): 2970, 2910, 1690, 1485, 1440, 1240, 1040, 935 cm^{-1}.

Ethyl 2-(1,3-benzodioxol-5-yl)ethenylcarbamate, **10a**.

A solution of *meta*-chloroperbenzoic acid (83 mg; 0.48 mmol) in methylene chloride (5 ml) was added to a solution of the carbamate **9a** (150 mg; 0.435 mmol) in methylene chloride (5 ml) at 0°C under nitrogen. The mixture was stirred at 0°C for 1 h, diluted with 30 ml of chloroform, washed with 20 ml of saturated aq. $NaHCO_3$, and dried over Na_2SO_4. Evaporation of the solvent gave the crude sulfoxide which was taken up in toluene (10 ml) and stirred at reflux under nitrogen for 4 h. After

cooling to room temperature, the toluene was evaporated and residue was purified by preparative tlc on silica gel with benzene as eluent. Isolation of the carbamate **10a** (R_f = 0.24) gave 60.3 mg (0.256 mmol; 59%). ^{1}H Nmr: δ 7.07 (1H, bd, *J* = 15.1 Hz), 6.83 (1H, bs), 6.71 (2H, bs), 6.45 (1H, bs), 5.93 (2H, s), 5.89 (1H, bd, *J* = 15.1 Hz), 4.22 (2H, bq, *J* = 7.1 Hz), 1.30 (3H, bt, *J* = 7.1 Hz).

E-1,3-Benzodioxole-5-propenoic acid **11** (3.84 g; 20 mmol) was suspended in 50% aqueous acetone (100 ml) and cooled to 0°C. Triethylamine (5.2 ml; 38.5 mmol) in acetone (40 ml) was added dropwise, followed by ethyl chloroformate (3.8 ml; 40 mmol) in acetone (20 ml). The mixture was stirred at 0°C for 30 min and sodium azide (4.16 g; 64 mmol) in water (20 ml) was added. This mixture was stirred an additional 1.5 h and poured into 100 ml of ice water. The acyl azide was extracted with 3 x 100 ml of chloroform. The combined extracts were washed with 100 ml of brine, dried over Na_2SO_4, and evaporated. The crude acyl azide thus obtained was taken up directly in ethanol (100 ml) and stirred at reflux under nitrogen for 3 h. After cooling to room temperature, the ethanol was evaporated and the residue was recrystallized from aq. ethanol to give 3.05 g (12.98 mmol; 64.9%) of carbamate **10a**. This could be recrystallized from methanol to give the pure carbamate **10a**, mp 91-92°C. The ^{1}H nmr was identical with that reported above. Ir ($CHCl_3$): 3410, 1720, 1660, 1500, 1485, 1250, 1040, 930 cm^{-1}. Ms (*m/z*): 235 (M^+), 189 (M^+ - EtOH, base). High resolution ms (*m/z*): 235.0846, calcd for $C_{12}H_{13}NO_4$, 235.0845; 189.0424, calcd for $C_{10}H_7NO_3$, 189.0426.

Ethyl 2-(1,3-benzodioxol-5-yl)ethenylmethylcarbamate, **10b**.

A solution of *meta*-chloroperbenzoic acid (75 mg; 0.43 mmol) in methylene chloride (5 ml) was added to a solution of the carbamate **9b** (141.7 mg; 0.395 mmol) in methylene chloride (5 ml) at 0°C under nitrogen. The mixture was stirred at 0°C for 1 h, diluted with 30 ml of chloroform, washed with 20 ml of saturated aq. $NaHCO_3$ and dried over Na_2SO_4. Evaporation of the solvent gave the crude sulfoxide which was taken up in toluene (10 ml) and stirred at reflux under nitrogen for 4 h. After cooling to room temperature, the toluene was evaporated and the residue was purified by preparative tlc on silica gel with benzene as eluent. Isolation of the carbamate **10b** (R_f = 0.26) gave 67.5 mg (0.271 mmol; 68.6%). ^{1}H Nmr: δ 7.50 (1H, m), 6.86 (1H, bs), 6.74 (2H, bs), 5.92 (2H, s), 5.75 (1H, d, *J* = 14.6 Hz), 4.26 (2H, q, *J* = 7.3 Hz), 3.16 (3H, s), 1.33 (3H, t, *J* = 7.3 Hz).

A solution of the carbamate **10a** (235 mg; 1 mmol) in THF (20 ml) was added dropwise to a suspension of sodium hydride (48 mg; 50% in oil; 1 mmol) in THF (5 ml) under nitrogen. The mixture was stirred at room temperature for 2 h and methyl iodide (0.1 ml; 1.5 mmol) in THF (5 ml) was added. The mixture was stirred at room temperature for 4 h and diluted with 30 ml of water. The carbamate **10a** was extracted with 3 x 30 ml of chloroform and the combined extracts were washed with 20 ml of brine and dried over Na_2SO_4. Evaporation of the solvent gave 256 mg of the enamide **10b** (quant.). This could be crystallized from methanol to give the pure enamide **10b**, mp 53-54°C. The ^{1}H nmr was identical with that reported above. Ir ($CHCl_3$): 2970, 2880, 1700, 1650, 1480, 1440, 1320, 1240, 1150, 1040, 935 cm^{-1}. Ms (*m/z*): 249 (M^+, base). High resolution ms (*m/z*): 249.0997, calcd for $C_{13}H_{15}NO_4$, 249.1001.

1-Bromo-3,5-hexadiene, **13a**.

Cyclopropyl bromide (10 g; 82.6 mmol) was added dropwise to magnesium (1.7 g; 69 mmol) in THF (40 ml) under nitrogen at a rate sufficient to maintain a gentle reflux. The mixture was stirred at reflux an additional 30 min after the addition was

complete. The solution of cyclopropyl Grignard reagent was then cooled to 0°C and acrolein (3.3 ml; 48.6 mmol) in THF (15 ml) was added dropwise. The mixture was stirred at room temperature overnight and quenched by addition of 2 ml of water followed by 25 ml of 10% aq. $NaHSO_3$. The crude cyclopropyl vinyl carbinol thus formed was extracted with 3 x 50 ml of diethyl ether. The combined extracts were washed with 25 ml of water, 10% aq. $NaHSO_3$, and brine, and dried over Na_2SO_4. Evaporation of the solvent gave 5.5 g of crude alcohol. This alcohol was cooled to 0°C and concentrated hydrobromic acid (11 ml) was added dropwise with vigorous stirring over approximately 3 min. The mixture was stirred at 0°C for an additional 5 min and then diluted with water. The crude bromide **13a** was extracted with 3 x 50 ml of diethyl ether. The combined extracts were washed with 25 ml of water, saturated aq. $NaHCO_3$, and brine, and dried over Na_2SO_4. Evaporation of the solvent gave the crude bromide **13a** which was distilled from calcium sulfate to give 3.15 g (19.56 mmol; 40% overall) of 1-bromo-3,5-hexadiene **13a**, bp 67° C/16 mm. lit.[15] bp 75° C/40 mm. ^{1}H Nmr (60 MHz): δ 6.80 - 4.90 (5H, m), 3.67 (2H, t, J = 6.5 Hz), 2.70 (2H, q, J = 6.5 Hz).

2-(2-Bromoethyl)furan, **13b**.

To diethyl ether (20 ml) at -78°C under nitrogen, was added *n*-butyllithium (40 ml; 2.5 M; 0.1 mol). After stirring at -78°C for 15 min, a solution of furan (7.3 ml; 0.1 mol) in diethyl ether (15 ml) was added slowly. The mixture was stirred at -78°C for 1 h, and then allowed to warm slowly to room temperature. Stirring was continued for 2 h before cooling the mixture to -78°C again. Ethylene oxide (approx. 10 ml; excess) was condensed into the mixture at -78°C and the mixture was allowed to warm slowly to room temperature again with vigorous stirring. After 1 h at room temperature, the reaction was quenched by addition of 10 ml of water, followed by 5 g of ammonium chloride. The mixture was diluted with water and extracted with 3 x 100 ml of diethyl ether. The combined extracts were washed with 75 ml of brine, dried over Na_2SO_4, and evaporated. Distillation of the residue gave 6.85 g (61.2 mmol; 61.2%) of pure 2-furanethanol, bp 88°C/20 mm. Lit.[18] bp 80-82° C/12 mm. ^{1}H Nmr (60 MHz): δ 7.30 (1H, dd, J = 2, 1 Hz), 6.27 (1H, dd, J = 3, 2 Hz), 6.08 (1H, dd, J = 3, 1 Hz), 3.83 (2H, bt, J = 7 Hz), 2.85 (2H, t, J = 7 Hz), 2.23 (1H, bs). Triethylamine (5 ml; 35.7 mmol) was added to a solution of 2-furanethanol (1g; 8.93 mmol) in diethyl ether (50 ml) under nitrogen and the mixture was cooled at 0°C. A solution of methanesulfonyl chloride (0.77 ml; 10 mmol) in diethyl ether (10 ml) was added slowly and the mixture was stirred at 0°C for 30 min. Water (50 ml) was added and the mesylate was extracted with 2 x 50 ml of diethyl ether. The combined extracts were washed with 30 ml of dilute aq. hydrochloric acid, saturated aq. $NaHCO_3$, and brine, and dried over Na_2SO_4. Evaporation of the solvent gave 1.67 g (8.68 mmol; 97.3%) of crude mesylate. ^{1}H Nmr (60 MHz): δ 7.35 (1H, dd, J = 2, 1 Hz), 6.33 (1H, dd, J = 3.5, 2 Hz), 6.18 (1H, dd, J = 3.5, 1 Hz), 4.45 (2H, t, J = 6.5 Hz), 3.10 (2H, t, J = 6.5 Hz), 2.92 (3H, s). Lithium bromide (3.8 g; 44 mmol) was added to a solution of the mesylate (4.91 g; 22.05 mmol) in THF (25 ml), and the mixture was stirred at reflux under nitrogen for 2 h. After cooling to room temperature, the mixture was diluted with water, and the bromide was extracted with 3 x 50 ml of diethyl ether. The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated. The residue was distilled to give 3.09 g (17.7 mmol; 80.1%) of pure bromide **13b**, bp 72°C/16 mm. ^{1}H Nmr: δ 7.36 (1H, dd, J = 2, 1 Hz), 6.33 (1H, dd, J = 3.4, 2 Hz), 6.15 (1H, dd, J = 3.4, 1 Hz), 3.60 (2H, t, J = 7.8 Hz), 3.22 (2H, t, J = 7.8 Hz).

Methyl α-phenylthio-1,3-benzodioxole-5-acetate, **14**.

A solution of the nitrile **7** (6.1 g; 22.7 mmol) in methanol (200 ml) was saturated with hydrochloric acid and then stirred at reflux under nitrogen overnight. After cooling to room temperature, the mixture was diluted with 200 ml of water and extracted with 3 x 200 ml of diethyl ether. The combined extracts were washed with 50 ml of water, saturated aq. $NaHCO_3$, and brine, and dried over Na_2SO_4. Evaporation of the solvent gave 6 g of crude ester **14**. Recrystallization from benzene/ligroine gave 5.8 g (19.2 mmol; 84.6%) of crude **14**. This was recrystallized again from petroleum ether to give the pure ester **14**, mp 62-63°C. ^{1}H Nmr: δ 7.35 - 7.15 (5H, m), 6.96 (1H, d, *J* = 1.9 Hz), 6.76 (1H, dd, *J* = 8.3, 1.9 Hz), 6.64 (1H, d, *J* = 8.3 Hz), 5.88 (2H, s), 4.76 (1H, s), 3.60 (3H, s). Ir ($CHCl_3$): 3000, 2950, 2890, 1740, 1510, 1495, 1445, 1250, 1150, 1040, 930 cm^{-1}. Ms (*m/z*): 302 (M^+), 193 (M^+-SPh, base). Anal. Calcd for $C_{16}H_{14}O_4S$: C, 63.56; H, 4.67. Found: C, 63.54; H, 4.60.

α-Phenylthio-1,3-benzodioxoleacetaldehyde, **15**.

Diisobutylaluminum hydride (3.7 ml; 1 M; 3.7 mmol) was added dropwise to a solution of the ester **14** (604 mg; 2 mmol) in toluene (15 ml) at -78°C under nitrogen. The mixture was stirred at 78°C for 40 min and quenched by dropwise addition of 1 ml of methanol. After stirring 30 min at -78°C, 25 ml of saturated aq. sodium potassium tartrate was added and the mixture allowed to warm to room temperature. This was then diluted with 25 ml of water and extracted with 3 x 30 ml of chloroform. The combined extracts were washed with 20 ml of water and brine, dried over Na_2SO_4, and evaporated. The residue consisted of the crude aldehyde **15**, with toluene as the only major contaminant. Kugelrohr distillation of the residue at an oven temperature of 155°C at 0.1 mm pressure gave 441.5 mg (1.62 mmol; 81%) of pure aldehyde **15**.

n-Butyllithium (2.5 ml; 2.4 M; 6mmol) was added to a solution of 5-(phenylthio)methyl-1,3-benzodioxole (1.22 g; 5 mmol) in THF (10 ml) under nitrogen at 0°C. The mixture was stirred at 0°C for 30 min to complete formation of the anion. The solution was then added dropwise via syringe to a solution of ethyl formate (0.82 ml; 10 mmol) in THF (2 ml) at 0°C. This mixture was stirred at room temperature under nitrogen for 1 h, and then poured into 30 ml of dilute aq. hydrochloric acid. The aldehyde **15** was extracted with 3 x 25 ml of diethyl ether and the combined extracts were washed with 20 ml of saturated aq. $NaHCO_3$, and brine, and dried over Na_2SO_4. The residue after evaporation of the solvent was purified by column chromatography on silica gel with benzene as eluent. Collecting the major fraction (R_f = 0.42) gave 415.1 mg (1.53 mmol; 30.5%) of pure aldehyde **15**. The aldehyde **15** prepared by either of the above methods showed the following spectral properties. ^{1}H Nmr: δ 9.50 (1H, d, *J* = 4.9 Hz), 7.50 - 7.20 (5H, m), 6.86 (1H, bs), 6.81 (2H, bs), 5.96 (2H, s), 4.65 (1H, d, *J* = 4.9 Hz). Ir (neat): 2900, 1720, 1610, 1590, 1505, 1490, 1445, 1250, 1040, 930, 810, 745, 685 cm^{-1}. Ms (*m/z*): 272 (M^+), 243 (M^+-CHO), 133 (M^+-CHO-PhSH, base). High resolution ms (*m/z*): 272.0510, calcd for $C_{15}H_{12}O_3S$, 272.0507; 243.0478, calcd for $C_{14}H_{11}O_2S$, 243.0479; 133.0295, calcd for $C_8H_5O_2$, 133.0290.

3,5-Hexadienol *p*-toluenesulfonate, **17**.

p-Toluenesulfonyl chloride (12.6 g; 66 mmol) was added in portions to a solution of 3,5-hexadienol[17] (5.78 g; 59 mmol) in pyridine (20 ml) under nitrogen at 0°C. After the addition was complete, the mixture was allowed to warm to room temperature with stirring over 3.5 h. The mixture was diluted with 50 ml of water and extracted with 2 x 50 ml of diethyl ether. The combined extracts were washed with 25 ml of water, dilute aq. hydrochloric acid, saturated aq. $NaHCO_3$, and brine, and dried over Na_2SO_4. Evaporation of the solvent gave 11.6 g (46 mmol; 78%) of tosylate **17**[15] which was used

without purification. ^{1}H Nmr (60 MHz): δ 7.77 and 7.32 (4H, AB, J = 8 Hz), 6.50 - 4.90 (5H, m), 4.05 (2H, t, J = 6 Hz), 2.45 (3H, s), 2.42 (2H, q, J = 6 Hz).

1-Azido-3,5-hexadiene, **18**.

From 1-bromo-3,5-hexadiene, **13a**.

Potassium azide (6.8 g; 84.5 mmol) and 18-crown-6 (264 mg; 1 mmol) were added to a solution of 1-bromo-3,5-hexadiene **13a** (2.7 g; 16.9 mmol) in acetonitrile (80 ml) and the mixture was stirred at reflux under nitrogen for 4 h. After cooling to room temperature, 100 ml of water was added and the azide was extracted with 3 x 70 ml of petroleum ether. The combined extracts were washed with 50 ml of water and brine, and dried over Na_2SO_4. Evaporation of the solvent left 1.8 g (14.6 mmol; 86.6%) of crude azide **18**.

From the tosylate **17**

Potassium azide (8.9 g; 109.6 mmol) and 18-crown-6 (264 mg; 1 mmol) were added to a solution of the tosylate **17** (13.8 g; 54.8 mmol) in acetonitrile (150 ml) and the mixture was stirred at reflux under nitrogen for 16 h. After cooling to room temperature, 200 ml of water was added and the azide was extracted with 3 x 150 ml of pentane. The combined extracts were washed with 75 ml of water and brine, and dried over Na_2SO_4. Evaporation of the solvent left 6.57 g (53.4 mmol; 97.5%) of crude azide **18**. The crude azide **18** prepared by either of the above methods showed the following spectral properties. ^{1}H Nmr (60 MHz): δ 6.70 - 4.90 (5H, m), 3.67 (2H, t, J = 6.5 Hz), 2.38 (2H, q, J = 6.5 Hz). Ir (neat): 2930, 2100, 1600, 1340, 1250, 990, 950, 895 cm^{-1}.

3,5-Hexadienamine, **16a**.

A solution of crude azide **18** (6.57 g; 53.4 mmol) in diethyl ether (75 ml) was added dropwise to a suspension of lithium aluminum hydride (1.4 g; 36.8 mmol) in diethyl ether (100 ml) under nitrogen, at a rate sufficient to maintain a gentle reflux. The mixture was stirred at reflux 2 h after the addition was complete. After cooling to 0°C, the reaction was quenched by careful addition of 1.4 ml of water, 1.4 ml of 15% aq. NaOH, and 4.2 ml of water. The organic phase was separated and the residual solid washed with 2 x 100 ml of diethyl ether. The combined extracts were washed with 70 ml of brine, dried over Na_2SO_4, and concentrated under vacuum. The diethyl ether still remaining was removed by distillation under one atmosphere nitrogen. Distillation of the residue gave the amine **16a** (3.04 g; 31.34 mmol; 58.7%), bp 55° C/20mm. The ir showed a weak absorption at 2100 cm^{-1} indicating minor contamination of the amine **16a** with the azide **18**. ^{1}H Nmr (60 MHz): δ 7.70 - 4.80 (5H, m), 2.75 (2H, t, J = 6 Hz), 2.25 (2H, q, J = 6 Hz), 1.13 (2H, s). Ir (neat): 3310, 3240, 2880, 1640, 1600, 1010, 910, 830 cm^{-1}.

2-Furanethanamine, **16b**.

A solution of sodium methoxide (prepared from 4.8 g of sodium and 50 ml of methanol) was added dropwise to a solution of nitromethane (12 g; 0.196 mol) and furfural (20 g; 0.208 mol) in methanol (40 ml) at 0°C under nitrogen. The mixture was stirred at 0°C an additional 5 min after the addition was complete. Diethyl ether (70 ml) was added and the salt was collected by filtration, washed with diethyl ether and air dried. The salt was dissolved in 100 ml of water and added to an ice-cold mixture of 200 ml of hydrochloric acid and 600 ml of water. The crude nitroethylene was collected by filtration and washed

with water. Recrystallization from ligroine gave 15.4 g (0.111 mol; 56.5%) of pure 2-(2-furyl)nitroethylene, mp 74-75°C. Lit.[14] mp 75-76°C. ^{1}H Nmr (60 MHz): δ 7.83 and 7.45 (2H, AB, J = 13 Hz), 7.57 (1H, d, J = 2 Hz), 6.88 (1H, d, J = 4 Hz), 6.55 (1H, dd, J = 4, 2 Hz). Ir ($CHCl_3$): 3120, 3030, 1640, 1505, 1315, 1210, 1020, 970, 950, 880, 770 cm^{-1}. A solution of 2-(2-furyl)nitroethylene (14.75 g; 0.106 mol) in diethyl ether (300 ml) was added to a suspension of lithium aluminum hydride (8 g; 0.212 mol) in diethyl ether (700 ml) at 0°C under nitrogen. After the addition was complete, the mixture was stirred at a gentle reflux for 16 h. After cooling to room temperature, the reaction was quenched by careful addition of 8 ml of water, 8 ml of 15% aq. NaOH, and 24 ml of water. The solid was removed by filtration and washed thoroughly with diethyl ether. The combined organic phases were washed with 150 ml of water and brine, dried over Na_2SO_4, and evaporated. Distillation of the residue gave 6.32 g (56.94 mmol; 53.7%) of 2-furanethanamine **16b**, bp 67° C/20 mm. Lit.[14] bp 60-70° C/20 mm. ^{1}H Nmr (60 MHz): δ 7.25 (1H, d, J = 2 Hz), 6.23 (1H, dd, J = 3, 2 Hz), 6.00 (1H, d, J = 3 Hz), 2.90 (4H, m), 1.08 (2H, s).

N-3,5-Hexadienyl α-phenylthio-1,3-benzodioxole-5-ethanamine, **19a**.

The aldehyde **15** was prepared by treatment of the ester **14** (1.2 g; 4 mmol) with diisobutylaluminum hydride (7.4 ml; 1 M; 7.4 mmol) as described above. The crude aldehyde obtained was immediately taken up in methanol (15 ml). A solution of the amine **16a** (776 mg; 8 mmol) in methanol (15 ml) was added. Sodium acetate (1 g; 12 mmol), acetic acid (0.7 ml; 12 mmol) and sodium sulfate (200 mg) were added and the mixture was stirred at room temperature under nitrogen for 36 h. Sodium cyanoborohydride (250 mg; 4 mmol) was added and the mixture was stirred at room temperature under nitrogen for an additional 2 h. Dilute hydrochloric acid was added until the pH of the solution stayed less than 1, and the mixture was stirred at room temperature for 1 h. The hydrochloric salt of the amine **19a** was then extracted with 3 x 50 ml of chloroform. The combined extracts were evaporated and the residue was triturated with benzene. The hydrochloric salt of the amine **19a** precipitated slowly upon standing in the refrigerator. The solid was collected and washed with benzene to give 887.8 mg (2.28 mmol; 57%) of amine hydrochloride salt. The salt could be recrystallized from benzene to give the pure hydrochloric salt of the amine **19a**, mp 166-167°C (dec). The amine **19a** regenerated from the pure hydrochloric salt showed the following spectral properties. ^{1}H Nmr: δ 7.35 - 7.15 (5H, m), 6.83 (1H, s), 6.70 (2H, s), 6.35 - 5.95 (2H, m), 5.93 (2H, s), 5.60 (1H, m), 5.00 (2H, m), 4.28 (1H, t, J = 7.3 Hz), 3.01 (2H, d, J = 7.3 Hz), 2.66 (2H, t, J = 6.8 Hz), 2.21 (2H, q, J = 6.8 Hz), 1.80 (1H, bs). Ir ($CHCl_3$): 2920, 2870, 2800, 1501, 1480, 1380, 1240, 1110, 1040 cm^{-1}. Ms (*m/z*): 286 (M^+-C_5H_7), 110 (M^+-$ArCH_2SPh$, base). High resolution ms (*m/z*): 286.0893, calcd for $C_{16}H_{16}NO_2S$, 286.0902; 110.0969, calcd for $C_7H_{12}N$, 110.0970.

N-2-(2-Furylethyl) α-phenylthio-1,3-benzodioxole-5-ethanamine, **19b**.

The aldehyde **15** was prepared by treatment of the ester **14** (1.2 g; 4 mmol) with diisobutylaluminum hydride (7.4 ml; 1 M; 7.4 mmol) as described above. The crude aldehyde obtained was immediately taken up in methanol (15 ml). A solution of the amine **16b** (444 mg; 4 mmol) in methanol (15 ml) was added. Sodium acetate (1 g; 12 mmol), acetic acid (0.7 ml; 12 mmol) and sodium cyanoborohydride (250 mg, 4 mmol) were then added and the mixture was stirred at room temperature under nitrogen for 2 h. Dilute aq. hydrochloric acid was added until the pH of the solution stayed less than 1. The mixture

was stirred at room temperature for 1 h. The hydrochloride salt of the amine **19b** was extracted with 3 x 50 ml of chloroform. The combined extracts were evaporated to an oily residue, which was triturated with benzene. After standing several hours in the refrigerator, the amine hydrochloride salt of **19b** could be obtained. This salt could be crystallized from chloroform/benzene to give the pure hydrochloric salt, mp 167-169°C. The amine **19b** regenerated from the pure hydrochloride salt showed the following spectral properties. ^{1}H Nmr: δ 7.30 - 7.15 (6H, m), 6.82 (1H, s), 6.68 (2H, s), 6.25 (1H, dd, J = 2.9, 1 Hz), 5.97 (1H, d, J = 2.9 Hz), 5.93 (2H, s), 4.27 (1H, t, J = 7.3 Hz), 3.02 (2H, d, J = 7.3 Hz), 2.86 (2H, m), 2.77 (2H, m), 1.42 (1H, bs). Ir (neat): 2900, 1585, 1501, 1480, 1440, 1240, 1040, 930, 730 cm^{-1}. Ms (*m/z*): 286 (M^+- furylCH$_2$), 124 (M^+-ArCHSPh, base). High resolution ms (*m/z*): 286.0919, calcd for $C_{16}H_{16}NO_2S$, 286.0902; 124.0761, calcd for $C_7H_{10}NO$, 124.0763.

Ethyl [2-(1,3-benzodioxol-5-yl)ethenyl]-3,5-hexadienylcarbamate, **2a**.

The amine generated from the hydrochloride salt (390 mg; 1 mmol) was taken up in THF (20 ml) and triethylamine (0.6 ml: 4 mmol) was added. The mixture was cooled to 0°C under nitrogen and ethyl chloroformate (0.2 ml; 2 mmol) was added. The mixture was allowed to warm to room temperature and stirred under nitrogen for 2 h. Water (50 ml) was added and the carbamate **20a** was extracted with 3 x 30 ml of chloroform. The combined extracts were washed with 20 ml of dilute aq. hydrochloric acid, saturated aq. $NaHCO_3$, and brine, and dried over Na_2SO_4. Evaporation of the solvent gave the crude carbamate **20a** which was taken up in methylene chloride (10 ml) and cooled to 0°C under nitrogen. A solution of *meta*-chloroperbenzoic acid (190 mg; 1.1 mmol) in methylene chloride (10 ml) was added and the mixture was stirred at 0°C for 1 h. The mixture was diluted with 50 ml of chloroform, washed with 20 ml of saturated aq. $NaHCO_3$, and dried over Na_2SO_4. Evaporation of the solvent gave the crude sulfoxide which was taken up in toluene (20 ml). The mixture was stirred at reflux under nitrogen for 2 h. After cooling to room temperature, the toluene was evaporated and the residue was purified by column chromatography on silica gel with benzene as eluent. Isolation of the carbamate **2a** (R_f = 0.24) gave 220.8 mg (0.7 mmol; 70%). The carbamate **2a** could be Kugelrohr distilled at an oven temperature of 165°C at 0.1 mm. ^{1}H Nmr: δ 7.42 (1H, m), 6.86 (1H, bs), 6.74 (2H, bs), 6.40 - 6.00 (2H, bs), 5.93 (2H, s), 5.78 (1H, d, J = 15.1 Hz), 5.70 (1H, m), 5.10 (2H, m), 4.25 (2H, q, J = 7.0 Hz), 3.70 (2H, bt, J = 7.3 Hz), 2.42 (2H, bt, J = 7.3 Hz), 1.32 (3H, t, J = 7.0 Hz). Ir ($CHCl_3$): 2950, 1700, 1650, 1490, 1445, 1410, 1350, 1240, 1050, 1010, 945 cm^{-1}. Ms (*m/z*): 315 (M^+, base), 248 (M^+-C_5H_7). High resolution ms (*m/z*): 315.1460, calcd for $C_{18}H_{21}NO_4$, 315.1471; 248.0939, calcd for $C_{13}H_{14}NO_4$, 248.0923.

Ethyl [2-(1,3-benzodioxol-5-yl)ethenyl][2-(2-furylethyl)]carbamate, **2b**.

The amine **19b** regenerated from the amine hydrochloride (403.5 mg; 1 mmol) was taken up in THF (20 ml) and triethylamine (0.6 ml; 4 mmol) was added. The mixture was cooled to 0°C under nitrogen and ethyl chloroformate (0.2 ml: 2 mmol) was added. The mixture was allowed to warm to room temperature and stirred under nitrogen for 2 h. Water (30 ml) was added and the carbamate **20b** was extracted with 3 x 30 ml of chloroform. The combined extracts were washed with 20 ml of dilute aq. hydrochloric acid, saturated aq. $NaHCO_3$, and brine, and dried over Na_2SO_4. Evaporation of the solvent

gave the carbamate **20b** which was taken up in methylene chloride (10 ml) and cooled to 0°C for 1 h. The mixture was diluted with 50 ml of chloroform and washed with 20 ml of saturated aq. $NaHCO_3$ and brine, and dried over Na_2SO_4. Evaporation of the solvent gave the crude sulfoxide which was taken up in toluene (20 ml) The mixture was stirred at reflux under nitrogen for 12 h. After cooling to room temperature, the toluene was evaporated and the residue was purified by column chromatography on silica gel with benzene as eluent to give 239.2 mg (0.727 mmol; 72.7%) of the carbamate **2b** (R_f = 0.21). The carbamate **2b** could be Kugelrohr distilled at an oven temperature of 175°C at 0.1 mm. ^{1}H Nmr: δ 7.47 (1H, m), 7.36 (1H, d, *J* = 2.0 Hz), 6.86 (1H, s), 6.74 (2H, s), 6.30 (1H, dd, *J* = 3.4, 2.0 Hz), 6.09 (1H, d, *J* = 3.4 Hz), 5.94 (2H, s), 5.79 (1H, d, *J* = 15.1 Hz), 4.22 (2H, bq, *J* = 6 Hz), 3.91 (2H, bt, *J* = 7.3 Hz), 2.96 (2H, bt, *J* = 7.3 Hz), 1.32 (3H, bt, *J* = 6 Hz). Ir ($CHCl_3$): 1710, 1655, 1510, 1490, 1450, 1415, 1230, 1040, 940 cm^{-1}. Ms (*m/z*): 329 (M^+, base), 248 (M^+ - furylCH_2). *High resolution ms (m/z): 329.1262, calcd for* $C_{18}H_{19}NO_5$, 329.1262; 248.0949, calcd for $C_{13}H_{14}NO_4$, 248.0923.

ACKNOWLEDGEMENT.

We thank the National Institutes of Health for support of this work.

REFERENCES AND NOTES

1. Dedicated to the memory of Tetsuji Kametani.
2. Taken from the Ph. D. thesis of SJM, UCLA, 1981.
3. For an excellent recent review on the *Amaryllidaceae* alkaloids, see: S. F. Martin, *The Alkaloids*, Vol. 30, pp. 251-376, Academic Press, 1987. For syntheses and synthetic approaches, see ref 4.
4. a) R. K. Boeckman, Jr., S. W. Goldstein, and M. A. Walters, *J. Am. Chem. Soc.*, 1988, **110**, 8250. b) R. K. Boeckman, Jr., J. P. Sabatucci, S. W. Goldstein, D. M. Springer, and P. F. Jackson, *J. Org. Chem.*, 1986, **51**, 3740. c) B. Umezawa, O. Hoshino, S. Sawaki, H. Sashida, K. Mori, Y. Hamada, K. Kotera, and Y. Iitaka, *Tetrahedron*, 1984, **40**, 1783. d) S. F. Martin, C. Tu, M. Kimura, and S. H. Simonsen, *J. Org. Chem.*, 1982, **47**, 3634. e) S. F. Martin and C. Tu, *J. Org. Chem.*, 1981, **46**, 3763. f) T. Sano, N. Kashiwaba, J. Toda, Y. Tsuda, and H. Irie, *Heterocycles*, 1980, **14**, 1097. g) G. Stork and D. J. Morgans, *J. Am. Chem. Soc.*, 1979, **101**, 7110. h) B. Umezawa, O. Hoshino, S. Sawaki, H. Sashida, and K. Mori, *Heterocycles*, 1979, **12**, 1475. i) Y. Tsuda, T. Sano, J. Taga, K. Isobe, J. Toda, S. Takagi, M. Yamaki, M. Murata, H. Irie, and H. Tanaka, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1358. j) O. Moller, E.-M. Steinberg, and K. Torssell, *Acta Chem. Scand. Ser. B*, 1978, **32**, 98.
5. J. Obrecht, L. Hellberg, and R. Somanathan, *J. Chem. Soc., Chem. Commun.*, 1987, 1219.
6. L. F. Cason and C. C. Wanser, *J. Am. Chem Soc.*, 1951, **73**, 142.
7. A. Pelter, P. Satyanarayana, and R. S. Ward, *Tetrahedron Lett.*, 1981, **22**, 1549.
8. I. H. Sánchez, F. J. Lopez, H. J. Flores, and M. I. Larraza, *Heterocycles*, 1983, **20**, 247.
9. For other examples of this substitution of cyano for thiophenyl in dithioacetals, see: F. Pochat and E. Levas,

Tetrahedron Lett., 1976, 1491.

10. J. Weinstock, *J. Org. Chem.*, 1961, **26**, 3511.
11. R. D. Haworth, W. H. Perkin, Jr., and J. Rankin, *J. Chem. Soc.*, 1924, **125**, 1686.
12. While the ethyl carbamate **10a** was unknown (to the best of our knowledge), the corresponding methyl carbamate was a known compound.[13] This compound, prepared in 62% yield from **11** by the identical route using methanol, had an analogous proton nmr spectrum to that of **10a**.
13. M. Furdik, A. Grozdjakova, and A. Kanala, *Acta Fac. Rerum Nat. Univ. Comenianae, Chimia*, 1963, **7**, 557 (*Chem. Abs.*, 1964, **61**, 8286f).
14. W. C. McCarthy and R. J. Kahl, *J. Org. Chem.*, 1956, **21**, 1118.
15. M. E. H. Howden, A. Maercker, J. Burdon, and J. D. Roberts, *J. Am. Chem. Soc.*, 1966, **88**, 1732.
16. R. V. Stevens, R. E. Cherpeck, B. L. Harrison, J. Lai, and R. Lapalme, *J. Am. Chem. Soc.*, 1976, **98**, 6317.
17. S. F. Martin, C. Tu, and T. Chou, *J. Am. Chem. Soc.*, 1980, **102**, 5274.
18. D. J. Chadwick, J. Chambers, G. D. Meakins, and R. L. Snowden, *J. Chem. Soc., Perkin Trans. 1*, 1975, 523.

Received, 11th August, 1989