Regioselective Synthesis of Acylpyrroles

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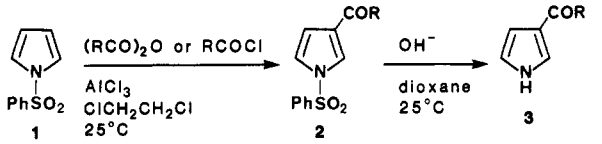
The regioselective synthesis of several pyrrole derivatives is described. $AlCl_3$-catalyzed acylation reactions of 1-(phenylsulfonyl)pyrrole (1) give 3-acyl derivatives, whereas the corresponding BF_3·OEt_2-catalyzed reactions give 2-acyl derivatives predominantly. Mild alkaline hydrolysis gives the corresponding acyl-1*H*-pyrroles in excellent yields. $AlCl_3$-catalyzed reactions of 1 with 1,1-dichloromethyl methyl ether and oxalyl chloride give 1-(phenylsulfonyl)-2-formylpyrrole (**6**) and 1-(phenylsulfonyl)-2-(chlorocarbonyl)pyrrole (**7**), respectively. 3-Pyrrolylacetic acid (**10**) was prepared by thallium(III) nitrate promoted rearrangement of 1-(phenylsulfonyl)-3-acetylpyrrole (**2a**). Trifluoroacetic anhydride catalyzed cyclization of 4-[1-(phenylsulfonyl)-3-pyrrolyl]butyric acid (**14**) gives 1-(phenylsulfonyl)-7-oxo-4,5,6,7-tetrahydroindole (**17**). Attempts to cyclize **14** at the 4-position have been unsuccessful.

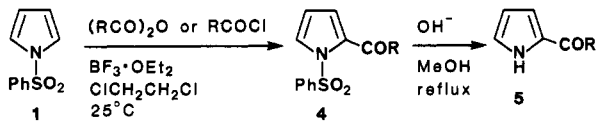
The regioselective synthesis of pyrrole derivatives has been the subject of considerable interest in recent years.[1-3] The regioselective introduction of 2-acyl substituent has been accomplished in two ways: (1) direct electrophilic substitution of pyrroles;[4,5] (2) lithiation of pyrroles at C-2 and condensation of the derived Grignard reagent with 2-pyridyl thiol esters.[6,7] However, regioselective synthesis of 3-acylpyrroles has been a stubborn problem, requiring the use of indirect methods involving several steps. A typical expedient is the introduction of an electron-withdrawing substituent at C-2 followed by an electrophilic substitution at C-4 and subsequent removal of the 2-substituent.[8-10] Some 1-alkyl-3-acylpyrroles are also obtainable in moderate to good yields by acid-catalyzed isomerization of the corresponding 2-substituted pyrroles.[11] This method is not viable, however, for the synthesis of 3-acyl-1*H*-pyrroles.

Recently we,[12] and others,[13] have published preliminary reports on a high-yield and highly regioselective synthesis of 3-acylpyrroles in which 1-(phenylsulfonyl)pyrrole (**1**)[14] is used as a substrate in $AlCl_3$-catalyzed Friedel–Crafts acylation reactions. The phenylsulfonyl group is readily removed by subsequent alkaline hydrolysis, thus providing a convenient synthesis of 3-acyl-1*H*-pyrroles. We have since undertaken detailed studies of this synthetically useful subject, and as a result we have developed a new methodology in which the preferential introduction of an acyl substituent either in the 2- or 3-position can be controlled. In this paper the synthetic aspects of this methodology are discussed in detail.

Results and Discussion

Synthetic Methods. Reaction of 1-(phenylsulfonyl)-pyrrole (**1**) and acyl chlorides or acid anhydrides in the presence of $AlCl_3$ at 25 °C in 1,2-dichloroethane solution gives essentially quantitative yields of the corresponding 3-acylated products **2**. Mild basic hydrolysis gives 3-





acyl-1*H*-pyrroles **3**. Table I summarizes the results of the two-step synthesis of 3-acylpyrroles **3**. In all cases, with the exception of entry **f**, the reactions were essentially regiospecific, and only traces (less than 2%) of the 2-isomer could be detected by careful GC or HPLC analysis of the total crude reaction products. In the case of entry **f**, a 1:9 mixture of **4f** and **2f** was isolated as a solid from which pure **2f** was obtained by recrystallization. The simplicity and high overall yield of this sequence should make this the method of choice for the synthesis of 3-acylpyrroles.

These acylation reactions can be carried out at much lower temperatures or in other solvents such as dichloromethane and nitromethane to give similar results. For example, acylation with acetyl chloride conducted at −78 °C in dichloromethane went to completion in 12 min (1-mmol scale) to afford a 1:99 mixture of **4a** and **2a**. Acylation with amounts of $AlCl_3$ less than indicated in Table I resulted in an incomplete conversion both at −78 °C and at 25 °C. Less regioselective results were obtained when other Lewis acids such as $SnCl_4$, $TiCl_4$, $ZnCl_2$, and $FeCl_3$ were used as catalysts: **4a** was the major isomer in the presence of $SnCl_4$ or $ZnCl_2$, while **2a** was the predominant isomer in the presence of $TiCl_4$ or $FeCl_3$. Observation of this catalytic effect on the isomer distribution between **4a** and **2a** led us to examine the effect of a mild Lewis acid, BF_3·OEt_2, on this reaction. The effect of this catalyst is to essentially reverse the regioselectivity of acylation relative to the $AlCl_3$-catalyzed reactions. Table II is a summary of the results of BF_3·OEt_2-catalyzed acylation of **1** with representative acylating reagents for the formation of 2-acylpyrroles **5**. Although not as completely regioselective as the $AlCl_3$-catalyzed reactions (5–15% of the 3-isomers **2** are observed), the products are readily purified and obtained in good yields. Again, basic hydrolysis provides the desired 2-acyl-1*H*-pyrroles **5**. Thus, these two

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Table I. $AlCl_3$-Catalyzed Acylation of 1 with Representative Acylating Reagents for the Formation of 3-Acylpyrroles (3)

compd	reagent	mole ratio of 1/reagent/catalyst	time, h	R	% yield[a] 2	% yield[a] 3
a	acetic anhydride	1:3:6	2	CH_3	99[b]	93
b	benzoyl chloride	1:1.1:1.2	1.5	C_6H_5	99[c]	93
c	cyclopropanecarboxylic acid chloride	1:1.1:1.2	2	cyclopropyl	99[c]	100
d	4-chlorobutyryl chloride	1:2:2	0.3	$CH_2CH_2CH_2Cl$	92	84[d]
e	3-carbomethoxypropionyl chloride	1:3:6	1.5	$CH_2CH_2CO_2CH_3$	100[e]	84
f	succinic anhydride	1:1.1:2.2	2	$CH_2CH_2CO_2H$	97[f]	84

[a] Isolated yield. [b] Small amounts (<1.5%) of the 2-isomer detected by GC. [c] Traces (<0.1%) of the 2-isomer detected by GC. [d] Yield of 3c.[4] [e] Small amounts (2%) of the 2-isomer detected by GC. [f] Yield of 1:9 mixture of 2- and 3-isomers; isolated yield of 2f after recrystallization is 48%.

Table II. $BF_3 \cdot OEt_2$-Catalyzed Acylation of 1 with Representative Acylating Reagents for the Formation of 2-Acylpyrroles (5)

compd	reagent	mole ratio of 1/reagent/catalyst	time	R	% yield[a] 4	% yield[a] 5
a	acetic anhydride	1:3:6	1.5 h	CH_3	83	95
b	benzoyl chloride	1:3:3	7 d	C_6H_5	75	95
c	cyclopropanecarboxylic acid chloride	1:3:3	18 h	cyclopropyl	69	93
d	4-chlorobutyryl chloride	1:2:2	2 d	$CH_2CH_2CH_2Cl$	56[b]	50[c]
e	3-carbomethoxypropionyl chloride	1:3:6	2 d	$CH_2CH_2CO_2CH_3$	42	
f	succinic anhydride	1:3:6	7 d	$CH_2CH_2CO_2H$	0[d]	

[a] Isolated yield. [b] 30% of 1 recovered. [c] Yield of 4c.[4] Prolonged base treatment provides 5c. [d] 1 recovered unchanged.

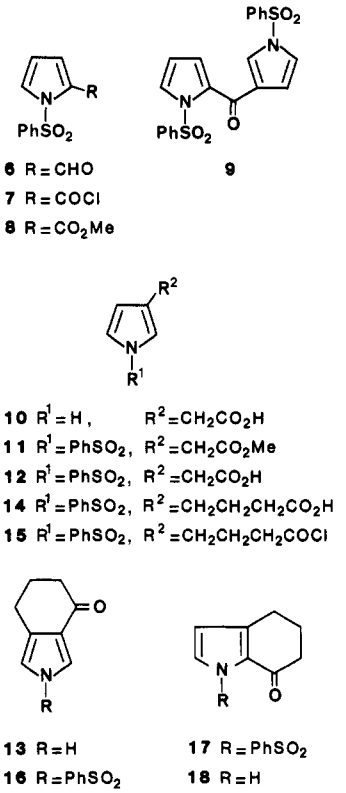
procedures represent a versatile methodology for the synthesis of isomerically pure 2- or 3-acylpyrroles using 1 as a starting material.

We have also observed that trifluoroacetic anhydride catalyzes the reaction of 1 and acetic acid at 25 °C to afford an excellent yield of **4a**. This acylation reaction may involve the formation of acetyl trifluoroacetate as an active intermediate, since the reaction of 1 and acetic anhydride in the presence of trifluoroacetic acid at 25 °C gave a similar result. No trifluoroacylation product could be detected in these cases.[15] We have also applied this type of acylation successfully to a synthesis of tetrahydroindoles (see following discussion). This may provide a general method for 2-acylation of 1 without the necessity of preforming the acid chlorides or anhydrides of the acylating species.

The assignment of structure **4a** is based on a UV λ_{max} (MeOH) signal at 274.5 nm (ϵ 9600) and the presence of a triplet (J = 3.4 Hz) at 6.37 ppm (C4 H) in the ^1H NMR spectrum. In addition, **4a** was converted by alkaline hydrolysis to the known 2-acetylpyrrole. The structure of **2a** is based on a UV λ_{max} (MeOH) signal at 238 nm (ϵ 19 200) and the ^1H NMR spectrum, in which the C-4 proton appears as a double doublet (J = 1.5 and 3.3 Hz at 6.67 ppm) and was firmly established by conversion to the known 3-acetylpyrrole.[16,17] The structures of all other products were assigned by analogy.

One-Carbon Acylations. All attempts to apply our methodology to selectively introduce one-carbon acyl units at C-3 have failed. Reaction of 1 with 1,1-dichloromethyl methyl ether in the presence of $AlCl_3$ afforded 1-(phenylsulfonyl)-2-formylpyrrole (**6**, Chart I) exclusively; similar results were obtained under a variety of conditions

Chart I



(changing solvent, catalyst, and temperature).

Regioselective 2-acylation was also observed in the reaction of 1 and oxalyl chloride[18] in the presence of $AlCl_3$ to give an essentially quantitative yield of **7** which was characterized as its methyl ester **8**. Thus, it appears that the regioselectivity of one-carbon acylation is totally re-

(15) Acylation of pyrrole with acetic acid–trifluoroacetic anhydride has been reported to give a 6% yield of 2-(trifluoroacetyl)pyrrole as the only isolated product. On the other hand, reaction of 2-acetylpyrrole with acetic acid–trifluoroacetic anhydride has been reported to give the 2,5-(19%) and 2,4-diacetyl (46%) derivatives (see ref 16).

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versed from that observed for other acyl species.[19]

It is interesting to note that the first time this acylation was attempted 9 was isolated as the major component of the reaction mixture along with 7. As can be seen in the structure 9, the carbonyl function is linked to the 2- and 3-positions of the pyrryl nuclei. Subsequently, we have observed that the first attack of oxalyl chloride yields 7. We have shown that pure 7 reacts cleanly with 1 at C-3 in the presence of $AlCl_3$ to yield 9 in good yield (68%). Thus it is apparent that in the first experiment 7 was first formed but then further reacted with excess 1 present in the reaction mixture.

Further Extensions. The ready availability of 3-acylpyrroles in quantity by this methodology suggests further extensions for the efficient preparation of other interesting 3-substituted pyrroles. The 3-pyrrolylacetic acids have relevance in the chemistry of porphyrins and antiinflammatory drugs. To our knowledge no practical preparation of 1*H*-3-pyrrolylacetic acid (10) has been reported in the literature. Although the ethyl ester of 10 has been reported, it was detected only as the minor product in the $Cu(OSO_2CF_3)_2$-promoted reaction of pyrrole and ethyl diazoacetate.[20] Thus, conversion of **2a** into 10 was attempted. Treatment of **2a** with thallium(III) nitrate (TTN) in methanol in the presence of $HClO_4$ afforded a 66% yield of methyl 3-pyrrolylacetate (11).[21] Hydrolysis of the ester in aqueous LiOH gave the corresponding acid 12. The phenylsulfonyl group, having served its purpose, was removed by treatment of 11 (or 12) with 5 N NaOH in boiling methanol to give a quantitative yield of 10. This type of reaction (**2a** → 11) normally does not proceed cleanly due to the well-known instability of nondeactivated pyrroles toward oxidative conditions.[1,21] The success of the TTN-catalyzed rearrangement is a reflection of the stability imparted to the pyrrole system by the phenylsulfonyl group.

Synthesis of Indole Derivatives. Since we have observed that $AlCl_3$-catalyzed acylations of 1 yield 3-acylated derivatives, we thought of applying this methodology to an internal cyclization with the ultimate objective of providing an entry to an isoindole system, e.g., 13. The required acid 14 and its acid chloride 15 for the cyclization are readily available from **2f**. Thus, Clemmensen reduction of **2f** gave an 81% yield of 14. Treatment of 14 with oxalyl chloride at 25 °C smoothly gave unstable 15 which cyclized at 25 °C even in the absence of any catalyst to give 17. Addition of freshly prepared 15 to a suspension of $AlCl_3$ in 1,2-dichloroethane solution also gave 17 as a sole product. The production of 17 was found to be most efficient when 14 was reacted with trifluoroacetic anhydride. Subsequent hydrolysis gave the known 18.[22] Thus, although we did not obtain 13, this approach does provide an entry to the 7-hydroxyindoles, a class of compounds not readily available by other routes.[22]

Mechanism. The striking regioselectivity and sensitivity to Lewis acids of acylation of 1 deserves some comments from a mechanistic point of view. We present here three possible mechanistic explanations for the observed regiocontrol in this reaction.

(1) The possibility exists that kinetic acylation is predominantly at C-2 in all cases to yield 4 but that subsequent acyl migration[11] would allow the production of 3-acylpyrroles. However, this possibility would seem to be ruled out by the results of the following experiment: Addition of $AlCl_3$ (1 equiv) at 25 °C to **4a** produces a stable (for at least 24 h in an NMR tube) complex [^{1}H NMR (CD_2Cl_2) δ 2.95 (3 H, s), 6.75 (1 H), 8.40 (1 H)] from which **4a** is regenerated upon an aqueous workup (1 N HCl).

(2) Alternatively the reason could be predominantly steric. Thus, a strong Lewis acid might complex with the phenylsulfonyl group which, by increasing the effective bulk of the substituent, would disfavor 2-substitution. However, we have been unable to detect any evidence (^{1}H NMR, UV, etc.) for such complexation under the reaction conditions.[23] Furthermore, it is difficult to explain the results of one-carbon acylations and internal cyclization (15 → 17) by using this type of steric argument. An example of predominant 3-substitution of pyrrole in the gas phase where steric and medium effects cannot play any important role has recently been reported.[24]

(3) Finally we have considered electronic factors. CNDO calculations show that the larger electron density in 1 is located at C-3 while the higher HOMO coefficient is at C-2.[12] We have also observed by ^{13}C NMR spectroscopy that $AlCl_3$ significantly deshields the carbonyl carbon of acetyl chloride (36-ppm downfield shift) while the chemical shift of the carbonyl carbon of a 1:1 mixture of acetyl chloride and BF_3·OEt_2 remains virtually unchanged, indicating that there is a large difference in the degree of positive charge on the carbonyl carbon of acylating species in the presence of $AlCl_3$ and BF_3·OEt_2.[25] Thus we speculate that the highly polarized species, e.g., $CH_3COCl \rightarrow AlCl_3$,[26] prefers to attack at C-3 (charge control) while the less polarized species prefers to attack at C-2 (orbital control). Although we prefer this hypothesis over the other two noted above, it is difficult to rationalize the results of one-carbon acylations and internal cyclization by using this hypothesis. Equally, none of these possible explanations can fully explain our results.[27]

Conclusion

We have established a versatile methodology for the synthesis of isomerically pure 2- and 3-acylpyrroles. The easy access to 3-acyl-1*H*-pyrroles is especially significant since few useful syntheses of this class of compounds exist to date.[28]

Experimental Section

General Methods. Infrared spectra were recorded by using a Perkin-Elmer 267 grating infrared spectrophotometer. ^{1}H NMR

(19) This type of behavior was also observed elsewhere.[13]

(20) Maryanoff, B. E. *J. Org. Chem.* **1979**, *44*, 4410.

(21) The thallium(III) nitrate promoted rearrangement of 4-acetylpyrrole-2-carboxylates has been reported: Kenner, G. W.; Smith, K. M.; Unsworth, J. F. *J. Chem. Soc., Chem. Commun.* **1973**, 43.

(22) Julia, M.; Pascal, Y. R. *Chim. Ther.* **1970**, *4*, 279.

(23) Although the possibility that such a complex may exist and serve to direct the regioselectivity of acylation cannot be totally excluded, we feel that the weight of evidence on hand argues strongly against such a rationale. When 1 and $AlCl_3$ are mixed in 1,2-dichloroethane, there is no evidence of complex formation by ^{1}H NMR and UV, and the mixture remains heterogenous.

(24) Speranza, M. *J. Chem. Soc., Chem. Commun.* **1981**, 1177.

(25) For studies on the effects of Lewis acid strength on carbonyl compounds, see: Childs, R. F.; Hor, Y.-C. *Can. J. Chem.* **1977**, *55*, 3495. Childs, R. F.; Mulholland, D. L.; Nixon, A. *Can J. Chem.* **1982**, *60*, 801.

(26) This type of donor–acceptor complex of 1:1 acetyl chloride–$AlCl_3$ in inert solvents such as 1,2-dichloroethane, dichloromethane, and sulfur dioxide has been well documented. See: Olah, G. A.; Moffat, M. E.; Kuhn, S. J.; Hardie, B. A. *J. Am. Chem. Soc.* **1964**, *86*, 2198. Wilinski, J.; Kurland, R. J. *Ibid.* **1978**, *100*, 2233. Glavincevski, B.; Brownstein, S. *J. Org. Chem.* **1982**, *47*, 1005.

(27) There is also a possibility that kinetic acylation takes place at C-2 to yield a σ complex and that immediate acyl migration occurs at this stage prior to deprotonation. However, extremely rapid formation of 2 in the $AlCl_3$-catalyzed reaction has prevented us from exploring this possibility: for example, addition of 1 (1 equiv) at 25 °C to a 1:1 mixture of acetyl chloride and $AlCl_3$ instantly (less than 10 s) produces a product Lewis acid complex whose ^{1}H NMR spectrum is superimposable to that of a 1:1 complex prepared from **2a** and $AlCl_3$: ^{1}H NMR (CD_2Cl_2) δ 3.00 (3 H, s), 6.93 (1 H), 7.33 (1 H), 8.47 (1 H).

(28) Chadwick, D. J.; Hodgson, S. T. *J. Chem. Soc., Perkin Trans. 1* **1983**, 93.

spectra were recorded with a Varian EM-390 90-MHz spectrometer. UV spectra were determined in CH_3OH by using a Varian Cary 210 spectrophotometer. Gas chromatographic data were obtained with a Hewlett-Packard 5840A gas chromatograph (FID) by using a 20-in. column of 10% UCW-982 on 80–100-mesh Chromosorb WAW-DMCSB3. The flow of the carrier gas (He) was ca. 24 mL/min. Mass spectra were recorded by Morgan Schaffer. Elemental analyses were performed at Guelph Chemical Laboratories Ltd. Melting points were determined with an Electrothermal melting point apparatus and are uncorrected. All reactions were carried out in an atmosphere of N_2. 1-(Phenylsulfonyl)pyrrole was prepared by a literature procedure.[14] All reagents and catalysts are commercial grade.

1-(Phenylsulfonyl)-3-acetylpyrrole (2a). To a suspension of anhydrous $AlCl_3$ (40 g, 0.30 mol) in 500 mL of 1,2-dichloroethane at 25 °C was added slowly acetic anhydride (15.3 g, 0.15 mol). The resulting solution was stirred at 25 °C for 10 min, a solution of **1** (10.35 g, 0.05 mol) in 25 mL of 1,2-dichloroethane was added, and the mixture was stirred at 25 °C for 2 h. (The reaction was nearly completed after 10 min.) The reaction was quenched with ice and water, and the product was extracted into dichloromethane. Concentration at reduced pressure gave crystals (12.3 g, 99%). GC analysis showed 98.5% **2a**. Recrystallization from ligroin (bp 60–110 °C) gave pure **2a**: mp 97–99 °C; IR (KBr) 3125, 1672, 1664, 1376, 1183, 1176, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40 (3 H, s, $COCH_3$), 6.67 (1 H, dd, J = 1.5, 3.3 Hz, C4 H), 7.13 (1 H, dd, J = 2.3, 3.3 Hz, C5 H), 7.4–7.7 (3 H, m), 7.75 (1 H, dd, J = 1.5, 2.3 Hz, C2 H), 7.85–8.0 (2 H, m); UV (MeOH) λ_{max} 220 nm (ϵ 12 700), 238 (19 200); GC (175 °C) t_R = 6.07 min. Anal. Calcd for $C_{12}H_{11}NO_3S$: C, 57.82; H, 4.45; N, 5.62; S, 12.86. Found: C, 57.73; H, 4.63; N, 5.71; S, 12.70.

1-(Phenylsulfonyl)-3-benzoylpyrrole (2b). To a suspension of anhydrous $AlCl_3$ (4.0 g, 0.030 mol) in 50 mL of 1,2-dichloroethane at 25 °C was added slowly benzoyl chloride (3.93 g, 0.028 mol). The resulting solution was stirred at 25 °C for 10 min, a solution of **1** (5.175 g, 0.025 mol) in 10 mL of 1,2-dichloroethane was added slowly, and the mixture was stirred at 25 °C for 90 min. The reaction was quenched with ice and water, and the product was extracted into dichloromethane. Removal of the solvent and chromatography of the residue in a column of silica gel, eluting with 1:19 ethyl acetate–toluene, afforded a 1:>1000 mixture of **4b** and **2b** as a solid: 7.7 g (99%); mp 69–72 °C; IR (KBr) 3140, 1657, 1640, 1380, 1180, 1066 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.77 (1 H, dd, J = 1.5, 3.3 Hz, C4 H), 7.20 (1 H, dd, J = 2.3, 3.3 Hz, C5 H), 7.35–8.00 (11 H, m); UV (MeOH) λ_{max} 248 nm (ϵ 19 060); GC (235 °C) t_R = 10.69 min. Anal. Calcd for $C_{17}H_{13}NO_3S$: C, 65.58; H, 4.21; N, 4.50; S, 10.30. Found: C, 65.48; H, 4.35; N, 4.50; S, 10.15.

1-(Phenylsulfonyl)-3-pyrrolyl Cyclopropyl Ketone (2c). To a suspension of anhydrous $AlCl_3$ (4.0 g, 0.03 mol) in 50 mL of 1,2-dichloroethane at 25 °C was added dropwise cyclopropanecarboxylic acid chloride (2.93 g, 0.028 mol). The resulting solution was stirred at 25 °C for 15 min, a solution of **1** (5.175 g, 0.025 mol) in 10 mL of 1,2-dichloroethane was added, and the mixture was stirred at 25 °C for 2 h. The reaction was quenched with ice and water, and the product was extracted into dichloromethane. The extracts were washed with water, dried over Na_2SO_4, and concentrated to give crystalline **2c**: 6.84 g (99%); mp 84–86 °C; IR (KBr) 3140, 1660, 1375, 1178, 1102 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83–1.27 (4 H, m), 2.2–2.5 (1 H, m), 6.72 (1 H, dd, J = 1.5, 3.3 Hz, C4 H), 7.17 (1 H, dd, J = 2.3, 3.3 Hz, C5 H), 7.4–8.0 (3 H, m); UV (MeOH) λ_{max} 239 nm (ϵ 19 500); GC (200 °C) t_R = 6.40 min. Anal. Calcd for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N, 5.09; S, 11.65. Found: C, 60.91; H, 4.85; N, 5.16; S, 11.77.

1-[1-(Phenylsulfonyl)-3-pyrrolyl]-4-chloro-1-butanone (2d). To a suspension of anhydrous $AlCl_3$ (532 mg, 4 mmol) in 8 mL of 1,2-dichloroethane at 25 °C was added dropwise 4-chlorobutyryl chloride (0.45 mL, 4 mmol). The resulting solution was stirred at 25 °C for 10 min, a solution of **1** (414 mg, 2 mmol) in 2 mL of 1,2-dichloroethane was added, and the mixture was stirred at 25 °C for 20 min. The reaction was quenched with 0.5 N HCl, and the product was extracted into dichloromethane. The extracts were washed with brine, 0.1 N NaOH, and brine, dried over Na_2SO_4, and concentrated at reduced pressure. Analysis of the residue by HPLC (μ-Porasil, 1:10 ethyl acetate–hexane) showed a 1:200 mixture of **4d** and **2d**, respectively. Chromatography in a column of silica gel (70–230 mesh), eluting with 3:10 ethyl acetate–hexane, gave **2d**: 572 mg (92%); mp 67–68 °C; IR (KBr) 3140, 1680, 1380, 1190, 1180, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.20 (2 H, quintet), 2.95 (2 H, t, CH_2CO), 3.70 (2 H, t, CH_2Cl), 6.70 (1 H, dd, J = 1.5, 3.4 Hz, C4 H), 7.15 (1 H, dd, J = 2.3, 3.4 Hz, C5 H), 7.4–7.7 (3 H, m), 7.80 (1 H, dd, J = 1.5, 2.3 Hz, C2 H), 7.85–8.0 (2 H, m); UV (MeOH) λ_{max} 219 nm (ϵ 15 400), 238 (23 600). Anal. Calcd for $C_{14}H_{14}NO_3SCl$: C, 53.93; H, 4.53; N, 4.49; S, 10.28. Found: C, 53.88; H, 4.71; N, 4.30; S, 10.08.

Methyl 4-[1-(Phenylsulfonyl)-3-pyrrolyl]-4-oxobutyrate (2e). To a suspension of $AlCl_3$ (80 g, 0.6 mol) in 500 mL of 1,2-dichloroethane was added dropwise 3-carbomethoxypropionyl chloride (45.2 g, 0.3 mol) at 25 °C. The resulting solution was stirred for 10 min, a solution of **1** (20.7 g, 0.1 mol) in 100 mL of 1,2-dichloroethane was added, and the mixture was stirred at 25 °C for 90 min. The reaction mixture was poured into ice and water (1000 mL) and the organic layer collected. The aqueous layer was extracted with dichloromethane (2 × 100 mL), and the combined organic layer was washed thoroughly with water, dried over Na_2SO_4, and concentrated under reduced pressure to give a 2:98 mixture of **4e** and **2e** as a solid residue (32 g, 100%). Crystallization from toluene–hexane gave **2e** as colorless needles: mp 137–139 °C; IR (KBr) 1740, 1685, 1370, 1170, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.67 (2 H, t), 3.10 (2 H, t), 3.67 (3 H, s), 6.68 (1 H, dd, J = 1.5, 3.4 Hz, C4 H), 7.17 (1 H, dd, J = 2.3, 3.4 Hz, C5 H), 7.4–7.7 (3 H, m), 7.80 (1 H, dd, J = 1.5, 2.3 Hz, C2 H), 7.85–8.0 (2 H, m); UV (MeOH) λ_{max} 238 nm (ϵ 19 590); GC (220 °C) t_R = 6.49 min. Anal. Calcd for $C_{15}H_{15}NO_5S$: C, 56.07; H, 4.70; N, 4.36; S, 9.98. Found: C, 56.13; H, 4.80; N, 4.38; S, 10.26.

4-[1-(Phenylsulfonyl)-3-pyrrolyl]-4-oxobutyric Acid (2f). To a suspension of $AlCl_3$ (29.33 g, 0.22 mol) in 400 mL of 1,2-dichloroethane was added at 25 °C succinic anhydride (11.0 g, 0.11 mol), and the mixture was stirred at 25 °C for 15 min, during which time the solids dissolved. A solution of **1** (20.7 g, 0.1 mol) in 50 mL of 1,2-dichloroethane was added, and the mixture was stirred at 25 °C for 90 min. The reaction was quenched with ice and water (500 mL) and the product extracted with dichloromethane. The organic layer was washed with water, dried over Na_2SO_4 and concentrated to give a 1:9 mixture of **4f** and **2f** as a colorless solid (29.8 g, 97%). Crystallization from dichloromethane gave pure **2f**: 14.88 g (48%); mp 125–127 °C; IR (KBr) 3600–2500, 1710, 1685, 1370, 1187, 1126, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.73 (2 H, t), 3.10 (2 H, t), 6.72 (1 H, dd, J = 1.5, 3.4 Hz, C4 H), 7.18 (1 H, dd, J = 2.3, 3.4 Hz, C5 H), 7.4–8.1 (6 H, m); UV (MeOH) λ_{max} 237 nm (ϵ 21 100). Anal. Calcd for $C_{14}H_{13}NO_5S$: C, 54.71; H, 4.26; N, 4.56; S, 10.43. Found: C, 54.54; H, 4.34; N, 4.52; S, 10.36.

General Procedure for the Hydrolysis of 2. A solution of **2c** (3.84 g, 14 mmol) in 50 mL of dioxane was stirred with 50 mL of 5 N NaOH at 25 °C for 17 h. The organic layer was collected, and the aqueous layer was thoroughly extracted with ethyl acetate. The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated at reduced pressure to give **3c** as a solid material, 1.9 g (100%). Recrystallization from toluene–hexane gave light pink crystals: (1.48 g); mp 104–106 °C; IR (KBr) 3220, 1622, 1520, 1254, 937 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.77–1.27 (4 H, m), 2.27–2.57 (1 H, m), 6.6–6.83 (2 H, m, C4,5 H), 7.5 (1 H, m, C2 H), 9.93 (1 H, br, NH). Anal. Calcd for C_8H_9NO: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.14; H, 6.68; N, 10.28.

4-(3-Pyrrolyl)-4-oxobutyric acid (3f): mp 169–170 °C; IR (KBr) 3600–2500, 3390, 1730, 1620, 1233, 1140, 1097 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.53 (2 H, t), 3.00 (2 H, t), 6.50 (1 H, m, C4 H), 6.87 (1 H, m, C5 H), 7.63 (1 H, m, C2 H), 10.3–12.0 (2 H, br, NH and CO_2H). Anal. Calcd for $C_8H_9NO_3$: C, 57.48; H, 5.42; N, 8.38. Found: C, 57.56; H, 5.41; N, 8.40.

1-(Phenylsulfonyl)-2-acetylpyrrole (4a). To a solution of acetic anhydride (225 mg, 2.2 mmol) in 6 mL of 1,2-dichloroethane at 25 °C was added $BF_3 \cdot OEt_2$ (625 mg, 4.4 mmol). The mixture was stirred for 10 min, a solution of **1** (414 mg, 2 mmol) in 2 mL of 1,2-dichloroethane was added, and the mixture was stirred at 25 °C for 90 min. The reaction was quenched with cold water, and the reaction products were extracted into dichloromethane. The residue remaining after concentration at reduced pressure was chromatographed in a column of silica gel (70–230 mesh), eluting with 1:4 ethyl acetate–toluene, to afford unconsumed **1** (43 mg), **4a** (414 mg, 83%), and **2a** (22 mg, 4.4%). Recrystalli-

zation from hexane gave pure **4a**: mp 96–98 °C; IR (KBr) 3165, 1680, 1360, 1185, 1145 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.35 (3 H, s, $COCH_3$), 6.37 (1 H, t, J = 3.4 Hz, C4 H), 7.07 (1 H, dd, J = 1.5, 3.4 Hz, C3 H), 7.43–7.67 (3 H, m), 7.87 (1 H, dd, J = 1.5, 3.4 Hz, C5 H), 7.97–8.10 (2 H, m); UV (MeOH) λ_{max} 224 nm (ϵ 10400), 238 (11700), 268 (sh, 8900), 274.5 (9600); GC (175 °C) t_R = 4.39 min. Anal. Calcd for $C_{12}H_{11}NO_3S$: C, 57.82; H, 4.45; N, 5.62; S, 12.86. Found: C, 57.88; H, 4.41; N, 5.46; S, 13.01.

1-(Phenylsulfonyl)-2-benzoylpyrrole (4b). To a solution of benzoyl chloride (1.8 mL, 14.5 mmol) and $BF_3{\cdot}OEt_2$ (1.8 mL, 14.5 mmol) in 50 mL of dichloromethane was added 1 (1.0 g, 4.83 mmol), and the mixture was stirred at 25 °C for 7 days. The mixture was washed with 1 N HCl and brine, dried over Na_2SO_4, and concentrated at reduced pressure. The residue was chromatographed in a column of silica gel (Waters PrepLC/System 500A), eluting with 1:5 ethyl acetate–hexane, to afford crystalline **4b**: 1.12 g (75%); mp 134–136 °C; IR (KBr) 3150, 1650, 1450, 1435, 1360, 1330 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.35 (1 H, t, J = 3.4 Hz, C4 H), 6.72 (1 H, dd, J = 1.5, 3.4 Hz, C3 H) 7.35–8.30 (11 H, m); UV (MeOH) λ_{max} 248 nm (ϵ 15280), 288 (11940); GC (235 °C) t_R = 9.39 min. Anal. Calcd for $C_{17}H_{13}NO_3S$: C, 65.58; H, 4.21; N, 4.50; S, 10.30. Found: C, 65.48; H, 4.12; N, 4.62; S, 10.10.

1-(Phenylsulfonyl)-2-pyrrolyl Cyclopropyl Ketone (4c). To a solution of $BF_3{\cdot}OEt_2$ (6.18 g, 43.5 mmol) in 25 mL of 1,2-dichloroethane at 25 °C was added cyclopropanecarbonyl chloride (4.55 g, 43.5 mmol). The mixture was stirred for 10 min, a solution of 1 (3.0 g, 14.5 mmol) in 10 mL of 1,2-dichloroethane was added, and the mixture was stirred at 25 °C for 18 h. The reaction was quenched with cold water, and the reaction products were extracted into dichloromethane. The extracts were washed with water, dried over Na_2SO_4, and concentrated in vacuo. The residue was chromatographed in a column of silica gel (70–230 mesh), eluting with 1:5 ethyl acetate–toluene, to afford **4c**: 2.74 g (69%); mp 139–141 °C; IR (KBr) 1666, 1360, 1170, 1142 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8–1.2 (4 H, m), 2.2–2.5 (1 H, m), 6.35 (1 H, t, J = 3.4 Hz, C4 H), 7.20 (1 H, dd, J = 1.5, 3.4 Hz, C3 H), 7.4–7.70 (3 H, m), 7.80 (1 H, dd, J = 1.5, 3.4 Hz, C3 H), 7.9–8.15 (2 H, m); UV (MeOH) λ_{max} 224 nm (ϵ 12480), 237 (12150), 274 (11600); GC (200 °C) t_R = 4.12 min. Anal. Calcd for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N, 5.09; S, 11.65. Found: C, 61.18; H, 4.80; N, 5.05; S, 11.76.

1-[1-(Phenylsulfonyl)-2-pyrrolyl]-4-chloro-1-butanone (4d). To a solution of 4-chlorobutyryl chloride (0.45 mL, 4 mmol) in 8 mL of 1,2-dichloroethane at 25 °C was added $BF_3{\cdot}OEt_2$ (568 mg, 4 mmol). The mixture was stirred for 10 min, a solution of 1 (414 mg, 2.0 mmol) in 2 mL of 1,2-dichloroethane was added, and the mixture was stirred at 25 °C for 2 days. The mixture was quenched with 0.5 N HCl, and the products were extracted into dichloromethane. The extracts were washed with brine, dried over Na_2SO_4, and concentrated at reduced pressure. The residue was chromatographed in a column of silica gel (Waters Prep LC/System 500A), eluting with 1:4 ethyl acetate–hexane, to afford unconsumed 1 (120 mg, 30%), **4d** (347 mg, 56%), and **2d** (32 mg, 5%). The spectral data for **4d** follow: mp 61–63 °C; IR (KBr) 3140, 2970, 1685, 1370, 1170, 1145 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.10 (2 H, quintet), 2.90 (2 H, t, CH_2CO), 3.50 (2 H, t, CH_2Cl), 6.40 (1 H, t, J = 3.4 Hz, C4 H), 7.10 (1 H, dd, J = 1.5, 3.4 Hz, C3 H), 7.45–7.70 (3 H, m), 7.90 (1 H, dd, J = 1.5, 3.4 Hz, C5 H), 8.0–8.1 (2 H, m); UV (MeOH) λ_{max} 224 nm (ϵ 11800), 237 (12900), 268 (sh, 10300), 274 (11200). Anal. Calcd for $C_{14}H_{14}NO_3SCl$: C, 53.93; H, 4.53; N, 4.49; S, 10.28. Found: C, 53.91; H, 4.62; N, 4.43; S, 10.27.

Methyl 4-[1-(Phenylsulfonyl)-2-pyrrolyl]-4-oxobutyrate (4e). To a solution of 3-carbomethoxypropionyl chloride (3.7 mL, 30 mmol) and $BF_3{\cdot}OEt_2$ (7.4 mL, 60 mmol) in 50 mL of 1,2-dichloroethane was added a solution of 1 (2.07 g, 10 mmol) in 10 mL of 1,2-dichloroethane at 25 °C. The resulting solution was stirred at 25 °C for 2 days and poured into ice–water. The product was extracted with dichloromethane, and the extracts were washed with 0.5 N HCl, water, 0.1 N NaOH, and brine and dried over Na_2SO_4. The residue remaining after concentration at reduced pressure was chromatographed in a column of silica gel (70–230 mesh), eluting with 1:10 ethyl acetate–toluene, to give a 85:15 mixture of **4e** and **2e** as determined by GC. Recrystallization from methanol gave pure **4e**: 1.36 g (42%); mp 139–142 °C; IR (KBr) 1740, 1683, 1358, 1170, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.63 (2 H, t), 3.05 (2 H, t), 3.63 (3 H, s), 6.35 (1 H, t, J = 3.4, C4 H), 7.13 (1 H, dd, J = 1.5, 3.4 Hz, C3 H), 7.4–7.7 (3 H, m), 7.80 (1 H, dd, J = 1.5, 3.4 Hz, C5 H), 7.95–8.1 (2 H, m); UV (MeOH) λ_{max} 237 nm (ϵ 12470); 269 (sh, 10180), 274 (10720); GC (220 °C) t_R = 4.11 min. Anal. Calcd for $C_{15}H_{15}NO_5S$: C, 56.07; H, 4.70; N, 4.36; S, 9.98. Found: C, 56.01; H, 4.79; N, 4.46; S, 9.76.

General Procedure for the Hydrolysis of 4. A solution of **4c** (826 mg, 3 mmol) in 5 mL of 5 N NaOH and 5 mL of methanol was refluxed for 3.5 h, and the methanol was evaporated at reduced pressure. The aqueous residue was extracted with ethyl acetate, and the extracts were washed with brine, dried over Na_2SO_4, and concentrated at reduced pressure to give 2-pyrrolyl cyclopropyl ketone (**5c**): 378 mg (93%); mp 68–70 °C. Recrystallization from hexane gave crystals, mp 71–72.5 °C (lit.[4] mp 71.5 °C).

4-[1-(Phenylsulfonyl)-2-pyrrolyl]-4-oxobutyric Acid (4f). A mixture of **4e** (1.0 g, 3.1 mmol) and $LiOH{\cdot}H_2O$ (168 mg, 4.0 mmol) in 10 mL of THF and 10 mL of water was stirred at 25 °C for 30 min. The mixture was diluted with water and acidified with 1 N HCl, and the resulting solid material was collected by filtration, washed with water, and dried under reduced pressure to give **4f**: 790 mg (83%); mp 183–184 °C; IR (KBr) 3600–2500, 1715, 1684, 1360, 1247, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.6 (2 H, t), 3.10 (2 H, t), 6.40 (1 H, t, J = 3.4 Hz, C4 H), 7.20 (1 H, q, J = 1.5, 3.4 Hz, C3 H), 7.47–7.7 (3 H, m), 7.83 (1 H, dd, J = 1.5, 3.4 Hz, C5 H), 7.9–8.1 (2 H, m); UV (MeOH) λ_{max} 237 nm (ϵ 12950), 268 (sh, 10350), 274 (10680). Anal. Calcd for $C_{14}H_{13}NO_5S$: C, 54.71; H, 4.26; N, 4.56; S, 10.43. Found: C, 54.72; H, 4.39; N, 4.50; S, 10.41.

Acylation of 1 with Acetic Acid–Trifluoroacetic Anhydride. To a stirred, ice-cooled solution of 1 (1.0 g, 4.83 mmol), 10 mL of trifluoroacetic anhydride, and 10 mL of dichloromethane was added 1.0 mL (17.5 mmol) of acetic acid. The solution was stirred at 25 °C for 2 h and concentrated at reduced pressure to give 1.20 g (100%) of solid which was a 97.6:2.4 mixture of **4a** and **2a** as determined by GC. Recrystallization from hexane–chloroform gave **4a**: 1.0 g (83%); mp 96–98 °C.

Acylation of 1 with Acetic Anhydride–Trifluoroacetic Acid. A solution of 1 (207 mg, 1 mmol), 0.28 mL of acetic anhydride, 0.45 mL of trifluoroacetic acid, and 4 mL of dichloromethane was stirred at 25 °C for 27 h. The workup gave 235 mg of solid which had essentially the same proportions of **4a** and **2a** as above.

1-(Phenylsulfonyl)-2-formylpyrrole (6). To a stirred, ice-cooled mixture of 1 (10.35 g, 0.050 mol) and $AlCl_3$ (15.73 g, 0.118 mol) in 150 mL of 1,2-dichloroethane was added dropwise 1,1-dichloromethyl methyl ether (8.0 g, 0.070 mol). The resulting solution was stirred at 0 °C for 3 h and then poured into a mixture of ice and water. The organic layer was collected, and the aqueous layer was extracted thoroughly with dichloromethane. The combined extracts were washed with water and brine, dried over Na_2SO_4, and concentrated at reduced pressure to give an oil which solidified on standing; 11.6 g (99%). Recrystallization from ligroin afforded **6** as white needles: mp 78–79 °C; IR (KBr) 1660, 1428, 1375, 1190, 1154 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.40 (1 H, t, J = 3.4 Hz, C4 H), 7.13 (1 H, dd, J = 1.5, 3.4 Hz, C3 H), 7.4–7.67 (4 H, m), 7.83–8.0 (2 H, m), 9.93 (1 H, s, CHO); ^1H NMR (Me_2SO-d_6) δ 6.53 (1 H, t, J = 3.4 Hz, C4 H), 7.27 (1 H, dd, J = 1.5, 3.4 Hz, C3 H), 7.53–7.8 (3 H, m), 7.90 (1 H, dd, J = 1.5, 3.4 Hz, C5 H), 7.97–8.13 (2 H, m), 9.87 (1 H, s, CHO); UV (MeOH) λ_{max} 224 nm (ϵ 10260), 238 (9400), 275 (8770), 283 (sh, 8750). Anal. Calcd for $C_{11}H_9NO_3S$: C, 56.16; H, 3.86; N, 5.95; S, 13.63. Found: C, 56.44; H, 4.17; N, 6.12; S, 13.88.

1-(Phenylsulfonyl)-2-(chlorocarbonyl)pyrrole (7). To an ice-cooled suspension of $AlCl_3$ (3.33 g, 25 mmol) in 50 mL of 1,2-dichloroethane was added 2.2 mL (25 mmol) of oxalyl chloride. The resulting solution was stirred at 0 °C for 20 min, a solution of 1 (1.04 g, 5 mmol) in 5 mL of 1,2-dichloroethane was added, and the mixture was stirred at 25 °C for 50 min. The mixture was poured into a mixture of ice and water (ca. 100 mL) and the product extracted into diethyl ether. The organic fraction was washed with water, dried over Na_2SO_4, and concentrated at reduced pressure to give 7 as a brown oil: 1.29 g (96%); IR (film on NaCl) 3140, 1754, 1188, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.43 (1 H, t, J = 3.4 Hz, C4 H), 7.35–8.3 (7 H, m). This sample (300 mg) was refluxed in 50 mL of methanol for 30 min and concen-

trated at reduced pressure. The residual oil was chromatographed in a column of silica gel (70–230 mesh), eluting with benzene, to give **8** as an oil (190 mg) which solidified on standing: mp 92–93 °C; IR (KBr) 3170, 1730, 1360, 1266, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.70 (3 H, s), 6.30 (1 H, t, J = 3.4 Hz, C4 H), 7.0 (1 H, dd, J = 1.5, 3.4 Hz, C3 H), 7.35–8.1 (6 H, m); UV (MeOH) λ_{max} 229 nm (ϵ 15 100), 259 (9410). Anal. Calcd for $C_{12}H_{11}NO_4S$: C, 54.33; H, 4.18; N, 5.28; S, 12.09. Found: C, 54.62; H, 4.06; N, 5.35; S, 11.85.

1-(Phenylsulfonyl)-2-pyrrolyl 1-(Phenylsulfonyl)-3-pyrrolyl Ketone (9). To a suspension of $AlCl_3$ (1.18 g, 8.9 mmol) in 10 mL of dichloromethane at 25 °C was added dropwise oxalyl chloride (0.37 mL, 4.3 mmol). The resulting solution was stirred at 25 °C for 10 min, and a solution of **1** (0.80 g, 3.9 mmol) in 5 mL of dichloromethane was added. The mixture was stirred at 25 °C for 60 min, and **1** (0.72 g, 3.5 mmol) was added. The mixture was stirred for 20 h and quenched with 0.5 N HCl, and the product was extracted into dichloromethane. The extracts were washed successively with brine, 0.1 N NaOH, and brine, dried over Na_2SO_4, and concentrated at reduced pressure. The residual oil was chromatographed in a column of silica gel (70–230 mesh), eluting with 1:20 ethyl acetate–toluene, to give **9** as an oil which solidified on standing: 590 mg (37%); mp 152–153 °C; IR (KBr) 3130, 1655, 1375 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.40 (1 H, t, J = 3.3 Hz, C4 H), 6.75 (1 H, dd, J = 1.5, 3.3 Hz, C4′ H), 6.85 (1 H, dd, J = 1.8, 3.3 Hz, C3 H), 7.20 (1 H, dd, J = 2.2, 3.3 Hz, C5′ H), 7.5–8.2 (12 H, m); UV (MeOH) λ_{max} 220 nm (ϵ 20 800), 245 (19 970), 266 (sh, 10 850), 275 (10 900), 292 (12 000). Anal. Calcd for $C_{21}H_{16}N_2O_5S_2$: C, 57.26; H, 3.66; N, 6.36; S, 14.56. Found: C, 57.26; H, 3.68; N, 6.21; S, 14.26.

1-(Phenylsulfonyl)-3-(carbomethoxymethyl)pyrrole (11). A mixture of **2a** (10.8 g, 43.4 mmol), thallium trinitrate trihydrate (21.14 g, 47.6 mmol), and 2 mL of 70% perchloric acid in 200 mL of methanol was stirred at 25 °C for 22 h and filtered. The filtrate was concentrated at reduced pressure, diluted with diethyl ether, and filtered. The filtrate was washed thoroughly with water and then 10% aqueous $NaHCO_3$. Removal of the solvent from the dried (Na_2SO_4) fraction and chromatography of the residual oil on a column of silica gel (70–230 mesh), eluting with 1:4 ethyl acetate–toluene, gave **11**: 8.03 g (66.4%); mp 54–56 °C; IR (KBr) 3165, 1743, 1376, 1189, 1179, 1067 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.47 (2 H, s), 3.68 (3 H, s), 6.27 (1 H, t, J = 3.4 Hz, C4 H), 7.10 (2 H, superimposed d, J = 3.4 Hz, C2,5 H), 7.4–7.97 (5 H, m). Anal. Calcd for $C_{13}H_{13}NO_4S$: C, 55.90; H 4.69; N, 5.01; S, 11.48. Found: C, 55.87; H, 4.84; N, 4.98; S, 11.30.

1-(Phenylsulfonyl)-3-pyrrolylacetic Acid (12). A mixture of **11** (1.395 g, 5 mmol), lithium hydroxide hydrate (0.84 g, 20 mmol), 5 mL of THF, and 5 mL of water was stirred at 25 °C for 45 min, diluted with 50 mL of water, and washed once with ethyl acetate. The aqueous fraction was acidified with 6 N HCl and the product extracted into ethyl acetate. The extracts were washed with brine, dried over Na_2SO_4, and concentrated at reduced pressure to give **12** as a solid, 1.32 g (100%). Recrystallization from toluene–hexane gave crystals: 1.11 g (84%); mp 99–100 °C; IR (KBr) 3500–2500, 1720, 1365, 1200, 1180, 1170, 1097, 1063 cm^{-1}; ^1H NMR ($CDCl_3$) 3.48 (2 H, s), 6.28 (1 H, t, J = 3.4 Hz, C4 H), 7.13 (2 H, superimposed d, J = 3.4 Hz, C2,5 H), 7.35–7.97 (5 H, m), 10.40 (1 H, br). Anal. Calcd for $C_{12}H_{11}NO_4S$: C, 54.32; H, 4.18; N, 5.28; S, 12.09. Found: C, 54.23; H, 4.14, N, 5.26; S, 12.44.

3-Pyrrolylacetic Acid (10). A mixture of **11** (2.0 g, 7 mmol), 15 mL of 5 N NaOH, and 15 mL of methanol was refluxed for 2.5 h, and the methanol was evaporated at reduced pressure. The aqueous residue was washed with ethyl acetate, acidified with 12 N HCl, and saturated with NaCl, and the product was extracted into ethyl acetate. The extracts were dried over Na_2SO_4 and concentrated at reduced pressure to give a solid which was triturated in hexane and filtered. Crystallization from toluene–hexane gave **10** as crystals: 0.65 g (72.5%); mp 90–91 °C; IR (KBr) 3500–2400, 3390, 1700, 1277, 1210, 1070, 1065 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 3.33 (2 H, s), 5.97 (1 H, m, C4 H), 6.65 (2 H, m, C2,5 H), 10.0–12.0 (2 H, br). Anal. Calcd for $C_6H_7NO_2$: C, 57.59; H, 5.64; N, 11.20. Found: C, 57.66; H, 5.57; N, 11.27.

4-[1-(Phenylsulfonyl)-3-pyrrolyl]butyric Acid (14). A mixture of zinc metal (45.8 g) and mercuric chloride (4.58 g) in 60 mL of water and 3 mL of 12 N HCl was stirred at 25 °C for 20 min, and the solvent was decanted. To the solid were added 28 mL of water, 66 mL of 12 N HCl, 300 mL of toluene, and **2f** (18 g, 0.058 mol). The mixture was refluxed for 16 h and cooled. The organic fraction was collected. The aqueous layer was shaken with toluene and the combined organic fraction washed with water, dried over Na_2SO_4, and concentrated at reduced pressure to give **14** as a solid, 13.9 g (80.9%). Recrystallization from toluene gave crystals: mp 92–94 °C; IR (KBr) 3500–2500, 1708, 1368, 1182, 1172, 1104 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 1.67 (2 H, quintet), 2.0–2.47 (4 H, m), 3.35 (1 H, br, CO_2H), 6.27 (1 H, dd, J = 1.5, 3.0 Hz, C4 H), 7.13 (1 H, m, C2 H), 7.27 (1 H, dd, J = 2.3, 3.0 Hz, C5 H), 7.5–8.0 (5 H, m). Anal. Calcd for $C_{14}H_{15}NO_4S$: C, 57.32; H, 5.15; N, 4.78; S, 10.93. Found: C, 57.39; H, 5.13; N, 4.66; S, 10.96.

Cyclization of 14. A solution of **14** (293 mg, 1 mmol) in 2 mL of oxalyl chloride was stirred at 25 °C for 1 h: ^1H NMR (oxalyl chloride) δ 2.02 (2 H, quintet), 2.54 (2 H, t), 2.90 (2 H, t), 6.19 (1 H, m, C4 H), 6.93 (1 H, m, C2 H), 7.06 (1 H, m, C5 H), 7.43–7.94 (5 H, m). The excess reagent was removed at 25 °C at reduced pressure. The residue was dissolved in 3 mL of 1,2-dichloroethane and added to a suspension of $AlCl_3$ (400 mg, 3 mmol) in 5 mL of 1,2-dichloroethane at 25 °C. The resulting solution was stirred for 45 min, the reaction was quenched with ice–water, and the product was extracted into dichloromethane. The only detectable product by TLC and ^1H NMR analyses of the extract was **17**.

1-(Phenylsulfonyl)-7-oxo-4,5,6,7-tetrahydroindole (17). A solution of **14** (1.63 g, 5.56 mmol) and 5 mL of trifluoroacetic anhydride in 20 mL of dichloromethane was stirred at 25 °C for 30 min and concentrated at reduced pressure. The residual oil was chromatographed in a column of silica gel (70–230 mesh), eluting with 1:10 ethyl acetate–toluene, to give **17**: 0.98 g (64%); mp 115–117 °C; IR (KBr) 1670, 1370, 1180, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.00 (2 H, quintet), 2.37 (2 H, t), 2.70 (2 H, t), 6.22 (1 H, d, J = 3.0 Hz, C3 H), 7.4–7.67 (3 H, m), 7.73 (1 H, d, J = 3.0 Hz, C2 H), 8.0–8.2 (2 H, m); UV (MeOH) λ_{max} 223 nm (ϵ 8910), 260 (sh, 11 700), 267 (12 030), 273 (11 950). Anal. Calcd for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N, 5.09; S, 11.65. Found: C, 61.11; H, 4.98; N, 5.22; S, 11.42.

7-Oxo-4,5,6,7-tetrahydroindole (18). A solution of **17** (250 mg, 0.91 mmol) in 10 mL of THF and 10 mL of 5 N NaOH was stirred under reflux for 44 h. The product was extracted into ethyl acetate, and the extract was washed with brine, dried over Na_2SO_4, and concentrated at reduced pressure to give **18** as a solid: 100 mg (81.5%); mp 91–93 °C. Recrystallization from hexane gave crystals: mp 95–96 °C (lit.[22] mp 95 °C); IR (KBr) 3260, 2935, 2860, 1635, 1415, 778 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.14 (2 H, quintet), 2.53 (2 H, t), 2.78 (2 H, t), 6.10 (1 H, m, C3 H), 7.05 (1 H, m, C2 H), 10.5 (1 H, br).

Preparation of ^{13}C NMR Samples. Acetyl chloride-*1*-^{13}C (90% enriched, 0.144 mL) was added to a suspension of $AlCl_3$ (267 mg, 1 equiv) in CD_2Cl_2 (4.0 mL). The spectra of the resulting solution were recorded at 30 and −60 °C on a Varian CFT-20 spectrometer. The chemical shift of the carbonyl carbon of the uncomplexed acetyl chloride was 169.9 ppm from $(CH_3)_4Si$ with CD_2Cl_2 (53.1 ppm) as the internal reference standard. In a similar fashion, acetyl chloride-*1*-^{13}C (0.175 mL) was added to a solution of BF_3·OEt_2 (0.30 mL, 1 equiv) in CD_2Cl_2 (4.0 mL).

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Registry No. **1**, 16851-82-4; **2a**, 81453-98-7; **2b**, 81453-99-8; **2c**, 81454-00-4; **2d**, 81454-00-4; **2e**, 86688-87-1; **2f**, 81454-02-6; **3a**, 1072-82-8; **3b**, 7126-41-2; **3c**, 81454-03-7; **3e**, 81454-04-8; **3f**, 81454-05-9; **4a**, 86688-88-2; **4b**, 86688-89-3; **4c**, 86688-90-6; **4d**, 86688-91-7; **4e**, 86695-72-9; **4f**, 86688-92-8; **5a**, 1072-83-9; **5b**, 7697-46-3; **5c**, 30625-80-0; **6**, 86688-93-9; **7**, 86688-94-0; **8**, 57850-02-9; **9**, 86688-95-1; **10**, 86688-96-2; **11**, 86688-97-3; **12**, 86688-98-4; **14**, 86688-99-5; **17**, 86689-00-1; **18**, 23456-78-2; $AlCl_3$, 7446-70-0; BF_3·OEt_2, 109-63-7; benzoyl chloride, 98-88-4; cyclopropanecarboxylic acid chloride, 4023-34-1; 4-chlorobutyryl chloride, 4635-59-0; 3-carbomethoxypropionyl chloride, 1490-25-1; succinic anhydride, 108-30-5; acetic anhydride, 108-24-7; dichloromethyl methyl ether, 4885-02-3; oxalyl chloride, 79-37-8; thallium trinitrate, 13746-98-0.