THE PREPARATION OF HETEROCYCLIC APPENDED VINYLOGOUS IMINIUM SALTS AND THEIR APPLICATION TO THE REGIOSELECTIVE PREPARATION OF BIHETEROCYCLIC SYSTEMS[1]

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Abstract- The synthesis of heterocyclic appended vinylogous iminium salts is described along with their conversion to heterocyclic appended pyrimidines, triazolopyrimidines, and pyrroles.

We have previously reported[2] the preparation of a novel thiophene appended chloropropeniminium salt from the corresponding vinylogous amide and it's condensation with guanidines and glycinates to give the corresponding thienylpyrimidines and thienylpyrroles, respectively. The ability to prepare such biheterocycles represents an important strategy[3] in organic synthesis and provides interesting substances for subsequent biological evaluation.[4] We would now like to report our more comprehensive findings in which we describe the regiochemically controlled preparation of biheterocyclic systems which contain thiophenes, pyrroles and furans as one component and pyrimidines, pyrroles and triazolo[1,5-*a*]pyrimidines as the second component.

The first step in this synthetic strategy is to take an appropriate acylthiophene, acylfuran or acylpyrrole ,which are commercially available, and convert them to the respective vinylogous amides by treatment with *N,N*-dimethylformamide dimethyl acetal (DMFA) as depicted in Scheme 1 and Table 1. The 2-thienylvinylogous amide had been reported in our earlier paper.[2]

Scheme 1

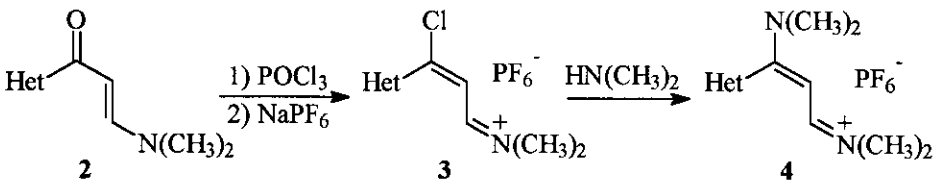
1 **2**

Table 1

Compound	Het	Yield %
2a	2-Furyl	94
2b	3-Pyrrolyl	93
2c	2-Pyrrolyl	92
2d	3-Thienyl	93
2e[2]	2-Thienyl	95

All of the aminomethylenations worked well and the respective vinylogous amides were prepared cleanly and in high isolated yields. The corresponding chloropropeniminium salts (3) and vinamidinium salts (4) were subsequently produced by reaction of the appropriate vinylogous amides with phosphorous oxychloride followed by treatment with dimethylamine. These results are reported in Scheme 2 and Table 2 and all salts (3 and 4) gave characteristic spectral properties consistent with their proposed structures.

Scheme 2



2 **3** **4**

Table 2

Het	Compound	Yield %[a]	Compound	Yield %[b]
2-Furyl	**3a**	91	**4a**	76
3-Pyrrolyl	**3b**	75	**4b**	64
2-Pyrrolyl	**3c**	78	**4c**	69
3-Thienyl	**3d**	84	**4d**	73
2-Thienyl[2]	**3e**	89	**4e**	71

[a]two-step overall yield from 1

[b]three-step overall yield from 1

In order to demonstrate the synthetic utility of these heterocyclic building blocks, the respective vinamidinium salts (4) reacted with guanidine in the presence of sodium hydride and DMF to produce pyrimidines with the various heterocyclic groups appended at the 4 position. The reactions were clean, gave good yields of the novel heterocyclic appended pyrimidines and the results are reported in Table 3.

Scheme 3

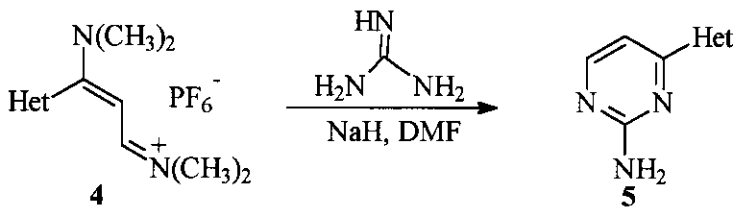
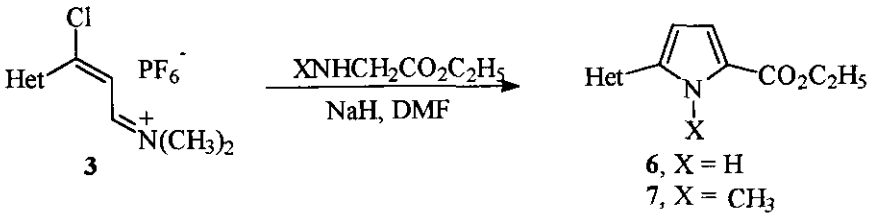


Table 3

Compound	Het	Yield %
5a	2-Furyl	78
5b	3-Pyrrolyl	65
5c	2-Pyrrolyl	81
5d	3-Thienyl	82
5e	2-Thienyl[2]	90

We have recently reported regiocontrolled syntheses of 2,5- and 2,3-disubstituted pyrroles[5,6] based on differences by which ethyl *N*-methylglycinate reacts with chloropropeniminium salts (3) versus unsymmetrical vinamidinium salts (4). The amino group of the amino acid ester tends to exchange at the chlorine bearing carbon of the chloropropeniminium salt by a proposed electronically driven process. Alternatively, the amino group of the amino acid ester exchanges at the less substituted amine bearing position of the vinamidinium salt by a proposed sterically driven process. The subsequent amine exchanged compounds undergo rapid azomethine ylid mediated cyclization to give the respective 2,5- and 2,3-disubstituted pyrrole systems. All of the regiochemical structural assignments for these pyrroles were carefully made with the aid of the NOESY NMR technique.[5,6] Application of this approach to the heterocyclic appended chloropropeniminium salts and vinamidinium salts yields the biheterocyclic pyrrole derivatives depicted in Tables 4 and 5. This approach allows for the preparation of bipyrrole systems[7] with different regiochemical attachments as well as similar analogs where a furan or thiophene[8] is regiospecifically attached to the pyrrole backbone. Such methodology provides an alternative strategy to cross coupling reactions.

Scheme 4



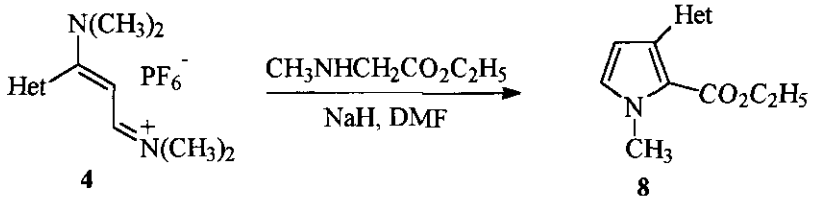
3

6, X = H
7, X = CH_3

Table 4

Het	Compound	Yield %	Compound	Yield %
2-Furyl	**6a**	60	**7a**	55
3-Pyrrolyl	**6b**	49	**7b**	67
2-Pyrrolyl	**6c**	35	**7c**	47
3-Thienyl	**6d**	75	**7d**	49
2-Thienyl[2]	**6e**	75	**7e**	55

Scheme 5



4

8

Table 5

Compound	Het	Yield %
8a	2-Furyl	61
8b	3-Pyrrolyl	45
8c	2-Pyrrolyl	50
8d	3-Thienyl	48
8e	2-Thienyl	44

We have also reported that unsymmetrically substituted vinamidinium salts[9] react in a regiocontrolled manner with 3-aminotriazole to produce 7-substituted triazolo[1,5-*a*]pyrimidines. The regiochemistry in this case was established by comparison of spectral properties of these triazolopyrimidines with compounds of known structure. Application of this technique to the heterocyclic appended vinamidinium salts (4) produces the

corresponding 7-heterocyclic appended triazolopyrimidines and thereby provides a useful entry into this class of interesting heterocyclic systems. Compounds (9d) and (9e) have been previously reported[10] in a U.S. patent.

Scheme 6

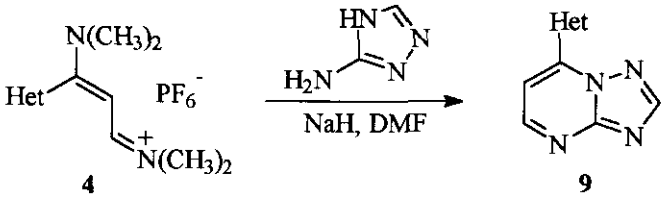


Table 6

Compound	Het	Yield %
9a	2-Furyl	53
9b	3-Pyrrolyl	65
9c	2-Pyrrolyl	42
9d[10]	3-Thienyl	58
9e[10]	2-Thienyl	85

In summary, a group of novel regiospecific, heterocyclic appended vinylogous iminium salts have been prepared. These materials react with a series of nucleophilic substances and provide entry to systems that contain pyrrole, thiophene and furan attached in a regiochemically defined manner to a variety of important heterocyclic frameworks.

EXPERIMENTAL

The following procedures are typical of the experimental conditions used for the preparation of pyrroles, pyrimidines, and triazolopyrimidines. The vinylogous iminium salts were prepared by standard methods.[5,6] All melting points and boiling points are uncorrected and all purified compounds gave a single spot upon tlc analysis on silica gel 7GF using an ethyl acetate/hexane mixture as eluent.

E-3-Dimethylamino-1-(3-thienyl)propenone (2d): Into a 250-mL one-neck round-bottom flask were placed 10.0 g (79 mmol) of 3-acetylthiophene, 18.9 g (158 mmol) of *N,N*-dimethylformamide dimethyl acetal and 50 mL of dry DMF. The flask was equipped with a condenser and stir bar and was heated at reflux overnight. After cooling to rt, the solvent was removed in vacuo leaving 13.2 g (93%) of solid . Additional purification was not needed, however, an analytical sample can be prepared by radial chromatography using a gradient elution of hexane and ethyl acetate. This compound exhibited the following

properties: mp 102-104 °C; ^{1}H NMR (DMSO-d_6) δ 2.91 (s, 3H), 3.14 (s, 3H), 5.75 (d, J = 12.2 Hz, 1H), 7.52 (m, 2H), 7.65 (d, J = 12.2 Hz, 1H), and 8.20 (m, 1H); ^{13}C NMR (DMSO-d_6) δ 38.9, 46.2, 93.9, 127.9, 128.9, 130.5, 146.8, 155.3, and 182.6; FTIR (KBr pellet) 3072, 1642, 1552 cm^{-1}; HRMS calcd for $C_9H_{11}NOS$ 181.0561, found 181.0562.

E-3-Dimethylamino-1-(2-furyl)propenone (2a): This compound was prepared in 94% yield in a manner similar to compound **(2d)**. This material exhibited the following properties: mp 91-93 °C; ^{1}H NMR (DMSO-d_6) δ 2.90 (s, 3H), 3.15 (s, 3H), 5.66 (d, J = 12.4 Hz, 1H), 6.61 (dd, J = 3.4 Hz, J = 1.6 Hz, 1H) 7.12 (d, J = 3.4 Hz, 1H), 7.69 (d, J = 12.4 Hz, 1H), and 7.80 (d, J = 1.6 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 38.8, 46.2, 92.4, 113.7, 114.9, 146.6, 155.1, 156.3, and 177.3; FTIR (KBr pellet) 3087, 1639, 1576, 1541 cm^{-1}; HRMS calcd for $C_9H_{11}NO_2$ 165.0790, found 165.0793.

E-3-Dimethylamino-1-(3-pyrrolyl)propenone (2b): This compound was prepared in 93% yield in a manner similar to compound **(2d)** . This material exhibited the following properties: mp 126-128 °C; ^{1}H NMR (DMSO-d_6) δ 2.95 (br s, 6H), 3.64 (s, 3H), 5.53 (d, J = 12.6 Hz, 1H), 6.40 (m, 1H), 6.97 (m, 1H), 7.36 (s, 1H), and 7.48 (d, J = 12.6 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 37.7, 46 (br), 94.5, 109.9, 124.4, 126.7, 129.0, 153.2, and 184.0; FTIR (KBr pellet) 1634, 1536 cm^{-1}; HRMS calcd for $C_{10}H_{14}N_2O$ 178.1106, found 178.1104.

E-3-Dimethylamino-1-(2-pyrrolyl)propenone (2c): This compound was prepared in 92% yield in a manner similar to compound **(2d)**. This material exhibited the following properties: mp 98-100 °C; ^{1}H NMR (DMSO-d_6) δ 2.97 (br s, 6H), 3.88 (s, 3H), 5.63 (d, J = 12.5 Hz, 1H), 6.02 (m, 1H), 6.84 (m, 1H), 6.90 (m, 1H), and 7.49 (d, J = 12.5 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 38.6, 46 (br), 94.5, 108.6, 116.5, 130.4, 134.0, 153.5, and 181.1; FTIR (KBr pellet) 1636, 1561 cm^{-1}; HRMS calcd for $C_{10}H_{14}N_2O$ 178.1106, found 178.1106.

3-Chloro-3-(3-thienyl)prop-2-en-1-ylidenedimethyliminium Hexafluorophosphate (3d): Into a dry 250 mL one-neck round-bottom flask were placed 14.0 g (77 mmol) of vinylogous amide and 50 mL of dry methylene chloride. While swirling frequently, 11.82 g (77 mmol) of phosphorous oxychloride were added dropwise. The reaction was allowed to stir at rt for 30 min followed by removing the solvent in vacuo. The residue was dissolved in a minimal amount of methanol and added to a solution containing 300 mL of methanol and 25.95 g (154 mmol) of sodium hexafluorophosphate at 0 °C. The chloropropeniminium salt precipitated out completely after 5 min of vigorous stirring. The solid was filtered and *dried in vacuo leaving 22.4 g (84%). Additional purification was not needed, however, an* analytical sample can be prepared by recrystallization from ethanol. This compound exhibited the following properties: mp 181-183 °C; ^{1}H NMR (DMSO-d_6) δ 3.65 (s, 3H), 3.75 (s, 3H), 7.62 (d, J = 10.2 Hz, 1H), 7.85-8.00 (m, 2H), 8.60 (m, 1H), and 8.94 (d, J = 10.2 Hz,

1H); ^{13}C NMR (DMSO-d_6) δ 44.0, 51.1, 115.5, 128.2, 131.2, 136.4, 139.4, 152.6, and 167.0; FTIR (KBr pellet) 3130, 1648, 1575, 835 cm^{-1}; HRMS calcd for $C_9H_{11}NClS^+$ 200.0301, found 200.0306.

3-Chloro-3-(2-furyl)prop-2-en-1-ylidenedimethyliminium Hexafluorophosphate (3a): This compound was prepared in 91% yield in a manner similar to compound (**3d**). This material exhibited the following properties: mp 145-147 °C (decomp); ^{1}H NMR (DMSO-d_6) δ 3.63 (s, 3H), 3.75 (s, 3H), 6.96 (dd, J = 3.5 Hz, J = 1.7 Hz, 1H), 7.45 (d, J = 10.5 Hz, 1H), 7.68 (d, J = 3.5 Hz, 1H), 8.29 (d, J = 1.7 Hz, 1H), and 8.89 (d, J = 10.5 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 43.8, 51.0, 112.6, 116.7, 122.9, 144.9, 150.5, 152.4, and 165.8; FTIR (KBr pellet) 1657, 1601, 833 cm^{-1}; HRMS calcd for $C_9H_{11}NOCl^+$ 184.0529, found 184.0521.

3-Chloro-3-(3-pyrrolyl)prop-2-en-1-ylidenedimethyliminium Hexafluorophosphate (3b): This compound was prepared in 75% yield in a manner similar to compound (**3d**). This material exhibited the following properties: mp 172-174 °C (decomp); ^{1}H NMR (DMSO-d_6) δ 3.51 (s, 3H), 3.63 (s, 3H), 3.73 (s, 3H), 6.93 (m, 1H), 7.03 (m, 1H), 7.19 (d, J = 10.5 Hz, 1H), 7.85 (m, 1H), and 8.69 (d, J = 10.5 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 38.4, 42.9, 50.2, 109.0, 110.9, 123.6, 128.5, 132.0, 155.7, and 165.5; FTIR (KBr pellet) 1636, 1570, 840 cm^{-1}; HRMS calcd for $C_{10}H_{14}N_2Cl^+$ 197.0846, found 197.0853.

3-Chloro-3-(2-pyrrolyl)prop-2-en-1-ylidenedimethyliminium Hexafluorophosphate (3c): This compound was prepared in 78% yield in a manner similar to compound (**3d**). This material exhibited the following properties: mp 157-158 °C (decomp); ^{1}H NMR (DMSO-d_6) δ 3.54 (s, 3H), 3.70 (s, 3H), 3.98 (s, 3H), 6.40 (dd, J = 2.4 Hz, J = 4.2 Hz, 1H), 6.96 (d, J = 10.4 Hz, 1H), 7.23 (dd, J = 4.2 Hz, J = 1.8 Hz, 1H), 7.52 (m, 1H), and 8.79 (d, J = 10.4 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 39.3, 43.2, 50.4, 110.7, 112.8, 124.6, 130.9, 138.7, 148.7, and 165.4; FTIR (KBr pellet) 3146, 1642, 1572, 838 cm^{-1}; HRMS calcd for $C_{10}H_{14}N_2Cl^+$ 197.0846, found 197.0855.

2-(3-Thienyl)-1,1,5,5-tetramethyl-1,5-diazapentadienium Hexafluorophosphate (4d): Into a 500 mL three-neck round-bottom flask were placed 200 mL of dry ethanol and and a stir bar. Gradually, 5.80 g (250 mmol) of sodium metal were added and allowed to stir until the reaction was complete. The mixture was cooled and 20.38 g (250 mmol) of dimethylamine hydrochloride were added while stirring. This solution was added to 10.0 g (29 mmol) of chloropropeniminium salt and stirred overnight. The resulting solid was filtered and dried in vacuo leaving 7.50 g (73%) of a solid. Additional purification was not needed, however, an analytical sample can be obtained by recrystallization from ethanol. This compound exhibited the following properties: mp 161-163 °C; ^{1}H NMR (DMSO-d_6) δ 2.98 (s, 3H), 3.15 (s, 3H), 3.18 (s, 3H), 3.33 (s, 3H), 5.60 (d, J = 11.7 Hz, 1H), 7.05 (d, J = 11.7

Hz, 1H), 7.21 (m, 1H), and 7.85 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 40.4, 43.1, 45.4, 48.9, 94.6, 129.6, 130.1, 130.8, 133.5, 163.4, and 169.4; FTIR (KBr pellet) 3075, 1635, 1567, 837 cm^{-1}; HRMS calcd for $C_{11}H_{17}N_2S^+$ 209.1112, found 209.1117.

2-(2-Furyl)-1,1,5,5-tetramethyl-1,5-diazapentadienium Hexafluorophosphate (4a): This compound was prepared in 76% yield in a manner similar to compound (**4d**). This material exhibited the following properties: mp 175-176 °C (decomp); ^{1}H NMR (DMSO-d_6) δ 3.19 (s, 3H), 3.28 (s, 3H), 3.05-3.50 (br s, 6H), 5.55 (d, J = 11.5 Hz, 1H), 6.82 (dd, J = 3.3 Hz, J = 1.8 Hz, 1H), 7.10 (d, J = 3.3 Hz, 1H), 7.49 (d, J = 11.5 Hz, 1H), and 8.11 (d, J = 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 40.6, 44 (br), 49.1, 94.6, 114.3, 121.9, 145.0, 148.4, 162.3, and 163.0; FTIR (KBr pellet) 1633, 1566, 838 cm^{-1}; HRMS calcd for $C_{11}H_{17}N_2O^+$ 193.1341, found 193.1342.

2-(3-Pyrrolyl)-1,1,5,5-tetramethyl-1,5-diazapentadienium Hexafluorophosphate (4b): This compound was prepared in 64% yield in a manner similar to compound (**4d**). This material exhibited the following properties: mp 172-173 °C; ^{1}H NMR ($CDCl_3$) δ 3.11 (s, 3H), 3.21 (s, 3H), 3.23 (s, 3H), 3.28 (s, 3H), 3.76 (s, 3H), 5.24 (d, J = 11.6 Hz, 1H), 6.12 (m, 1H), 6.71 (m, 1H), 7.03 (m, 1H), and 7.18 (d, J = 11.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 38.6, 40.2, 43.1, 45.6, 48.5, 94.2, 112.5, 115.9, 125.8, 128.7, 163.3, and 170.3; FTIR (KBr pellet) 1625, 1560, 842 cm^{-1}; HRMS calcd for $C_{12}H_{20}N_3^+$ 206.1657, found 206.1652.

2-(2-Pyrrolyl)-1,1,5,5-tetramethyl-1,5-diazapentadienium Hexafluorophosphate (4c): This compound was prepared in 69% yield in a manner similar to compound (**4d**). This material exhibited the following properties: mp 141-143 °C; ^{1}H NMR (DMSO-d_6) δ 2.87 (s, 3H), 3.15 (s, 3H), 3.19 (s, 3H), 3.29 (s, 3H), 3.47 (s, 3H), 5.64 (d, J = 11.4 Hz, 1H), 6.20-6.30 (m, 2H), and 7.10-7.20 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 36.3, 40.5, 42.6, 44.7, 49.0, 95.8, 111.0, 117.0, 124.5, 128.8, 164.0, and 165.8; FTIR (KBr pellet) 1638, 1569, 837 cm^{-1}; HRMS calcd for $C_{12}H_{20}N_3^+$ 206.1657, found 206.1646.

2-Amino-4-(3-thienyl)pyrimidine (5d): A 100 mL three-neck round-bottom flask was equipped with a stir bar, condenser, and placed under a nitrogen atmosphere. Into the flask was placed 0.282 g (7 mmol) of a 60% mineral oil dispersion of sodium hydride which was washed twice with dry hexane. The hexane was removed by cannula and part of a 40 mL portion of dry DMF along with 0.382 g (2.2 mmol) of guanidine carbonate were added. After stirring for 5 min, 1.00 g (2.8 mmol) of vinamidinium salt were added and the mixture was heated at 100 °C overnight. The reaction was cooled and the solvent was removed in vacuo. The residue was partitioned several times between water and chloroform. The combined chloroform extracts were dried over anhydrous $MgSO_4$ and concentrated. The crude product was passed through a short plug of silica gel and purified by radial chromatography using a gradient elution of hexane and ethyl acetate. An 82% yield (0.41 g)

of a solid was obtained. This compound exhibited the following properties: mp 237-239 °C; ^{1}H NMR (DMSO-d_6) δ 6.61 (s, 2H), 7.03 (d, J = 5.1 Hz, 1H), 7.63-7.73 (m, 2H), and 8.25 (s, 2H); ^{13}C NMR (DMSO-d_6) δ 107.8, 127.9, 128.3, 129.0, 142.3, 160.6, 161.6, and 165.5; FTIR (KBr pellet) 3324, 3175, 1648, 1561 cm^{-1}; HRMS calcd for $C_8H_7N_3S$ 177.0361, found 177.0356.

2-Amino-4-(2-furyl)pyrimidine (5a): This compound was prepared in 78% yield in a manner similar to compound (**5d**). This material exhibited the following properties: mp 211-213 °C; ^{1}H NMR (DMSO-d_6) δ 6.70 (br s, 3H), 6.89 (d, J = 5.1 Hz, 1H), 7.18 (m, 1H), 7.91 (s, 1H), and 8.29 (d, J = 5.1 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 105.7, 113.2, 114.2, 147.1, 153.5, 157.1, 160.8, and 165.4; FTIR (KBr pellet) 3331, 3181, 1650, 1560, 1480 cm^{-1}; HRMS calcd for $C_8H_7N_3O$ 161.0589, found 161.0590.

2-Amino-4-(3-pyrrolyl)pyrimidine (5b): This compound was prepared in 65% yield in a manner similar to compound (**5d**). This material exhibited the following properties: mp 212-214 °C; ^{1}H NMR (DMSO-d_6) δ 3.67 (s, 3H), 6.32 (s, 2H), 6.57 (m, 1H), 6.73 (d, J = 5.2 Hz, 1H), 6.78 (m, 1H), 7.42 (s, 1H), and 8.07 (d, J = 5.2 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 37.8, 106.5, 108.8, 124.4, 124.8, 125.1, 159.2, 163.1, and 165.3; FTIR (KBr pellet) 3313, 3164, 1651, 1575, 1457 cm^{-1}; HRMS calcd for $C_9H_{10}N_4$ 174.0905, found 174.0905.

2-Amino-4-(2-pyrrolyl)pyrimidine (5c): This compound was prepared in 81% yield in a manner similar to compound (**5d**). This material exhibited the following properties: mp 141-143 °C; ^{1}H NMR (DMSO-d_6) δ 4.01 (s, 3H), 6.09 (m, 1H), 6.47 (s, 2H), 6.78-6.83 (m, 2H), 6.94 (s, 1H), and 8.10 (d, J = 5.3 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 39.1, 107.6, 109.5, 115.1, 130.4, 131.0, 159.0, 160.8, and 164.7; FTIR (KBr pellet) 3283, 3152, 1627, 1582, 1456 cm^{-1}; HRMS calcd for $C_9H_{10}N_4$ 174.0905, found 174.0900.

2-Carbethoxy-5-(3-thienyl)pyrrole (6d): A 100 mL three-neck round-bottom flask was equipped with a stir bar, condenser and placed under a nitrogen atmosphere. Into the flask was placed 0.56 g (14 mmol) of a 60% mineral oil dispersion of sodium hydride which was washed twice with dry hexane. The hexane was removed by cannula and 40 mL of dry DMF was added to the flask followed by 0.99 g (7.1 mmol) of glycine ethyl ester hydrochloride and 1.00 g (2.8 mmol) of vinamidinium salt . The reaction was stirred for 1 h at rt followed by heating at 100 °C overnight. The reaction was cooled to rt and the solvent was removed *in vacuo*. The residue was partitioned several times between water and chloroform. The combined chloroform extracts were dried over anhydrous $MgSO_4$ and concentrated. The crude product was passed through a short plug of silical gel and purified by radial chromatography using a gradient elution of hexane and ethyl acetate. A 75% yield (0.46 g) of a solid was obtained. This compound exhibited the following properties: mp 132-134 °C; ^{1}H NMR (DMSO-d_6) δ 1.30 (t, J = 7.0 Hz, 3H), 4.26 (q, J = 7.0 Hz, 2H), 6.55 (m,

1H), 6.82 (m, 1H), 7.60 (m, 2H), 8.00 (s, 1H), and 12.1 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 16.3, 61.3, 109.6, 118.1, 121.7, 124.1, 127.9, 128.4, 134.9, 135.2, and 162.2; FTIR (KBr pellet) 3310, 3105, 1687 cm^{-1}; HRMS calcd for $C_{11}H_{11}NO_2S$ 221.0511, found 221.0516.

2-Carbethoxy-5-(2-furyl)pyrrole (6a): This compound was prepared in 60% yield in a manner similar to compound **(6d)**. This material exhibited the following properties: mp 87-89 °C; ^{1}H NMR (DMSO-d_6) δ 1.30 (t, J = 7.0 Hz, 3H), 4.27 (q, J = 7.0 Hz, 2H), 6.44 (m, 1H), 6.57 (m, 1H), 6.83 (m, 1H), 7.01 (m, 1H), 7.70 (s, 1H), and 12.2 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 16.2, 61.5, 107.5, 108.5, 113.6, 118.0, 124.5, 130.5, 144.1, 148.6, and 162.1; FTIR (KBr pellet) 3305, 1677, 1263 cm^{-1}; HRMS calcd for $C_{11}H_{11}NO_3$ 205.0739, found 205.0739.

2-Carbethoxy-5-(3-pyrrolyl)pyrrole (6b): This compound was prepared in 49% yield in a manner similar to compound **(6d)**. This material exhibited the following properties: mp 109-111 °C; ^{1}H NMR (DMSO-d_6) δ 1.28 (t, J = 7.0 Hz, 3H), 3.62 (s, 3H), 4.23 (q, J = 7.0 Hz, 2H), 6.20 (m, 1H), 6.47 (m, 1H), 6.70 (m, 1H), 6.75 (m, 1H), 7.26 (s, 1H), and 12.2 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 16.6, 38.3, 62.1, 107.8, 108.0, 118.3, 118.9, 120.6, 123.0, 124.8, 136.0, and 163.5; FTIR (KBr pellet) 3330, 1655, 1313, 1155 cm^{-1}; HRMS calcd for $C_{12}H_{14}N_2O_2$ 218.1055, found 218.1059.

2-Carbethoxy-5-(2-pyrrolyl)pyrrole (6c): This compound was prepared in 35% yield in a manner similar to compound **(6d)**. This material exhibited the following properties: mp 75-77 °C; ^{1}H NMR (DMSO-d_6) δ 1.29 (t, J = 7.0 Hz, 3H), 3.69 (s, 3H), 4.25 (q, J = 7.0 Hz, 2H), 6.03 (m, 1H), 6.30 (m, 1H), 6.47 (m, 1H), 6.83 (m, 2H), and 11.8 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 16.3, 37.0, 61.2, 108.9, 109.8, 110.9, 118.0, 123.6, 126.1, 126.8, 131.9, and 162.1; FTIR (KBr pellet) 3310, 1691, 1296, 1240 cm^{-1}; HRMS calcd for $C_{12}H_{14}N_2O_2$ 218.1055, found 218.1058.

2-Carbethoxy-1-methyl-5-(3-thienyl)pyrrole (7d): A 100 mL three-neck round-bottom flask was equipped with a stir bar, condenser and placed under nitrogen. Into the flask was placed 0.44 g (11 mmol) of a 60% mineral oil dispersion of sodium hydride which was washed twice with dry hexane. The hexane was removed by cannula and 40 mL of dry DMF was added to the flask followed by 0.67 g (4.3 mmol) of sarcosine ethyl ester hydrochloride and 1.00 g (2.9 mmol) of chloropropeniminium salt . The reaction was heated at 100 °C overnight. The reaction was cooled to rt and the solvent was removed *in vacuo*. The residue was partitioned several times between water and chloroform. The combined chloroform extracts were dried and concentrated. The crude product was passed through a short plug of silical gel and purified by radial chromatography using a gradient elution of hexane and ethyl acetate. A 49% yield (0.33 g) of a liquid was obtained. This compound exhibited the following properties: bp 98 °C at 0.05 torr; ^{1}H NMR (DMSO-d_6) δ 1.29 (t, J = 7.1 Hz, 3H), 3.81 (s, 3H), 4.23 (q, J = 7.1 Hz, 2H), 6.31 (d, J = 4.0 Hz, 1H), 6.92 (d, J = 4.0 Hz,

1H), 7.35 (m, 1H), and 7.69-7.74 (m, 2H); ^{13}C NMR (DMSO-d_6) δ 16.1, 35.9, 61.2, 110.6, 119.0, 124.5, 125.9, 128.6, 130.1, 133.7, 138.1, and 162.3; FTIR (CCl_4) 3106, 1698, 1247, 1108 cm^{-1}; HRMS calcd for $C_{12}H_{13}NO_2S$ 235.0667, found 235.0677.

2-Carbethoxy-5-(2-furyl)-1-methylpyrrole (7a): This compound was prepared in 55% yield in a manner similar to compound (**7d**). This material exhibited the following properties: bp 79 °C at 0.1 torr; ^{1}H NMR (DMSO-d_6) δ 1.29 (t, J = 7.1 Hz, 3H), 4.01 (s, 3H), 4.24 (q, J = 7.1 Hz, 2H), 6.45 (d, J = 4.0 Hz, 1H), 6.66 (m, 1H), 6.81 (m, 1H), 6.93 (d, J = 4.0 Hz, 1H), and 7.82 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 16.1, 35.9, 61.4, 109.9, 110.6, 113.6, 119.2, 124.9, 133.0, 145.0, 147.2, and 162.2; FTIR (CCl_4) 3109, 1702, 1248, 1109 cm^{-1}; HRMS calcd for $C_{12}H_{13}NO_3$ 219.0895, found 219.0895.

2-Carbethoxy-1-methyl-5-(3-pyrrolyl)pyrrole (7b): This compound was prepared in 67% yield in a manner similar to compound (**7d**). This material exhibited the following properties: bp 108 °C at 0.1 torr; ^{1}H NMR (DMSO-d_6) δ 1.27 (t, J = 7.0 Hz, 3H), 3.67 (s, 3H), 3.90 (s, 3H), 4.20 (q, J = 7.0 Hz, 2H), 6.11 (d, J = 3.9 Hz, 1H), 6.26 (m, 1H), 6.82 (m, 1H), 6.84 (d, J = 3.9 Hz, 1H), and 7.04 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 16.2, 35.6, 37.6, 60.9, 108.4, 110.1, 115.8, 119.4, 122.8, 123.0, 124.4, 139.4, and 162.4; FTIR (CCl_4) 3108, 1691, 1299, 1244, 1105 cm^{-1}; HRMS calcd for $C_{13}H_{16}N_2O_2$ 232.1212, found 232.1216.

2-Carbethoxy-1-methyl-5-(2-pyrrolyl)pyrrole (7c): This compound was prepared in 47% yield in a manner similar to compound (**7d**). This material exhibited the following properties: bp 97 °C at 0.1 torr; ^{1}H NMR (DMSO-d_6) δ 1.29 (t, J = 7.1 Hz, 3H), 3.49 (s, 3H), 3.72 (s, 3H), 4.25 (q, J = 7.1 Hz, 2H), 6.13 (m, 1H), 6.21 (m, 1H), 6.25 (d, J = 4.0 Hz, 1H), and 6.94 (m, 2H); ^{13}C NMR (DMSO-d_6) δ 16.2, 35.6, 36.0, 61.2, 109.2, 112.1, 113.0, 118.6, 124.4, 124.6, 125.9, 134.1, and 162.3; FTIR (CCl_4) 3105, 1702, 1247, 1108 cm^{-1}; HRMS calcd for $C_{13}H_{16}N_2O_2$ 232.1212, found 232.1216.

2-Carbethoxy-1-methyl-3-(3-thienyl)pyrrole (8d): A 100 mL three-neck round-bottom flask was equipped with a stir bar, condenser and placed under nitrogen. Into the flask was placed 0.56 g (14 mmol) of a 60% mineral oil dispersion of sodium hydride which was washed twice with dry hexane. The hexane was removed by cannula and 40 mL of dry DMF was added to the flask followed by 1.09 g (7.0 mmol) of sarcosine ethyl ester hydrochloride and 1.00 g (2.8 mmol) of vinamidinium salt . The reaction was stirred at room temperature for 1 h and heated at 100 °C overnight. The reaction was cooled to room temperature and the solvent was removed *in vacuo*. The residue was partitioned several times between water and chloroform. The combined chloroform extracts were dried over anhydrous $MgSO_4$ and concentrated. The crude product was passed through a short plug of silical gel and purified by radial chromatography using a gradient elution of hexane and

ethyl acetate. A 48% yield (0.32 g) of a liquid was obtained. This compound exhibited the following properties: bp 80 °C at 0.1 torr; ^{1}H NMR (DMSO-d_6) δ 1.16 (t, J = 7.1 Hz, 3H), 3.84 (s, 3H), 4.16 (q, J = 7.1 Hz, 2H), 6.22 (d, J = 2.6 Hz, 1H), 7.09 (d, J = 2.6 Hz, 1H), 7.22 (m, 1H), and 7.40-7.50 (m, 2H); ^{13}C NMR (DMSO-d_6) δ 15.7, 39.1, 61.3, 111.4, 120.1, 124.1, 126.0, 128.9, 130.8, 131.3, 138.0, and 162.7; FTIR (CCl_4) 3108, 1690, 1278, 1108 cm^{-1}; HRMS calcd for $C_{12}H_{13}NO_2S$ 235.0667, found 235.0671.

2-Carbethoxy-3-(2-furyl)-1-methylpyrrole (8a): This compound was prepared in 61% yield in a manner similar to compound **(8d)**. This material exhibited the following properties: bp 76 °C at 0.05 torr; ^{1}H NMR (DMSO-d_6) δ 1.28 (t, J = 7.1 Hz, 3H), 3.85 (s, 3H), 4.26 (q, J = 7.1 Hz, 2H), 6.40 (d, J = 2.6 Hz, 1H), 6.52 (m, 1H), 6.83 (m, 1H), 7.13 (d, J = 2.6 Hz, 1H), and 7.65 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 15.9, 39.3, 61.7, 109.2, 110.0, 113.2, 119.5, 123.8, 131.2, 143.3, 150.7, and 162.3; FTIR (CCl_4) 3108, 1692, 1277, 1109 cm^{-1}; HRMS calcd for $C_{12}H_{13}NO_3$ 219.0895, found 219.0900.

2-Carbethoxy-1-methyl-3-(3-pyrrolyl)pyrrole (8b): This compound was prepared in 45% yield in a similar manner to compound **(8d)**. This material exhibited the following properties: bp 114 °C at 0.1 torr; ^{1}H NMR (DMSO-d_6) δ 1.29 (t, J = 7.1 Hz, 3H), 3.61 (s, 3H), 3.79 (s, 3H), 4.23 (q, J = 7.1 Hz, 2H), 6.16 (m, 1H), 6.25 (m, 1H), 6.63 (m, 1H), 6.98 (m, 1H), and 7.07 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 16.4, 38.2, 40.2, 61.8, 111.1, 111.7, 120.0, 120.4, 123.0, 123.7, 130.6, and 164.0; FTIR (CCl_4) 3106, 1686, 1414, 1301, 1262, 1107 cm^{-1}; HRMS calcd for $C_{13}H_{16}N_2O_2$ 232.1212, found 232.1220.

2-Carbethoxy-1-methyl-3-(2-pyrrolyl)pyrrole (8c): This compound was prepared in 50% yield in a manner similar to compound **(8d)**. This material exhibited the following properties: bp 80 °C at 0.1 torr; ^{1}H NMR (DMSO-d_6) δ 1.02 (t, J = 7.0 Hz, 3H), 3.36 (s, 3H), 3.88 (s, 3H), 4.03 (q, J = 7.0 Hz, 2H), 5.86 (m, 1H), 5.98 (m, 1H), 6.07 (d, J = 2.1 Hz, 1H), 6.73 (s, 1H), and 7.12 (d, J = 2.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 16.0, 36.2, 39.7, 61.7, 108.9, 110.5, 113.7, 123.1, 123.5, 126.3, 130.2, 130.8, and 163.4; FTIR (CCl_4) 3105, 1692, 1409, 1208, 1111 cm^{-1}; HRMS calcd for $C_{13}H_{16}N_2O_2$ 232.1212, found 232.1218.

2-Carbethoxy-1-methyl-3-(2-thienyl)pyrrole (8e): This compound was prepared in 44% yield in a manner similar to compound **(8d)**. This material exhibited the following properties: bp 74 °C at 2 torr; ^{1}H NMR (DMSO-d_6) δ 1.20 (t, J = 7.1 Hz, 3H), 3.84 (s, 3H), 4.20 (q, J = 7.1 Hz, 2H), 6.27 (m, 1H), 7.04 (m, 1H), 7.11 (m, 1H), 7.24 (m, 1H), and 7.45 (m, 1H); ^{13}C NMR (DMSO-d_6) δ 15.7, 39.2, 61.5, 111.7, 120.1, 126.5, 126.8, 128.2, 128.6, 130.9, 139.0, and 162.4; FTIR (CCl_4) 3106, 1695, 1412, 1276, 1113 cm^{-1}; HRMS calcd for $C_{12}H_{13}NO_2S$ 235.0667, found 235.0663.

7-(3-Thienyl)-1,2,4-triazolo[1,5-*a*]pyrimidine (9d): This compound was prepared in 58% yield in a manner similar to compound (**5d**). This material exhibited the following properties: mp 173-175 °C; ^{1}H NMR ($CDCl_3$) δ 7.38 (d, J = 4.4 Hz, 1H), 7.55 (dd, J = 2.8 Hz, J = 5.4 Hz, 1H), 7.83 (d, J = 5.4 Hz, 1H), 8.61 (s, 1H), 8.85 (d, J = 4.4 Hz, 1H), and 9.14 (d, J = 2.8 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 109.7, 129.3, 129.6, 131.7, 135.1, 143.4, 156.6, 157.4, and 157.6; FTIR (KBr pellet) 3110, 1604, 1540, 797 cm^{-1}; HRMS calcd for $C_9H_6N_4S$ 202.0313, found 202.0314.

7-(2-Furyl)-1,2,4-triazolo[1,5-*a*]pyrimidine (9a): This compound was prepared in 53% yield in a manner similar to compound (**5d**). This material exhibited the following properties: mp 211-212 °C; ^{1}H NMR ($CDCl_3$) δ 6.77 (m, 1H), 7.55 (d, J = 4.8 Hz, 1H), 7.78 (m, 1H), 8.23 (d, J = 3.6 Hz, 1H), 8.61 (s, 1H), and 8.85 (d, J = 4.8 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 106.4, 115.6, 122.2, 138.3, 144.3, 150.0, 156.4, 157.1, and 157.7; FTIR (KBr pellet) 3121, 1620, 1542, 775 cm^{-1}; HRMS calcd for $C_9H_6N_4O$ 186.0542, found 186.0545.

7-(3-Pyrrolyl)-1,2,4-triazolo[1,5-*a*]pyrimidine (9b): This compound was prepared in 65% yield in a manner similar to compound (**5d**). This material exhibited the following properties: mp 179-181 °C; ^{1}H NMR (DMSO-d_6) δ 3.82 (s, 3H), 7.07 (m, 1H), 7.11 (m, 1H), 7.64 (d, J = 5.0 Hz, 1H), 8.39 (m, 1H), 8.74 (s, 1H), and 8.75 (d, J = 5.0 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 38.2, 106.4, 110.7, 114.1, 126.4, 130.3, 145.1, 155.5, 157.1, and 157.5; FTIR (KBr pellet) 3101, 1606, 1558, 810cm^{-1}; HRMS calcd for $C_{10}H_9N_5$ 199.0858, found 199.0868.

7-(2-Pyrrolyl)-1,2,4-triazolo[1,5-*a*]pyrimidine (9c): This compound was prepared in 42% yield in a manner similar to compound (**5d**). This material exhibited the following properties: mp 149-150 °C; ^{1}H NMR ($CDCl_3$) δ 3.83 (s, 3H), 6.39 (m, 1H), 7.00 (m, 1H), 7.05 (d, J = 4.7 Hz, 1H), 7.21 (m, 1H), 8.54 (s, 1H), and 8.79 (d, J = 4.7 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 38.2, 109.8, 110.5, 120.0, 123.4, 132.2, 141.6, 155.9, 157.0, and 157.5; FTIR (KBr pellet) 3108, 1604, 1555, 729 cm^{-1}; HRMS calcd for $C_{10}H_9N_5$ 199.0858, found 199.0859.

7-(2-Thienyl)-1,2,4-triazolo[1,5-*a*]pyrimidine (9e): This compound was prepared in 85% yield in a manner similar to compound (**5d**). This material exhibited the following properties: mp 209-211 °C; ^{1}H NMR (DMSO-d_6) δ 7.45 (dd, J = 4.0 Hz, J = 5.0 Hz, 1H), 8.03 (d, J = 5.0 Hz, 1H), 8.22 (d, J = 5.0 Hz, 1H), 8.60 (d, J = 4.0 Hz, 1H), 8.85 (s, 1H), and 8.91 (d, J = 5.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 107.7, 130.5, 132.5, 135.0, 135.7, 143.8, 155.7, 157.7, and 158.1; FTIR (KBr pellet) 3119, 1635, 1573, 840 cm^{-1}; HRMS calcd for $C_9H_6N_4S$ 202.0313, found 202.0327.

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