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Solvent controlled divergent syntheses of polysubstituted pyrroles and pyrrolo[2,3-*b*]-1,4-thiazines

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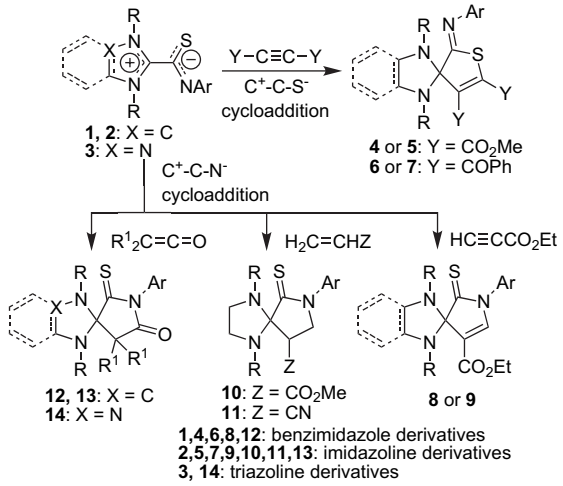
ABSTRACT

The reaction of 2-imidazolyl carbene-derived 2-arylthiocarbamoyl imidazolium salts with ethyl propiolate proceeded via the solvent dependent tandem [3+2] cycloaddition and subsequent ring transformation processes. While the reaction in butanone yielded 3-amino-2-vinylthiopyrroles as the major products, use of benzene as the solvent led to the predominant formation of pyrrolo[2,3-*b*][1,4]thiazines. This work disclosed a unique ring transformation of imidazoline-spiro-pyrrolines to pyrrolo[2,3-*b*][1,4]thiazines, which provides a simple route to both multifunctional pyrroles and pyrrolo[2,3-*b*][1,4]thiazines that are otherwise difficult to synthesize.

1. Introduction

Nucleophilic *N*-heterocyclic carbenes including 2-benzimidazolyl, 2-imidazolinyl, 2-imidazolyl, 3-triazolyl, and 2-thiazolyl carbenes are known to react with aryl isothiocyanates to form stable zwitterions, 2-thiocarbamoyl benzimidazolium,[1] -imidazolinium,[2,3] -imidazolium,[4] -triazolium,[5] and -thiazolium inner salts,[6,7] respectively. Recently, we found that these *N*-heterocyclic carbene-derived inner salts are unique ambident bis-dipolar compounds.[8,9] These zwitterions can act as either C^+–C–S^- or C^+–C–N^- 1,3-dipoles toward different dipolarophiles, and the site selectivity of reaction is controlled by the nature of dipolarophiles. For example, 2-arylthiocarbamoyl benzimidazolium **1** and imidazolinium salts **2** reacted with dimethyl acetylenedicarboxylate (DMAD) or dibenzoylacetylene to give spiro-thiophene derivatives **4**–**7** via the C^+–C–S^- cycloaddition pathway,[8a,b] whereas in the reaction with ethyl propiolate, methyl acrylate, acrylonitrile or ketenes, they behaved as C^+–C–N^- dipolar species and produced spiro-pyrroles **8**–**14** predominantly (Scheme 1).[8a–c]

Our studies have also revealed that the outcome of the [3+2] cycloaddition reactions of *N*-heterocyclic carbene-derived dipoles was also regulated by the structures of carbenes, exemplified by the reactions between different carbene-derived 1,3-dipoles with DMAD. As described in Scheme 1, 2-arylthiocarbamoyl benzimidazolium **1** or imidazolinium salts **2** reacted with DMAD to produce the expected [3+2] cycloaddition products, spiro-thiophenes **4** or **5**.[8a,b] However, the same reaction of 2-arylthiocarbamoyl imidazolium salts **15** or thiazolium salts **18** with DMAD afforded imidazoline substituted olefins **17**[9a] or thieno[2,3-*b*]pyrazines **20**,[9b] respectively (Scheme 2). Although both the monoheterocycle **17** and the fused heterocycle **20** can be derived,



Scheme 1. The reaction of 2-arylthiocarbamoyl benzimidazolium **1**, imidazolinium **2** or triazolium salts **3** with electron-deficient alkynes, alkenes or ketenes.

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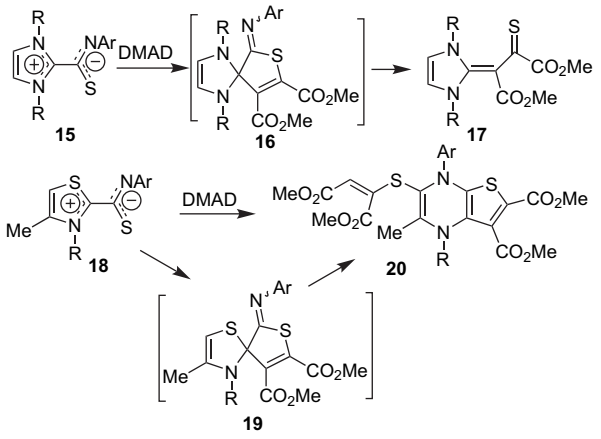


Scheme 2. The reaction of 2-arylthiocarbamoyl imidazolium salts **15** or thiazolium salts **18** with DMAD.

respectively, from the expected spiro-intermediates **16** and **19**, it was surprising that the two structurally similar intermediates, imidazoline-spiro-dihydrothiophene **16** and thiazoline-spiro-dihydrothiophene **19**, followed dramatically different ring transformation pathways. The imidazoline substituted olefin **17** was apparently derived from fragmentation of the thiophene ring of **16**. On the contrary, the thieno[2,3-*b*]pyrazine **20** was formed by expansion of the thiazole ring of spiro-intermediate **19**.

In order to gain a better understanding of the chemistry of *N*-heterocyclic carbene-derived ambident dipolar compounds and to further explore their synthetic applications, we undertook the current study of the reaction of 2-thiocarbamoyl imidazolium inner salts with ethyl propiolate. Interestingly, the reaction produced, predominantly, novel 3-amino-2-vinylthiopyrrole or pyrrolo[2,3-*b*]-1,4-thiazine derivatives in different solvents. We herein report our observations.

2. Results and discussion

In this work, 2-arylthiocarbamoyl imidazolium salts **15** were prepared from the reaction of aryl isothiocyanates with imidazole carbenes generated in situ from the imidazolium salts with sodium hydride.[9a] We started our investigation with the reaction between *N*,*N*′-dibenzyl-2-phenylthiocarbamoyl imidazolium salt **15a** and ethyl propiolate. Initially, the reaction with **15a** was examined in dichloroethane. Under refluxing condition, interestingly, two isomeric substituted pyrroles **22a** and **23a**, and pyrrolo[2,3-*b*][1,4]thiazine **24a** were isolated, albeit in very low yields (Scheme 3, R=Bn; Table 1, entries 1 and 2).

To optimize the reaction conditions, the reaction was then carried out by varying solvent, temperature, and the ratio of starting materials. The outcome of the reaction was found to be strongly dependent upon the solvent employed. To our delight, by using different solvents, not only the yield of major product can be significantly improved, but also the selectivity of the reaction can be reversed. For example, as shown in Table 1, the less polar solvents such as benzene and THF allowed selective formation of

Table 1
Reaction of *N*,*N*′-dibenzyl-2-phenylthiocarbamoyl imidazolium inner salt **15a** with ethyl propiolate under different conditions

Entry	Reaction conditions				Yield of product (%)		
	15a/**21** R=Bn	Sol.	Temp[a] (°C)	*T* (h)	**22a**	**23a**	**24a**
1	1:3	DCE[b]	70–80	5	14	9	7
2	1:5	DCE	70–80	4	19	8	12
3	1:3	THF	60–70	5	16	6	41
4	1:1	Benzene	60–70	18	6	3	26
5	1:3	Benzene	60–70	5	12	6	46
6	1:5	Benzene	80–90	3	15	6	35
7	1:3	Acetone	50–60	5	35	18	7
8	1:3	Butanone	70–80	5	41	6	5
9	1:5	Butanone	70–80	5	50	6	—
10	1:5	CH_3CN	70–80	3	21	18	7

[a] Oil bath temperature.
[b] DCE=1,2-dichloroethane.

pyrrolo[2,3-*b*][1,4]thiazine **24a** (entries 3–6). On the contrary, the more polar solvents including acetone and butanone favored the formation of pyrrole **22a** (entries 7–9). Other conditions, such as reaction temperature and ratio of starting materials, did affect the yields of products, but no reversal of the selectivity of the reaction was observed. It should be pointed out that the product **24a** was somewhat unstable on silica gel and in solvents, probably due to its water sensitive imino group. Thus, the isolation of **24a** has to be performed quickly using flash chromatography.

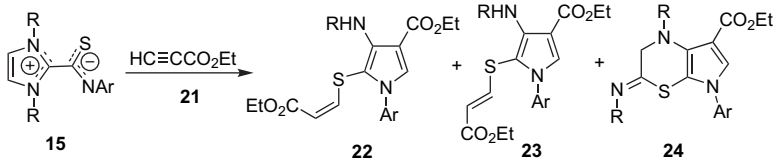
The scope of the reaction was then studied by using dipoles **15** bearing different substituents. In order to allow selective preparation of 3-amino-2-vinylthiopyrroles **22**, the reactions of imidazolium salts **15** with ethyl propiolate were performed in butanone under refluxing condition. As compiled in Table 2, as for the formation of 3-amino-2-vinylthiopyrroles, the nature of the substituents on the imidazolium salts has a marginal effect on the reaction. All dipoles **15a**–**15i** bearing either alkyl or benzyl groups reacted with ethyl propiolate smoothly to produce (*Z*)-2-vinylthiopyrroles **22** in 44–53% yields, along with (*E*)-isomer **23** (6–15%), and sometimes pyrrolothiazines **24** (5–8%) was produced in these reactions.

Multifunctional pyrroles constitute the key structural feature of many natural products[10] and bioactive synthetic compounds.[11]

Table 2
Reaction of 2-phenylthiocarbamoyl imidazolium salts **15** with ethyl propiolate in butanone

Entry	**15**	R, Ar	Yield of product[a] (%)		
1	**15a**	Bn, Ph	**22a**, 50	**23a**, 6	**24a**, —[c]
2	**15b**	*p*-ClBn, Ph	**22b**, 44	**23b**, 12	**24b**, —[c]
3	**15c**	3,4-Cl_2Bn, Ph	**22c**, 53	**23c**, 15	**24c**, 8
4	**15d**	Bn, *p*-CH_3OPh	**22d**, 48	**23d**, —[b]	**24d**, —[c]
5	**15e**	Bn, *p*-ClPh	**22e**, 52	**23e**, —[b]	**24e**, 6
6	**15f**	*p*-ClBn, *p*-ClPh	**22f**, 53	**23f**, —[b]	**24f**, 6
7	**15g**	3,4-Cl_2Bn, *p*-CH_3Ph	**22g**, 51	**23g**, —[b]	**24g**, 5
8	**15h**	*i*-Pr, Ph	**22h**, 48	**23h** —[b]	**24h**, —[c]
9	**15i**	*n*-Bu, Ph	**22i**, 49	**23i**, —[b]	**24i**, —[c]

[a] Reaction conditions: **15**/**21**=1:5, butanone, 80–85 °C, 3–8 h.
[b] *E*-isomer **23** was isolated in 10–15% yields without characterization.
[c] Pyrrolothiazine **24** was not isolated.



Scheme 3. The reaction of 2-arylthiocarbamoyl imidazolium inner salts **15** with ethyl propiolate.

They are also important synthetic intermediates in construction of more complicated heterocycles.[12] Our current study provides a simple route to 3-amino-2-vinylthiopyrrole-4-carboxylates **22**, which are valuable intermediates for further elaborations.

Our second intention was to optimize the formation of the pyrrolo[2,3-*b*][1,4]thiazines **24** by use of benzene as solvent. As illustrated in Table 3, when reacted with ethyl propiolate in dry benzene at 60–70 °C, different benzyl-substituted dipoles **15** produced pyrrolothiazines **24** in 37–49% yields, along with small amounts of pyrroles **22** and **23**. On the other hand, it was observed that the alkyl group substituted pyrrolothiazines, such as **24h** and **24i** (R=*iso*-propyl and *n*-butyl), were less stable than the benzyl-substituted analogs. They partially decomposed during the isolation and purification process, and the pure products **24h** and **24i** were not isolated.

The structures of all products were elucidated on the basis of spectroscopic data and microanalysis. The NMR spectra, mass spectral data, and elemental analyses indicated that the products **22** and **23** were isomers derived from one dipole and two ethyl propiolate molecules, while the products **24** were the [1+1] adducts of dipoles **15** with ethyl propiolate. Since spectroscopic data did not allow full verification of the structures, X-ray diffraction analyses were carried out to unambiguously assign that the product **22a** was (*Z*) ethyl 3-benzylamino-2-(2-ethoxycarbonylvinylthio)-1-phenylpyrrole-4-carboxylate and **24a** was ethyl 1-benzyl-3-benzylimino-5-phenyl-2,3-dihydropyrrolo[2,3-*b*][1,4]thiazine-7-carboxylate (Fig. 1).[13] The *Z* and *E* isomers, **22** and **23**, can be easily differentiated by the *J* value of two vinyl protons in the ^{1}H NMR spectra.

The formation of the fused pyrrolo[2,3-*b*][1,4]thiazine **24** from the 2-thiocarbamoyl imidazolium salt **15** with ethyl propiolate was unexpected, although the ethoxycarbonyl-substituted pyrrole substructure was conceivable based on the [3+2] cycloaddition between the C^+–C–N dipolar moiety of **15** and ethyl propiolate. The proposed mechanism for the formation of substituted pyrroles **22**, **23** and pyrrolo[2,3-*b*][1,4]thiazines **24** is indicated in Scheme 4. [3+2] Cycloaddition of the C^+–C–N^- dipole of **15** with ethyl propiolate forms imidazoline-spiro-pyrroline intermediate **25**. Selective C–N bond cleavage of the imidazoline ring of **25** gives rise to a zwitterion **26A**, which is tautomerized with **26B**. Electrocyclization reaction of **26A** results in the formation of the fused-ring intermediate **27**, which isomerizes into the pyrrolo[2,3-*b*][1,4]thiazine derivative **24**. S-Nucleophilic addition of zwitterion **26B** to ethyl propiolate forms a pair of 2-vinylthio-3-pyrryl iminium intermediates **30** and **31**. Hydrolysis of iminium salts **30** and **31** with a trace amount of water in the solvent and/or in the chromatographic elution leads to the formation of pyrroles **22** and **23** (Scheme 4). The fact that the polar solvents favored the formation of pyrroles **22** supported this mechanism, since polar solvents should stabilize the zwitterion intermediates **26A** and **26B**, and therefore should slow down the electrocyclization.

Table 3
Reaction of 2-phenylthiocarbamoyl imidazolium salts **15** with ethyl propiolate in benzene

Entry	**15**	R, Ar	Yield of product[a] (%)		
1	**15a**	Bn, Ph	**22a**, 12	**23a**, 6	**24a**, 46
2	**15b**	*p*-ClBn, Ph	**22b**, 10	**23b**, 6	**24b**, 49
3	**15c**	3,4-Cl_2Bn, Ph	**22c**, 10	**23c**, 7	**24c**, 37
4	**15d**	Bn, *p*-CH_3OPh	**22d**, 14	**23d**, —[b]	**24d**, 43
5	**15e**	Bn, *p*-ClPh	**22e**, 11	**23e**, —[b]	**24e**, 44
6	**15f**	*p*-ClBn, *p*-ClPh	**22f**, 10	**23f**, —[b]	**24f**, 49
7	**15g**	3,4-Cl_2Bn, *p*-CH_3Ph	**22g**, 8	**23g**, —[b]	**24g**, 46
8	**15j**	*p*-ClBn, *p*-CH_3Ph	**22j**, 10	**23j**, —[b]	**22j**, 42
9	**15k**	3,4-Cl_2Bn, *p*-CH_3OPh	**22k**, 12	**23k**, 8	**24k**, 37

[a] Reaction conditions: **15**/**21**=1:3, 60–70 °C, 5–8 h.
[b] By-products **23** were isolated in 5–8% yields without full characterization.

Comparison of the current reactions with those between different heterocyclic carbene-derived 1,3-dipoles and various dipolarophiles described in our earlier publications[8,9] reveals some significant observations. Firstly, different ambident dipoles derived from various *N*-heterocyclic carbenes and aryl isothiocyanates have the same chemo-selectivity between their C–C–S or C–C–N species toward the same dipolarophile. Secondly, among the [3+2] cycloaddition reactions that we have examined, those of 2-thiocarbamoyl benzimidazolium, -imidazolinium, and -triazolium inner salts with various dipolarophiles always produce the expected cycloadducts, spiro-thiophenes or spiro-pyrroles.[8] On the other hand, the reaction of 2-thiocarbamoyl imidazolium[9a] and -thiazolium inner salts[9b] with different dipolarophiles generally afford mono- or fused-heterocycles via ring transformation of the spiro-intermediates. Finally, on the basis of the transformation products of the spiro-intermediates, thiazoline-spiro-dihydrothiophene **19**, imidazoline-spiro-dihydrothiophene **16**, and imidazoline-spiro-pyrroline **25**, the ring-opening aptitude in these spiro-heterocycles is thiazoline>dihydrothiophene>imidazoline>pyrroline.

In summary, we have shown that the 2-imidazolyl carbene-derived 2-thiocarbamoyl imidazolium salts are able to undergo different tandem reactions with ethyl propiolate. The reaction was highly solvent dependent. In non-polar solvent such as benzene, the reaction proceeded via a [3+2] cycloaddition followed by a novel ring transformation of imidazoline-spiro-pyrroline to produce fused-ring pyrrolo[2,3-*b*][1,4]thiazine as the major product. When reaction was performed in butanone, however, the reaction yielded predominantly 3-amino-2-vinylthiopyrrole derivatives. This work not only enriches the chemistry of 1,3-dipolar cycloaddition and ring transformation reactions, but also provides a very simple synthetic route to pyrrolo[2,3-*b*][1,4]thiazine and polyfunctionalized pyrrole derivatives, which are not readily prepared by other methods and are potentially amenable to further transformations.

3. Experiment section

3.1. General

Melting points are uncorrected. ^{1}H NMR (500 or 300 MHz) and ^{13}C NMR (125 or 75 MHz) were recorded in the solvent as indicated. Benzene was dried by distilling from sodium benzophenone ketyl, while the commercial butanone was used directly. The 2-arylthiocarbamoyl imidazolium inner salts **15** were prepared according to our earlier publication.[9a]

3.2. General procedure for the reaction of 2-arylthiocarbamoyl imidazolium inner salts 15 with ethyl propiolate in butanone

At ambient temperature, the 2-arylthiocarbamoyl imidazolium inner salts **15** (1 mmol) were mixed with ethyl propiolate (5 mmol) in butanone (30 mL). The mixture was stirred at 80–85 °C for 3–8 h. After removal of the solvent under vacuum, the products **22**–**24** were isolated by chromatography on silica gel eluting with petroleum ether and ethyl acetate (8:1).

3.3. General procedure for the reaction of 2-arylthiocarbamoyl imidazolium inner salts 15 with ethyl propiolate in benzene

At ambient temperature, the 2-arylthiocarbamoyl imidazolium inner salts **15** (1 mmol) were mixed with ethyl propiolate (3 mmol) in dry benzene (30 mL). The mixture was stirred at 60–65 °C for 5–8 h under nitrogen atmosphere. After removal of the solvent under vacuum, the products **24** and the mixture of by-products **22** and **23**

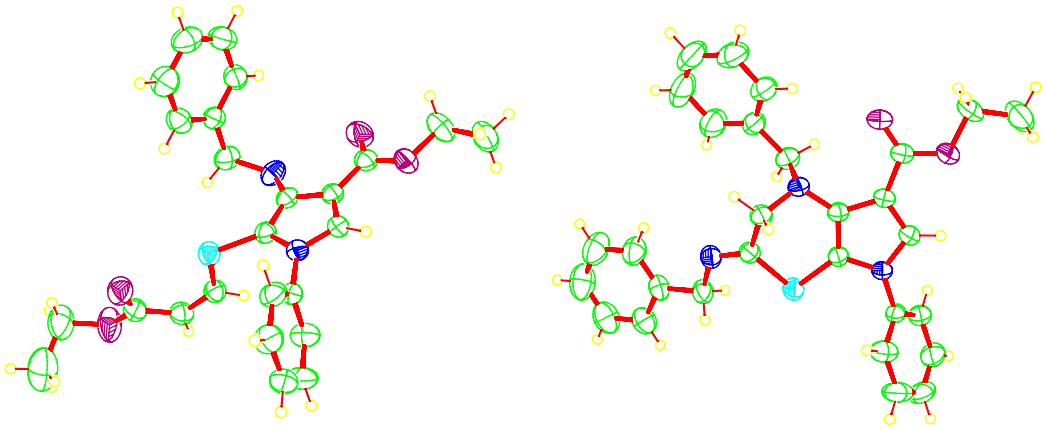


Figure 1. The ORTEP drawing of single-crystal structures of compounds **22a** and **24a**.

were isolated by flash chromatography on a silica gel column eluting with a mixture of petroleum ether (30–60 °C) and ethyl acetate (5:1 to 3:1). The two isomers **22** and **23** were further separated by chromatography a silica gel column (petroleum ether/ethyl acetate=8:1).

*3.3.1. (Z) Ethyl 4-benzylamino-5-(2-ethoxycarbonylvinylthio)-1-phenyl-1H-pyrrole-3-carboxylate (**22a**)*

Yield 50% (butanone), 12% (benzene), mp 83–84 °C; IR ν (cm^{-1}): 3334, 3116, 1698, 1681; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.36–7.44 (m, 6H), 7.21–7.33 (m, 5H), 6.67 (d, J=10.1 Hz, 1H), 6.00 (br, 1H), 5.59 (d, J=10.1 Hz, 1H), 4.71 (s, 2H), 4.30 (q, J=7.1 Hz, 2H), 4.16 (q, J=7.1 Hz, 2H), 1.33 (t, J=7.1 Hz, 3H), 1.27 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 166.2, 165.3, 153.5, 143.0, 140.2, 138.4, 129.1, 128.4, 127.9, 127.6, 126.9, 126.6, 113.1, 105.0, 104.2, 60.2, 59.7, 49.5, 14.5, 14.3; MS (ESI): 451 (M+1). Anal. Calcd for $C_{25}H_{26}N_2O_4S$: C, 66.64; H, 5.82; N, 6.22. Found: C, 66.72; H, 5.79; N, 6.15.

*3.3.2. (E) 4-Benzylamino-5-(2-ethoxycarbonylvinylthio)-1-phenyl-1H-pyrrole-3-carboxylate (**23a**)*

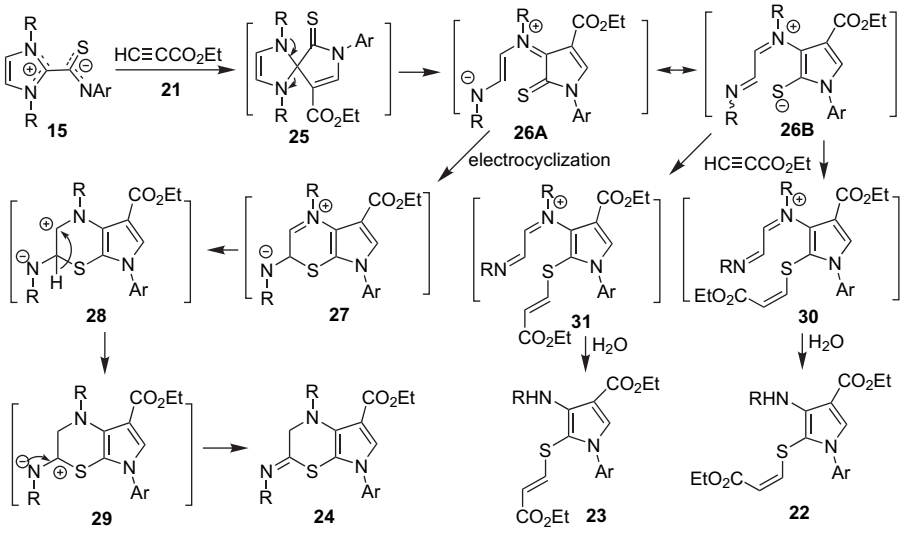
Yield 6% (benzene or butanone), mp 64–65 °C; IR ν (cm^{-1}): 3396, 1704, 1683; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.39 (s, 1H), 7.29–7.31 (m, 3H), 7.22–7.26 (m, 3H), 7.14–7.19 (m, 5H), 6.09 (br, 1H), 5.31 (d, J=14.6 Hz, 1H), 4.59 (s, 2H), 4.22 (q, J=7.1 Hz, 2H), 4.05 (q, J=7.1 Hz, 2H), 1.26 (t, J=7.1 Hz, 3H), 1.18 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 165.3, 165.1, 147.7, 144.5, 140.2, 138.2, 129.7, 128.9, 128.4, 128.3, 127.4, 126.9, 126.3, 116.0, 104.7, 95.5, 60.3, 59.7, 48.6, 14.5, 14.3; MS (ESI): 451 (M+1). Anal. Calcd for $C_{25}H_{26}N_2O_4S$: C, 66.64; H, 5.82; N, 6.22. Found: C, 66.69; H, 5.83; N, 6.14.

*3.3.3. Ethyl 1-benzyl-3-(benzylimino)-5-phenyl-1,2,3,5-tetrahydropyrrolo[2,3-b][1,4]thiazine-7-carboxylate (**24a**)*

Yield 46% (benzene), mp 141–142 °C; IR ν (cm^{-1}): 1708, 1612; ^1H NMR (500 MHz, C_6D_6) δ (ppm): 7.91 (d, J=7.2 Hz, 2H), 7.55 (s, 1H), 7.47 (d, J=7.5 Hz, 2H), 7.33 (d, J=7.6 Hz, 2H), 7.29 (d, J=8.2 Hz, 2H), 7.19–7.24 (m, 2H), 7.02–7.13 (m, 5H), 4.63 (s, 2H), 4.52 (s, 2H), 4.37 (q, J=7.1 Hz, 2H), 4.07 (s, 2H), 1.23 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 163.3, 154.5, 138.8, 137.9, 137.6, 132.3, 129.74, 129.67, 128.5, 128.2, 127.8, 127.3, 127.0, 126.8, 124.4, 112.2, 111.1, 59.9, 57.7, 57.5, 56.5, 14.6; MS (ESI): 482 (M+1). Anal. Calcd for $C_{29}H_{27}N_3O_2S$: C, 72.32; H, 5.65; N, 8.73. Found: C, 72.02; H, 5.71; N, 8.75.

*3.3.4. (Z) Ethyl 4-(4-chlorobenzyl)amino-5-(2-ethoxycarbonyl vinylthio)-1-phenyl-1H-pyrrole-3-carboxylate (**22b**)*

Yield 44% (butanone), 10% (benzene), mp 100–101 °C; IR ν (cm^{-1}): 3382, 1697; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.42 (s, 1H), 7.41–7.44 (m, 2H), 7.38 (t, J=7.2 Hz, 1H), 7.23–7.32 (m, 6H), 6.64 (d, J=10.1 Hz, 1H), 5.60 (d, J=10.1 Hz, 1H), 4.68 (s, 2H), 4.31 (q, J=7.1 Hz,



Scheme 4. The proposed mechanism for the formation of pyrroles **22**, **23** and pyrrolo[2,3-*b*][1,4]thiazines **24**.

2H), 4.17 (q, *J*=7.1 Hz, 2H), 1.36 (t, *J*=7.1 Hz, 3H), 1.28 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 166.2, 165.3, 153.0, 142.2, 138.7, 138.3, 132.6, 129.1, 129.0, 128.5, 128.0, 126.7, 113.2, 105.1, 104.8, 60.2, 59.8, 48.8, 14.5, 14.3; MS (EI): 125 (100), 215 (54), 261 (53), 313 (55), 333 (54), 451 (45), 484 (M^+, 50%). Anal. Calcd for $C_{25}H_{25}ClN_2O_4S$: C, 61.91; H, 5.20; N, 5.78. Found: C, 61.76; H, 5.30; N, 5.71.

*3.3.5. (E) Ethyl 4-(4-chlorobenzyl)amino-5-(2-ethoxycarbonyl-vinylthio)-1-phenyl-1H-pyrrole-3-carboxylate (**23b**)*

Yield 12% (butanone), 6% (benzene), mp 68–69 °C; IR ν (cm^{-1}): 3373, 1701; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.49 (s, 1H), 7.41–7.42 (m, 3H), 7.29 (s, 4H), 7.25 (d, *J*=7.1 Hz, 2H), 7.21 (d, *J*=14.6 Hz, 1H), 6.27 (br s, 1H), 5.35 (d, *J*=14.6 Hz, 1H), 4.66 (s, 2H), 4.33 (q, *J*=7.0 Hz, 2H), 4.17 (q, *J*=7.0 Hz, 2H), 1.37 (t, *J*=7.0 Hz, 3H), 1.29 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 165.3, 165.0, 147.3, 144.1, 138.9, 138.2, 132.5, 129.7, 128.9, 128.6, 128.5, 128.3, 126.3, 116.1, 104.7, 95.6, 60.4, 59.8, 47.7, 14.5, 14.3; HRMS (TOF-EI): 484.1228 (M+1), $C_{25}H_{25}ClN_2O_4S$ required 484.1224.

*3.3.6. Ethyl 1-(4-chlorobenzyl)-3-(4-chlorobenzylimino)-5-phenyl-1,2,3,5-tetrahydropyrrolo[2,3-b][1,4]thiazine-7-carboxylate (**24b**)*

Yield 49% (benzene), mp 151–152 °C; IR ν (cm^{-1}): 1704, 1631, 1623; ^{1}H NMR (500 MHz, C_6D_6) δ (ppm): 7.60 (d, *J*=8.1 Hz, 2H), 7.52 (s, 1H), 7.24–7.26 (m, 3H), 7.15 (d, *J*=8.2 Hz, 2H), 7.05–7.13 (m, 5H), 4.46 (s, 2H), 4.35 (q, *J*=7.1 Hz, 2H), 4.28 (s, 2H), 3.95 (s, 2H), 1.21 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ (ppm): 162.7, 153.5, 138.0, 137.6, 136.8, 133.4, 133.1, 132.8, 131.2, 129.5, 129.1, 128.6, 128.5, 126.9, 124.3, 111.7, 111.6, 59.6, 56.73, 56.68, 56.1, 14.4; MS (EI): 125 (100), 549 (M^+, 1.5%). Anal. Calcd for $C_{29}H_{25}Cl_2N_3O_2S$: C, 63.27; H, 4.58; N, 7.63. Found: C, 63.45; H, 4.96; N, 7.58.

*3.3.7. (Z) Ethyl 4-(3,4-dichlorobenzyl)amino-5-(2-ethoxycarbonyl-vinylthio)-1-phenyl-1H-pyrrole-3-carboxylate (**22c**)*

Yield 53% (butanone), 10% (benzene), mp 123–125 °C; IR ν (cm^{-1}): 3378, 1697, 1684; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.41–7.45 (m, 3H), 7.38 (d, *J*=5.9 Hz, 1H), 7.35 (d, *J*=8.2 Hz, 1H), 7.26 (d, *J*=7.5 Hz, 2H), 7.20 (dd, *J*=8.3, 1.6 Hz, 1H), 6.56 (d, *J*=10.0 Hz, 1H), 5.56 (d, *J*=10.0 Hz, 1H), 4.67 (s, 3H), 4.32 (q, *J*=7.1 Hz, 2H), 4.16 (q, *J*=7.1 Hz, 2H), 1.36 (t, *J*=7.1 Hz, 3H), 1.28 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 166.1, 165.4, 152.8, 142.2, 141.0, 138.3, 132.3, 130.5, 130.2, 129.4, 129.1, 128.5, 128.3, 128.1, 126.74, 126.68, 113.2, 105.0, 60.2, 59.8, 48.2, 14.5, 14.3; MS (EI): 104 (70), 159 (78), 215 (95), 261 (100), 313 (80), 518 (M^+, 33%). Anal. Calcd for $C_{25}H_{24}Cl_2N_2O_4S$: C, 57.81; H, 4.66; N, 5.39. Found: C, 58.32; H, 4.76; N, 5.24.

*3.3.8. (E) Ethyl 4-(3,4-dichlorobenzyl)amino-5-(2-ethoxycarbonyl-vinylthio)-1-phenyl-1H-pyrrole-3-carboxylate (**23c**)*

Yield 15% (butanone), 7% (benzene), mp 77–79 °C; IR ν (cm^{-1}): 3381, 1701, 1679; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.50 (s, 1H), 7.45 (d, *J*=1.5 Hz, 1H), 7.41–7.42 (m, 3H), 7.38 (d, *J*=8.2 Hz, 1H), 7.24–7.26 (m, 2H), 7.20 (dd, *J*=8.2, 1.0 Hz, 1H), 7.16 (d, *J*=14.6 Hz, 1H), 5.31 (d, *J*=14.6 Hz, 1H), 4.65 (s, 2H), 4.34 (q, *J*=7.1 Hz, 2H), 4.15 (q, *J*=7.1 Hz, 2H), 1.38 (t, *J*=7.1 Hz, 3H), 1.28 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 165.3, 164.9, 146.9, 142.8, 140.5, 138.0, 132.5, 130.7, 130.4, 129.8, 129.3, 128.9, 128.5, 126.6, 126.3, 116.2, 104.9, 60.5, 60.0, 47.5, 14.5, 14.3; HRMS (TOF-EI): 518.0840, $C_{25}H_{24}Cl_2N_2O_4S$ required 518.0834.

*3.3.9. Ethyl 1-(3,4-dichlorobenzyl)-3-(3,4-dichlorobenzylimino)-5-phenyl-1,2,3,5-tetrahydropyrrolo[2,3-b][1,4]thiazine-7-carboxylate (**24c**)*

Yield 37% (benzene), mp 173–174 °C; IR ν (cm^{-1}): 1698, 1635; ^{1}H NMR (500 MHz, C_6D_6) δ (ppm): 7.88 (s, 1H), 7.50 (s, 1H), 7.42 (s, 1H), 7.25–7.27 (m, 1H), 7.19 (d, *J*=8.2 Hz, 1H), 7.15 (d, *J*=8.2 Hz, 1H), 7.11–7.12 (m, 4H), 7.06–7.08 (m, 1H), 6.93 (d, *J*=8.0 Hz, 1H), 4.34 (s, 2H), 4.33 (q, *J*=7.2 Hz, 2H), 4.10 (s, 2H), 3.84 (s, 2H), 1.22 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 163.2, 155.5, 138.9, 138.0, 137.6, 132.6, 132.2, 131.8, 131.4, 130.4, 130.2, 129.8, 129.7, 128.9, 128.5, 127.0, 127.03, 124.5, 111.7, 110.9, 60.6, 56.7, 56.6, 55.9, 14.5; MS (EI): 159 (75), 161 (55), 227 (98), 273 (100), 617 (M^+, 1.5%), 619 (M+2, 2). Anal. Calcd for $C_{29}H_{23}Cl_4N_3O_2S$: C, 56.23; H, 3.74; N, 6.78. Found: C, 56.48; H, 4.05; N, 6.63.

*3.3.10. (Z) Ethyl 4-benzylamino-5-(2-ethoxycarbonylvinylthio)-1-(4-methoxyphenyl)-1H-pyrrole-3-carboxylate (**22d**)*

Yield 48% (butanone), 14% (benzene), mp 94–95 °C; IR ν (cm^{-1}): 3359, 3333, 1688, 1570; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37 (d, *J*=6.9 Hz, 2H), 7.37 (s, 1H), 7.32 (t, *J*=7.7 Hz, 2H), 7.24 (t, *J*=7.3 Hz, 1H), 7.17 (d, *J*=8.8 Hz, 2H), 6.92 (d, *J*=8.8 Hz, 2H), 6.68 (d, *J*=10.1 Hz, 1H), 6.10 (br, 1H), 5.59 (d, *J*=10.1 Hz, 1H), 4.71 (s, 2H), 4.30 (q, *J*=7.1 Hz, 2H), 4.17 (q, *J*=7.1 Hz, 2H), 3.85 (s, 3H), 1.34 (t, *J*=7.1 Hz, 3H), 1.28 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 166.2, 165.3, 159.2, 153.5, 142.4, 140.2, 131.4, 128.5, 128.4, 127.9, 127.6, 126.9, 114.2, 113.0, 104.7, 60.2, 59.6, 55.5, 49.6, 14.5, 14.3; MS (MALDI-TOF): 480 (M^+). Anal. Calcd for $C_{26}H_{28}N_2O_5S$: C, 64.98; H, 5.87; N, 5.83. Found: C, 64.61; H, 6.02; N, 5.80.

*3.3.11. Ethyl 1-benzyl-3-(benzylimino)-5-(4-methoxyphenyl)-1,2,3,5-tetrahydropyrrolo[2,3-b][1,4]thiazine-7-carboxylate (**24d**)*

Yield 43% (benzene), mp 105–106 °C; IR ν (cm^{-1}): 1702, 1627, 1618; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.47 (s, 1H), 7.45 (d, *J*=7.7 Hz, 1H), 7.25–7.39 (m, 10H), 7.02 (d, *J*=8.8 Hz, 2H), 4.41 (s, 2H), 4.37 (q, *J*=7.1 Hz, 2H), 4.32 (s, 2H), 3.96 (br s, 2H), 3.89 (s, 3H), 1.37 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 163.4, 159.5, 154.7, 138.9, 137.6, 131.8, 130.8, 129.8, 128.5, 128.2, 127.8, 127.3, 127.0, 126.9, 126.1, 114.7, 112.7, 110.6, 59.9, 57.7, 57.5, 56.6, 55.6, 14.6; MS (MALDI-TOF): 510 (M−1). Anal. Calcd for $C_{30}H_{29}N_3O_3S$: C, 70.43; H, 5.71; N, 8.21. Found: C, 70.15; H, 6.01; N, 8.00.

*3.3.12. (Z) Ethyl 4-benzylamino-5-(2-ethoxycarbonylvinylthio)-1-(4-chlorophenyl)-1H-pyrrole-3-carboxylate (**22e**)*

Yield 52% (butanone), 11% (benzene), mp 79–80 °C; IR ν (cm^{-1}): 3399, 1701, 1679; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.40 (d, *J*=6.8 Hz, 2H), 7.39 (s, 1H), 7.37 (d, *J*=7.5 Hz, 2H), 7.32 (t, *J*=7.5 Hz, 2H), 7.25 (d, *J*=7.0 Hz, 1H), 7.21 (d, *J*=8.5 Hz, 2H), 6.65 (d, *J*=10.0 Hz, 1H), 5.61 (d, *J*=10.0 Hz, 1H), 4.71 (s, 2H), 4.31 (q, *J*=7.1 Hz, 2H), 4.18 (q, *J*=7.1 Hz, 2H), 1.34 (t, *J*=7.1 Hz, 3H), 1.29 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 166.2, 165.1, 153.0, 143.1, 140.1, 137.0, 133.8, 129.3, 128.4, 128.3, 127.8, 127.6, 126.9, 113.4, 105.4, 104.1, 60.2, 59.8, 49.4, 14.5, 14.3; MS (MALDI-TOF): 485 (M+1). Anal. Calcd for $C_{25}H_{25}ClN_2O_4S$: C, 61.91; H, 5.20; N, 5.78. Found: C, 61.86; H, 5.75; N, 5.47.

*3.3.13. Ethyl 1-benzyl-3-(benzylimino)-5-(4-chlorophenyl)-1,2,3,5-tetrahydropyrrolo[2,3-b][1,4]thiazine-7-carboxylate (**24e**)*

Yield 44% (benzene), mp 133–134 °C; IR ν (cm^{-1}): 1707, 1636; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.50 (d, *J*=6.6 Hz, 2H), 7.49 (s, 1H), 7.45 (d, *J*=7.1 Hz, 2H), 7.36–7.39 (m, 6H), 7.27–7.31 (m, 4H), 4.42 (s, 2H), 4.37 (q, *J*=7.1 Hz, 2H), 4.32 (s, 2H), 3.95 (s, 2H), 1.37 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 163.2, 154.0, 138.7, 137.5, 136.3, 134.1, 132.6, 129.9, 129.7, 128.5, 128.2, 127.8, 127.4, 127.0, 126.6, 125.7, 112.2, 111.5, 60.0, 57.6, 56.4, 14.6; MS (MALDI-TOF): 515 (M^+). Anal. Calcd for $C_{29}H_{26}ClN_3O_2S$: C, 67.49; H, 5.08; N, 8.14. Found: C, 67.36; H, 5.23; N, 8.05.

*3.3.14. (Z) Ethyl 4-(4-chlorobenzyl)amino-5-(2-ethoxycarbonyl-vinylthio)-1-(4-chlorophenyl)-1H-pyrrole-3-carboxylate (**22f**)*

Yield 53% (butanone), 10% (benzene), mp 116–117 °C; IR ν (cm^{-1}): 3390, 1699, 1678; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.40 (d, *J*=8.7 Hz, 2H), 7.39 (s, 1H), 7.26–7.31 (m, 4H), 7.20 (d, *J*=9.0 Hz, 2H),

6.61 (dd, J=10.0, 3.2 Hz, 1H), 5.62 (dd, J=10.0, 1.5 Hz, 1H), 4.68 (s, 2H), 4.31 (q, J=7.1 Hz, 2H), 4.18 (q, J=7.1 Hz, 2H), 1.35 (t, J=7.1 Hz, 3H), 1.30 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 166.1, 165.2, 152.7, 142.7, 138.8, 136.8, 133.9, 132.5, 129.3, 128.9, 128.5, 128.3, 127.8, 113.6, 105.3, 104.2, 60.3, 59.8, 48.6, 14.5, 14.3; MS (MALDI-TOF): 519 (M+1), 541 (M+Na^+). Anal. Calcd for $C_{25}H_{24}Cl_2N_2O_4S$: C, 57.81; H, 4.66; N, 5.39. Found: C, 57.67; H, 4.79; N, 5.39.

3.3.15. Ethyl 1-(4-chlorobenzyl)-3-(4-chlorobenzylimino)-5-(4-chlorophenyl)-1,2,3,5-tetrahydropyrrolo[2,3-b][1,4]thiazine-7-carboxylate (**24f**)

Yield 49% (benzene), mp 149–150 °C; IR ν (cm^{-1}): 1711, 1637; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.51 (d, J=8.7 Hz, 2H), 7.49 (s, 1H), 7.34–7.38 (m, 6H), 7.25–7.28 (m, 4H), 4.36 (q, J=7.4 Hz, 2H), 4.36 (s, 2H), 4.27 (s, 2H), 3.91 (br s, 2H), 1.37 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 163.1, 154.3, 137.1, 136.2, 136.1, 134.3, 133.2, 132.9, 132.4, 131.0, 129.9, 129.1, 128.7, 128.4, 126.7, 125.8, 111.9, 111.3, 60.0, 56.9, 56.8, 56.4, 14.5; MS (MALDI-TOF): 582 (M−1). Anal. Calcd for $C_{29}H_{24}Cl_3N_3O_2S$: C, 59.55; H, 4.14; N, 7.18. Found: C, 59.48; H, 4.41; N, 6.82.

3.3.16. (Z) Ethyl 4-(3,4-dichlorobenzyl)amino-5-(2-ethoxycarbonylvinylthio)-1-(p-tolyl)-1H-pyrrole-4-carboxylate (**22g**)

Yield 51% (butanone), 8% (benzene), mp 111–112 °C; IR ν (cm^{-1}): 3339, 1697, 1685; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.45 (s, 1H), 7.39 (s, 1H), 7.35 (d, J=8.3 Hz, 1H), 7.19–7.22 (m, 3H), 7.12 (d, J=7.8 Hz, 2H), 6.56 (d, J=10.0 Hz, 1H), 6.20 (br, 1H), 5.56 (d, J=10.0 Hz, 1H), 4.66 (s, 2H), 4.31 (q, J=7.1 Hz, 2H), 4.16 (q, J=7.0 Hz, 2H), 2.39 (s, 3H), 1.36 (t, J=7.1 Hz, 3H), 1.28 (t, J=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 166.1, 165.4, 153.0, 142.0, 141.0, 138.1, 135.8, 132.3, 130.5, 130.2, 129.7, 129.4, 128.5, 126.7, 126.5, 113.2, 104.8, 60.2, 59.7, 48.2, 21.1, 14.5, 14.3; MS (MALDI-TOF): 531 (M−1), 555 (M+Na^+). Anal. Calcd for $C_{26}H_{26}Cl_2N_2O_4S$: C, 58.54; H, 4.91; N, 5.25. Found: C, 58.37; H, 5.25; N, 5.57.

3.3.17. Ethyl 1-(3,4-dichlorobenzyl)-3-(3,4-dichlorobenzylimino)-5-(p-tolyl)-1,2,3,5-tetrahydropyrrolo[2,3-b][1,4]thiazine-7-carboxylate (**24g**)

Yield 46% (benzene), mp 147–148 °C; IR ν (cm^{-1}): 1707, 1632; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.53 (s, 1H), 7.50 (s, 1H), 7.47 (s, 1H), 7.44 (d, J=8.2 Hz, 1H), 7.26–7.37 (m, 6H), 7.18 (d, J=8.2 Hz, 1H), 4.36 (q, J=7.1 Hz, 2H), 4.32 (s, 2H), 4.27 (s, 2H), 3.92 (s, 2H), 2.46 (s, 3H), 1.37 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 161.3, 153.5, 137.1, 136.7, 136.1, 133.2, 130.6, 130.3, 129.6, 129.5, 129.1, 128.5, 128.4, 128.2, 127.7, 127.0, 125.1, 122.5, 110.2, 108.7, 58.1, 54.9, 54.7, 54.0, 19.2, 12.6; MS (MALDI-TOF): 630 (M−1). Anal. Calcd for $C_{30}H_{25}Cl_4N_3O_2S$: C, 56.89; H, 3.98; N, 6.63. Found: C, 56.63; H, 4.24; N, 6.28.

3.3.18. (Z) Ethyl 4-(iso-propyl)amino-5-(2-ethoxycarbonylvinylthio)-1-phenyl-1H-pyrrole-3-carboxylate (**22h**)

Yield 48% (butanone), mp 107–108 °C; IR ν (cm^{-1}): 3370, 1688; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.44 (t, J=7.3 Hz, 2H), 7.43 (s, 1H), 7.38 (t, J=7.4 Hz, 1H), 7.30 (d, J=7.6 Hz, 2H), 6.84 (d, J=10.0 Hz, 1H), 5.73 (d, J=10.1 Hz, 1H), 5.32 (br, 1H), 4.30 (q, J=7.1 Hz, 2H), 4.18 (q, J=7.1 Hz, 2H), 4.16–4.26 (m, 1H), 1.36 (t, J=7.1 Hz, 3H), 1.28 (t, J=7.1 Hz, 3H), 1.21 (d, J=6.2 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 166.3, 165.3, 153.4, 142.5, 138.6, 129.1, 128.5, 127.9, 126.6, 113.5, 105.5, 104.2, 60.2, 59.6, 45.4, 23.6, 14.5, 14.3; MS (EI): 215 (50), 341 (50), 369 (45), 402 (M^+, 100%). Anal. Calcd for $C_{21}H_{26}N_2O_4S$: C, 62.66; H, 6.51; N, 6.96. Found: C, 62.62; H, 6.84; N, 6.95.

3.3.19. (Z) Ethyl 4-(n-butyl)amino-5-(2-ethoxycarbonylvinylthio)-1-phenyl-1H-pyrrole-3-carboxylate (**22i**)

Yield 49% (butanone), mp 40–42 °C; IR ν (cm^{-1}): 3375, 1698; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.28–7.37 (m, 3H), 7.31 (s, 1H), 7.29 (dd, J=6.8, 2.0 Hz, 2H), 6.77 (d, J=10.0 Hz, 1H), 5.62 (d, J=10.0 Hz, 1H), 4.21 (q, J=7.1 Hz, 2H), 4.08 (q, J=7.1 Hz, 2H), 3.39 (t, J=6.9 Hz, 2H), 1.52 (qt, J=7.6 Hz, 2H), 1.30–1.40 (m, 2H), 1.26 (t, J=7.1 Hz, 3H), 1.18 (t, J=7.1 Hz, 3H), 0.85 (t, J=7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 166.3, 165.4, 154.2, 143.9, 138.5, 129.1, 128.4, 127.9, 126.6, 113.1, 104.7, 103.5, 60.2, 59.6, 45.6, 32.4, 20.1, 14.5, 14.3, 14.0; HRMS (TOF-EI): 416.1775, $C_{22}H_{28}N_2O_4S$ required 416.1770.

3.3.20. (E) Ethyl 4-(4-chlorobenzyl)amino-5-(2-ethoxycarbonylvinylthio)-1-(p-tolyl)-1H-pyrrole-3-carboxylate (**22j**)

Yield 10% (benzene), mp 103–104 °C; IR ν (cm^{-1}): 3359, 1697, 1683; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.38 (s, 1H), 7.30 (d, J=8.5 Hz, 2H), 7.26 (d, J=8.5 Hz, 2H), 7.21 (d, J=8.1 Hz, 2H), 7.13 (d, J=8.2 Hz, 2H), 6.64 (d, J=10.0 Hz, 1H), 6.11 (br, 1H), 5.59 (d, J=10.0 Hz, 1H), 4.67 (s, 3H), 4.30 (q, J=7.1 Hz, 2H), 4.17 (q, J=7.1 Hz, 2H), 2.39 (s, 3H), 1.34 (t, J=7.1 Hz, 3H), 1.29 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 166.1, 165.3, 153.1, 142.6, 139.0, 138.0, 135.9, 132.5, 129.6, 128.9, 128.5, 128.4, 126.4, 113.2, 104.9, 104.6, 60.1, 59.6, 48.8, 21.0, 14.4, 14.3; MS (MALDI-TOF): 499 (M+1), 521 (M+Na^+). Anal. Calcd for $C_{26}H_{27}ClN_2O_4S$: C, 62.58; H, 5.45; N, 5.61. Found: C, 62.31; H, 5.27; N, 5.39.

3.3.21. Ethyl 1-(4-chlorobenzyl)-3-(4-chlorobenzylimino)-5-(p-tolyl)-1,2,3,5-tetrahydropyrrolo[2,3-b][1,4]thiazine-7-carboxylate (**24j**)

Yield 42% (benzene), mp 159–160 °C; IR ν (cm^{-1}): 1708, 1614; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.49 (s, 1H), 7.37 (d, J=8.2 Hz, 2H), 7.34 (d, J=8.4 Hz, 2H), 7.31 (d, J=6.0 Hz, 4H), 7.27 (d, J=9.4 Hz, 2H), 7.25 (d, J=8.7 Hz, 2H), 4.36 (q, J=7.1 Hz, 2H), 4.35 (s, 2H), 4.27 (s, 2H), 3.92 (br s, 2H), 2.45 (s, 3H), 1.37 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 163.3, 154.9, 138.5, 137.3, 136.2, 135.3, 133.2, 132.8, 131.9, 131.0, 130.2, 129.1, 128.6, 128.3, 126.9, 124.4, 112.1, 110.7, 59.9, 56.9, 56.7, 56.6, 21.1, 14.6, 14.2; MS (MALDI-TOF): 562 (M−1). Anal. Calcd for $C_{30}H_{27}Cl_2N_3O_2S$: C, 63.83; H, 4.82; N, 7.44. Found: C, 63.49; H, 5.05; N, 7.33.

3.3.22. (Z) Ethyl 4-(2,4-dichlorobenzyl)amino-5-(2-ethoxycarbonylvinylthio)-1-(4-methoxyphenyl)-1H-pyrrole-3-carboxylate (**22k**)

Yield 12% (benzene), mp 99–100 °C; IR ν (cm^{-1}): 3394, 1707, 1676; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.45 (s, 1H), 7.37 (s, 1H), 7.35 (d, J=8.4 Hz, 1H), 7.21 (d, J=8.1 Hz, 1H), 7.16 (d, J=8.3 Hz, 2H), 6.92 (d, J=8.7 Hz, 2H), 6.56 (d, J=9.9 Hz, 1H), 5.56 (d, J=9.9 Hz, 1H), 4.67 (s, 2H), 4.31 (q, J=7.0 Hz, 2H), 4.17 (q, J=7.1 Hz, 2H), 3.85 (s, 3H), 1.36 (t, J=7.1 Hz, 3H), 1.29 (t, J=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 166.1, 165.4, 159.3, 153.0, 141.9, 141.1, 132.3, 131.3, 130.5, 130.2, 129.4, 128.6, 128.0, 126.7, 114.2, 113.2, 104.9, 104.6, 60.2, 59.7, 55.5, 48.2, 14.5, 14.3; MS (MALDI-TOF): 548 (M^+), 571 (M+Na^+). Anal. Calcd for $C_{26}H_{26}Cl_2N_2O_5S$: C, 56.83; H, 4.77; N, 5.10. Found: C, 56.89; H, 4.84; N, 5.20.

3.3.23. (E) Ethyl 4-(2,4-dichlorobenzyl)amino-5-(2-ethoxycarbonylvinylthio)-1-(4-methoxyphenyl)-1H-pyrrole-3-carboxylate (**23k**)

Yield 8% (benzene), mp 79–80 °C; IR ν (cm^{-1}): 3390, 1707, 1681; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.45 (s, 2H), 7.37 (d, J=8.2 Hz, 1H), 7.15–7.20 (m, 4H), 6.91 (d, J=8.9 Hz, 2H), 5.30 (d, J=14.6 Hz, 1H), 4.64 (s, 2H), 4.34 (q, J=7.1 Hz, 2H), 4.15 (q, J=7.1 Hz, 2H), 3.85 (s, 3H), 1.38 (t, J=7.1 Hz, 3H), 1.29 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 165.3, 164.9, 159.5, 147.1, 142.8, 140.7, 132.4, 130.9, 130.7, 130.4, 129.9, 129.3, 127.6, 126.6, 116.2, 114.0, 104.6, 60.4, 59.9, 55.5, 47.5, 14.5, 14.3; MS (MALDI-TOF): 549 (M+1), 571 (M+Na^+). Anal. Calcd for $C_{26}H_{26}Cl_2N_2O_5S$: C, 56.83; H, 4.77; N, 5.10. Found: C, 56.76; H, 4.66; N, 4.80.

*3.3.24. Ethyl 1-(3,4-dichlorobenzyl)-3-(3,4-dichlorobenzylimino)-5-(4-methoxyphenyl)-1,2,3,5-tetrahydropyrrolo[2,3-b][1,4]thiazine-7-carboxylate (**24k**)*

Yield 37% (benzene), mp 144–145 °C; IR ν (cm^{-1}): 1702, 1633; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.51 (s, 1H), 7.47 (d, J=5.0 Hz, 2H), 7.44 (d, J=8.2 Hz, 1H), 7.26–7.36 (m, 4H), 7.18 (d, J=8.0 Hz, 1H), 7.03 (d, J=8.0 Hz, 2H), 4.36 (q, J=7.1 Hz, 2H), 4.31 (s, 2H), 4.28 (s, 2H), 3.97 (s, 2H), 3.90 (s, 3H), 1.37 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 163.3, 159.6, 155.5, 139.0, 138.0, 132.6, 132.2, 131.4, 131.2, 131.0, 130.5, 130.4, 130.1, 129.7, 129.0, 127.1, 127.0, 126.1, 114.8, 112.5, 110.5, 60.0, 56.8, 56.6, 55.9, 55.6, 14.6; HRMS (TOF-EI): 647.0367, $C_{30}H_{25}Cl_4N_3O_3S$ required 647.0371.

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References and notes

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13. CCDC 680483 and 680482 [**22a** and **24a**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.