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A NEW ADDITION-REARRANGEMENT OF [1,4]THIAZINE-2-THIONES WITH ARYL-1,2,4-TRIAZOLINE-3,5-DIONES

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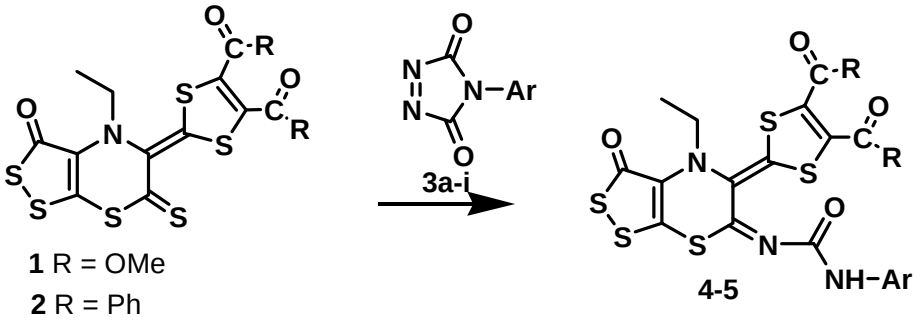
Abstract –Arylcarbamoylimino derivatives of the (1,3-dithiol-2-ylidene)-[1,2]dithiolo[3,4-*b*][1,4]thiazine ring system were synthesized by a new addition-rearrangement reaction of [1,2]dithiolo[1,4]thiazine-2-thiones with 4-aryl-1,2,4-triazoline-3,5-diones.

INTRODUCTION

The reaction of Hünig's base (*N*-ethyldiisopropylamine) or related amines and disulfur dichloride (S_2Cl_2) constitutes a very fast way to the synthesis of very complex sulfur-nitrogen heterocycles, such as bis[1,2]dithiolo[1,4]thiazines,[1] bis[1,2]dithiolopyrroles,[2] [1,2]dithiolo[1,4]thiazine,[3] and bis[1,2]dithiolylamines.[4] A careful control of the reaction conditions and the presence of oxygen or nitrogen nucleophiles permitted the selective trapping of reactive electrophilic intermediates generated in the reaction, on the way to stable final products. A good combination of reagents and reaction sequences gave rise to the preparation of each heterocycle in a one-pot reaction that sometimes implied up to fifteen different steps. Some of the products obtained by these sequential multicomponent reactions have shown a very good reactivity in 1,3-dipolar cycloaddition reactions,[5] therefore expanding the possibilities for the preparation of new heterocyclic derivatives. In this paper we report the preparation of arylcarbamoylimino[1,2]dithiolo[1,4]thiazines (**4a-i**) and (**5a-d**) obtained by a new addition-rearrangement reaction of [1,2]dithiolo[1,4]thiazine-2-thiones (**1**-**2**) with 4-aryl-1,2,4-triazoline-3,5-diones (**3a-i**).

RESULTS AND DISCUSSION

We recently reported that the [1,2]dithiolo[1,4]thiazine (**1**), obtained by cycloaddition of a 5-thioxobis[1,2]dithiolo[1,4]thiazin-3-one with dimethyl acetylenedicarboxylate (DMAD), was unable to undergo a further cycloaddition of DMAD or dibenzoylacetylene (DBA) to give bis-cycloadducts.[6] Looking for new cycloadditions on the heterodiene system of this compound we performed the reaction of **1** (1 equiv.) with the commercial 4-phenyl-1,2,4-triazoline-3,5-dione (**3a**) (2.5 equiv.) which is considered one of the most powerful dienophiles,[7] in refluxing chlorobenzene for three hours expecting to obtain a 1:1 cycloadduct. After working up of the reaction residue we obtained a new compound (**4a**) as an orange solid of mp 81-82 ºC (48%) (Scheme 1).



4 R = OMe

a (48%), Ar = C_6H_5
b (60%), Ar = *p*-ClC_6H_4
c (52%), Ar = *p*-BrC_6H_4
d (45%), Ar = *p*-$CH_3C_6H_4$
e (42%), Ar = *p*-$CH_3OC_6H_4$
f (64%), Ar = *m*-ClC_6H_4
g (95%), Ar = 2,4-$Cl_2C_6H_3$
h (23%), Ar =
i (43%), Ar =

5 R = C_6H_5

a (84%), Ar = C_6H_5
b (23%), Ar = *p*-ClC_6H_4
c (44%), Ar = *p*-BrC_6H_4
d (44%), Ar = *p*-$CH_3C_6H_4$

Scheme 1. Preparation of carbamoylimino derivatives.

MS spectrum (FAB^+) of **4a** showed a molecular peak of 567 amu that corresponded to a product in which 73 amu (NSCO from the MH^+ ion, detected by HRMS [FAB^+]) were lost as comparing to the mass of the expected 1:1 adduct. ^1H NMR of **4a** showed five coupled aromatic protons plus a broad singlet in the aromatic region (an NH group confirmed by IR spectrum), in addition to two methoxy and one methyl groups, and two diastereotopic methylenic protons (two groups of six signals), indicating the presence of conformers. Its ^{13}C NMR spectrum showed four carbonyl and one imino groups, 10 sp^2 carbon signals, and four alkyl signals. Two of the more intense signals (the *ortho*- and *para*-*C*H phenyl carbons[8]) appeared doubled with much smaller signals, indicating an unequal mixture (10:1) of geometric carbamide isomers,

from which the structure (**4a**) was deduced. Assignment of structure (**4a**) to the isolated product was confirmed by comparison with its chloroderivative (**4b**) whose structure was proved by X-Ray crystallography (see below).

We then prepared other 4-aryl-1,2,4-triazoline-3,5-diones (**3b-i**) by reaction of commercial aryl isocyanates with methyl hydrazinocarboxylate, followed by cyclization of the 4-aryl-1-methoxycarbonyl-semicarbazides to the corresponding 4-arylurazoles,[9] that were subsequently oxidized with *N*-bromo-succinimide to **3b-i**[10,11] and subjected to *in situ* reaction with **2** in the same conditions previously used for the reaction with **3a**. After column chromatography, the *N*-arylcarbamoylimino(1,3-dithiol-2-ylidene)-[1,2]dithiolo[3,4-*b*][1,4]thiazines (**4b-i**) were obtained in 23-95% yields. The best yield was obtained by using the dichlorophenyltriazolinedione (**3g**). Mono-halogenated triazolinediones (**3b-c**,**f**) gave better yields than the ones bearing alkoxy or alkyl groups (**3d-e**,**h-i**) or none (**3a**). The structure of **4b** was confirmed by single crystal X-Ray diffraction (Figure 1). Remarkable distances were the dithiole sulfur-imine nitrogen S(2)···N(2): 2.693(1) Å and the thiazine sulfur-carbamoyl oxygen S(3)···O(6): 2.593(1) Å, both indicating intramolecular interactions.

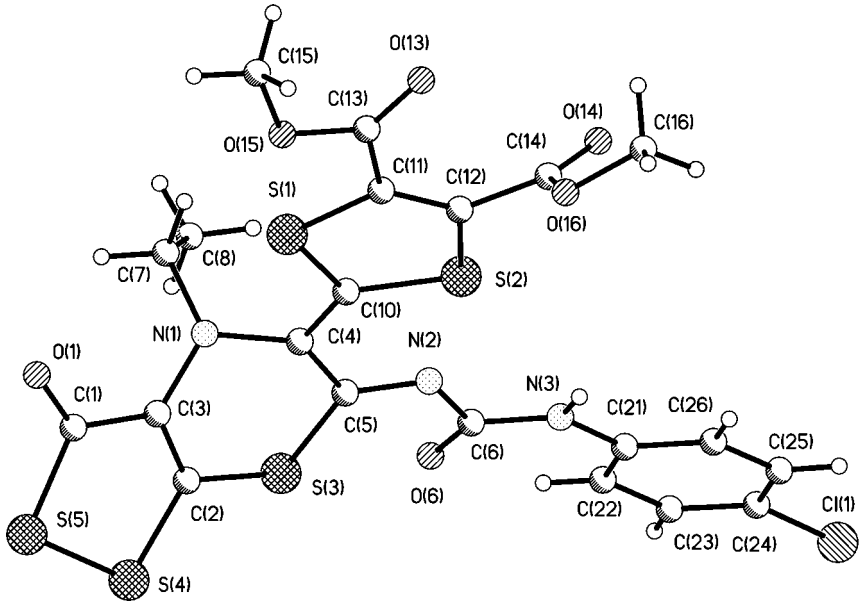
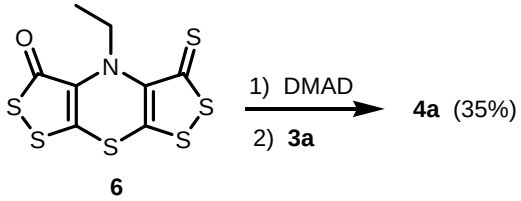


Figure 1. The molecular structure of 4b.

Compound (**4a**) was also obtained in one pot from a precursor bisdithiolothione. Thus, DMAD (1.5 equiv) was added to a solution of **6**[1] (1 equiv.) in chlorobenzene, heated under reflux for 1 h, and then **3a** (1.5 equiv.) was added to the resulting solution and heated under reflux for additional 3 h. Column chromatography of the residue afforded **4a** in 35% yield, which is approximately the same overall yield obtained in the two-stages process. It is noteworthy that, by this methodology, compound (**4a**) was

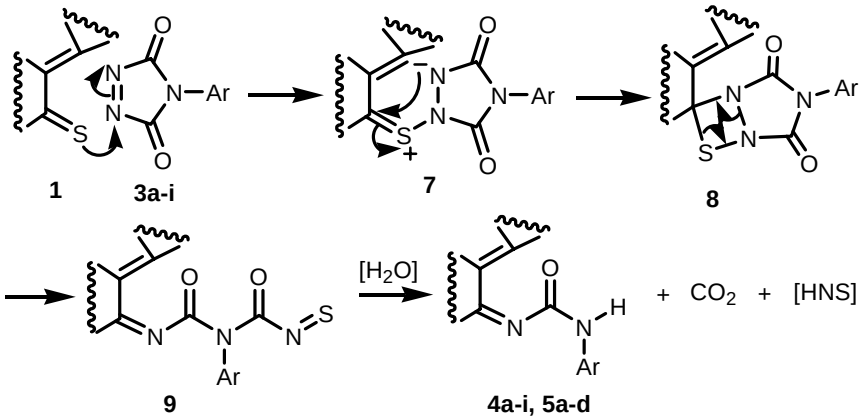
prepared in two steps from Hünig's base, disulfur dichloride, dimethyl acetylenedicarboxylate and phenyltriazolinedione, that are all commercial compounds.



Scheme 2. One-pot preparation of 4a.

Then we performed the reaction of the dithiolothiazine (**2**) (1 equiv.) and triazolines (**3a-i**) (2.5 equiv.) in refluxing chlorobenzene for 15 min to 4 h. In this way, the 2-(arylcarbamoylimino)[1,2]dithiolo[1,4]-thiazines (**5a-d**) were obtained in 23-84% yields (Scheme 1). The best yield was obtained from the phenyltriazolinedione (**3a**). Although **2** reacted with all triazolinediones (**3a-i**), completing the reaction in 15 min for the most active examples (**3b**,**f-g**) essayed, the yields were very low. In many cases the expected products were not isolated due to their instability at the temperature required for the reaction, giving rise to tar (detected as baseline on TLC) and consumption of the starting materials.

The fact that the best yields for **4a-i** were obtained from the most electrophilic triazolines (**3b-c**,**f-g**), bearing halogen atoms in the aryl group, suggested that the reaction should start by a nucleophilic attack of the nucleophilic thione sulfur from **1** to one electrophilic nitrogen of **3a-i** (rather than by [2+2] cycloaddition of **1** with **3a-i** followed by attack of the anionic nitrogen to the cationic thione carbon in **7** to form a fused four-membered cyclic intermediate (**8**) that rearranges to a unstable bis-ureimido thionitroso compound (**9**), which is hydrolyzed during workup to give the isolated products (**4a-i**) and (**5a-d**) (Scheme 3).



Scheme 3. Reaction mechanism.

Attempts of catalyzing the reaction by $Sc(OTf)_3$ in dichloromethane at room temperature were unsuccessful and in refluxing chlorobenzene conducted to extensive decomposition of starting materials. These facts supported a mechanism governed by a sulfur-nitrogen nucleophilic attack in which the halogen atoms in the triazoline increased the electrophilic character of nitrogen atoms.

CONCLUSION

It was reported that the reaction of 4-aryl-1,2,4-triazoline-3,5-diones with 1,2-dithiole-3-thiones gave 1,2-dithiolylidene-1,2,4-triazoline-3,5-diones[12] and with 1,3-dithiole-2-thiones gave 1,3-dithiolylide ne-1,2,4-triazoline-3,5-diones,[13] and activated sulfur heterocycles such as pyrimidinethiazolium salts gave pyrimidinyltriazolines,[14] therefore the triazolinedione system was conserved in all final products. The now reported reaction of [1,2]dithiolo[1,4]thiazine-2-thiones (**1**-**2**) with 4-aryl-1,2,4-triazoline-3,5-diones (**3a-i**) is the first case in which the triazoline system from **3a-i** is converted into a carbamoylimino group through a new rearrangement. The arylcarbamoylimino group[15] has shown pharmacological value (antidiarrheal lidamidine hydrochloride,[16,17] central nervous system agents[18]). The now reported reaction is a new and straightforward pathway to the synthesis of arylcarbamoylimino-heterocycles with potential pharmacological utility.

EXPERIMENTAL

General Remarks: Compounds (**1**,[6] **2**,[6] **6**,[1] **3b**,**d-f**[10] and **3c**[11]) were prepared as described, and **3g-i** were prepared similarly. Compound (**3a**), arylisocyanates and methyl hydrazinocarboxylate were purchased and used without further purification. Aromatic and chlorinated solvents were distilled from phosphorus pentoxide. Melting points were not corrected. Column chromatography was carried out on a medium pressure Gilson liquid chromatography apparatus, with silica gel C60 (Merck). Petroleum ether refers to the fraction bp 40-60 ºC. NMR: Varian Unity Inova 400 (δ_H = 7.24, δ_C = 77.0). FT-IR: Nicolet Impact 410. MS: VG-AutoSpec (70 eV).

***N*-Phenylcarbamoylimino[1,2]dithiolo[1,4]thiazines (4a) and (5a):** Triazolinedione (**3a**) (48 mg, 0.273 mmol) was added to a stirred solution of **1** (50 mg, 0.107 mmol) or **2** (60 mg, 0.107 mmol) in chlorobenzene (10 mL) and the mixture was refluxed for 3 h **(4a)** or 4 h **(5a)**. Then the solvent was removed in the rotary evaporator and the resulting residue was purified by flash chromatography (SiO_2, petroleum ether-dichlorometane 1:4).

Dimethyl 3-Oxo-4-ethyl-5-(1,3-dithiol-2-ylidene)-6-(*N*-phenylcarbamoylimino)[1,2]dithiolo[3,4-*b*]-[1,4]thiazine-4',5'-dicarboxylate (4a): Orange solid (29 mg, 48%), mp 81-82 ºC (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.62 (d, *J* = 7.7 Hz, 2H, Phenyl), 7.52 (s, br, 1H, NH), 7.37 (t, *J* = 7.7 Hz, 2H, Phenyl), 7.14 (t, *J* = 7.7 Hz, 1H, Phenyl), 3.93 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.59 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 3.22 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 1.16 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 185.6 (*C*=O heterocycle), 162.2, 160.3 and 159.6 (3 × *C*=O), 157.6 (*C*=N), 151.9, 151.1, 137.5, 136.0 and 133.0 (5 × sp^2 *tertiary* C + *aromatic* C), 129.1 and 124.5 (2 × *C*H Ar), 120.6 (sp^2 *tertiary* C), 119.3 (*C*H Ar), 118.9 (sp^2 *tertiary* C), 53.7 (O*C*H_3), 53.6 (O*C*H_3), 46.5 (*C*H_2), 13.6 (*C*H_3); IR (KBr cm^{-1}) ν 3353 (N-H), 2924, 1731 (C=O), 1661

(C=O), 1429, 1258; MS (FAB^+) *m/z* 567 (M^+, 38), 538 (32), 475 (38), 462 (42), 448 (12), 419 (55), 119 (85), 91 (100); HRMS (FAB^+), M^+(found) = 566.9665 $C_{21}H_{17}N_3O_6S_5$ requires 566.9721. Anal. Calcd for $C_{21}H_{17}N_3O_6S_5$: C, 44.43; H, 3.02; N, 7.40. Found: C, 44.69; H, 3.37; N, 6.95.

3-Oxo-4-ethyl-5-(4,5-dibenzoyl-1,3-dithiol-2-ylidene)-6-(*N*-phenylcarbamoylimino)[1,2]dithiolo-[3,4-*b*][1,4]thiazine (5a): Orange solid (60 mg, 84%), mp 133-134 ºC (decomp) (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.61-7.11 (m, 15H, Phenyl), 7.08 (s, br, 1H, NH), 3.66 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 3.32 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 1.21 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 187.5, 186.7 and 185.5 (3 × *C*=O), 162.2 (*C*=O carbamide), 157.7 (*C*=N), 151.7, 151.4, 143.1, 140.0, 137.5, 136.9 and 136.7 (7 × sp^2 *tertiary* C + *aromatic* C), 134.0 (*C*H Ar), 133.1 (sp^2 *tertiary* C), 129.1, 128.8, 128.7 and 124.4 (4 × *C*H Ar), 120.4 (sp^2 *tertiary* C), 119.2 (*C*H Ar), 46.6 (*C*H_2), 13.6 (*C*H_3); IR (KBr cm^{-1}) ν 3426 (N-H), 2924, 1660 (C=O), 1638 (C=O), 1431, 1259; MS (FAB^+) *m/z* 660 (M + 1, 10), 659 (M^+, 7), 281 (14), 221 (17), 207 (17); HRMS (FAB^+) M^+(found) = 659.0137, $C_{31}H_{21}N_3O_4S_5$ requires 659.0136. Anal. Calcd for $C_{31}H_{21}N_3O_4S_5$: C, 56.43; H, 3.21; N, 6.37. Found: C, 56.74; H, 3.56; N, 5.99.

***N*-Arylcarbamoylimino[1,2]dithiolo[1,4]thiazines (4b-i, 5a-d) (Typical Procedure):** *N*-Bromo-succinimide (NBS) (98 mg, 0.550 mmol) was added to a chilled stirred solution of 4-arylurazole (0.272 mmol) in dichloromethane (10 mL) and the mixture was stirred for 20 min at 0 ºC. Then the solvent was evaporated in the rotary evaporator and the crude triazolinedione (**3b-i**, 0.272 mmol), obtained as a pink solid, was added to a stirred solution of **1** (50 mg, 0.107 mmol) in chlorobenzene (10 mL) and the mixture was heated under reflux for 3 h. Similarly, the crude 4-aryl-1,2,4-triazoline-3,5-dione was added to a stirred solution of **2** (60 mg, 0.107 mmol) in chlorobenzene (10 mL) and the mixture was heated under reflux for 4 h (**5a**), 15 min (**5b**), 30 min (**5c**) or heated at 110 ºC for 2 h (**5d**). Then the solvent was evaporated in the rotary evaporator and the resulting residue was purified by flash chromatography (SiO_2, petroleum ether-dichloromethane 1:4).

Dimethyl 3-Oxo-4-ethyl-5-(1,3-dithiol-2-ylidene)-6-{*N*-(4-chlorophenyl)carbamoylimino}[1,2]di-thiolo[3,4-*b*][1,4]thiazine-4',5'-dicarboxylate (4b): Orange solid (39 mg, 60%), mp 231-232 ºC (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.58 (d, *J* = 9.0 Hz, 2H, Aryl), 7.52 (s, br, 1H, NH), 7.33 (d, *J* = 9.0 Hz, 2H, Aryl), 3.93 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.59 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 3.22 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 1.16 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 185.6 (*C*=O heterocycle), 162.7, 160.3 and 159.6 (3 × *C*=O), 157.6 (*C*=N), 151.8, 151.6, 136.1, 133.1, 132.3, 130.9 and 129.42 (7 × sp^2 *tertiary* C + *aromatic* C), 129.1 (*C*H Aryl), 120.7 (sp^2 *tertiary* C), 120.5 (*C*H Aryl), 53.7 (OCH_3), 53.7 (OCH_3), 46.6 (CH_2), 13.6 (*C*H_3); IR (KBr cm^{-1}) ν 3339 (N-H), 2924, 1721 (C=O), 1657 (C=O), 1511, 1428,

1200; MS (FAB^+) *m/z* 602 (M^+ + 1, 2), 307 (16), 154 (100). HRMS (FAB^+), M^+(found) = 600.9350 $C_{21}H_{16}N_3O_6ClS_5$ requires 600.9331. Anal. Calcd for $C_{21}H_{16}N_3O_6ClS_5$: C, 41.89; H, 2.68; N, 6.98. Found: C, 42.29; H, 2.46; N, 7.39.

X-Ray Diffraction Study of 4b: Crystals were grown by slow diffusion of petroleum ether into concentrated solutions of **4b** in chloroform at room temperature. A crystal of dimensions $0.28 \times 0.13 \times 0.04$ mm^3 was attached to a glass fibre and transferred to a Bruker AXS SMART 1000 diffractometer with graphite monochromatized Mo Kα X-radiation and a CCD area detector. A full sphere of the reciprocal space was collected up to $2\theta = 46.70$ º. Raw frame data were integrated with the SAINT[19] program to obtain a set of 11373 collected reflections. The structure was solved by direct methods with SHELXTL.[20] A semi-empirical absorption correction was applied with the program SADABS.[21] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were set in calculated positions and refined as riding atoms, with a common thermal parameter. All calculations and graphics were made with SHELXTL. Final R values were R_1= 0.0436 for 1782 observed reflections with $I>2\sigma(I)$, and wR_2 = 0.0604 for all 3628 independent data. CCDC-203526 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Dimethyl 3-Oxo-4-ethyl-5-(1,3-dithiol-2-ylidene)-6-{*N*-(4-bromophenyl)carbamoylimino}[1,2]dithiolo[3,4-*b*][1,4]thiazine-4',5'-dicarboxylate (4c): Orange solid (36 mg, 52%), mp 209-210 ºC (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.53 (d, *J* = 8.8 Hz, 2H, Aryl), 7.47 (d, *J* = 8.8 Hz, 2H, Aryl), 7.45 (s, br, 1H, NH), 3.93 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.59 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 3.22 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 1.16 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 185.6 (*C*=O heterocycle), 162.7, 160.3, 159.6 (3 × *C*=O), 157.5 (*C*=N), 151.8, 151.6, 136.8, 136.0, 133.1 and 132.3 (6 × sp^2 *tertiary* C + *aromatic* C), 132.1 and 120.8 (6 × *C*H Aryl), 120.4 and 117.0 (2 × sp^2 *tertiary* C + *aromatic* C), 53.8 and 53.7 (2 × O*C*H_3), 46.6 (*C*H_2), 13.6 (*C*H_3); IR (KBr cm^{-1}) ν 3426 (N-H), 2923, 1723 (C=O), 1660 (C=O), 1511, 1431, 1261, 1200; MS (FAB^+) *m/z* 648 (M + 3, 8), 647 (M + 2, 6), 646 (M + 1, 5); HRMS (FAB^+) M^+(found) = 644.8856 $C_{21}H_{16}N_3O_6BrS_5$ requires 644.8826. Anal. Calcd for $C_{21}H_{16}N_3O_6BrS_5$: C, 39.01; H, 2.49; N, 6.50. Found: C, 39.36; H, 2.24; N, 6.17.

Dimethyl 3-Oxo-4-ethyl-5-(1,3-dithiol-2-ylidene)-6-{*N*-(4-methylphenyl)carbamoylimino}[1,2]dithiolo[3,4-*b*][1,4]thiazine-4',5'-dicarboxylate (4d): Orange solid (28 mg, 45%), mp 241-242 ºC (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.50 (d, *J* = 8.4 Hz, 2H, Aryl), 7.46 (s, br, 1H, NH), 7.17 (d, *J* = 8.4 Hz, 2H, Aryl), 3.93 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.59 (six signals, double

quartet, J = 14.2 Hz, J = 7.1 Hz, 1H, ½CH_2), 3.22 (six signals, double quartet, J = 14.2 Hz, J = 7.1 Hz, 1H, ½CH_2), 1.16 (t, J = 7.1 Hz, 3H, CH_3), ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 185.3 (C=O heterocycle), 161.6, 160.0 and 159.3 (3 × C=O), 157.3 (*C*=N), 151.7, 150.6, 135.6, 134.6, 133.9, 132.7, 131.8 (7 × sp^2 *tertiary* C + *aromatic* C), 129.3 (*C*H Aryl), 120.3 (sp^2 *tertiary* C), 118.9 (*C*H Aryl), 53.4 (O*C*H_3), 53.3 (O*C*H_3), 46.2 (*C*H_2), 20.6 (*C*H_3), 13.3 (*C*H_3); IR (KBr cm^{-1}) ν 3398 (N-H), 2925, 1740 (C=O), 1666 (C=O), 1512, 1253; MS (FAB$^+$) *m/z* 582 (M + 1, 42), 475 (22); HRMS (FAB$^+$) M^+(found) = 580.9898 $C_{22}H_{19}N_3O_6S_5$ requires 580.9877. Anal. Calcd for $C_{22}H_{19}N_3O_6S_5$: C, 45.42; H, 3.29; N, 7.22. Found: C, 45.78; H, 2.94; N, 6.97.

Dimethyl 3-Oxo-4-ethyl-5-(1,3-dithiol-2-ylidene)-6-{*N*-(4-methoxyphenyl)carbamoylimino}[1,2]dithiolo[3,4-*b*][1,4]thiazine-4',5'-dicarboxylate (4e): Orange solid (27 mg, 42%), mp 216-218 ºC (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.53 (d, J = 9.0 Hz, 2H, Aryl), 7.45 (s, 1H, NH), 6.90 (d, J = 9.0 Hz, 2H, Aryl), 3.93 (s, 3H, CO_2CH_3), 3.90 (s, 3H, CO_2CH_3), 3.81 (s, 3H, OCH_3), 3.59 (six signals, double quartet, J = 14.0 Hz, J = 7.0 Hz, 1H, ½CH_2), 3.22 (six signals, double quartet, J = 14.0 Hz, J = 7.0 Hz, 1H, ½CH_2), 1.16 (t, J = 7.0 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 185.6 (C=O heterocycle), 161.8, 160.3 and 159.7 (3 × *C*=O), 157.6 (*C*=N), 156.5, 152.0, 150.7, 135.9, 132.9, 130.9 and 130.5 (7 × sp^2 *tertiary* C + *aromatic* C), 121.0 (*C*H Ar), 120.5 (sp^2 *tertiary* C), 114.2 (*C*H Ar), 55.5 (O*C*H_3), 53.7 and 53.6 (2 × CO_2*C*H_3), 46.5 (*C*H_2), 13.6 (*C*H_3); IR (KBr cm^{-1}) ν 3337 (N-H), 2924, 1723 (C=O), 1650 (C=O), 1510, 1247; MS (FAB$^+$) *m/z* 598 (M + 1, 11), 309 (20), 231 (80); HRMS (FAB$^+$) M^+(found) = 596.9825 $C_{22}H_{19}N_3O_7S_5$ requires 596.9827. Anal. Calcd for $C_{22}H_{19}N_3O_7S_5$: C, 44.21; H, 3.20; N, 7.03. Found: C, 43.78; H, 3.54; N, 6.78.

Dimethyl 3-Oxo-4-ethyl-5-(1,3-dithiol-2-ylidene)-6-{*N*-(3-chlorophenyl)carbamoylimino}[1,2]dithiolo[3,4-*b*][1,4]thiazine-4',5'-dicarboxylate (4f): Orange solid (41 mg, 64%), mp 192-193 ºC (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.75 (s, 1H, Aryl), 7.61 (s, br, 1H, NH), 7.46 (d, J = 8.0 Hz, 1H, Aryl), 7.27 (t, J = 8.0 Hz, 1H, Aryl), 7.10 (d, J = 8.0 Hz, 1H, Aryl), 3.93 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 3.58 (six signals, double quartet, J = 14.4 Hz, J = 7.2 Hz, 1H, ½CH_2), 3.21 (six signals, double quartet, J = 14.4 Hz, J = 7.2 Hz, 1H, ½CH_2), 1.16 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 185.5 (*C*=O, heterocycle), 162.8, 160.3 and 159.5 (3 × *C*=O), 157.5 (*C*=N), 151.7, 138.8, 136.2, 134.8, 133.1 and 132.1 (6 × sp^2 *tertiary* C + *aromatic* C), 130.0 and 124.3 (2 × *C*H Aryl), 120.6 sp^2 *tertiary* C), 119.2 and 117.2 (2 × *C*H Aryl), 53.8 and 53.7 (2 × O*C*H_3), 46.5 (*C*H_2), 13.6 (CH_3); IR (KBr cm^{-1}) ν 3371 (N-H), 2924, 1725 (C=O), 1661 (C=O), 1413, 1196; MS (FAB$^+$) *m/z* 602 (M + 1, 5), 371 (8), 307 (10), 219 (6), 154 (100); HRMS (FAB$^+$) M^+(found) = 600.9338 $C_{21}H_{16}N_3O_6ClS_5$ requires 600.9331. Anal. Calcd for $C_{21}H_{16}N_3O_6ClS_5$: C, 41.89; H, 2.68; N, 6.98. Found: C, 42.28; H, 3.05; N, 6.66.

Dimethyl 3-Oxo-4-ethyl-5-(1,3-dithiol-2-ylidene)-6-{*N*-(2,4-dichlorophenyl)carbamoylimino}[1,2]-dithiolo[3,4-*b*][1,4]thiazine-4',5'-dicarboxylate (4g): Orange solid (65 mg, 95%), mp 229-230 ºC (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.37 (d, *J* = 8.0 Hz, 1H, Aryl), 8.02 (s, br, 1H, NH), 7.41 (s, 1H, Aryl), 7.29 (d, *J* = 8.0 Hz, 1H, Aryl), 3.92 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.60 (six signals, double quartet, *J* = 14.2 Hz, *J* = 7.1 Hz, 1H, ½CH_2), 3.22 (six signals, double quartet, *J* = 14.2 Hz, *J* = 7.1 Hz, 1H, ½CH_2), 1.17 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 185.4 (*C*=O, heterocycle), 162.5, 159.7 and 159.6 (3 × *C*=O), 157.1 (*C*=N), 152.5, 151.3, 135.4, 133.3, 133.1, 130.9 and 129.0 (7 × sp^2 *tertiary* C + *aromatic* C), 128.8 and 128.0 (2 × *C*H Ar), 122.9 (sp^2 *tertiary* C), 120.7 (*C*H Ar), 53.7 and 53.6 (2 × O*C*H_3), 46.6 (CH_2), 13.5 (CH_3); IR (KBr cm^{-1}) ν 3406 (NH), 2923, 1732 (C=O), 1674 (C=O), 1504, 1430, 1193; MS (FAB$^+$) *m/z* 636 (M + 1, 100), 578 (33), 521 (55), 460 (82); HRMS (FAB$^+$) M^+(found) = 634.8954 $C_{21}H_{15}N_3O_6Cl_2S_5$ requires 634.8942. Anal. Calcd for $C_{21}H_{15}N_3O_6Cl_2S_5$: C, 39.62; H, 2.37; N, 6.60. Found: C, 39.32; H, 2.65; N, 6.31.

Dimethyl 3-Oxo-4-ethyl-5-(1,3-dithiol-2-ylidene)-6-{*N*-[(3,4-methylenedioxy)phenyl]carbamoyl-imino}[1,2]dithiolo[3,4-*b*][1,4]thiazine-4',5'-dicarboxylate (4h): Orange solid (15 mg, 23%), mp 267-269 ºC (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.95 (s, 2H, Aryl), 6.99 (s, 1H, Aryl), 5.99 (s, 2H, CH_2O_2), 3.91 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.60 (six signals, double quartet, *J* = 14.0 Hz, *J* = 7.0 Hz, ½CH_2), 3.22 (six signals, double quartet, *J* = 14.0 Hz, *J* = 7.0 Hz, ½CH_2), 1.17 (t, *J* = 7.0 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 185.5 (*C*=O heterocycle), 161.6, 159.7 and 159.6 (3 × *C*=O), 157.0 (*C*=N), 151.8, 151.4, 147.7, 144.5, 135.3, 133.2, 133.0, 129.8 and 120.7 (9 × sp^2 *tertiary* C + *aromatic* C), 111.7 (*C*H Ar), 103.5 (*C*H_2O_2), 102.1 and 102.0 (2 × *C*H Ar), 53.7 and 53.5 (2 × O*C*H_3), 46.5 (*C*H_2), 13.5 (*C*H_3); IR (KBr cm^{-1}) ν 3390 (N-H), 2923, 1741 (C=O), 1666 (C=O), 1503, 1200; MS (FAB$^+$) *m/z* 612 (M + 1, 5), 475 (10); HRMS (FAB$^+$) (M + 1)(found) = 611.9661 $C_{22}H_{18}N_3O_8S_5^+$ requires 611.9697. Anal. Calcd for $C_{22}H_{17}N_3O_8S_5$: C, 43.20; H, 2.80; N, 6.87. Found: C, 43.56; H, 3.15; N, 6.55.

Dimethyl 3-Oxo-4-ethyl-5-(1,3-dithiol-2-ylidene)-6-{*N*-(9*H*-fluoren-2-yl)carbamoylimino}[1,2]dithi-olo[3,4-*b*][1,4]thiazine-4',5'-dicarboxylate (4i): Orange solid (30 mg, 43%), mp 240-242 ºC (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.98 (s, 1H, NH), 7.72-7.23 (m, 7H, Aryl), 3.95 (s, 2H, CH_2-Aryl), 3.88 (s, 6H, 2 × OCH_3), 3.57 (six signals, double quartet, *J* = 14.2 Hz, *J* = 7.1 Hz, 1H, ½CH_2), 3.20 (six signals, double quartet, *J* = 14.2 Hz, *J* = 7.1 Hz, 1H, ½CH_2), 1.16 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 185.5 (C=O heterocycle), 161.8, 160.3 and 159.5 (3 × *C*=O), 157.5 (*C*=N), 152.1, 151.1, 144.4, 143.1, 141.1, 138.1, 136.4, 136.1, 133.0, 131.9, 129.2 (11 × sp^2 *tertiary* C + *aromatic* C), 126.7, 126.3, 124.8, 120.1, 119.4, 118.0, 115.9 (7 × *C*H Ar), 53.7 and 53.6 (2 × O*C*H_3), 46.5 and 37.0 (2 × *C*H_2), 13.5 (*C*H_3); IR (KBr cm^{-1}) ν 3418 (N-H), 2923, 1728 (C=O), 1660 (C=O), 1445, 1260, 1204; MS

(FAB$^+$) *m/z* 656 (M + 1, 11), 475 (9); HRMS (FAB$^+$) M$^+$(found) = 655.0007 $C_{28}H_{21}N_3O_6S_5$ requires 655.0034. Anal. Calcd for $C_{28}H_{21}N_3O_6S_5$: C, 51.28; H, 3.23; N, 6.41. Found: C, 51.53; H, 3.01; N, 6.12.

3-Oxo-4-ethyl-5-(4,5-dibenzoyl-1,3-dithiol-2-ylidene)-6-{*N*-(4-chlorophenyl)carbamoylimino}[1,2]-dithiolo[3,4-*b*][1,4]thiazine (5b): Orange solid (17 mg, 23%), mp 72-73 ºC (decomp) (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.48 (m, 8H, Aryl), 7.26 (m, 7H, Aryl + NH), 3.68 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 3.28 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 1.20 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 186.5, 186.4, 184.6 and 178.4 (4 × *C*=O), 154.2 (*C*=N), 149.0, 142.9, 139.6, 136.6, 136.5 (5 × sp^2 *tertiary* C + *aromatic* C), 134.0 (*C*H Ar, DEPT), 133.8 and 131.5 (2 × sp^2 *tertiary* C), 128.8 and 128.7 (2 × *C*H Ar, DEPT), 118.5 (sp^2 *tertiary* C), 45.6 (*C*H_2, DEPT), 13.7 (*C*H_3, DEPT); IR (KBr cm^{-1}) ν 3426 (N-H), 2923, 1659 (C=O), 1644 (C=O), 1536, 1447, 1262; MS (FAB$^+$) *m/z* 664 (M – 29, 12), 395 (12), 221 (12), 207 (11). Anal. Calcd for $C_{31}H_{20}N_3O_4ClS_5$: C, 53.63; H, 2.90; N, 6.05. Found: C, 53.87; H, 3.23; N, 5.78.

3-Oxo-4-ethyl-5-(4,5-dibenzoyl-1,3-dithiol-2-ylidene)-6-{*N*-(4-bromophenyl)carbamoylimino}[1,2]-dithiolo[3,4-*b*][1,4]thiazine (5c): Orange solid (35 mg, 44%), mp 94-95 ºC (decomp) (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.60 (s, br, 1H, NH), 7.45 (m, 10H, Aryl), 7.24 (m, 4H, Aryl), 3.62 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 3.28 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 1.19 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 187.5, 186.6, 185.4 and 162.6 (4 × *C*=O), 157.6 (*C*=N), 151.9, 151.6, 143.1, 140.0, 136.8, 136.7 (6 × sp^2 *tertiary* C + *aromatic* C), 134.0 and 132.0 (2 × *C*H Ar, DEPT), 130.9 (sp^2 *tertiary* C), 128.8, 128.7 and 120.7 (3 × *C*H Ar, DEPT), 116.9 (sp^2 *tertiary* C), 46.5 (*C*H_2, DEPT), 13.6 (*C*H_3, DEPT); IR (KBr cm^{-1}) ν 3425 (N-H), 2923, 1659 (C=O), 1643 (C=O), 1536, 1446, 1262, 1201; MS (FAB$^+$) *m/z* 740 (M + 3, 3), 739 (M + 2, 2), 738 (M + 1, 2), 391 (5), 192 (7); HRMS (FAB$^+$) M$^+$(found) = 736.9225 $C_{31}H_{20}N_3O_4BrS_5$ requires 736.9241. Anal. Calcd for $C_{31}H_{20}N_3O_4BrS_5$: C, 50.40; H, 2.73; N, 5.69. Found: C, 50.69; H, 3.04; N, 5.38.

3-Oxo-4-ethyl-5-(4,5-dibenzoyl-1,3-dithiol-2-ylidene)-6-{*N*-(4-methylphenyl)carbamoylimino}[1,2]-dithiolo[3,4-*b*][1,4]thiazine (5d): Orange solid (32 mg, 44%), mp 104-105 ºC (decomp) (CH_2Cl_2-petroleum ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.50 (m, 5H, Aryl + NH), 7.47 (m, 2H, Aryl), 7.26 (m, 6H, Aryl), 7.15 (d, *J* = 8.0 Hz, 2H, Aryl), 3.65 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 3.31 (six signals, double quartet, *J* = 14.4 Hz, *J* = 7.2 Hz, 1H, ½CH_2), 2.64 (s, 3H, CH_3), 1.21 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 187.5, 186.7, 185.5 and 161.9 (4 × *C*=O), 157.6 (*C*=N), 151.8, 151.1, 143.1, 139.9, 136.9, 136.7, 134.9 and 134.1 (8 × sp^2 *tertiary* C + *aromatic* C), 133.9, 129.6, 129.0 and 128.8 (4 × *C*H Ar, DEPT), 120.5 (sp^2 *tertiary* C), 119.2 (*C*H Ar, DEPT), 46.6 (*C*H_2, DEPT), 20.9 and 13.7 (2 × *C*H_3, DEPT); IR (KBr cm^{-1}) ν 3425 (N-H), 2923, 1659 (C=O), 1644 (C=O), 1537, 1446, 1262; MS (FAB$^+$) *m/z* 674 (M +1, 7), 327 (11), 281 (22), 207 (23); HRMS (FAB$^+$) M$^+$(found)

= 673.0294 $C_{32}H_{23}N_3O_4S_5$ requires 673.0292. Anal. Calcd for $C_{32}H_{23}N_3O_4S_5$: C, 57.06; H, 3.44; N, 6.24. Found: C, 57.39; H, 3.71; N, 5.91.

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