Supporting Information

Synthesis, chemistry and dynamic NMR study of new atropisomeric 4-dialkylamino-5-chloro-1,2-dithiol-3-thiones

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N-(2-*N*'-isopropyl-*N*'-2,2-dimethylpropylaminoethyl)phthalimide **1a** was prepared as described.[1] Benzene was distilled from phosphorus pentoxide. The reactions were carried out in anhydrous solvents, under nitrogen atmosphere and in oven-dried glassware. Melting points were determined in capillary tubes and are uncorrected. Products were isolated by flash chromatography using 230-400 mesh silica gel or on a medium-pressure Gilson liquid cromatography apparatus, with silica gel C60 (Merck). Petroleum ether refers to the fraction bp 40-60 °C.

Synthesis of *N*-(2-*N´*-isopropyl-*N´*-2,2-dimethylpropylaminoethyl)phtalimide (1b). Pivalaldehyde (30 mmol) was added to a stirred solution of N-isopropylaminoethanol (24 mmol) and a small amount of p-toluensulfonic acid in toluene (50 ml). The reaction mixture was refluxed for 10 hours using a Dean-Stark. The mixture, without further purification, was added dropwise to a stirred suspension of $LiAlH_4$ (1.125 g, 29 mmol) in anhydrous ether (20 ml). The stirring was continued under reflux for 3 hours. Once finished, the reaction was quenched by addition of water (1.12 ml), NaOH 5% (1.12 ml) and water (3.36 ml) at 0 °C. The mixture was filtered and the solvent was evaporated under reduced pressure. The mixture was purified by flash chromatography (CH_2Cl_2/EtOAc) to yield ***N*-Isopropyl-*N*-2,2-dimethylpropylaminoethanol.** 3.6 g (87%). Colorless liquid, bp 213-215°C. ^{1}H RMN (200 MHz, $CDCl_3$): 0.80 (s, 9H), 0.89 (d, *J* = 6.7, 6H), 2.01 (s, 2H); 2.46 (t, *J* = 5.6, 2H), 2.81 (hept, *J* = 6.7, 1H), 3.06 (br s, 1H), 3.38 (t, *J* = 5.6, 2H). ^{13}C RMN (50 MHz, $CDCl_3$): 18.1 (2 x CH_3), 28.6 (3 x CH_3),

[1] (a) Moore, M. B.; Rapala, R. T. *J. Am. Chem. Soc.* **1946**, *68*, 1657-1658. (b) Chiti, S. *Farm. Ed. Sci.* **1958**, *13*, 261 and 276.

32.4 (C_q), 51.7 (CH), 52.4 (CH_2), 58.8 (CH_2), 63.4 (CH_2). MS (EI, 70 eV) *m/z* 173 (M^+, 1.8), 116 (100).

A solution of thionyl chloride (22 mmol) in chloroform (25 ml) was added dropwise to a solution of aminoalcohol (11 mmol) in chloroform (25 ml). The mixture was refluxed for 3 hours. The solvent and thionyl chloride added in excess were removed by destilation. The residue was treated with NaOH 50% solution and extracted with CH_2Cl_2. The organic layer was dried and the solvent was eliminated under reduced pressure. To the residue dissolved in DMF (20 ml) was added potassium phthalimide (24 mmol). The mixture was stirred at room temperature overnight. The mixture was quenched by addition of CH_2Cl_2 (50 ml) and water (200 ml). The organic phase was decanted and the aqueous layer was extracted with CH_2Cl_2. The combined organic fractions were washed with a $NaHCO_3$ solution and brine. The organic fraction was dried and evaporated under reduced pressure. The residue was treated with petroleum ether (150 ml) and a a white solid precipitated, after filtration the organic solvent was washed with water, decanted and dried. The solvent was removed under reduced pressure. The solid was isolated by flash chromatography (Hexane/EtOAc).

***N*-(2-*N´*-Isopropyl-*N´*-2,2-dimethylpropylaminoethyl)phthalimide (1b).** 2.46 g (74%). White solid, mp 48-49 ºC. ^{1}H RMN (200 MHz, $CDCl_3$): 0.73 (s, 9H); 0.87 (d, *J* = 6.7, 6H), 2.06 (s, 2H); 2.50-2.58 (m, 2H), 2.86 (hept, *J* = 6.7, 1H), 3.57-3.64 (m, 2H), 7.55-7.73 (m, 4H, H_{Ar}), ^{13}C RMN (50 MHz, $CDCl_3$): 18.1 (2 x CH_3), 28.2 (3 x CH_3), 32.3 (C_q), 37.8 (CH_2), 50.3 (CH_2), 52.0 (CH), 62.9 (CH_2), 123.0 (CH_{Ar}), 132.1 (C_{Ar}), 133.7 (CH_{Ar}), 168.2 (2 x C=O). MS (EI, 70 eV) *m/z* 302 (M^+, 0.5), 245 (100), 174 (72).

Synthesis of 5-chloro-1,2-dithiole-3-thiones. Disulfur dichloride (10 mmol) was added dropwise at –40°C to a stirred solution of isopropylamine **1a-b** (2 mmol) and DABCO (8 mmol) dissolved in chloroform (50 ml). The stirring was continued at –40°C for 15 min and at room temperature for 3 days. The mixture was quenched by addition of triethylamine (13 mmol) at –20°C and stirred for an additional 2 hours at room temperature. The mixture was filtered over celite and the solvent was evaporated under reduced pressure. The resulting solid was purified by MPLC (light petroleum, and then light petroleum-CH_2Cl_2 mixtures) to give the corresponding product.

4-(*N*-2-Phthalimidoethyl-*N*-isopropyl)amine-5-chloro-1,2-dithiole-3-thione (2a). 0.34 g (43%). Brown solid, mp 153-154°C. ^{1}H RMN (400 MHz, $CDCl_3$): 1.00-1.40 (m, 6H); 3.47-3.87 (m, 5H); 7.66-7.83 (m, 4H, H_{Ar}). ^{13}C RMN (100 MHz, $CDCl_3$): 22.2 (2 x CH_3), 37.8 (CH_2), 42.8 (CH_2), 53.2 (CH), 123.0 (CH_{Ar}), 132.0 (C_{Ar}), 133.8 (CH_{Ar}),

150.2 (Csp^2), 158.0 (Csp^2), 168.1 (2 x C=O), 209.3 (C=S). IR (KBr, cm^{-1}) ν 3450, 2968, 1700 (C=O), 1397, 1290 (C=S), 1028, 723. MS (EI, 70 eV) *m/z* 398 (M^+, 6), 222 (90), 180 (100), 174 (65), 49 (70). HRMS, M^+ = 397.9977 $C_{16}H_{15}ClN_2O_2S_3$ requires 397.9984. Anal.calcd for $C_{16}H_{15}ClN_2O_2S_3$: C, 48.17; H, 3.79; N, 7.02. Found: C, 48.17; H, 3.69; N, 6.95.

4-(*N*-2-Phthalimidoethyl-*N*-2,2-dimethylpropyl)amine-5-chloro-1,2-dithiol-3-thione (2b). 0.26 g (30%). Orange solid, mp 135-136°C. ^1H RMN (400 MHz, $CDCl_3$): 0.87 (s, 9H), 2.94-3.03 (m, 1H), 3.33-3.78 (m, 5H), 7.66-7.88 (m, 4H, H_{Ar}). ^{13}C RMN (100 MHz, $CDCl_3$): 27.6 (3 x CH_3), 34.6 (Cq), 36.5 (CH_2), 52.3 (CH_2), 62.6 (CH_2), 123.1 (CH_{Ar}), 132.0 (C_{Ar}), 133.9 (CH_{Ar}), 150.9 (Csp^2), 155.5 (Csp^2), 168.1 (2 x C=O), 208.4 (C=S). IR (KBr, cm^{-1}) ν 1772, 1709 (C=O), 1466, 1433, 1395, 1364 (C=S). MS (EI, 70 eV) *m/z* 426 (M^+, 21), 369 (100), 266 (35), 174 (79).

Synthesis of 5-dialkylamine-1,2-dithiol-3-thiones. A mixture of 5-chloro-1,2-dithiole-3-thione **2a** (0.1 mmol) and the corresponding amine (0.1 mmol) in chloroform (3 ml) was refluxed for 1 hour. The solvent was removed under reduced pressure and the residue was purified by flash chromatography with hexane /EtOAc.

4-(*N*-2-Phthalimidoethyl-*N*-isopropyl)amine-5-pyrrolidinyl-1,2-dithiole-3-thione 3a. 25 mg (60%). Brown solid, mp 178-180 ºC. ^1H RMN (400 MHz, $CDCl_3$): 1.07 (d, *J* = 6.2, 3H), 1.26 (d, *J* = 6.2, 3H), 1.90-2.00 (m, 4H), 3.36-3.43 (m, 1H), 3.70-3.85 (m, 4H), 3.86-3.97 (m, 2H), 4.00-4.09 (m, 1H), 4.37 (hept, *J* = 6.2, 1H), 7.70-7.87 (m, 4H, H_{Ar}). ^{13}C RMN (100 MHz, $CDCl_3$): 21.3 (CH_3), 22.3 (CH_3), 25.0 (2 x CH_2), 37.8 (CH_2), 48.5 (CH_2), 50.4 (CH), 52.4 (2 x CH_2), 123.1 (CH_{Ar}), 131.5 (Csp^2), 132.0 (C_{Ar}), 133.9 (CH_{Ar}), 168.1 (C=O), 174.4 (Csp^2), 199.9 (C=S). IR (KBr, cm^{-1}) ν 1463, 2974, 1709 (C=O), 1500, 1274 (C=S). EM (FAB^+) *m/z* 434 (M^+ + 1, 100), 174 (17). HRMS, M^+ = 433.0942 $C_{20}H_{23}N_3O_2S_3$ requires 433.0952.

4-(*N*-2-Phthalimidoethyl-*N*-isopropyl)amine-5-morfolinyl-1,2-dithiole-3-thione 3b. 37 mg (82%). Brown solid. mp 162-164 ºC. ^1H RMN (400 MHz, $CDCl_3$): 1.03 (d, *J* = 6.3, 3H), 1.21 (d, *J* = 6.3, 3H), 3.27-3.33 (m, 1H), 3.73-3.90 (m, 7H), 3.97-4.05 (m, 4H), 4.25 (hept, *J* = 6.3, 1H), 7.67-7.80 (m, 4H, H_{Ar}). ^{13}C RMN (100 MHz, $CDCl_3$): 22.1 (CH_3), 22.2 (CH_3), 38.1 (CH_2), 47.9 (CH_2), 50.4 (2 x CH_2), 50.8 (CH), 66.5 (2 x CH_2), 123.4 (CH_{Ar}), 132.2 (C_{Ar}), 134.2 (CH_{Ar}), 168.3 (C=O), 176.8 (Csp^2), 204.5 (C=S). IR (KBr, cm^{-1}) ν 2961, 1708 (C=O), 1397, 1274 (C=S). EM (FAB^+) *m/z* 450

(M^++ 1, 100). HRMS, M^+ = 449.0897 $C_{20}H_{23}N_3O_3S_3$ requires 449.0902. Anal.calcd for $C_{20}H_{23}N_3O_3S_3$: C, 53.43; H, 5.16; N, 9.35. Found: C, 53.29; H, 5.05; N, 9.17.

Synthesis of 5-dialkylamine-1,2-dithiol-3-thiones with phthalimide ring-opening. A mixture of 5-chloro-1,2-dithiole-3-thione **2a** (0.1 mmol) and the corresponding amine (1 mmol) in chloroform (3 ml) was refluxed for 1 hour. The solvent was removed under reduced pressure and the residue was purified by flash chromatography with hexane /EtOAc.

4-[*N*-2-{(2'-Pyrrolidinylcarbonyl)phenylcarboxamide}ethyl-*N*-isopropyl]amine-5-pyrrolidinyl-1,2-dithiole-3-thione 4a. 47 mg (95%). Red oil. ^{1}H RMN (400 MHz, $CDCl_3$): 1.00 (d, *J* = 6.3, 3H), 1.11 (d, *J* = 6.3, 3H), 1.78-1.85 (m, 2H), 1.87-2.10 (m, 6H), 3.00-3.15 (m, 3H), 3.32-3.42 (m, 1H), 3.47-3.56 (m, 1H), 3.58-3.62 (m, 2H), 3.70-3.82 (m, 5H), 4.26 (hept, *J* = 6.3, 1H), 7.21-7.47 (m, 4H, H_{Ar}, NH), 7.72-7.78 (m, 1H, H_{Ar}). ^{13}C RMN (100 MHz, $CDCl_3$): 21.5 (CH_3), 22.8 (CH_3), 24.8 (CH_2), 25.3 (2 x CH_2), 26.1 (CH_2), 40.0 (CH_2), 46.0 (CH_2), 49.0 (CH_2), 50.1 (CH_2), 50.4 (CH), 52.8 (2 x CH_2), 126.5 (CH_{Ar}), 128.7 (CH_{Ar}), 129.2 (CH_{Ar}), 131.1 (CH_{Ar}), 131.8 (Csp^2), 132.7 (C_{Ar}), 137.1 (C_{Ar}), 167.6 (C=O), 170.1 (C=O), 174.7 (Csp^2), 199.6 (C=S). IR (KBr, cm^{-1}) ν 3292, 2974, 1622 (C=O), 1501, 1277 (C=S). EM (FAB^+) *m/z* 505 (M^++1, 22), 434 (33), 202 (100). HRMS, M^+ = 504.1684 $C_{24}H_{32}N_4O_2S_3$ requires 504.1687.

General procedure for the synthesis of thioacyl chlorides. Dialkyl acetylenedicarboxylate (0.1 mmol) was added to a solution of 1,2-dithiole-3-thione **2a-b** (0.25 mmol) in benzene (5 ml). The resulting mixture was refluxed for 45 min. The thioacyl chloride was isolated for characterization after elimination of the eluent by rotatory evaporator at room temperature.

Diethyl 6-(*N*-2-phthalimidoethyl-*N*-isopropyl)amine-6-chlorothiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 5a: 0.14 g (100%). Red solid, mp 80-82°C. ^{1}H RMN (400 MHz, $CDCl_3$): 1.01 (d, *J* = 6.2, 3H), 1.23-1.57 (m, 9H), 3.31-3.50 (m, 2H), 3.56 (hept, *J* = 6.2, 1H), 3.70-3.96 (m, 2H), 4.18-4.41 (m, 4H), 7.61-7.84 (m, 4H, H_{Ar}). ^{13}C RMN (100 MHz, $CDCl_3$): 13.4 (CH_3), 13.6 (CH_3), 19.7 (CH_3), 23.0 (CH_3), 38.1 (CH_2), 50.8 (CH_2), 54.6 (CH), 62.6 (CH_2), 62.8 (CH_2), 122.9 (CH_{Ar}), 132.4 (C_{Ar}), 133.4 (CH_{Ar}), 134.9 (Csp^2), 135.5 (Csp^2), 137.5 (Csp^2), 159.2 (C=O), 159.5 (C=O), 167.5 (2 x C=O), 174.4 (Csp^2), 182.4 (C=S). IR (KBr, cm^{-1}) ν 3469, 2973, 1715(C=O), 1573, 1403, 1250 (C=S), 1091, 1018. EM (FAB^+) *m/z* 568 (M^+, 7), 533 (41), 174 (100).

Dimethyl 6-(*N*-2-phthalimidoethyl-*N*-isopropyl)amine-6-chlorothiocarbonyl-1,4-ditiafulvene-2,3-dicarboxylate 5b: 0.14 g (100%). Red sticked solid. ^{1}H RMN (400

MHz, C_6D_5Cl): 1.09 (d, *J* = 6.3, 3H), 1.45 (d, *J* = 6.3, 3H), 3.57-3.76 (m, 9H) 3.98-4.02 (m, 2H), 7.43-7.48 (m, 2H, H_{Ar}), 7.71-7.74 (m, 2H, H_{Ar}).^{13}C RMN (100 MHz, C_6D_5Cl): 20.1 (CH_3), 23.4 (CH_3), 38.5 (CH_2), 51.4 (CH_2), 53.3 (CH_3), 53.4 (CH_3), 55.0 (CH), 123.2 (CH_{Ar}), 132.5 (C_{Ar}), 133.8 (CH_{Ar}), 134.4 (Csp^2), 135.5 (Csp^2), 182.4 (C=S), 174.6 (Csp^2), 167.8 (2 x C=O), 159.9 (C=O), 137.9 (Csp^2), 159.7 (C=O).

Diethyl 6-(*N*-2-phthalimidoethyl-*N*-2,2-dimethylpropyl)amine-6-chlorothiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 5c: 0.15 g (100%). Brown oil. ^{1}H RMN (400 MHz, $CDCl_3$): 0.97 (s, 9H), 1.27-1.40 (m, 3H), 2.95 (d, *J* = 14.5, 1H), 3.12-3.33 (m, 1H), 3.33 (d, *J* = 14.5, 1H), 3.40-3.62 (m, 1H), 3.75-4.01 (m, 2H), 4.22-4.41 (m, 4H), 7.66-7.82 (m, 4H, H_{Ar}). ^{13}C RMN (100 MHz, $CDCl_3$): 13.8 (CH_3), 13.9 (CH_3), 28.4 (3 x CH_3), 33.1 (Cq), 37.1 (CH_2), 54.3 (CH_2), 63.0 (CH_2), 63.2 (CH_2), 67.2 (CH_2), 123.1 (CH_{Ar}), 131.8 (C_{Ar}), 133.9 (CH_{Ar}), 140.6 (Csp^2), 159.1 (C=O), 159.2 (C=O), 167.8 (2 x C=O), 170.3 (Csp^2), 181.6 (C=S).

Dimethyl 6-(*N*-2-phthalimidoethyl-*N*-2,2-dimethylpropyl)amine-6-chlorothiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 5d: 0.14 g (100%). Brown oil. ^{1}H RMN (400 MHz, $CDCl_3$): 1.09 (d, *J* = 6.3, 3H), 1.45 (d, *J* = 6.3, 3H), 3.57-3.76 (m, 9H), 3.98-4.02 (m, 2H), 7.43-7.48 (m, 2H, H_{Ar}), 7.71-7.74 (m, 2H, H_{Ar}). ^{13}C RMN (100 MHz, $CDCl_3$): 20.1 (CH_3), 23.4 (CH_3), 38.5 (CH_2), 51.4 (CH_2), 53.3 (CH_3), 53.4 (CH_3), 55.0 (CH), 123.2 (CH_{Ar}), 132.5 (C_{Ar}), 133.8 (CH_{Ar}), 134.4 (Csp^2), 135.5 (Csp^2), 137.9 (Csp^2), 159.7 (C=O), 159.9 (C=O), 167.8 (2 x C=O), 174.6 (Csp^2), 182.4 (C=S). EM (FAB^+) *m/z* 568 (M^+, 4), 570 (M^++2, 3), 533 (86), 174 (100).

General procedure for the synthesis of thioacid derivatives. Once the formation of the thioacyl chlorides was achieved, over the reaction mixture was added the corresponding nucleophile (2.5 eq) at room temperature. The mixture was stirred for 1 hour and then evaporated to dryness under reduced pressure. The residue was purified by flash chromatography with hexane/EtOAc as eluent.

Diethyl 6-(*N*-2-phthalimidoethyl-*N*-isopropyl)amine-6-pyrrolidinylthiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 6a. 0.13 g (90%). Red solid, mp 113-114^{o}C. ^{1}H RMN (400 MHz, $CDCl_3$): 1.22-1.40 (m, 12H), 2.05-2.11 (m, 4H), 2.87-2.95 (m, 2H), 3.40 (hept, *J* = 6.4, 1H), 3.57-3.65 (m, 2H), 3.89-3.99 (m, 4H), 4.17-4.31 (m, 4H), 7.65-7.81 (m, 4H, H_{Ar}). ^{13}C RMN (100 MHz, $CDCl_3$): 14.2 (2 x CH_3), 22.0 (2 x CH_3), 25.5 (2 x CH_2), 38.7 (CH_2), 46.0 (CH_2), 52.9 (2 x CH_2), 56.0 (CH), 62.7 (CH_2), 62.9 (CH_2), 123.4 (CH_{Ar}), 127.0 (Csp^2), 128.9 (Csp^2), 131.9 (Csp^2), 132.3 (C_{Ar}), 133.4 (Csp^2), 134.2 (CH_{Ar}), 159.7 (C=O), 160.5 (C=O), 168.3 (2 x C=O), 190.7 (C=S). IR (KBr, cm^{-1}) ν

2968, 2870, 1715 (C=O), 1586, 1391, 1240 (C=S), 1018. EM (FAB^+) *m/z* 603 (M^+, 100). HRMS, M^+ = 603.1531 $C_{28}H_{33}N_3O_6S_3$ requires 603.1531.

Diethyl 6-(*N*-2-phthalimidoethyl-*N*-isopropyl)amine-6-morfolinylthiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 6b. 0.13 g (80%). Red solid, mp 100-102°C. ^{1}H RMN (200 MHz, $CDCl_3$): 1.22-1.40 (m, 12H). 2.92-3.00 (m, 2H), 3.41 (hept, *J* = 6.4, 1H), 3.57-3.65 (m, 2H), 3.81-3.86 (m, 4H), 4.14-4.30 (m, 8H), 7.66-7.80 (m, 4H, H_{Ar}). ^{13}C RMN (50 MHz, $CDCl_3$): 13.9 (2 x CH_3), 21.6 (2 x CH_3), 38.5 (CH_2), 46.1 (CH_2), 50.2 (2 x CH_2), 56.0 (CH), 62.5 (CH_2), 62.6 (CH_2), 66.5 (2 x CH_2), 123.1 (CH_{Ar}), 128.8 (Csp^2), 129.3 (Csp^2), 131.9 (C_{Ar}), 133.0 (Csp^2), 133.9 (CH_{Ar}), 159.2 (C=O), 160.1 (C=O), 168.0 (2 x C=O), 194.2 (C=S). IR (KBr, cm^{-1}) ν 1773, 1734, 1715 (C=O), 1267, 1248 (C=S), 1150. EM (FAB^+) *m/z* 619 (M^+, 100). HRMS, M^+ = 619.1472 $C_{28}H_{33}N_3O_7S_3$ requires 619.1481. Anal.calcd for $C_{28}H_{33}N_3O_7S_3$: C, 54.26; H, 5.37; N, 6.78. Found: C, 54.27; H, 5.40; N, 6.73.

Dimethyl 6-(*N*-2-phthalimidoethyl-*N*-isopropyl)amine-6-pyrrolidinylthiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 6c. 0.09 g (65%). Red sticked solid. ^{1}H RMN (200 MHz, $CDCl_3$): 1.30 (d, *J* = 6.4, 6H), 2.07-2.14 (m, 4H), 2.90-2.99 (m, 2H), 3.42 (hept, *J* = 6.4, 1H), 3.60-3.68 (m, 2H), 3.80 (s, 3H), 3.83 (s, 3H), 3.89-3.99 (m, 4H), 7.68-7.84 (m, 4H, H_{Ar}). ^{13}C RMN (50 MHz, $CDCl_3$): 21.6 (2 x CH_3), 25.2 (2 x CH_2), 30.9 (CH_2), 38.4 (CH_2), 45.7 (CH_2), 52.7 (2 x CH_2), 53.1 (CH_3), 53.3 (CH_3), 55.7 (CH), 123.2 (CH_{Ar}), 126.3 (Csp^2), 128.6 (Csp^2), 132.0 (C_{Ar}), 133.1 (Csp^2), 133.9 (CH_{Ar}), 159.8 (C=O), 160.6 (C=O), 168.0 (2 x C=O), 190.4(C=S). IR (KBr, cm^{-1}) ν 1737, 1714 (C=O), 1430, 1390, 1255 (C=S). EM (FAB^+) *m/z* 575 (M^+, 100). HRMS, M^+ = 575.1224 $C_{26}H_{29}N_3O_6S_3$ requires 575.1219.

Diethyl 6-(*N*-2-phthalimidoethyl-*N*-2,2-dimethylpropyl)amine-6-pyrrolidinylthiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 6d. 0.11 g (70%). Orange oil. ^{1}H RMN (200 MHz, $CDCl_3$): 0.92 (s, 9H), 1.29 (t, *J* = 7.1, 3H), 1.34 (t, *J* = 7.1, 3H), 2.00-2.03 (m, 4H), 2.67 (s, 2H), 3.30-3.34 (m, 2H), 3.83-3.86 (m, 4H), 3.97-4.01 (m, 2H), 4.25 (q, *J* = 7.1, 2H), 4.30 (q, *J* = 7.1, 2H), 7.61-7.75 (m, 4H, H_{Ar}). ^{13}C RMN (50 MHz, $CDCl_3$): 13.9 (2 x CH_3), 28.3 (3 x CH_3), 25.5 (2 x CH_2), 33.4 (Cq), 37.1 (CH_2), 52.7 (2 x CH_2), 54.8 (CH_2), 62.5 (CH_2), 62.7 (CH_2), 64.9 (CH_2), 123.1 (CH_{Ar}), 125.1 (Csp^2), 129.2 (Csp^2), 132.1 (C_{Ar}), 132.9(Csp^2), 133.8 (CH_{Ar}), 134.3 (Csp^2), 159.5 (C=O), 160.1 (C=O), 168.0 (2 x C=O), 190.0 (C=S). EM (FAB^+) *m/z* 631 (M^+, 100), 561 (43).

Diethyl 6-(*N*-2-phthalimidoethyl-*N*-2,2-dimethylpropyl)amine-6-morfolinylthiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 6e. 0.06 g (40%). Orange solid, mp

195-196°C. ^{1}H RMN (400 MHz, $CDCl_3$): 0.91 (s, 9H), 1.29 (t, *J* = 7.0, 3H), 1.33 (t, *J* = 7.0, 3H), 2.68 (s, 2H), 3.33-3.37 (m, 2H), 3.73-3.84 (m, 4H), 3.97-4.01 (m, 2H), 4.02-4.15 (m, 2H), 4.26 (q, *J* = 7.0, 2H), 4.30 (q, *J* = 7.0, 2H), 7.67-7.81 (m, 4H, H_{Ar}). ^{13}C RMN (100 MHz, $CDCl_3$): 13.9 (2 x CH_3), 28.2 (3 x CH_3), 33.3 (Cq), 37.2 (CH_2), 50.3 (2 x CH_2), 55.8 (CH_2), 62.6 (CH_2), 62.8 (CH_2), 65.1 (CH_2), 66.7 (2 x CH_2), 123.1 (CH_{Ar}), 127.3 (Csp^2), 129.9 (Csp^2), 132.1 (C_{Ar}), 132.5 (Csp^2), 132.7 (Csp^2), 133.8 (CH_{Ar}), 159.3 (C=O), 160.0 (C=O), 168.0 (2 x C=O), 194.0 (C=S). IR (KBr, cm^{-1}) ν 3439, 2943, 1712 (C=O), 1390, 1272 (C=S), 1011. EM (FAB^+) *m/z* 647 (M^+, 100), 561 (20). HRMS, M^+ = 647.1745 $C_{30}H_{37}N_3O_7S_3$ requires 647.1794. Anal.calcd for $C_{30}H_{37}N_3O_7S_3$: C, 55.62; H, 5.76; N, 6.49. Found: C, 55.69; H, 5.60; N, 6.29.

Dimethyl 6-(*N*-2-phthalimidoethyl-*N*-2,2-dimethylpropyl)amine-6-pyrrolidinyl-thiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 6f. 0.04 g (30%). Orange oil. ^{1}H RMN (200 MHz, $CDCl_3$): 0.94 (s, 9H), 2.01-2.08 (m, 4H), 2.71 (s, 2H), 3.31-3.35 (m, 2H), 3.82-3.86 (m, 10H), 3.98-4.02 (m, 2H), 7.70-7.82 (m, 4H, H_{Ar}). ^{13}C RMN (50 MHz, $CDCl_3$): 25.2 (2 x CH_3), 28.3 (3 x CH_3), 33.5 (Cq), 37.1 (CH_2), 52.7 (CH_2), 53.4 (CH_3), 55.0 (2 x CH_2), 65.0 (CH_2), 123.2 (CH_{Ar}), 124.7 (Csp^2), 129.5 (Csp^2), 132.1 (C_{Ar}), 132.7 (Csp^2), 133.8 (CH_{Ar}), 134.5 (Csp^2), 159.9 (C=O), 160.0 (C=O), 168.1 (2 x C=O), 190.1 (C=S). IR (KBr, cm^{-1}) ν 3463, 2953, 1715 (C=O), 1388, 1257 (C=S), 1016. EM (FAB^+) *m/z* 603 (M^+, 100), 533 (11). HRMS, M^+ = 603.1525 $C_{28}H_{33}N_3O_6S_3$ requires 603.1532.

General procedure for the synthesis of thioacid derivatives with phthalimide ring-opening. Once the formation of the acyl chlorides was achieved, over the reaction mixture was added the corresponding nucleophile (10 eq) at room temperature. The mixture was stirred for 1 hour and then evaporated to dryness under reduced pressure. The residue was purified by flash chromatography with hexane/EtOAc as eluent.

Diethyl 6[*N*-2-{(2'-pyrrolidinylcarbonyl)phenylcarboxamide}ethyl-*N*-isopropyl]-amine-6-pyrrolidinylthiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 7a. 0.12 g (70%). Red oil. ^{1}H RMN (400 MHz, $CDCl_3$): 1.09 (d, J = 6.3, 6H), 1.15-1.35 (m, 6H), 1.76-1.92 (m, 4H), 1.96-2.03 (m, 4H), 2.98-3.14 (m, 5H), 3.32-3.41 (m, 2H), 3.57 (t, *J* = 6.7, 2H), 3.74-3.80 (m, 4H), 4.14-4.34 (m, 4H), 7.19-7.23 (m, 1H, H_{Ar}), 7.30-7.43 (m, 2H, H_{Ar}), 7.61-7.71. (m, 2H, H_{Ar}, NH), ^{13}C RMN (100 MHz, $CDCl_3$): 14.2 (2 x CH_3), 22.0 (2 x CH_3), 24.8 (CH_2), 25.4 (2 x CH_2), 26.1 (CH_2), 39.1 (CH_2), 44.3 (CH_2), 45.8 (CH_2), 48.9 (CH_2), 52.9 (2 x CH_2), 54.5 (CH), 62.8 (CH_2), 62.9 (CH_2), 120.4 (Csp^2),

126.8 (CH_{Ar}), 128.2 (CH_{Ar}), 129.0 (CH_{Ar}), 130.1 (Csp^2), 131.0 (CH_{Ar}), 131.5 (Csp^2), 132.3 (Csp^2), 132.9 (C_{Ar}), 137.9 (C_{Ar}), 159.8 (C=O), 160.1 (C=O), 167.5 (C=O), 170.1 (C=O), 191.8 (C=S). IR (KBr, cm^{-1}) ν 3525-3145, 1732 (C=O), 1615, 1250 (C=S). EM (FAB^+) *m/z* 674 (M^+, 100), 603 (77).

Diethyl 6-[*N*-2-{(2'-morfolinylcarbonyl)phenylcarboxamide}ethyl-*N*-isopropyl]-amine-6-morfolinylthiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 7b. 0.09 g (50%). Red oil. ^1H RMN (400 MHz, $CDCl_3$): 1.09 (d, *J* = 6.3, 6H), 1.15-1.35 (m, 6H), 2.98-3.14 (m, 5H), 3.39-3.43 (m, 2H), 3.53-3.61 (m, 2H), 3.69-3.78 (m, 8H), 4.00-4.08 (m, 4H), 4.19-4.26 (m, 4H), 7.19-7.23 (m, 1H, H_{Ar}), 7.30-7.43 (m, 2H, H_{Ar}), 7.61-7.71 (m, 2H, H_{Ar}, NH). ^{13}C RMN (100 MHz, $CDCl_3$): 13.8 (2 x CH_3), 21.7 (2 x CH_3), 38.7 (CH_2), 42.0 (CH_2), 44.0 (CH_2), 47.5 (CH_2), 50.1 (2 x CH_2), 54.2 (CH), 62.6 (CH_2), 62.7 (CH_2), 66.2 (2 x CH_2), 66.3 (CH_2), 66.5 (CH_2), 121.2 (Csp^2), 126.6 (CH_{Ar}), 127.5 (CH_{Ar}), 128.8 (CH_{Ar}), 130.1 (Csp^2), 130.7 (CH_{Ar}), 131.8 (Csp^2), 133.2 (C_{Ar}), 136.1 (C_{Ar}), 159.3 (C=O), 159.6 (C=O), 166.8 (C=O), 170.2 (C=O), 195.1 (C=S). IR (KBr, cm^{-1}) ν 3280, 2968, 1733 (C=O), 1616, 1427, 1256 (C=S), 1109, 1012. EM (FAB^+) *m/z* 706 (M^+, 100), 620 (59). HRMS, M^+ = 706.2149 $C_{32}H_{42}N_4O_8S_3$ requires 706.2165.

Dimethyl 6[*N*-2-{(2'-pyrrolidinylcarbonyl)phenylcarboxamide}ethyl-*N*-isopropyl]-amine-6-pyrrolidinylthiocarbonyl-1,4-ditiafulvene-2,3-dicarboxylate 7c. 0.11 g (65%). Orange solid, mp 118-120°C. ^1H RMN (400 MHz, $CDCl_3$): 1.15 (d, *J* = 6.5, 6H), 1.82-1.98 (m, 4H), 2.02-2.12 (m, 4H), 3.03-3.07 (m, 2H), 3.11-3.20 (m, 3H), 3.39-3.42 (m, 2H), 3.58-3.73 (m, 6H), 3.79 (s, 3H), 3.81 (s, 3H), 7.24-7.26 (m, 1H, H_{Ar}), 7.36-7.45 (m, 2H, H_{Ar}), 7.64 (t, *J* = 5.8, 1H, NH), 7.72-7.74 (m, 2H, H_{Ar}). ^{13}C RMN (100 MHz, $CDCl_3$): 22.0 (2 x CH_3), 24.8 (CH_2), 25.4 (CH_2), 26.1 (CH_2), 39.1 (CH_2), 44.4 (CH_2), 45.8 (CH_2), 48.9 (CH_2), 52.9 (2 x CH_3), 54.5 (CH), 61.7 (CH_2), 120.2 (Csp^2), 126.8 (CH_{Ar}), 128.2 (CH_{Ar}), 129.0 (CH_{Ar}), 130.1 (Csp^2), 131.0 (CH_{Ar}), 131.8 (Csp^2), 132.3 (Csp^2), 132.8 (C_{Ar}), 137.9 (C_{Ar}), 160.2 (C=O), 160.5 (C=O), 167.5 (C=O), 170.1 (C=O), 191.7 (C=S). IR (KBr, cm^{-1}) ν 1728 (C=O), 1647, 1614, 1429, 1255 (C=S). EM (FAB^+) *m/z* 647 (M^+ + 1, 100). HRMS, M^+ = 646.1959 $C_{30}H_{38}N_4O_6S_3$ requires 646.1954. Anal.calcd for $C_{30}H_{38}N_4O_6S_3$: C, 55.70; H, 5.92; N, 8.66. Found: C, 55.61; H, 5.82; N, 8.45.

Diethyl 6-[*N*-2-{(2'-pyrrolidinylcarbonyl)phenylcarboxamide}ethyl-*N*-2,2-dimethylpropyl]amine-6-pyrrolidinylthiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 7d. 0.07 g (40%). Brown oil. ^1H RMN (200 MHz, $CDCl_3$): 0.80 (s, 9H), 1.17-1.34 (m,

6H), 1.79-1.99 (m, 8H), 2.58 (br s, 2H), 3.11-3.17 (m, 2H), 3.31-3.40 (m, 2H), 3.44-3.64 (m, 4H), 3.80-3.91 (m, 4H), 4.20-4.31 (m, 4H), 7.21-7.41 (m, 3H, H_{Ar}), 7.66-7.70 (m, 1H, H_{Ar}), 8.22-8.27 (m, 1H, NH). ^{13}C RMN (50 MHz, $CDCl_3$): 14.2 (2 x CH_3), 24.8 (2 x CH_2), 26.0 (2 x CH_2), 28.4 (3 x CH_3), 34.1 (Cq), 38.3 (CH_2), 45.8 (CH_2), 48.8 (CH_2), 53.2 (2 x CH_2), 53.8 (CH_2), 62.9 (CH_2), 63.0 (CH_2), 65.8 (CH_2), 117.4 (Csp^2), 126.8 (CH_{Ar}), 128.1 (CH_{Ar}), 128.8 (CH_{Ar}), 130.3 (Csp^2), 130.8 (CH_{Ar}), 132.5 (Csp^2), 133.1 (C_{Ar}), 133.2 (Csp^2), 138.2 (C_{Ar}), 159.8 (C=O), 160.0 (C=O), 167.5 (C=O), 170.1 (C=O), 191.0 (C=S). IR (KBr, cm^{-1}) ν 3600-3150, 1732 (C=O), 1630, 1425, 1235 (C=S). EM (FAB^+) *m/z* 702 (M^+, 100), 632 (83).

Diethyl 6-[*N*-2-{(2'-morfolinylcarbonyl)phenylcarboxamide}ethyl-*N*-2,2-dimethyl-propyl]amine-6-morfolinylthiocarbonyl-1,4-dithiafulvene-2,3-dicarboxylate 7e. 0.07 g (40%). Brown oil. ^{1}H RMN (200 MHz, $CDCl_3$): 0.85 (s, 9H), 1.25-1.38 (m, 6H), 2.64 (br s, 2H), 3.24-3.26 (m, 2H), 3.42-3.50 (m, 2H), 3.51-3.70 (m, 8H), 3.71-3.95 (m, 8H), 4.22-4.42 (m, 4H), 7.23-7.50 (m, 3H, H_{Ar}), 7.68-7.72 (m, 1H, H_{Ar}), 8.01-8.12 (m, 1H, NH). ^{13}C RMN (50 MHz, $CDCl_3$): 13.9 (2 x CH_3). 28.1 (3 x CH_3), 33.8 (Cq), 38.2 (CH_2), 42.1 (CH_2), 47.6 (CH_2), 50.4 (CH_2), 53.3 (CH_2), 62.7 (CH_2), 62.8 (CH_2), 65.4 (CH_2), 66.6 (CH_2), 118.4 (Csp^2), 126.7 (CH_{Ar}), 127.7 (CH_{Ar}), 128.8 (CH_{Ar}), 130.6 (CH_{Ar}), 130.8 (Csp^2), 132.1 (Csp^2), 133.7 (C_{Ar}), 136.2 (C_{Ar}), 159.4 (C=O), 159.7 (C=O), 167.1 (C=O), 170.2 (C=O), 194.7 (C=S). IR (KBr, cm^{-1}) ν 3640-3180, 1719 (C=O),1643, 1275, 1253 (C=S). EM (FAB^+) *m/z* 734 (M^+, 100), 648 (57).

Dimethyl 6-[*N*-2-{(2'-pyrrolidinylcarbonyl)phenylcarboxamide}ethyl-*N*-2,2-dimethylpropyl]amine-6-pyrrolidinylthiocarbonyl-1,4-ditiafulvene-2,3-dicarboxylate 7f. 0.05 g (30%). Brown oil. ^{1}H RMN (200 MHz, $CDCl_3$): 0.84 (s, 9H), 1.79-2.04 (m, 8H), 2.63 (s, 2H), 3.18 (t, J = 6.51, 2H), 3.35-3.40 (m, 2H), 3.52-3.68 (m, 4H), 3.82 (s, 3H), 3.90 (s, 3H), 3.87-3.94 (m, 4H), 7.25-7.49 (m, 3H, H_{Ar}), 7.70-7.75 (m, 1H, H_{Ar}), 8.26 (t, J = 5.71, 1H, NH). ^{13}C RMN (50 MHz, $CDCl_3$): 24.5 (CH_2), 25.8 (CH_2), 28.2 (3 x CH_3), 33.8 (Cq), 38.1 (CH_2), 45.5 (CH_2), 48.6 (CH_2), 53.7 (CH_3), 60.0 (CH_2), 64.3 (CH_2), 65.5 (CH_2), 117.0 (Csp^2), 126.6 (CH_{Ar}), 127.8 (CH_{Ar}), 128.6 (CH_{Ar}), 130.0 (Csp^2), 130.6 (CH_{Ar}), 132.2 (Csp^2), 132.9 (C_{Ar}), 133.2 (Csp^2), 137.9 (C_{Ar}), 160.0 (C=O), 160.2 (C=O), 167.3 (C=O), 169.8 (C=O), 190.7 (C=S). IR (KBr, cm^{-1}) ν 3445, 2951, 1716 (C=O), 1591, 1466, 1392, 1258 (C=S), 1018. EM (FAB^+) *m/z* 674 (M^+, 91), 604 (66), 202 (100).