Supporting Information

Tin-free radical cyclizations for the synthesis of 7-azaoxindoles, 7-azaindolines, tetrahydro [1, 8] naphthyridines and tetrahydro-5H-pyrido[2, 3-b]azepin-8-ones.

Eric Bacqué¹, Myriem El Qacemi² and Samir Zard^{2*}

¹ *Aventis pharma, 94400 Vitry sur Seine, France.*

² *Laboratoire de Synthèse Organique associé au CNRS
Ecole Polytechnique, 91128 Palaiseau, France*

General considerations

All reactions were carried under an inert atmosphere. Commercial reagents were used as received without further purification. All products were purified by using silica gel SDS 60 C. C. 40-63 or by crystallisation. NMR spectra were recorded in CDCl₃ with TMS as an internal standard at room temperature on a Bruker AMX400 operating at 400 MHz for ¹H and 100 MHz for ¹³C. Infrared Absorption spectra were recorded with a Perkin-Elmer 1600 Fourier Transform Spectrophotometer. Mass spectra were recorded with a HP 5989B mass spectrometer. Melting points were determined by Reichert microscope apparatus and were uncorrected.

Experimental section

(6-Chloro-pyridin-2-yl)-cyclopropyl-amine 2a : compound **2a** was prepared by heating a solution of 516 mg of 2,6-dichloropyridine and 2 mL of cyclopropylamine (8.3 eq) in a sealed tube at 150°C for 20 hours. The excess of amine was then evaporated in vacuo. The crude mixture was purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 95:5) to give the aminopyridine **2a** in 76% yield as a colorless oil. ¹H NMR (CDCl₃, 400 MHz) δ 7.41 (t, 1H, CHar., J = 8 Hz), 6.61 (dd, 2H, CHar., J = 8 Hz), 5.28 (bs, 1H, NH), 2.47 (m, 1H, CH), 0.78 (m, 2H, CH₂), 0.53 (m, 2H, CH₂) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 159.7 (Car.), 149.3 (Car.), 140.0 (CHar.), 112.4 (CHar.), 103.8 (CHar.), 23.8 (CH), 7.62 (CH₂) ppm. IR (neat) 3414, 3272, 2975, 1597, 1564, 1504, 1435, 1361, 1156, 1139, 1024, 1009, 893, 776, 733 cm⁻¹. MS (CI+NH₃) m/z 169, 171 (MH⁺).

tert-Butyl-(6-chloro-pyridin-2-yl)-amine 2b : compound **2b** was prepared by heating a solution of 1.725 g of 2,6-dichloropyridine and 7.5 mL of *tert*-butylamine (6.2 eq) in a sealed tube at 180 °C for 4 days. The amine was then evaporated in vacuo. The crude mixture was

Deleted: 7.

Deleted: 7.

dissolved in dichloromethane, treated with saturated aqueous Na_2CO_3 , extracted with dichloromethane, dried and concentrated under reduced pressure to give compound **2b** (>99 % yield) as a yellow oil which was used with no further purification. ^1H NMR (CDCl_3 , 400 MHz) δ 7.29 (t, 1H, *CHar.*, $J = 8$ and 7 Hz), 6.52 (d, 1H, *CHar.*, $J = 7$ Hz), 6.32 (d, 1H, *CHar.*, $J = 8$ Hz), 4.67 (bs, 1H, *NH*), 1.42 (s, 9H, $\text{C}(\text{CH}_3)_3$) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 158.0 (Car.), 149.3 (Car.), 139.2 (*CHar.*), 111.2 (*CHar.*), 106.2 (*CHar.*), 50.9, $\text{C}(\text{CH}_3)_3$, 29.3 ($\text{C}(\text{CH}_3)_3$) ppm. IR (neat) 3423, 2965, 1592, 1560, 1497, 1437, 1388, 1337, 1225, 1156, 1138, 987, 774 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 185, 187 (MH^+).

Butyl-(6-chloro-pyridin-2-yl)-amine 2c : compound **2c** was prepared by heating a solution of 1.415 g of 2,6-dichloropyridine and 7.5 mL of butylamine (8 eq) in a sealed tube at 140 °C for 18 hours. The amine was then evaporated in vacuo. The crude mixture was dissolved in dichloromethane, treated with saturated aqueous Na_2CO_3 , extracted with dichloromethane, dried and concentrated under reduced pressure to give compound **2c** (93 % yield) as a yellow oil which was used with no further purification. ^1H NMR (CDCl_3 , 400 MHz) δ 7.33 (t, 1H, *CHar.*, $J = 8$ Hz), 6.53 (d, 1H, *CHar.*, $J = 8$ Hz), 6.23 (d, 1H, *CHar.*, $J = 8$ Hz), 4.80 (bs, 1H, *NH*), 3.20 (q, 2H, NCH_2 , $J = 7$ Hz), 1.56 (quin, 2H, CH_2 , $J = 7$ Hz), 1.38 (sex, 2H, CH_2 , $J = 7$ Hz), 0.92 (t, 3H, CH_3 , $J = 7$ Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 158.8 (Car.), 149.4 (Car.), 139.7 (*CHar.*), 111.4 (*CHar.*), 113.6 (*CHar.*), 41.8 (CH_2N), 31.2 (CH_2), 20.0 (CH_2), 13.8 (CH_3) ppm. IR (neat) 3427, 3287, 2957, 1598, 1565, 1504, 1435, 1393, 1328, 1164, 1125, 1091, 979, 772 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 185, 187 (MH^+); 141, 143 (MH^+-44).

tert-Butyl-(4,6-dichloro-pyridin-2-yl)-amine 2d : compound **2d** was prepared by heating a solution of 1.05 g of 2,4,6-trichloropyridine and 6.5 mL of *tert*-butylamine (10 eq) in a sealed tube at 180 °C for 64 hours. The amine was then evaporated in vacuo. The crude mixture was dissolved in dichloromethane, treated with saturated aqueous Na_2CO_3 , extracted with dichloromethane, dried and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (silica gel, petroleum ether-dichloromethane, 10:0 to 96:4) to give compound **2b** (75 % yield) as a colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 6.55 (s, 1H, *CHar.*), 6.29 (s, 1H, *CHar.*), 4.73 (bs, 1H, *NH*), 1.40 (s, 9H, $\text{C}(\text{CH}_3)_3$) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 158.2 (Car.), 150.1 (Car.), 145.4 (Car.), 111.5 (*CHar.*), 105.9 (*CHar.*), 51.4 ($\text{C}(\text{CH}_3)_3$), 29.2 ($\text{C}(\text{CH}_3)_3$) ppm. IR (neat) 3426, 2970, 1579, 1555, 1450, 1453, 1420, 1364, 1218, 1148, 1007, 810 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 219, 221, 223 (MH^+).

Deleted: 2

Deleted: 5

Deleted: 5

Deleted: 2

Deleted:

Deleted: 7.

Deleted: 7.

Deleted: 7.

Deleted: 6.8

Deleted: 3

Deleted: 3

Deleted: 3

Formatted: No underline

Butyl-(4,6-dichloro-pyridin-2-yl)-amine 2e : compound **2e** was prepared by refluxing 990 mg of 2,4,6-trichloropyridine and 5.2 mL of butylamine (9.7 eq) for 19 hours and then the amine was evaporated in vacuo. The crude mixture was purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 9:1) to give the aminopyridine **2e** in 37% yield as a white solid. ^1H NMR (CDCl_3 , 400 MHz) δ 6.58 (s, 1H, CHar.), 6.24 (s, 1H, CHar.), 4.84 (bs, 1H, NH), 3.19 (m, 2H, CH_2NH), 1.59 (m, 2H, CH_2), 1.40 (m, 2H, CH_2 , $J = 7$ Hz), 0.95 (t, 3H, CH_3 , $J = 7$ Hz) ppm ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 159.0 (Car.), 150.1 (Car.), 146.0 (Car.), 111.7 (CHar.), 103.5 (CHar.), 41.9 (CH_2N), 31.1 (CH_2), 20.0 (CH_2), 13.7 (CH_3) ppm. MS ($\text{CI}+\text{NH}_3$) m/z 219, 221, 223 (MH^+).

Deleted: .3

Deleted: .3

Dithiocarbonic acid {[[(6-chloro-pyridin-2-yl)-cyclopropyl-carbamoyl]-methyl} ester ethyl ester 4a : a solution of aminopyridine **2a** (123 mg, 0.72 mmol) and chloroacetyl chloride (0.17 mL, 2.13 mmol, 2.9 eq) in toluene (6 mL) was refluxed for 2 hours. When the starting material was totally consumed, the crude mixture was cooled to room temperature, neutralized with saturated aqueous Na_2CO_3 , extracted with dichloromethane, dried and concentrated under reduced pressure. The residue was used with no further purification in the next reaction.

To a solution of the residue in acetone (6 mL) under argon was added Potassium *O*-Ethyl xanthate (140 mg, 0.87 mmol, 1.2 eq) and the reaction mixture was stirred for 1 h at room temperature. After consumption of all the starting material, acetone was evaporated and the resulting mixture was diluted with water, extracted with dichloromethane, dried and concentrated. The residue was purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 1:1) to give compound **4a** (64 % yield) as a yellow oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.69 (t, 1H, CHar., $J = 8$ Hz), 7.27 (d, 1H, CHar., $J = 8$ Hz), 7.21 (d, 1H, CHar., $J = 8$ Hz), 4.61 (q, 2H, OCH_2 , $J = 7$ Hz), 4.32 (s, 2H, CH_2S), 3.20 (m, 1H, CH), 1.40 (t, 3H, CH_3 , $J = 7$ Hz), 1.04 (m, 2H, CH_2), 0.67 (m, 2H, CH_2) ppm ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 213.7 ($\text{C}=\text{S}$), 168.6 ($\text{NC}=\text{O}$), 154.3 (Car.), 149.3 (Car.), 140.0 (CHar.), 121.8 (CHar.), 119.4 (CHar.), 70.5 (OCH_2), 40.8 (CH_2S), 30.2 (CHN), 13.7 (CH_3), 9.8 (CH_2) ppm. IR (neat) 2985, 1682, 1574, 1434, 1336, 1226, 1156, 1113, 1050, 797 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 330 (M).

Deleted: .0

Deleted: .0

Deleted: .0

Deleted: .0

Deleted: .0

Dithiocarbonic acid {[*tert*-butyl-(6-chloro-pyridin-2-yl)-carbamoyl]-methyl} ester ethyl ester **4b** : a solution of aminopyridine **2b** (1.05 g, 5.7 mmol), *N,N*-dimethylaniline (2.1 mL, 16.6 mmol, 2.9 eq) and chloroacetyl chloride (1.4 mL, 17.7 mmol, 3 eq) in 1,2-dichloroethane (50 mL) was refluxed for 7 hours. When starting material was totally consumed, the solution was cooled to room temperature. 1,2-dichloroethane was evaporated in vacuo and the crude mixture neutralized with saturated aqueous Na_2CO_3 , extracted with dichloromethane, dried and concentrated under reduced pressure. The residue was used with no further purification in the next reaction.

To a solution of the residue in acetone (50 mL) under argon was added Potassium *O*-Ethyl xanthate (2.6 g, 16.25 mmol, 2.8 eq) and the reaction mixture was stirred for 1 h at room temperature. After consumption of all the starting material, acetone was evaporated and the resulting mixture was diluted with water, extracted with dichloromethane, dried and concentrated. The residue was purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 3:2) to give compound **4b** (88 % yield) as a yellow oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.82 (t, 1H, *CHar.*, J = 8 Hz), 7.42 (d, 1H, *CHar.*, J = 8 Hz), 7.29 (d, 1H, *CHar.*, J = 8 Hz), 4.56 (q, 2H, OCH_2 , J = 7 Hz), 3.55 (s, 2H, CH_2S), 1.40 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.37 (t, 3H, CH_3 , J = 7 Hz) ppm ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 213.7 ($\text{C}=\text{S}$), 165.5 ($\text{NC}=\text{O}$), 154.2 (*Car.*), 150.7 (*Car.*), 140.6 (*CHar.*), 124.6 (*CHar.*), 123.7 (*CHar.*), 70.3 (OCH_2), 59.9 ($\text{C}(\text{CH}_3)_3$), 42.3 (CH_2S), 28.8 ($\text{C}(\text{CH}_3)_3$), 13.7 (CH_3) ppm. IR (neat) 2253, 1671, 1577, 1560, 1428, 1260, 1050, 909 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 346, 348 (M).

Formatted: Font color: Auto

Dithiocarbonic acid {[*butyl*-(6-chloro-pyridin-2-yl)-carbamoyl]-methyl}ester ethyl ester **4c** : a solution of aminopyridine **2c** (912 mg, 4.94 mmol) and chloroacetyl chloride (0.59 mL, 7.48 mmol, 1.5 eq) in toluene (15 mL) was refluxed for 1 hour. When starting material was totally consumed, the crude mixture was cooled to room temperature, neutralized with saturated aqueous Na_2CO_3 , extracted with dichloromethane, dried and concentrated under reduced pressure. The residue was used with no further purification in the next reaction.

To a solution of the residue in acetone (19 mL) under argon was added Potassium *O*-Ethyl xanthate (960 mg, 6 mmol, 1.2 eq) and the reaction mixture was stirred for 1 h at room temperature. After consumption of all the starting material, acetone was evaporated and the resulting mixture was diluted with water, extracted with dichloromethane, dried and concentrated. The residue was purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 7:3) to give compound **4c** (87 % yield) as a yellow oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.76 (t, 1H, *CHar.*, J = 8 Hz), 7.26 (d, 2H, *CHar.*, J = 8 Hz), 4.56 (q, 2H, OCH_2 , J = 7 Hz), 4.04 (s, 2H, CH_2S), 3.85 (t, 2H, NCH_2 , J = 8 Hz), 1.54 (quin, 2H, CH_2 , J = 8 Hz), 1.37 (t, 3H, CH_3 , J = 7 Hz), 1.29 (sext, 2H, CH_2 , J = 8 Hz), 0.87 (t, 3H, CH_3 , J = 8 Hz) ppm ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 213.5 ($\text{C}=\text{S}$), 166.5 ($\text{NC}=\text{O}$), 154.3 (*Car.*), 150.0 (*Car.*), 140.7 (*CHar.*), 122.4 (*CHar.*), 118.6 (*CHar.*), 70.4 (OCH_2), 48.4 (CH_2), 40.4 (CH_2),

30.0 (CH₂), 19.9 (CH₂), 13.6 (CH₃) ppm. IR (neat) 2958, 1670, 1579, 1432, 1379, 1306, 1218, 1141, 1112, 1054, 801 cm⁻¹. MS (CI+NH₃) m/z 347, 349 (MH⁺).

Dithiocarbonic acid {[*tert*-butyl-(4,6-dichloro-pyridin-2-yl)-carbamoyl]-methyl} ester ethyl ester **4d** : a solution of aminopyridine **2d** (411 mg, 1.87 mmol), N,N-dimethylaniline (0.7 mL, 5.55 mmol, 3 eq) and chloroacetyl chloride (0.45 mL, 5.70 mmol, 3 eq) in 1,2-dichloroethane (16 mL) was stirred under argon at room temperature for 6 hours and then refluxed for 15 hours. When starting material was totally consumed, the crude mixture was cooled to room temperature, neutralized with saturated aqueous Na₂CO₃, extracted with dichloromethane, dried and concentrated under reduced pressure. The residue was used with no further purification in the next reaction.

To a solution of the residue in acetone (20 mL) under argon was added Potassium *O*-Ethyl xanthate (1 g, 6.25 mmol, 3.3 eq) by portions and the reaction mixture was stirred for 3 h at room temperature. After consumption of all the starting material, acetone was evaporated and the resulting mixture was diluted with water, extracted with dichloromethane, dried and concentrated. The residue was purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 9:1) to give compound **4d** (72 % yield) as a yellow oil. ¹H NMR (CDCl₃, 400 MHz) δ 7.43 (s, 1H, CHar.), 7.29 (s, 1H, CHar.), 4.60 (q, 2H, OCH₂, J = 7 Hz), 3.56 (s, 2H, CH₂S), 1.40 (t, 3H, OCH₂CH₃, J = 7 Hz), 1.40 (s, 9H, C(CH₃)₃) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 213.9 (C=S), 165.5 (NC=O), 155.0 (Car.), 151.4 (Car.), 147.1 (Car.), 124.5 (2xCHar.), 70.7 (OCH₂), 60.4 (C(CH₃)₃), 42.3 (CH₂S), 28.9 (C(CH₃)₃), 13.8 (CH₃) ppm. IR (neat) 2978, 1681, 1563, 1544, 1384, 1228, 1050, 816 cm⁻¹. MS (CI+NH₃) m/z 380, 382, 384 (M), 324, 326, 328 (M-56).

Dithiocarbonic acid {[butyl-(4,6-dichloro-pyridin-2-yl)-carbamoyl]-methyl} ester ethyl ester **4e** : a solution of aminopyridine **2e** (205 mg, 0.94 mmol) and chloroacetyl chloride (0.15 mL, 1.9 mmol, 2 eq) in toluene (10 mL) was refluxed for 1.5 hours. When starting material was totally consumed, the crude mixture was cooled to room temperature, neutralized with saturated aqueous Na₂CO₃, extracted with dichloromethane, dried and concentrated under reduced pressure. The residue was used with no further purification in the next reaction.

To a solution of the residue in acetone (9 mL) under argon was added Potassium *O*-Ethyl xanthate (192 mg, 1.2 mmol, 1.3 eq) and the reaction mixture was stirred for 1 h at room temperature. After consumption of all the starting material, acetone was evaporated and the resulting mixture was diluted with water, extracted with dichloromethane, dried and concentrated. The residue was purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 4:1) to give compound **4e** (88 % yield) as a white solid. ¹H NMR

Deleted: .1

Deleted: .1

(CDCl₃, 400 MHz) δ 7.36 (bs, 1H, CHar.), 7.24 (s, 1H, CHar.), 4.60 (q, 2H, OCH₂, J = 7 Hz), 4.14 (s, 2H, CH₂S), 3.88 (t, 2H, NCH₂, J = 8 Hz), 1.58 (m, 2H, CH₂), 1.40 (t, 3H, OCH₂CH₃, J = 7 Hz), 1.32 (m, 2H, CH₂), 0.91 (t, 3H, CH₃, J = 7 Hz) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 213.4 (C=S), 166.9 (NC=O), 154.8 (Car.), 150.2 (Car.), 147.0 (Car.), 121.8 (CHar.), 118.3 (CHar.), 70.6 (OCH₂), 48.3 (CH₂S), 40.8 (CH₂N), 30.3 (CH₂), 19.9 (CH₂), 13.7 (CH₃), 13.7 (CH₃) ppm. IR (neat) 2958, 1681, 1567, 1457, 1415, 1378, 1294, 1227, 1161, 1111, 1049, 813 cm⁻¹. MS (CI+NH₃) m/z 381, 383, 385 (MH⁺).

6-Chloro-1-cyclopropyl-1,3-dihydro-pyrrolo[2,3-b]pyridin-2-one 5a : a solution of xanthate **4a** (150 mg, 0.45 mmol) in 1,2-dichloroethane (0.09 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 90 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.6 eq of DLP were added. the crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 1:1) to give compound **5a** (57 % yield) as pink crystals (m.p = 126°C, recrystallised with heptane/ethyl acetate). ¹H NMR (CDCl₃, 400 MHz) δ 7.38 (d, 1H, CHar., J = 8 Hz), 6.94 (d, 1H, CHar., J = 8 Hz), 3.45 (s, 2H, CH₂), 2.78-2.75 (m, 1H, CH), 1.06-1.01 (m, 4H, CH₂) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 174.6 (NC=O), 158.8 (Car.), 149.1 (Car.), 133.4 (CHar.), 117.3 (CHar.), 116.8 (Car.), 34.3 (CH₂), 22.3 (CHN), 5.6 (CH₂) ppm. IR (CH₂Cl₂) 1733, 1580, 1454, 1370, 1355, 1091 cm⁻¹. MS (CI+NH₃) m/z 209, 211 (MH⁺). Anal. calcd. for C₁₀H₉ClN₂O: C, 57.57; H, 4.35, found: C, 57.51; H, 4.36.

1-tert-Butyl-6-chloro-1,3-dihydro-pyrrolo[2,3-b]pyridin-2-one 5b : a solution of xanthate **4b** (216 mg, 0.62 mmol) in chlorobenzene (0.1 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 20 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.6 eq of DLP were added. the crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 3:2) to give compound **5b** (82 % yield) as red-orange crystals (m.p = 78°C, recrystallised with heptane/ethyl acetate). ¹H NMR (CDCl₃, 400 MHz) δ 7.34 (d, 1H, CHar., J = 8 Hz), 6.90 (d, 1H, CHar., J = 8 Hz), 3.43 (s, 2H, CH₂), 1.76 (s, 9H, C(CH₃)₃) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 175.0 (NC=O), 159.7 (Car.), 147.9 (Car.), 133.0 (CHar.), 117.7 (Car.), 116.7 (CHar.), 59.1 (C(CH₃)₃), 35.6 (CH₂), 28.8 (C(CH₃)₃) ppm. IR (CH₂Cl₂) 2984, 1727, 1614, 1577, 1426, 1418, 1346, 1301, 1265, 1201, 896 cm⁻¹. MS

Deleted: .1

Deleted: 7.6

Deleted: .1

Deleted: .3

Deleted: 69

Deleted: 68

Formatted: English U.K.

Field Code Changed

Formatted: Spanish Mexico

(CI+NH₃) m/z 225, 227 (MH⁺). Anal. calcd. for C₁₁H₁₃ClN₂O: C, 58.80 ; H, 5.83, found: C, 58.83 ; H, 5.91.

1-Butyl-6-chloro-1,3-dihydro-pyrrolo[2,3-b]pyridin-2-one 5c : a solution of xanthate **4c** (200 mg, 0.57 mmol) in 1,2-dichloroethane (0.1 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 90 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.6 eq of DLP were added. the crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 100:0 to 65:45) to give compound **5c** (73 % yield) as pink crystals (m.p = 60°C, recrystallised with heptane/ethyl acetate). ¹H NMR (CDCl₃, 400 MHz) δ 7.40 (d, 1H, CHar., J = 8 Hz), 6.93 (d, 1H, CHar., J = 8 Hz), 3.77 (t, 2H, NCH₂, J = 8 Hz), 3.50 (s, 2H, CH₂CO), 1.67 (quin, 2H, CH₂, J = 8 Hz), 1.35 (sex, 2H, CH₂, J = 8 Hz), 0.92 (t, 3H, CH₃, J = 8 Hz) ppm ; ¹³C NMR (CDCl₃, 100 MHz) δ 174.1 (NC=O), 158.2 (Car.), 149.0 (Car.), 133.4 (CHar.), 117.2 (Car.), 117.1 (CHar.), 39.1 (CH₂N), 34.3 (CH₂CO), 29.6 (CH₂), 20.0 (CH₂), 13.7 (CH₃) ppm. IR (CH₂Cl₂) 2960, 1724, 1608, 1580, 1467, 1358, 1224, 1089, 898 cm⁻¹. MS (CI+NH₃) m/z 224, 226 (M). Anal. calcd. for C₁₁H₁₃ClN₂O: C, 58.8 ; H, 5.83, found: C, 58.67 ; H, 5.68.

1-tert-Butyl-4,6-dichloro-1,3-dihydro-pyrrolo[2,3-b]pyridin-2-one 5d : a solution of xanthate **4d** (200 mg, 0.52 mmol) in chlorobenzene (0.1 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 20 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.7 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0) to give compound **5d** (74 % yield) as white crystals (m.p = 64°C, recrystallised with heptane). ¹H NMR (CDCl₃, 400 MHz) δ 6.94 (s, 1H, CHar.), 3.45 (s, 2H, CH₂), 1.74 (s, 9H, C(CH₃)₃) ppm ; ¹³C NMR (CDCl₃, 100 MHz) δ 173.8 (NC=O), 160.2 (Car.), 148.6 (Car.), 139.7 (Car.), 116.8 (CHar.), 116.6 (Car.), 59.7 (C(CH₃)₃), 35.0 (CH₂), 28.8 (C(CH₃)₃) ppm. IR (CH₂Cl₂) 2929, 1725, 1610, 1566, 1426, 1408, 1202, 1087 cm⁻¹. MS (CI+NH₃) m/z 259, 261, 263 (MH⁺), 204, 206, 208 (M-55). Anal. calcd. for C₁₁H₁₂Cl₂N₂O: C, 50.99 ; H, 4.67, found: C, 51.02 ; H, 4.77.

Deleted:

1-Butyl-4,6-dichloro-1,3-dihydro-pyrrolo[2,3-b]pyridin-2-one 5e : a solution of xanthate **4e** (117 mg, 0.30 mmol) in 1,2-dichloroethane (0.05 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (30 mol % per 90 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.8 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 100:0 to 8:2) to give compound **5e** (78 % yield) as white crystals (m.p = 83°C, recrystallised with heptane). ^1H NMR (CDCl_3 , 400 MHz) δ 6.97 (s, 1H, CHar.), 3.77 (t, 2H, NCH_2 , $J = 7$ Hz), 3.51 (s, 2H, CH_2CO), 1.66 (m, 2H, CH_2), 1.35 (m, 2H, CH_2), 0.94 (t, 3H, CH_3 , $J = 7$ Hz) ppm ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 172.9 (NC=O), 158.7 (Car.), 149.8 (Car.), 140.1 (Car.), 117.3 (CHar.), 116.1 (Car.), 39.6 (CH_2CO), 33.8 (CH_2N), 29.6 (CH_2), 19.9 (CH_2), 13.6 (CH_3) ppm. IR (CH_2Cl_2) 2990, 1732, 1606, 1571, 1465, 1437, 1315, 1295, 1272, 1087 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 259, 261, 263 (MH^+). Anal. calcd. for $\text{C}_{11}\text{H}_{13}\text{Cl}_2\text{N}_2\text{O}$: C, 50.99 ; H, 4.67, found: C, 50.75 ; H, 4.72.

Deleted: 3

Deleted: 3

Deleted: 5

Deleted: 3

Formatted: Subscript

Allyl-(6-chloro-pyridin-2-yl)-amine 6a : compound **6a** was prepared by heating a solution of 1.62 g (10.9 mmol) of 2,6-dichloropyridine and 5 mL of allylamine (66.6 mmol, 6.1 eq) in a sealed tube at 140 °C for 22 hours. The amine was then evaporated in vacuo. The crude mixture was dissolved in dichloromethane, treated with saturated aqueous Na_2CO_3 , extracted with dichloromethane, dried and concentrated under reduced pressure to give compound **6a** (quantitative) as a yellow oil which was used with no further purification. ^1H NMR (CDCl_3 , 400 MHz) δ 7.32 (t, 1H, CHar., $J = 7$ and 8 Hz), 6.54 (d, 1H, CHar., $J = 7$ Hz), 6.23 (d, 1H, CHar., $J = 8$ Hz), 5.91-5.83 (m, 1H, $\text{CH}=\text{CH}_2$), 5.28 (bs, 1H, NH), 5.23 (dd, 1H, $\text{CH}=\text{CH}_2$, $J = 17$ Hz), 5.13 (dd, 1H, $\text{CH}=\text{CH}_2$, $J = 10$ Hz), 3.88 (t, 2H, NCH_2 , $J = 5$ Hz) ppm ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 158.8 (Car.), 149.4 (Car.), 139.7 ($\text{CH}=\text{CH}_2$), 134.3 (CHar.), 116.2 ($\text{CH}_2=\text{CH}$), 111.9 (CHar.), 104.1 (CHar.), 44.6 (NCH_2) ppm. IR (neat) 3496, 3110, 2925, 1597, 1432, 1413, 1184, 931 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 170, 172 (MH^+), 154, 156 (MH^+-16).

Deleted: 5

Deleted: 2

Deleted: 5

Deleted: 2

Deleted: 1

Deleted: 4

Deleted: 3

But-3-enyl-(6-chloro-pyridin-2-yl)-amine 6b : compound **6b** was prepared by heating a solution of 1.516 g (10.2 mmol) of 2,6-dichloropyridine and 1.3 g of homoallylamine (18.2 mmol, 1.8 eq) in a sealed tube at 140 °C for 42 hours. The amine was then evaporated in vacuo. The crude mixture was dissolved in dichloromethane, treated with saturated aqueous Na_2CO_3 , extracted with dichloromethane, dried and concentrated under reduced pressure to give compound **6b** (87% yield) as an orange oil which was used with no further purification.

^1H NMR (CDCl_3 , 400 MHz) δ 7.32 (t, 1H, CHar. , $J = 7$ and 8 Hz), 6.53 (d, 1H, CHar. , $J = 7$ Hz), 6.23 (d, 1H, CHar. , $J = 8$ Hz), 5.81-5.74 (m, 1H, $\text{CH}=\text{CH}_2$), 5.11 (dd, 1H, $\text{CH}=\text{CH}_2$, $J = 16$ Hz), 5.08 (dd, 1H, $\text{CH}=\text{CH}_2$, $J = 10$ Hz), 4.76 (bs, 1H, NH), 3.28 (m, 2H, NCH_2), 2.34 (m, 2H, CH_2) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 158.8 (Car.), 149.5 (Car.), 139.7 ($\text{CH}=\text{CH}_2$), 135.2 (CHar.), 117.5 ($\text{CH}_2=\text{CH}$), 111.8 (CHar.), 104.1 (CHar.), 41.1 (NCH_2), 33.5 (CH_2) ppm. IR (neat) 3421, 3287, 2926, 1598, 1565, 1503, 1438, 1414, 1326, 1162, 979 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 183, 185 (MH^+), 141, 143 (MH^+-42).

N-Allyl-N-(6-chloro-pyridin-2-yl)-acetamide 7a : a solution of aminopyridine **6a** (976 mg, 5.78 mmol), DMAP (2.124 g, 17.4 mmol, 3 eq) and acetyl chloride (1.65 mL, 23.2 mmol, 4 eq) in dichloromethane (50 mL) was stirred under argon at room temperature for 2 hours. When starting material was totally consumed, the crude mixture was cooled to room temperature, neutralized with saturated aqueous Na_2CO_3 , extracted with dichloromethane, dried and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 2:3) to give compound **7a** (88 % yield) as a colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.66 (t, 1H, CHar. , $J = 8$ Hz), 7.29 (bs, 1H, CHar.), 7.16 (d, 1H, CHar. , $J = 8$ Hz), 5.88-5.80 (m, 1H, $\text{CH}=\text{CH}_2$), 5.10 (ddd, 3H, $\text{CH}=\text{CH}_2$, $J = 17.3$ Hz et 10 Hz), 4.47 (d, 2H, NCH_2 , $J = 5.3$ Hz), 2.13 (s, 3H, COCH_3) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.4 (NCO), 154.4 (Car.), 149.7 (Car.), 140.3 (CHar.), 133.1 (CHar.), 121.9 (CHar.), 118.9 ($\text{CH}=\text{CH}_2$), 117.2 ($\text{CH}_2=\text{CH}$), 50.2 (NCH_2), 23.5 (COCH_3) ppm. IR (neat) 3081, 1673, 1580, 1562, 1434, 1377, 1232, 1165, 986, 797 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 211, 213 (MH^+), 228, 231 (MH^++NH_3)

N-But-3-enyl-N-(6-chloro-pyridin-2-yl)-acetamide 7b : a solution of aminopyridine **6b** (359 mg, 1.96 mmol), DMAP (679 mg, 5.55 mmol, 2.8 eq) and acetyl chloride (0.55 mL, 7.73 mmol, 3.9 eq) in dichloromethane (20 mL) was stirred under argon at room temperature for one hour. When starting material was totally consumed, the crude mixture was cooled to room temperature, neutralized with saturated aqueous Na_2CO_3 , extracted with dichloromethane, dried and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 2:3) to give compound **7b** (97 % yield) as a colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.71 (t, 1H, CHar. , $J = 8$ Hz), 7.25 (bs, 1H, CHar.), 7.24 (d, 1H, CHar. , $J = 8$ Hz), 5.78-5.71 (m, 1H, $\text{CH}=\text{CH}_2$), 5.04 (d, 1H, $\text{CH}=\text{CH}_2$, $J = 17$ Hz), 5.01 (d, 1H, $\text{CH}=\text{CH}_2$, $J = 9$ Hz), 3.94 (t, 2H, NCH_2 , $J = 7.4$ Hz), 2.33 (m, 2H, CH_2), 2.08 (s, 3H, COCH_3) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.1 (NCO), 155.0 (Car.), 150.0 (Car.), 140.3 (CHar.), 134.9 (CHar.), 122.2 (CHar.), 119.9 ($\text{CH}=\text{CH}_2$), 116.9 ($\text{CH}_2=\text{CH}$), 47.1 (NCH_2), 32.7 (CH_2), 23.3 (COCH_3) ppm. IR (neat) 2980, 1667, 1580, 1563, 1440, 1382, 1309, 1164, 988 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 225, 227 (MH^+).

Dithiocarbonic acid (1-{[acetyl-(6-chloro-pyridin-2-yl)-amino]-methyl}-4-oxo-pentyl) ester ethyl ester 9a : olefin **7a** (260 mg, 1.23 mmol) and xanthate derivative (435 mg, 2.44 mmol, 1.99 eq) were dissolved in 1,2-dichloroethane (1.23 mmol / 1 mL) and refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added (5 mol %) to the refluxing solution, followed by additional portions (2.5 mol % every 90 min). The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 0.34 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 1:4) to give compound **9a** (84 % yield) as a yellow oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.75 (t, 1H, CHar. , $J = 8$ Hz), 7.30 (d, 1H, CHar. , $J = 8$ Hz), 7.28 (d, 1H, CHar. , $J = 8$ Hz), 4.56 (q, 2H, OCH_2 , $J = 7$ Hz), 4.32 (dd, 1H, NCH_2 , $J = 8$ and 14 Hz), 3.98 (dd, 1H, NCH_2 , $J = 7$ and 14 Hz), 3.86-3.82 (m, 1H, CHS), 2.65-2.61 (m, 2H, CH_2), 2.18-2.12 (m, 1H, CH), 2.12 (s, 3H, NCOCH_3), 2.06 (s, 3H, COCH_3), 1.80-1.74 (m, 1H, CH), 1.36 (t, 3H, OCH_2CH_3 , $J = 7$ Hz) ppm ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 213.1 ($\text{C}=\text{S}$), 207.5 (CO), 170.4 (NCOCH_3), 154.6 (Car.), 150.3 (Car.), 140.6 (CHar.), 122.9 (CHar.), 120.6 (CHar.), 70.2 (OCH_2), 49.9 (NCH_2), 49.3 (CHS), 40.3 (CH_2), 30.1 (COCH_3), 24.9 (CH_2), 23.2 (NCOCH_3), 13.7 (OCH_2CH_3) ppm. IR (neat) 2983, 1715, 1673, 1579, 1563, 1435, 1377, 1292, 1224, 1047, 737 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 389, 391 (MH^+), 269, 271 (MH^+-120).

Dithiocarbonic acid (1-{[acetyl-(6-chloro-pyridin-2-yl)-amino]-methyl}-5-chloro-4-oxo-pentyl) ester ethyl ester 9b : olefin **7a** (254 mg, 1.20 mmol) and xanthate derivative (850 mg, 4.0 mmol, 3.3 eq) were dissolved in 1,2-dichloroethane (0.6 mmol / 1 mL) and refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added (5 mol %) to the refluxing solution, followed by additional portions (2.5 mol % every 90 min). The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.38 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-ethyl

Deleted: 7.77 and 7.92

Deleted: 7.77

Deleted: 7.92

Deleted: .1

Deleted: 7.7

Deleted: et

Deleted: .1

Deleted: et

Deleted: .1

acetate, 10:0 to 1:4) to give compound **9b** (44 % yield) as a yellow oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.72 (t, 1H, *CHar.*, $J = 8$ Hz), 7.25 (d, 1H, *CHar.*, $J = 8$ Hz), 7.23 (d, 1H, *CHar.*, $J = 8$ Hz), 4.51 (q, 2H, OCH_2 , $J = 7$ Hz), 4.27 (dd, 1H, NCH_2 , $J = 8$ and 14 Hz), 4.10 (s, 2H, CH_2Cl), 3.93 (dd, 1H, NCH_2 , $J = 8$ and 14 Hz), 3.82-3.77 (m, 1H, *CHS*), 2.75-2.72 (m, 2H, CH_2), 2.17-2.11 (m, 1H, *CH*), 2.00 (s, 3H, NCOCH_3), 1.82-1.76 (m, 1H, *CH*), 1.32 (t, 3H, OCH_2CH_3 , $J = 7$ Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 212.8 ($\text{C}=\text{S}$), 201.5 (CO), 170.4 (NCOCH_3), 154.5 (*Car.*), 150.2 (*Car.*), 140.7 (*CHar.*), 122.9 (*CHar.*), 120.5 (*CHar.*), 70.3 (OCH_2), 49.8 (NCH_2), 49.0 (*CHS*), 48.2 (CH_2Cl), 36.6 (CH_2), 24.8 (CH_2), 23.1 (NCOCH_3), 13.7 (OCH_2CH_3) ppm. IR (neat) 2933, 1734, 1670, 1579, 1563, 1436, 1380, 1294, 1222, 1047, 733 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 424, 426, 428 (MH^+), 301, 303, 305 (MH^+-123).

Deleted: 7.8

Deleted: 7.

Deleted: 7.

Deleted: .1

Deleted: 7.

Deleted: .1

Deleted: 7.

Deleted: .1

Deleted: .1

Formatted: Spanish Mexico

Formatted: Spanish Mexico

Formatted: Spanish Mexico

Dithiocarbonic acid [1-{[acetyl-(6-chloro-pyridin-2-yl)-amino]-methyl}-4-oxo-4-(2-oxo-oxazolidin-3-yl)-butyl] ester ethyl ester **9c**: olefin **7a** (305 mg, 1.45 mmol) and xanthate derivative (710 mg, 2.85 mmol, 1.9 eq) were dissolved in 1,2-dichloroethane (0.72 mmol / 1 mL) and refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added (5 mol %) to the refluxing solution, followed by additional portions (2.5 mol % every 90 min). The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 0.3 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-ethyl acetate, 10:0 to 0:10) to give compound **9c** (87 % yield) as a white foam. ^1H NMR (CDCl_3 , 400 MHz) δ 7.74 (t, 1H, *CHar.*, $J = 8$ Hz), 7.29 (d, 1H, *CHar.*, $J = 8$ Hz), 7.28 (d, 1H, *CHar.*, $J = 8$ Hz), 4.55 (q, 2H, OCH_2 , $J = 7$ Hz), 4.40 (t, 2H, $\text{OCH}_2\text{CH}_2\text{N}$, $J = 8$ Hz), 4.36 (dd, 1H, NCH_2 , $J = 8$ and 14 Hz), 4.00 (t, 2H, $\text{OCH}_2\text{CH}_2\text{N}$, $J = 8$ Hz), 4.00 (m, 1H, NCH_2), 3.89-3.86 (m, 1H, *CHS*), 3.08-3.01 (m, 2H, CH_2), 2.26-2.20 (m, 1H, *CH*), 2.06 (s, 3H, NCOCH_3), 1.95-1.89 (m, 1H, *CH*), 1.36 (t, 3H, OCH_2CH_3 , $J = 7$ Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 213.1 ($\text{C}=\text{S}$), 172.3 (CONCO), 170.4 (NCOCH_3), 154.6 (NCOO), 153.5 (*Car.*), 150.4 (*Car.*), 140.6 (*CHar.*), 122.9 (*CHar.*), 120.7 (*CHar.*), 70.3 (OCH_2), 62.2 ($\text{NCH}_2\text{CH}_2\text{O}$), 50.0 (NCH_2), 49.2 (*CHS*), 42.5 ($\text{NCH}_2\text{CH}_2\text{O}$), 32.5 (CH_2), 25.8 (CH_2), 23.2 (NCOCH_3), 13.7 (OCH_2CH_3) ppm. IR (neat) 2925, 1782, 1701, 1672, 1580, 1563, 1439, 1387, 1223, 1046 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 461, 463 (MH^+), 399, 401 (MH^+-62), 337, 339 (MH^+-124), 285, 287 (MH^+-176).

Deleted: 7.

Deleted: 2

Deleted: 7.

Deleted: 2

Deleted: 7.

Deleted: 2

Deleted: .11

Deleted: 7.7

Deleted: .1

Deleted: .11

Formatted: English U.K.

Formatted: English U.K.

Formatted: English U.K.

Formatted: English U.K.

Formatted: English U.K.

Formatted: English U.K.

Dithiocarbonic acid (1-{{acetyl-(6-chloro-pyridin-2-yl)-amino}-methyl}-4-cyclopropyl-4-oxo-butyl) ester ethyl ester 9d : olefin **7a** (202 mg, 0.96 mmol) and xanthate derivative (460 mg, 2.25 mmol, 2.3 eq) were dissolved in 1,2-dichloroethane (1 mmol / 1 mL) and refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added (5 mol %) to the refluxing solution, followed by additional portions (2.5 mol % every 90 min). The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 0.7 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-ethyl acetate, 10:0 to 1:4) to give compound **9d** (77 % yield) as a yellow oil. ¹H NMR (CDCl₃, 400 MHz) δ 7.74 (t, 1H, CHar., J = 8 Hz), 7.29 (d, 1H, CHar., J = 8 Hz), 7.28 (d, 1H, CHar., J = 8 Hz), 4.55 (q, 2H, OCH₂, J = 7 Hz), 4.32 (dd, 1H, NCH₂, J = 7 and 14 Hz), 3.99 (dd, 1H, NCH₂, J = 7 and 14 Hz), 3.88-3.82 (m, 1H, CHS), 2.78-2.71 (m, 2H, CH₂), 2.18-2.15 (m, 1H, CH), 2.06 (s, 3H, NCOCH₃), 1.91-1.87 (m, 1H, CH), 1.81-1.78 (m, 1H, CH), 1.36 (t, 3H, OCH₂CH₃, J = 7 Hz) ppm ; ¹³C NMR (CDCl₃, 100 MHz) δ 213.1 (C=S), 209.6 (CO), 170.4 (NCOCH₃), 154.6 (Car.), 150.2 (Car.), 140.6 (CHar.), 122.8 (CHar.), 120.7 (CHar.), 70.2 (OCH₂), 50.0 (NCH₂), 49.4 (CHS), 40.1 (CH₂), 25.2 (CH₂), 23.2 (NCOCH₃), 20.7 (CH(CH₂)₂), 13.7 (OCH₂CH₃), 10.9 (CH(CH₂)₂) ppm. IR (neat) 2933, 1715, 1673, 1579, 1562, 1435, 1384, 1294, 1219, 1046, 806 cm⁻¹. MS (CI+NH₃) m/z 415, 417 (MH⁺), 388, 390 (MH⁺-27), 291, 293 (MH⁺-124).

Dithiocarbonic acid [1-{{acetyl-(6-chloro-pyridin-2-yl)-amino}-methyl}-3-(1-benzyl-1H-tetrazol-5-yl)-propyl] ester ethyl ester 9e : olefin **7a** (325 mg, 1.54 mmol) and xanthate derivative (938 mg, 3.20 mmol, 2.1 eq) were dissolved in 1,2-dichloroethane (0.77 mmol / 1 mL) and refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added (5 mol %) to the refluxing solution, followed by additional portions (2.5 mol % every 90 min). The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 0.57 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced

Deleted: 7.

Deleted: 7.

Deleted: 7.

Deleted: .1

Deleted: .1

pressure and purified by flash column chromatography (silica gel, petroleum ether-ethyl acetate, 10:0 to 0:10) to give compound **9e** (66 % yield) as a yellow foam. ^1H NMR (CDCl_3 , 400 MHz) δ 7.74 (t, 1H, *CHar.*, $J = 8$ Hz), 7.32 (m, 3H, *CHar.*), 7.27 (d, 1H, *CHar.*, $J = 8$ Hz), 7.24 (d, 1H, *CHar.*, $J = 8$ Hz), 7.17 (m, 2H, *CHar.*), 5.49 (dd, 2H, *NCH}_2*, $J = 19$ Hz), 4.50 (q, 2H, *OCH}_2*, $J = 7$ Hz), 4.31 (dd, 1H, *NCH}_2*, $J = 8$ and 14 Hz), 3.90 (dd, 1H, *NCH}_2*, $J = 8$ and 14 Hz), 3.83 (m, 1H, *CHS*), 2.93-2.82 (m, 2H, *CH}_2*), 2.32-2.29 (m, 1H, *CH*), 2.00 (s, 3H, *NCOCH}_3*), 2.03-1.94 (m, 1H, *CH*), 1.30 (t, 3H, *OCH}_2\text{CH}_3*, $J = 7$ Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 212.4 (*C=S*), 170.5 (*NCOCH}_3*), 154.4 (*Car.*), 154.2 (*NCN*), 150.4 (*Car.*), 140.9 (*CHar.*), 133.3 (*Car.*), 129.3 (*CHar.*), 128.9 (*CHar.*), 127.6 (*CHar.*), 123.1 (*CHar.*), 120.8 (*CHar.*), 70.4 (*OCH}_2*), 50.7 (*NCH}_2*), 49.5 (*NCH}_2*), 48.7 (*CHS*), 28.3 (*CH}_2*), 23.1 (*NCOCH}_3*), 20.7 (*CH}_2*), 13.7 (*OCH}_2\text{CH}_3*) ppm. IR (neat) 3684, 3430, 1670, 1605, 1438, 1223, 1050 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 505, 507 (MH^+), 446, 447 (MH^+-59).

Dithiocarbonic acid (1-{2-[acetyl-(6-chloro-pyridin-2-yl)-amino]-ethyl}-3-cyano-propyl) ester ethyl ester 9f: the olefin **7b** (400 mg, 1.78 mmol) and xanthate derivative (597 mg, 3.70 mmol, 2.1 eq) were dissolved in 1,2-dichloroethane (1.28 mmol / 1 mL) and refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added (5 mol %) to the refluxing solution, followed by additional portions (2.5 mol % every 90 min). The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 0.17 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 0:10) to give compound **9f** (97 % yield) as a yellow oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.71 (t, 1H, *CHar.*, $J = 8$ Hz), 7.27 (bs, 1H, *CHar.*), 7.21 (d, 1H, *CHar.*, $J = 8$ Hz), 4.58 (q, 2H, *OCH}_2*, $J = 7$ Hz), 3.96-3.92 (m, 2H, *NCH}_2*), 3.78 (m, 1H, *CHS*), 2.52-2.47 (m, 2H, *CH}_2\text{CN}*), 2.16-2.14 (m, 1H, *CH*), 2.06 (s, 3H, *COCH}_3*), 2.03-1.94 (m, 3H, *CH}_2* and *CH*), 1.38 (t, 3H, *OCH}_2\text{CH}_3*, $J = 7$ Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 212.5 (*C=S*), 170.2 (*NCO*), 154.7 (*Car.*), 150.0 (*Car.*), 140.6 (*CHar.*), 122.3 (*CHar.*), 119.2 (*CHar.*), 119.0 (*CN*), 70.4 (*OCH}_2*), 47.5 (*CHS*), 45.4 (*CH}_2*), 32.3 (*CH}_2*), 30.2 (*CH}_2*), 23.4 (*NCOCH}_3*), 14.8 (*CH}_2*), 13.7 (*OCH}_2\text{CH}_3*) ppm. IR (neat) 2982, 2936, 2246, 1672, 1580, 1562, 1434, 1385, 1290, 1222, 1164, 1111, 1047, 988, 736 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 385, 387 (M).

Dithiocarbonic acid (1-{2-[acetyl-(6-chloro-pyridin-2-yl)-amino]-ethyl}-4-oxo-pentyl) ester ethyl ester **9g** : the olefin **7b** (300 mg, 1.33 mmol) and xanthate derivative (454 mg, 2.55 mmol, 1.9 eq) were dissolved in 1,2-dichloroethane (0.9 mmol / 1 mL) and refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added (5 mol %) to the refluxing solution, followed by additional portions (2.5 mol % every 90 min). The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 0.24 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 1:9) to give compound **9g** (92 % yield) as a yellow oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.69 (t, 1H, CHar. , $J = 8$ Hz), 7.27 (bs, 1H, CHar.), 7.20 (d, 1H, CHar. , $J = 8$ Hz), 4.58 (q, 2H, OCH_2 , $J = 7$ Hz), 3.95 (t, 2H, NCH_2 , $J = 7$ Hz), 3.71 (m, 1H, CHS), 2.57 (t, 2H, CH_2CO , $J = 7$ Hz), 2.11 (s, 3H, CH_3), 2.07 (s, 3H, NCOCH_3), 2.07-1.92 (m, 3H, CH_2 and CH), 1.83-1.77 (m, 1H, CH), 1.38 (t, 3H, OCH_2CH_3 , $J = 7$ Hz) ppm ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 213.8 ($\text{C}=\text{S}$), 207.7 (CO), 170.3 (NCO), 154.8 (Car.), 150.0 (Car.), 140.6 (CHar.), 122.2 (CHar.), 119.3 (CHar.), 70.2 (OCH_2), 48.4 (CHS), 45.7 (NCH_2), 40.5 (CH_2), 33.0 (CH_2), 30.1 (COCH_3), 27.7 (CH_2), 23.5 (NCOCH_3), 13.8 (OCH_2CH_3) ppm. IR (neat) 2982, 2936, 1715, 1672, 1580, 1562, 1434, 1372, 1288, 1219, 1163, 1111, 1045, 987, 736 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 402 (M), 279, 281 (M-123).

4-(1-Acetyl-6-chloro-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-3-yl)-butan-2-one **10a** : a solution of xanthate **9a** (405 mg, 1.04 mmol) in chlorobenzene (0.1 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 20 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.7 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 1:4) to give compound **10a** (50 % yield) as white crystals (m.p. = 111°C, recrystallised with heptane/ethyl acetate). ^1H NMR (CDCl_3 , 400 MHz) δ 7.40 (d, 1H, CHar. , $J = 8$ Hz), 6.90 (d, 1H, CHar. , $J = 8$ Hz), 4.15 (dd, 1H, NCH_2 , $J = 10$ Hz and 12 Hz), 3.72 (dd, 1H, NCH_2 , $J = 12$ Hz and 6 Hz), 3.25 (m, 1H, CH), 2.62 (s, 3H, NCOCH_3), 2.50 (m, 2H, COCH_2), 2.14 (s, 3H, COCH_3), 2.05 (m, 1H, CH_2), 1.75 (m, 1H, CH_2) ppm ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 207.3 ($\text{C}=\text{O}$), 170.0 ($\text{NC}=\text{O}$), 155.2 (Car.), 148.5 (Car.), 135.0 (CHar.), 127.5 (Car.), 117.7 (CHar.), 51.8 (NCH_2), 39.9 (CH_2), 34.7 (CH), 30.2 (COCH_3), 28.5 (CH_2), 25.0 (NCOCH_3) ppm. IR (CH_2Cl_2) 3684, 3409, 1716, 1665, 1601, 1580, 1477, 1386, 1316 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 267, 269 (MH^+). Anal. calcd. for $\text{C}_{13}\text{H}_{15}\text{ClN}_2\text{O}_2$: C, 58.54 ; H, 5.67, found: C, 58.18 ; H, 5.64.

Deleted: 7.

Deleted: 7.

Deleted: .1

Deleted: .5

Deleted: .5

Deleted: .1

Deleted: 7.

Deleted: 7.

Deleted: .1

Deleted: .1

Deleted: 5.7

4-(1-Acetyl-6-chloro-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-3-yl)-1-chloro-butan-2-one

10b : a solution of xanthate **9b** (433 mg, 1.02 mmol) in chlorobenzene (0.07 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 20 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.6 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-ethyl acetate, 10:0 to 1:4) to give compound **10b** (45 % yield) as white crystals (mp = 82°C, recrystallisation with heptane/ethyl acetate). ¹H NMR (CDCl₃, 400 MHz) δ 7.43 (d, 1H, CHar., J = 8 Hz), 6.93 (d, 1H, CHar., J = 8 Hz), 4.19 (dd, 1H, NCH₂, J = 10 and 12 Hz), 4.07 (s, 2H, CH₂Cl), 3.76 (dd, 1H, NCH₂, J = 6 and 12 Hz), 3.33-3.25 (m, 1H, CH), 2.76-2.68 (m, 2H, CH₂), 2.65 (s, 3H, NCOCH₃), 2.14-2.06 (m, 1H, CH), 1.86-1.74 (m, 1H, CH) ppm ; ¹³C NMR (CDCl₃, 100 MHz) δ 201.8 (CO), 170.1 (NCOCH₃), 148.7 (Car.), 139.3 (Car.), 135.1 (CHar.), 127.2 (Car.), 117.8 (CHar.), 51.8 (NCH₂), 48.1 (CH₂Cl), 36.1 (CH₂), 34.8 (CH), 28.5 (CH₂), 25.0 (NCOCH₃) ppm. IR (CH₂Cl₂) 3684, 1713, 1665, 1602, 1580, 1438, 1384, 1316 cm⁻¹. MS (CI+NH₃) m/z 301, 303 (MH⁺), 269, 271 (MH⁺-32).

Deleted: 7.7

Deleted: 7

Deleted: .7

Deleted: 9.8

Deleted: 5.

Deleted: 3

3-[3-(1-Acetyl-6-chloro-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-3-yl)-propionyl]-oxazolidin-2-one

10c : a solution of xanthate **9c** (570 mg, 1.24 mmol) in chlorobenzene (0.1 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 20 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.4 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-ethyl acetate, 10:0 to 0:10) to give compound **10c** (66 % yield) as a yellow foam. ¹H NMR (CDCl₃, 400 MHz) δ 7.41 (d, 1H, CHar., J = 8 Hz), 6.87 (d, 1H, CHar., J = 8 Hz), 4.39 (t, 2H, OCH₂CH₂N, J = 8 Hz), 4.15 (m, 1H, NCH₂, J = 11 Hz), 3.98 (t, 2H, OCH₂CH₂N, J = 8 Hz), 3.76 (m, 1H, NCH₂, J = 5 and 12 Hz), 3.29-3.25 (m, 1H, CH), 2.95 (t, 2H, CH₂, J = 7 Hz), 2.58 (s, 3H, NCOCH₃), 2.09-2.01 and 1.87-1.82 (m, 2H, CH₂) ppm ; ¹³C NMR (CDCl₃, 100 MHz) δ 172.1 (NCOO), 169.8 (NCOCH₃), 155.2 (Car.), 153.5 (NCOCH₂), 148.3 (Car.), 135.1 (CHar.), 127.3 (Car.), 117.6 (CHar.), 62.2 (OCH₂), 51.8 (NCH₂), 42.4 (NCH₂), 34.9 (CH), 32.1 (CH₂), 29.3 (CH₂), 24.9

Deleted: 7.7

Deleted: 7.7

Deleted: .4

Deleted: .4

(NCOCH₃) ppm. IR (neat) 2926, 1781, 1701, 1665, 1600, 1579, 1432, 1386, 1260, 1114, 1041 cm⁻¹. MS (CI+NH₃) m/z 337, 339 (M).

Formatted: Spanish Mexico

Formatted: Spanish Mexico

3-(1-Acetyl-6-chloro-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-3-yl)-1-cyclopropyl-propan-1-one 10d : a solution of xanthate **9d** (283 mg, 0.68 mmol) in chlorobenzene (0.1 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 20 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.66 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-ethyl acetate, 10:0 to 3:7) to give compound **10d** (57 % yield) as yellow crystals (m.p. = 95°C, recrystallised with heptane/ethyl acetate). ¹H NMR (CDCl₃, 400 MHz) δ 7.41 (d, 1H, CHar., J = 8 Hz), 6.90 (d, 1H, CHar., J = 8 Hz), 4.16 (dd, 1H, NCH₂, J = 10 and 12 Hz), 3.75 (dd, 1H, NCH₂, J = 6 and 12 Hz), 3.29-3.22 (m, 1H, CH), 2.67-2.61 (m, 2H, CH₂), 2.63 (s, 3H, NCOCH₃), 2.08-2.03 (m, 1H, CH), 1.91-1.87 (m, 1H, CH), 1.78-1.75 (m, 1H, CH), 1.01-0.98 (m, 2H, CH₂), 0.89-0.86 (m, 2H, CH₂) ppm ; ¹³C NMR (CDCl₃, 100 MHz) δ 209.6 (CO), 170.0 (NCOCH₃), 155.2 (Car.), 148.4 (Car.), 135.1 (CHar.), 127.6 (Car.), 117.7 (CHar.), 51.9 (NCH₂), 39.7 (CH₂), 34.9 (CH), 28.8 (CH₂), 24.9 (NCOCH₃), 20.7 (CH(CH₂)₂), 11.1 (CH(CH₂)₂) ppm. IR (CH₂Cl₂) 3683, 1697, 1664, 1600, 1579, 1477, 1386, 1315, 1087 cm⁻¹. MS (CI+NH₃) m/z 293, 295 (MH⁺). Anal. calcd. for C₁₅H₁₇ClN₂O₂: C, 61.54 ; H, 5.85, found: C, 61.54 ; H, 6.01.

Deleted:

Deleted: 7.7

Deleted: 7.7

Deleted: 5.

1-{3-[2-(1-Benzyl-1H-tetrazol-5-yl)-ethyl]-6-chloro-2,3-dihydro-pyrrolo[2,3-b]pyridin-1-yl}-ethanone 10e : a solution of xanthate **9e** (520 mg, 1.03 mmol) in chlorobenzene (0.09 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 20 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.3 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 1:9) to give compound **10e** (43 % yield) as a yellow oil. ¹H NMR (CDCl₃, 400 MHz) δ 7.35-7.30 (m, 3H, CHar.), 7.28 (d, 1H, CHar., J = 8 Hz), 7.15-7.13 (m, 2H, CHar.), 6.84 (d, 1H, CHar., J = 8 Hz), 5.51 (s, 2H, NCH₂), 4.03 (dd, 1H, NCH₂, J = 12 Hz), 3.64 (dd, 1H, NCH₂, J = 5 and 12 Hz), 3.23 (m, 1H, CH), 2.74 (t, 2H, CH₂, J = 8 Hz), 2.59 (s, 3H, NCOCH₃), 2.09-1.99 and 1.84-1.77 (m, 2H, CH₂) ppm ; ¹³C NMR (CDCl₃, 100 MHz) δ 169.8 (NCOCH₃), 155.0 (Car.),

Deleted: 7.7

Deleted: 7.7

Deleted: 1.9 and 12.1

Deleted: .3

Deleted: .1

Deleted: 7.6

153.9 (NCN), 148.6 (Car.), 135.1 (CHar.), 133.1 (Car.), 129.3 (CHar.), 129.1 (CHar.), 127.4 (CHar.), 126.7 (Car.), 117.7 (CHar.), 51.5 (NCH₂), 50.9 (NCH₂), 34.4 (CH), 31.5 (CH₂), 24.9 (NCOCH₃), 20.3 (CH₂) ppm. IR (neat) 3687, 2304, 1666, 1601, 1580, 1438, 1385, 1316, 1244, 1087 cm⁻¹. MS (CI+NH₃) m/z 382, 384 (M).

3-(1-Acetyl-7-chloro-1,2,3,4-tetrahydro-[1,8]naphthyridin-4-yl)-propionitrile 10f : a solution of xanthate **9f** (670 mg, 1.73 mmol) in chlorobenzene (0.1 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 20 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.2 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 0:10) to give compound **10f** (72 % yield) as a yellow oil. ¹H NMR (CDCl₃, 400 MHz) δ 7.44 (d, 1H, CHar., J = 8 Hz), 7.01 (d, 1H, CHar., J = 8 Hz), 3.83 (m, 2H, NCH₂), 2.97 (m, 1H, CH), 2.47 (s, 3H, COCH₃), 2.41 (t, 2H, CH₂CN), 2.01-1.95 (m, 2H, 2xCH), 1.84-1.77 (m, 2H, 2xCH) ppm ; ¹³C NMR (CDCl₃, 100 MHz) δ 171.4 (NCO), 150.6 (Car.), 147.1 (Car.), 138.9 (CHar.), 124.2 (Car.), 119.4 (CHar.), 118.8 (CN), 40.4 (CH₂), 34.9 (CH), 29.2 (CH₂), 26.5 (CH₂), 26.0 (NCOCH₃), 15.0 (CH₂) ppm. IR (neat) 2994, 2246, 1733, 1667, 1586, 1563, 1434, 1371, 1313, 1269, 1110, 916, 732 cm⁻¹. MS (CI+NH₃) m/z 264 (MH⁺). Anal. calcd. for C₁₃H₁₄ClN₃O: C, 59.21 ; H, 5.35, found: C, 58.76 ; H, 5.39.

4-(1-Acetyl-7-chloro-1,2,3,4-tetrahydro-[1,8]naphthyridin-4-yl)-butan-2-one 10g : a solution of xanthate **9g** (500 mg, 1.24 mmol) in chlorobenzene (0.1 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 20 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.4 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 0:10) to give compound **10g** (74 % yield) as a colorless oil. ¹H NMR (CDCl₃, 400 MHz) δ 7.55 (d, 1H, CHar., J = 8 Hz), 7.07 (d, 1H, CHar., J = 8 Hz), 3.94-3.83 (m, 2H, NCH₂), 2.86-2.82 (m, 1H, CHS), 2.57 (t, 2H, CH₂CO, J = 7 Hz), 2.54 (s, 3H, CH₃), 2.20 (s, 3H, NCOCH₃), 2.07-1.92 (m, 3H, CH₂ and

Deleted: 7.

Deleted: 7.

Deleted: 7.9

Deleted: 7.9

Deleted: 5

CH), 1.80-1.72 (m, 1H, *CH*) ppm ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 207.6 (CO), 171.3 (NCO), 150.6 (Car.), 146.3 (Car.), 138.9 (CHar.), 126.0 (Car.), 119.2 (CHar.), 40.6 (NCH₂), 40.4 (CH₂), 35.1 (CH), 30.0 (COCH₃), 27.4 (CH₂), 26.9 (CH₂), 25.9 (NCOCH₃) ppm. IR (neat) 2939, 1715, 1668, 1585, 1558, 1434, 1369, 1311, 1269, 1221, 1163, 1109, 1006, 732 cm^{-1} . MS (CI+NH₃) m/z 281, 283 (MH^+).

Acetic acid 4-[butyl-(6-chloro-pyridin-2-yl)-carbamoyl]-2-ethoxythiocarbonylsulfanyl-butyl ester **11** : xanthate **4c** (200 mg, 0.58 mmol, 1 eq) and allyl acetate (0.25 mL, 2.31 mmol, 4 eq) were dissolved in 1,2-dichloroethane (1 mmol / 1 mL) and refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added (5 mol %) to the refluxing solution, followed by additional portions (2.5 mol % every 90 min). The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 0.35 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 3:2) to give compound **11** (51 % yield) as a yellow oil and compound **12** (10% yield) as a yellow oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.70 (t, 1H, *CHar.*, $J = 8$ Hz), 7.24 (d, 1H, *CHar.*, $J = 8$ Hz), 7.17 (bs, 1H, *CHar.*), 4.60 (q, 2H, OCH_2 , $J = 7$ Hz), 4.26 (dd, 1H, OCH_2 , $J = 5$ and 11 Hz), 4.18 (dd, 1H, OCH_2 , $J = 6$ and 11 Hz), 3.97-3.91 (m, 1H, *CHS*), 3.81 (t, 2H, NCH_2 , $J = 7$ Hz), 2.47-2.39 (m, 2H, CH_2), 2.23-2.19 (m, 1H, *CH*), 2.04 (s, 3H, COCH_3), 1.94-1.90 (m, 1H, *CH*), 1.53-1.45 (quin, 2H, CH_2 , $J = 7$ Hz), 1.39 (t, 3H, OCH_2CH_3 , $J = 7$ Hz), 1.30 (sex, 2H, CH_2 , $J = 7$ Hz), 0.87 (t, 3H, CH_3 , $J = 7$ Hz) ppm ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 212.8 ($\text{C}=\text{S}$), 171.4 (OCO), 170.6 ($\text{NC}=\text{O}$), 154.7 (Car.), 150.1 (Car.), 140.4 (CHar.), 122.4 (CHar.), 119.6 (CHar.), 70.2 (OCH_2), 65.7 (OCH_2), 48.8 (*CHS*), 47.8 (CH_2N), 32.2 (CH_2), 30.3 (CH_2), 26.4 (CH_2), 20.7 (COCH_3), 19.9 (CH_2), 13.6 (CH_3) ppm. IR (neat) 2958, 2933, 1745, 1667, 1580, 1564, 1434, 1384, 1224, 1160, 1142, 1111, 1048, 797, 735 cm^{-1} .

Acetic acid 9-butyl-2-chloro-8-oxo-6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-5-ylmethyl ester **12** : a solution of xanthate **11** (131 mg, 0.29 mmol) in 1,2-dichloroethane (0.1 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 90 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 2 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash

Deleted: 7.

Deleted: 7.

Deleted: .1

Deleted: 4.8

Deleted: .3

Deleted: .3

Deleted: .1

Deleted: .5

Deleted: and 7.3

Deleted: .1

Deleted: .3 and 7.5

Deleted: .3

column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 3:2) to give compound **12** (35 % yield) as a yellow oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.50 (d, 1H, CHar. , $J = 8$ Hz), 7.16 (d, 1H, CHar. , $J = 8$ Hz), 4.43 (dd, 1H, OCH_2 , $J = 11$ Hz), 4.33 (dd, 2H, OCH_2 , $J = 6$ and 11 Hz), 4.10-4.06 (m, 1H, NCH_2), 3.99-3.90 (m, 1H, NCH_2), 3.19 (m, 1H, CH), 2.46-2.39 (m, 2H, CH_2), 2.25-2.22 (m, 1H, CH), 2.03 (s, 3H, COCH_3), 1.79-1.74 (m, 1H, CH), 1.65-1.59 (m, 1H, CH), 1.51-1.48 (m, 1H, CH), 1.30-1.23 (m, 2H, CH_2), 0.88 (t, 3H, CH_3 , $J = 7$ Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 171.8 (OCO), 170.7 (NC=O), 154.9 (Car.), 148.3 (Car.), 137.2 (CHar.), 128.3 (Car.), 121.2 (CHar.), 63.9 (OCH_2), 45.7 (CH_2N), 37.1 (CH), 33.1 (CH_2), 31.7 (CH_2), 30.6 (CH_2), 20.7 (COCH_3), 20.3 (CH_2), 13.7 (CH_3) ppm. IR (neat) 2957, 1745, 1674, 1580, 1563, 1445, 1408, 1369, 1231, 1113, 1042, 810 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 324, 326 (M), 341, 343 ($\text{M}+\text{NH}_3$).

Pent-4-enoic acid butyl-(6-chloro-pyridin-2-yl)-amide 13 : a solution of aminopyridine **2c** (500 mg, 2.71 mmol), DMAP (772 mg, 6.32 mmol, 2.3 eq) and hept-4-enoyl chloride (2 eq, freshly prepared from 0.55 mL of hepten-4-oic acid and 0.51 mL of oxalyl chloride) in 1,2-dichloroethane (15 mL) was stirred for 1 hour and then refluxed for 2 hours. When starting material was totally consumed, the solution was cooled to room temperature. 1,2-dichloroethane was evaporated in vacuo and the crude mixture neutralized with saturated aqueous Na_2CO_3 , extracted with dichloromethane, dried and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 4:1) to give compound **13** (81 % yield) as a colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.70 (t, 1H, CHar. , $J = 8$ Hz), 7.24 (d, 1H, CHar. , $J = 8$ Hz), 7.19 (bs, 1H, CHar.), 5.83-5.73 (m, 1H, $\text{CH}=\text{CH}_2$), 5.02-4.98 (dd, 2H, $\text{CH}=\text{CH}_2$, $J = 17$ Hz), 3.83 (t, 2H, NCH_2 , $J = 8$ Hz), 2.40-2.34 (m, 4H, $\text{CH}_2\text{CH}_2\text{CO}$), 1.55-1.49 (quin, 2H, CH_2), 1.35-1.25 (sex, 2H, CH_2), 0.88 (t, 3H, CH_3 , $J = 7$ Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 172.1 (NC=O), 155.2 (Car.), 150.3 (Car.), 140.4 (CHar.), 137.4 (CHar.), 122.3 (CHar.), 119.8 ($\text{CH}=\text{CH}_2$), 115.3 ($\text{CH}_2=\text{CH}$), 47.8 (CH_2N), 34.5 (CH_2), 30.6 (CH_2), 29.5 (CH_2), 20.1 (CH_2), 13.8 (CH_3) ppm. IR (neat) 3370, 3079, 2959, 2873, 2362, 1718, 1668, 1579, 1435, 1386, 1162, 1111, 915, 797 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 267, 269 (MH^+).

Dithiocarbonic acid (1-{2-[butyl-(6-chloro-pyridin-2-yl)-carbamoyl]-ethyl}-4-oxo-pentyl) ester ethyl ester 14 : the olefin **13** (100 mg, 0.37 mmol) and xanthate derivative (145 mg, 0.81 mmol, 2.2 eq) were dissolved in 1,2-dichloroethane (0.7 mmol / 1 mL) and refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added (5 mol %) to the refluxing solution, followed by additional portions (2.5 mol % every 90 min). The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 0.24 eq of DLP were added. The crude mixture was then cooled to room temperature, concentrated under reduced

pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 2:3) to give compound **14** (88 % yield) as a colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.70 (t, 1H, *CHar.*, $J = 8$ Hz), 7.24 (d, 1H, *CHar.*, $J = 8$ Hz), 7.19 (bs, 1H, *CHar.*), 4.62 (q, 2H, OCH_2 , $J = 7$ Hz), 3.82 (t, 2H, NCH_2 , $J = 7$ Hz), 3.79-3.68 (m, 1H, *CHS*), 2.60 (t, 2H, CH_2CO , $J = 7$ Hz), 2.43 (m, 2H, CH_2CON), 2.18-2.14 (m, 1H, *CH*), 2.14 (s, 3H, COCH_3), 1.99-1.96 (m, 1H, *CH*), 1.91-1.83 (m, 2H, CH_2), 1.54-1.45 (quin, 2H, CH_2), 1.42 (t, 3H, OCH_2CH_3 , $J = 7$ Hz), 1.33-1.24 (sex, 2H, CH_2), 0.89 (t, 3H, CH_3 , $J = 7$ Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 213.8 ($\text{C}=\text{S}$), 207.5 ($\text{C}=\text{O}$), 171.6 ($\text{NC}=\text{O}$), 154.7 (*Car.*), 149.9 (*Car.*), 140.3 (*CHar.*), 122.2 (*CHar.*), 119.6 (*CHar.*), 69.9 (OCH_2), 50.4 (*CHS*), 47.6 (CH_2N), 40.5 (CH_2), 32.2 (CH_2), 30.2 (CH_2), 30.0 (CH_2), 29.6 (COCH_3), 28.2 (CH_2), 19.9 (CH_2), 13.7 (CH_3) ppm. IR (neat) 2960, 1714, 1666, 1579, 1563, 1434, 1386, 1285, 1213, 1160, 1142, 1111, 1047, 987, 797 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 445, 447 (MH^+), 338, 340 (MH^+-107), 322, 324 (MH^+-123).

9-Butyl-2-chloro-5-(3-oxo-butyl)-5,6,7,9-tetrahydro-pyrido[2,3-b]azepin-8-one 15 : a solution of xanthate **14** (147 mg, 0.33 mmol) in 1,2-dichloroethane (0.1 mmol / 1 mL) was refluxed for 15 min under argon. Lauroyl peroxide (DLP) was then added portionwise (20 mol % per 90 minutes) to the refluxing solution. The reaction being regularly monitored for the disappearance of the starting material by thin-layer chromatography, the starting material was totally consumed when 1.9 eq of DLP were added. the crude mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether-diethyl ether, 10:0 to 2:3) to give compound **15** (59 % yield) as a yellow oil and 20 % of the reduced product. ^1H NMR (CDCl_3 , 400 MHz) δ 7.51 (d, 1H, *CHar.*, $J = 8$ Hz), 7.15 (d, 1H, *CHar.*, $J = 8$ Hz), 4.11-4.04 and 3.92-3.85 (m, 2H, NCH_2), 2.76-2.71 (m, 1H, *CH*), 2.48-2.31 (m, 4H, CH_2CO and CH_2), 2.19-2.15 (m, 1H, CH_2CON), 2.12 (s, 3H, COCH_3), 2.02-1.92 (m, 2H, CH_2), 1.68-1.40 (m, 3H, CH_2), 1.27-1.22 (m, 2H, CH_2), 0.86 (t, 3H, CH_3 , $J = 7$ Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 207.3 ($\text{C}=\text{O}$), 172.1 ($\text{NC}=\text{O}$), 154.9 (*Car.*), 147.8 (*Car.*), 137.1 (*CHar.*), 130.7 (*Car.*), 121.2 (*CHar.*), 45.4 (CH_2N), 41.1 (CH_2), 36.9 (*CH*), 35.3 (CH_2), 33.6 (CH_2), 30.6 (CH_2), 30.0 (COCH_3), 25.4 (CH_2), 20.2 (CH_2), 13.7 (CH_3) ppm. IR (neat) 2956, 1715, 1673, 1575, 1562, 1444, 1407, 1373, 1299, 1145, 1106 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 323, 325 (MH^+).