Supporting Information

Tin-free Radical Sequences under Acidic Conditions. A Convergent Access to Azoles Containing Structures

Fabien Gagosz and Samir Z. Zard*

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

General Considerations

All reactions were carried out under an atmosphere of dry argon. Commercial reagents were used as received without further purification. All products were purified by flash column chromatography using silica gel SDS 60 C.C. 40-63. NMR spectra were recorded in CDCl₃ with TMS as an internal standard at ambient temperature on a Bruker AMX400 operating at 400 MHz for ¹H and 100 MHz for ¹³C. Infrared Absorption spectra were recorded as a solution in CCl₄ 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

Synthesis of olefins 2a-e

1-Allyl-[1,2,4]triazole (2a). To a stirred suspension of [1,2,3]triazole (6.9 g, 100 mmol) and allylbromide (12.1 ml, 140 mmol) in 100 ml of THF was added dropwise DBU (18.0 ml, 120 mmol) over 1 hour. The resulting mixture was stirred at room temperature for 12 hours, filtered and the cake washed with THF (100 ml). The filtrate was concentrated to residue and partitioned between water (200 ml) and EtOAc (400 ml and 100 ml). The combined organic layers were concentrated and the residue distilled under reduced pressure to afford **2a** (4.7 g, 43%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 4.72 (d, *J* = 5.8 Hz, 2H), 5.16-5.29 (m, 2H), 5.87-5.99 (m, 1H), 7.88 (s, 1H), 8.03 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 52.0, 119.8, 131.1, 142.8, 151.9. IR(CCl₄) 2933, 1529, 1502, 1418, 1346, 1273, 1202, 1138, 1014 cm⁻¹. MS (CI+NH₃) *m/z* 110 (MH⁺).

1-Buten-3-enyl-[1,2,4]triazole (2b). To a stirred suspension of [1,2,3]triazole (3.8 g, 55.5 mmol) and 4-bromo-but-1-ene (5.1 ml, 50 mmol) in 100 ml of THF was added dropwise DBU (9.1 ml, 61 mmol) over 1 hour. The resulting mixture was stirred at room temperature for 12 hours, filtered and the cake washed with THF (50 ml). The filtrate was concentrated to residue and partitioned between water (100 ml) and EtOAc (200 ml and 50 ml). The combined organic layers were concentrated and the residue distilled under reduced pressure to afford **2b** (3.2 g, 52%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 2.58 (td, J = 7.0, 6.8 Hz, 2H), 4.18 (t, J = 7.0 Hz, 2H), 4.98-5.04 (m, 2H), 5.61-5.73 (m, 1H), 7.89 (s, 1H), 8.00 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 35.9, 49.0, 118.4, 133.1, 143.0, 151.9. IR(CCl_4) 2982, 2947, 1642, 1258, 1503, 1449, 1434, 1362, 1345, 1273, 1203, 1139 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 124 (MH^+).

1-allyl-imidazole (2c). To a solution of imidazole (2.7 g, 40 mmol) in 75 ml of THF was added portionwise NaH (60% in mineral oil, 1.76 g, 44 mmol). The resulting mixture was refluxed for 1 hour. The solution was then cooled to room temperature and allylbromide (3.8 ml, 44 mmol) was added. The mixture was heated at 50°C for 3 hours, cooled to room temperature and diluted with ether. The ether extrates were combined, washed with brine, dried over MgSO_4 and concentrated. The crude product was distilled under reduced pressure to afford **2c** (1.38 g, 32%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 4.50 (d, J = 5.6 Hz, 2H), 5.10-5.25 (m, 2H), 5.85-5.97 (m, 1H), 6.87 (s, 1H), 7.03 (s, 1H), 7.43 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 49.3, 118.5, 119.7, 129.4, 132.8, 137.1. IR(CCl_4) 2922, 1646, 1502, 1437, 1420, 1294, 1279, 1230, 1108, 1073 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 109 (MH^+).

1-but-3-enyl-imidazole (2d). To a solution of imidazole (1.7 g, 25 mmol) in 50 ml of THF was added portionwise NaH (60% in mineral oil, 1.1 g, 27.5 mmol). The resulting mixture was refluxed for 1 hour. The solution was then cooled to room temperature and 4-bromo-but-1-ene (2.8 ml, 27.5 mmol) was added. The mixture was refluxed for 3 hours, cooled to room temperature and diluted with ether. The ether extrates were combined, washed with brine, dried over MgSO_4 and concentrated. The crude product was distilled under reduced pressure to afford **2d** (2.2 g, 72%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 2.51 (td, J = 7.0, 6.9 Hz, 2H), 3.99 (t, J = 7.0 Hz, 2H), 5.03-5.11 (m, 2H), 5.67-5.78 (m, 1H), 6.92 (s, 1H), 7.04 (s, 1H), 7.46 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 35.3, 46.3, 118.0, 118.7, 129.3, 133.5, 136.9. IR(CCl_4) 2981, 2936, 1641, 1503, 1457, 1437, 1357, 1283, 1229, 1110, 1075, 1034 cm^{-1} . MS ($\text{CI}+\text{NH}_3$) m/z 123 (MH^+).

1-but-3-enyl-benzimidazole (2e). To a solution of benzimidazole (2.95 g, 25 mmol) in 50 ml of THF was added portionwise NaH (60% in mineral oil, 1.1 g, 27.5 mmol). The resulting mixture was refluxed for 1 hour. The solution was then cooled to room temperature and 4-bromo-but-1-ene (2.8 ml, 27.5 mmol) was added. The mixture was refluxed for 3 hours, cooled to room temperature and diluted with ether. The ether extrates were combined, washed with brine, dried over MgSO₄ and concentrated. The crude product was distilled under reduced pressure to afford **2e** (2.8 g, 66%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 2.60 (td, *J*= 7.0, 6.9 Hz, 2H), 4.20 (t, *J*= 7.0 Hz, 2H), 4.99-5.09 (m, 2H), 5.69-5.80 (m, 1H), 7.25-7.33 (m, 2H), 7.37-7.42 (m, 1H), 7.79-7.83 (m, 1H), 7.87 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 34.0, 44.5, 109.6, 118.5, 120.4, 122.1, 122.8, 133.5, 142.9, 143.0. IR(CCl₄) 3004, 2935, 1615, 1494,; 1457, 1438, 1360, 1330, 1284, 1261, 1246, 1200 cm⁻¹. MS (CI+NH₃) *m/z* 173 (MH⁺).

Typical procedure for the synthesis of radical adducts 3a-f

Dithiocarbonic acid *O*-ethyl ester *S*-(4-oxo-1-[1,2,4]triazol-1-ylmethyl-pentyl) ester (3a).

A solution of dithiocarbonic acid *O*-ethyl ester *S*-(2-oxo-propyl) ester **1a** (178 mg, 1 mmol), olefin **2a** (218 mg, 2 mmol) and 10-camphorsulfonic acid (464 mg, 2 mmol) in 2 ml of 1,2-dichloroethane was refluxed for 15 min under argon. Lauroyl peroxide was then added portionwise (2 to 5 mol% / **1a** per hour) to the refluxing solution. When **1a** was totally consumed (after a global addition of 28 mg of lauroyl peroxide (0.07 mmol)), the crude mixture was cooled to room temperature, diluted with ether and washed with saturated aqueous NaHCO₃. The organic layer was dried over MgSO₄, filtered, concentrated and purified by flash column chromatography (silica gel, AcOEt-MeOH, 98:2) to give **3a** (215 mg, 75%) as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 1.38 (t, *J*= 7.1 Hz, 3H), 1.76-1.84 (m, 1H), 1.95-2.12 (m, 1H), 2.09 (s, 3H), 2.60 (t, *J*= 6.2 Hz, 2H), 4.04-4.14 (m, 1H), 4.45 (dd, *J*= 6.0, 6.0 Hz, 2H), 4.58 (q, *J*= 7.1 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 13.7, 24.7, 29.9, 40.3, 50.1, 52.9, 70.6, 143.9, 152.0, 206.7, 212.2. IR(CCl₄) 2935, 1718, 1507, 1364, 1223, 1048 cm⁻¹. MS (CI+NH₃) *m/z* 288 (MH⁺).

Dithiocarbonic acid *O*-ethyl ester *S*-(4-(4-fluoro-phenyl)-4-oxo-1-[1,2,4]triazol-1-ylmethyl-butyl) ester (3b). Pale yellow oil (88%). Silica gel, AcOEt-Petroleum ether, 70:30.

^1H NMR (400 MHz, CDCl_3) δ 1.33 (t, J = 7.3 Hz, 3H), 1.86-1.95 (m, 1H), 2.15-2.24 (m, 1H), 3.07-3.12 (m, 2H), 4.14-4.21 (m, 1H), 4.44 (dd, J = 14.2, 6.7 Hz, 1H), 4.50-4.56 (m, 2H), 4.53 (q, J = 7.3 Hz, 2H), 7.05 (dd, J = 8.6, 8.6 Hz, 2H), 7.89 (s, 1H), 7.88-7.91 (m, 2H), 8.15 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.6, 25.0, 35.3, 50.1, 52.8, 70.6, 115.6, 130.6, 132.8, 143.9, 151.9, 164.8, 196.6, 212.0. IR(CCl_4) 2984, 1691, 1599, 1503, 1273, 1227, 1156, 1138, 1052 cm^{-1} . MS (CI+ NH_3) m/z 246 (M-HS(CS)OEt+ H^+), 368 (MH^+).

Dithiocarbonic acid *O*-ethyl ester *S*-[3-(methyl-phenyl-carbamoyl)-1-[1,2,4]triazol-1-ylmethyl-propyl] ester (3c). Pale yellow oil (65%). Silica gel, AcOEt-Petroleum ether, 90:10. ^1H NMR (400 MHz, CDCl_3) δ 1.32 (t, J = 7.0 Hz, 3H), 1.68-1.78 (m, 1H), 1.96-2.06 (m, 1H), 2.08-2.22 (m, 2H), 3.17 (s, 3H), 4.05-4.13 (m, 1H), 4.32 (dd, J = 14.2, 6.6 Hz, 1H), 4.39 (dd, J = 14.2, 5.8 Hz, 1H), 4.51 (q, J = 7.0 Hz, 2H), 7.07 (d, J = 7.2 Hz, 2H), 7.27 (t, J = 7.2 Hz), 7.34 (t, J = 7.2 Hz), 7.83 (s, 1H), 8.06 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.6, 26.5, 31.0, 37.2, 49.8, 52.6, 70.3, 127.1, 127.8, 129.8, 143.5, 143.7, 151.8, 171.2, 212.1. IR(CCl_4) 2984, 2939, 1661, 1596, 1496, 1441, 1420, 1387, 1273, 1221, 1138, 1112, 1052 cm^{-1} . MS (CI+ NH_3) m/z 356 (M-HS(CS)OEt+ H^+), 379 (MH^+).

Dithiocarbonic acid *O*-ethyl ester *S*-[4-oxo-4-(2-oxo-oxazolidin-3-yl)-1-[1,2,4]triazol-1-ylmethyl-butyl] ester (3d). Pale yellow oil (82%). Silica gel, AcOEt. ^1H NMR (400 MHz, CDCl_3) δ 1.40 (t, J = 7.1 Hz, 3H), 1.89-1.99 (m, 1H), 2.13-2.26 (m, 2H), 2.34-2.42 (m, 2H), 2.96-3.16 (m, 2H), 3.68-3.75 (m, 1H), 4.00 (t, J = 7.9 Hz, 2H), 4.35 (t, J = 6.9 Hz, 2H), 4.41 (t, J = 7.9 Hz, 2H), 4.61 (q, J = 7.1 Hz, 2H), 7.94 (s, 1H), 8.10 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.8, 28.9, 32.4, 34.7, 42.6, 47.1, 47.7, 62.2, 70.6, 143.5, 152.3, 153.5, 172.4, 213.2. IR(CCl_4) 2984, 1792, 1704, 1503, 1386, 1361, 1264, 1222, 1139, 1111, 1048 cm^{-1} . MS (CI+ NH_3) m/z 253, 312, 373 (MH^+).

Dithiocarbonic acid *S*-(3-benzothiazol-2-yl-1-imidazol-1-ylmethyl-propyl) ester *O*-ethyl ester (3e). Pale yellow oil (61%). Silica gel, AcOEt. ^1H NMR (400 MHz, CDCl_3) δ 1.39 (t, J = 7.0 Hz, 3H), 2.03-2.14 (m, 1H), 2.27-2.37 (m, 1H), 3.14-3.24 (m, 1H), 3.28-3.37 (m, 1H), 4.10-4.21 (m, 2H), 4.29-4.36 (m, 1H), 4.62 (q, J = 7.0 Hz, 2H), 7.02 (s, 1H), 7.06 (s, 1H), 7.36 (dd, J = 8.1, 7.5 Hz, 1H), 7.46 (dd, J = 7.8, 7.4 Hz, 1H), 7.55 (s, 1H), 7.86 (d, J = 7.9 Hz, 1H), 7.95 (d, J = 8.1 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.8, 30.0, 31.4, 50.7, 50.7, 70.8,

119.6, 121.6, 122.7, 125.1, 126.2, 129.8, 135.1, 137.7, 153.2, 169.4, 212.2. IR(CCl₄) 2927, 1521, 1499, 1436, 1282, 1228, 1110, 1052 cm⁻¹. MS (CI+NH₃) m/z 318, 378 (MH⁺).

Dithiocarbonic acid *O*-ethyl ester *S*-[1-imidazol-1-ylmethyl-4-oxo-4-(2-oxo-oxazolidin-3-yl)-butyl] ester (3f). Pale yellow oil (79%). Silica gel, AcOEt-MeOH, 98:2. ¹H NMR (400 MHz, CDCl₃) δ 1.41 (t, *J*= 7.1 Hz, 3H), 1.91-2.00 (m, 1H), 2.08-2.26 (m, 3H), 2.97-3.17 (m, 2H), 3.70-3.77 (m, 1H), 4.01 (t, *J*= 8.1 Hz), 4.13 (t, *J*= 7.3 Hz, 2H), 4.42 (t, *J*= 8.1 Hz), 4.63 (q, *J*= 7.1 Hz, 2H), 6.93 (s, 1H), 7.06 (s, 1H), 7.49 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 13.8, 29.1, 32.4, 36.1, 42.6, 44.5, 47.7, 62.3, 70.6, 118.9, 129.8, 137.30, 153.6, 172.4, 213.1. IR(CCl₄) 2922, 1790, 1703, 1503, 1384, 1361, 1264, 1223, 1110, 1048 cm⁻¹. MS (CI+NH₃) m/z 106, 197, 312, 373 (MH⁺).

Transformation of radical adducts 3b,c,f

6-fluoro-4-[1,2,4]triazol-1-ylmethyl-3,4-dihydro-2*H*-naphthalen-1-one (4). A solution of **3b** (265 mg, 0.72 mmol) and 10-camphorsulfonic acid (167 mg, 0.72 mmol) in 3.5 ml of 1,2-dichloroethane was refluxed for 15 min under argon. Lauroyl peroxide was then added portionwise (10 mol% / **3b** per hour) to the refluxing solution. When **3b** was totally consumed (after a global addition of 315 mg of lauroyl peroxide (0.79 mmol)), the crude mixture was cooled to room temperature, diluted with ether and washed with saturated aqueous NaHCO₃. The organic layer was dried over MgSO₄, filtered, concentrated and purified by flash column chromatography (silica gel, AcOEt) to give **4** (132 mg, 75%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 1.90-1.98 (m, 1H), 2.16-2.26 (m, 1H), 2.60 (ddd, *J*= 17.8, 4.8, 4.8 Hz, 1H), 2.71 (ddd, *J*= 17.8, 12.4, 5.0 Hz, 1H), 3.58-3.65 (m, 1H), 4.39-4.50 (m, 2H), 6.67 (dd, *J*= 9.1, 2.3 Hz, 1H), 7.01 (ddd, *J*= 8.4, 8.4, 2.3 Hz, 1H), 7.95 (s, 1H), 7.98 (s, 1H), 8.04 (dd, *J*= 8.4, 6.1 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 24.6, 33.9, 38.4, 52.6, 114.8, 115.6, 128.7, 131.0, 143.7, 145.8, 152.5, 165.7, 195.2. IR(CCl₄) 2942, 1692, 1608, 1585, 1502, 1273, 1251, 1139, 1010 cm⁻¹. MS (CI+NH₃) m/z 246 (MH⁺). MP (Ethyl acetate-petroleum ether) 99-101°C. Anal. calcd. for C₁₃H₁₂FN₃O: C, 63.66; H, 4.93, found: C, 63.47; H, 5.02.

1-methyl-5-[1,2,4]triazol-1-ylmethyl-1,3,4,5-tetrahydro-benzo[*b*]azepin-one (5). A solution of **3c** (674 mg, 1.78 mmol) and 10-camphorsulfonic acid (412 mg, 1.78 mmol) in 9

ml of 1,2-dichloroethane was refluxed for 15 min under argon. Lauroyl peroxide was then added portionwise (10 mol% / **3c** per hour) to the refluxing solution. When **3c** was totally consumed (after a global addition of 780 mg of lauroyl peroxide (1.95 mmol)), the crude mixture was cooled to room temperature, diluted with ether and washed with saturated aqueous NaHCO₃. The organic layer was dried over MgSO₄, filtered, concentrated and purified by flash column chromatography (silica gel, AcOEt) to give **5** (164 mg, 36%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 1.74-1.92 (m, 1H), 2.22-2.40 (m, 3H), 3.38 (s, 3H), 3.54-3.64 (m, 1H), 4.42-4.52 (m, 1H), 4.54-4.70 (m, 1H), 7.14-7.26 (m, 3H), 7.32-7.40 (dd, *J*= 17.8, 4.8 Hz, 1H), 7.92 (s, 1H), 8.02 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 32.7 (2 C), 35.3, 39.0, 51.8, 123.1, 126.5, 128.4, 135.5, 143.3 (2 C), 152.1, 172.5. IR(CCl₄) 2943, 1671, 1601, 1503, 1494, 1454, 1369, 1273, 1139, 1110, 1009 cm⁻¹. MS (CI+NH₃) *m/z* 257 (MH⁺). MP (Ethyl acetate-petroleum ether) 114-115°C. Anal. calcd. for C₁₄H₁₆N₄O: C, 65.61; H, 6.29, found: C, 65.03; H, 6.41.

3-(3-6,7-dihydro-5H-pyrrolo[1,2-*a*]imidazol-7-yl-propionyl)-oxazolidin-2-one (6). A solution of **3f** (880 mg, 2.37 mmol) and 10-camphorsulfonic acid (550 mg, 2.37 mmol) in 10 ml of 1,2-dichloroethane was refluxed for 15 min under argon. Lauroyl peroxide was then added portionwise (10 mol% / **3f** per hour) to the refluxing solution. When **3f** was totally consumed (after a global addition of 1.04 g of lauroyl peroxide (2.60 mmol)), the crude mixture was cooled to room temperature, diluted with ether and washed with saturated aqueous NaHCO₃. The organic layer was dried over MgSO₄, filtered, concentrated and purified by flash column chromatography (silica gel, AcOEt-MeOH, 95:5) to give **6** (330 mg, 56%) as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 1.63-1.82 (m, 1H), 1.90-1.99 (m, 1H), 2.07-2.16 (m, 1H), 2.21-2.29 (m, 1H), 2.73-2.82 (m, 1H), 3.15 (t, *J*= 7.4 Hz, 2H), 3.83-3.95 (m, 2H), 3.98 (t, *J*= 7.8 Hz), 4.38 (t, *J*= 7.8 Hz), 6.81 (s, 1H), 6.99 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 28.0, 32.8, 33.5, 34.7, 42.5, 43.6, 62.1, 114.3, 132.9, 153.6, 156.5, 172.8. IR(CCl₄) 2922, 1790, 1705, 1384, 1360, 1269, 1223, 1110, 1087, 1045 cm⁻¹. MS (CI+NH₃) *m/z* 250 (MH⁺).

Radical cascades with olefin 2e

4-(2,3-dihydro-1H-benzo[*d*]pyrrolo[1,2-*a*]imidazol-3-yl)-butan-2-one (8a). A solution of xanthate **1a** (712 mg, 4 mmol), olefin **2a** (1.38 g, 8 mmol) and 10-camphorsulfonic acid (1.86

g, 8 mmol) in 8 ml of 1,2-dichloroethane was refluxed for 15 min under argon. Lauroyl peroxide was then added portionwise (10 mol% / **1a** per hour) to the refluxing solution. When **1a** was totally consumed (after a global addition of 796 mg of lauroyl peroxide (2 mmol)), the crude mixture was cooled to room temperature, diluted with ether and washed with saturated aqueous NaHCO₃. The organic layer was dried over MgSO₄, filtered, concentrated and purified by flash column chromatography (silica gel, AcOEt) to give an inseparable 1.9/1 mixture (1.92 g) of compounds **7a** and **8a**. A solution of this mixture and 10-camphorsulfonic acid (1.45 g, 6.24 mmol) in 20 ml of 1,2-dichloroethane was refluxed for 15 min under argon. Lauroyl peroxide was then added portionwise (10 mol% / **7a** per hour) to the refluxing solution. When **7a** was totally consumed (after a global addition of 1.76 g of lauroyl peroxide (4.51 mmol)), the crude mixture was cooled to room temperature, diluted with ether and washed with saturated aqueous NaHCO₃. The organic layer was dried over MgSO₄, filtered, concentrated and purified by flash column chromatography (silica gel, AcOEt) to give **8a** (519 mg, 57%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 1.97-2.04 (m, 2H), 2.17 (s, 3H), 2.25-2.33 (m, 1H), 2.74-2.96 (m, 3H), 3.17-3.25 (m, 1H), 3.91-3.97 (m, 1H), 4.05-4.10 (m, 1H), 7.18-7.22 (m, 2H), 7.23-7.28 (m, 1H), 7.70-7.72 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 26.9, 30.0, 33.4, 35.1, 41.0, 41.6, 109.5, 119.4, 121.6, 121.8, 131.9, 148.3, 162.9, 208.1. IR(CCl₄) 2939, 2886, 1717, 1621, 1258, 1449, 1409, 1370, 1354, 1297, 1276, 1217, 1162, 1005 cm⁻¹. MS (CI+NH₃) m/z 229 (MH⁺). MP (Ethyl acetate-petroleum ether) 68-69°C. Anal. calcd. for C₁₄H₁₆N₂O: C, 73.66; H, 7.06, found: C, 73.54; H, 7.16.

3-(2,3-dihydro-1H-benzo[d]pyrrolo[1,2-a]imidazol-3-yl)-N-methyl-N-phenylpropionamide (8b). A solution of xanthate **1c** (538 mg, 2 mmol), olefin **2a** (516 g, 3 mmol) and 10-camphorsulfonic acid (696 mg, 3 mmol) in 4 ml of 1,2-dichloroethane was refluxed for 15 min under argon. Lauroyl peroxide was then added portionwise (10 mol% / **1a** per hour) to the refluxing solution. When **1a** was totally consumed (after a global addition of 640 mg of lauroyl peroxide (1.6 mmol)), the crude mixture was cooled to room temperature, diluted with ether and washed with saturated aqueous NaHCO₃. The organic layer was dried over MgSO₄, filtered, concentrated and purified by flash column chromatography (silica gel, AcOEt) to give an inseparable 1.3/1 mixture (436 mg) of the radical adduct and **8b**. A solution of this mixture and 10-camphorsulfonic acid (260 mg, 1.12 mmol) in 6 ml of 1,2-dichloroethane was refluxed for 15 min under argon. Lauroyl peroxide was then added portionwise (10 mol% / radical adduct per hour) to the refluxing solution. When the radical adduct was totally consumed (after a global addition of 275 mg of lauroyl peroxide (0.66

mmol)), the crude mixture was cooled to room temperature, diluted with ether and washed with saturated aqueous NaHCO₃. The organic layer was dried over MgSO₄, filtered, concentrated and purified by flash column chromatography (silica gel, AcOEt) to give **8b** (236 mg, 37%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 1.94-2.04 (m, 1H), 2.10-2.20 (m, 1H), 2.22-2.31 (m, 1H), 2.36-2.50 (m, 2H), 2.76-2.86 (m, 1H), 3.18-3.24 (m, 1H), 3.26 (s, 3H), 3.92-4.00 (m, 1H), 4.02-4.10 (m, 1H), 7.17-7.23 (m, 4H), 7.24-7.34 (m, 2H), 7.36-7.42 (m, 2H), 7.64-7.69 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 29.1, 31.8, 33.4, 35.5, 37.4, 41.8, 109.5, 119.7, 121.6 (2 C), 121.8 (2 C), 127.4, 127.9, 129.9, 132.2, 144.0, 148.6, 163.1, 172.4. IR(CCl₄) 3063, 2947, 1658, 1596, 1258, 1496, 1449, 1408, 1387, 1331, 1275, 1125 cm⁻¹. MS (CI+NH₃) m/z 320 (MH⁺). MP (Ethyl acetate-petroleum ether) 112-113°C. Anal. calcd. for C₂₀H₂₁N₃O: C, 75.21; H, 6.63, found: C, 75.03; H, 6.76.

3-(3-2,3-dihydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]imidazol-3-ylpropionyl)-oxazolidin-2-one

(8c). A solution of xanthate **1d** (498 mg, 2 mmol), olefin **2a** (516 mg, 3 mmol) and 10-camphorsulfonic acid (696 mg, 3 mmol) in 4 ml of 1,2-dichloroethane was refluxed for 15 min under argon. Lauroyl peroxide was then added portionwise (10 mol% / **1a** per hour) to the refluxing solution. When **1a** was totally consumed (after a global addition of 320 mg of lauroyl peroxide (0.8 mmol)), the crude mixture was cooled to room temperature, diluted with ether and washed with saturated aqueous NaHCO₃. The organic layer was dried over MgSO₄, filtered, concentrated and purified by flash column chromatography (silica gel, AcOEt) to give an inseparable 1.9/1 mixture (645 mg) of the radical adduct and **8c**. A solution of this mixture and 10-camphorsulfonic acid (392 mg, 1.69 mmol) in 8 ml of 1,2-dichloroethane was refluxed for 15 min under argon. Lauroyl peroxide was then added portionwise (10 mol% / radical adduct per hour) to the refluxing solution. When the radical adduct was totally consumed (after a global addition of 481 mg of lauroyl peroxide (1.21 mmol)), the crude mixture was cooled to room temperature, diluted with ether and washed with saturated aqueous NaHCO₃. The organic layer was dried over MgSO₄, filtered, concentrated and purified by flash column chromatography (silica gel, AcOEt) to give **8c** (340 mg, 57%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 2.04-2.13 (m, 1H), 2.25-2.36 (m, 1H), 2.36-2.45 (m, 1H), 2.87-2.96 (m, 1H), 3.16-3.50 (m, 2H), 3.35-3.44 (m, 1H), 3.97 (t, *J* = 8.1 Hz, 2H), 3.99-4.06 (m, 1H), 4.16 (ddd, *J* = 8.9, 8.8, 4.2 Hz, 1H), 4.31-4.42 (m, 2H), 7.18-7.24 (m, 2H), 7.28-7.32 (m, 1H), 7.68-7.72 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 27.7, 32.8, 33.2, 35.3, 41.9, 42.6, 62.2, 109.6, 119.8, 121.8, 122.0, 132.2, 148.6, 153.6, 162.9, 172.7. IR(CCl₄) 3065,

3050, 1781, 1701, 1540, 1525, 1387, 1221, 1041 cm^{-1} . MS (CI+NH₃) m/z 300 (MH⁺). MP (Ethyl acetate-petroleum ether) 146-147°C. Anal. calcd. for C₁₆H₁₇N₃O₃: C, 64.20; H, 5.72, found: C, 64.23; H, 5.78.

Transformation of compound 8c

***N*-cyclopropyl-3-(2,3-dihydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]imidazol-3-yl)-propionamide**

(9a). To a solution of **8c** (100 mg, 0.33 mmol) in 1 ml of acetonitrile was added excess of cyclopropylamine (1 ml). The resulting mixture was stirred at room temperature for 10 hours, concentrated under reduced pressure and purified by flash column chromatography (silica gel, dichloromethane-MeOH, 98:2) to give **9a** (81 mg, 91%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 0.49-0.52 (m, 2H), 0.73-0.74 (m, 2H), 1.84-1.93 (m, 1H), 2.22-2.31 (m, 1H), 2.32-2.41 (m, 1H), 2.44-2.51 (m, 1H), 2.61-2.69 (m, 1H), 2.72-2.79 (m, 1H), 2.88-2.96 (m, 1H), 3.23-3.31 (m, 1H), 4.00-4.06 (m, 1H), 4.11-4.17 (m, 1H), 7.17 (bs, 1H), 7.22-7.24 (m, 2H), 7.30-7.32 (m, 1H), 7.67-7.69 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 6.4, 6.5, 22.7, 29.6, 33.6, 33.9, 34.9, 41.9, 109.8, 119.6, 121.9, 122.2, 132.1, 148.2, 162.9, 174.2. IR(CCl₄) 3298, 2949, 1677, 1641, 1524, 1450, 1414, 1298, 1277, 1219, 1148 cm^{-1} . MS (CI+NH₃) m/z 270 (MH⁺). MP (Ethyl acetate-petroleum ether) 156-158°C. Anal. calcd. for C₁₆H₁₉N₃O: C, 71.35; H, 7.11, found: C, 71.41; H, 7.16.

3-(2,3-dihydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]imidazol-3-yl)-1-[4-(3-trifluoromethyl-phenyl)-

piperazin-1-yl]-propan-1-one (9b). To a solution of **8c** (100 mg, 0.33 mmol) in 1 ml of acetonitrile was added excess of *N*-(3-trifluoromethylphenyl)piperazine (1 ml). The resulting mixture was refluxed for 10 hours, cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography (silica gel, dichloromethane-MeOH, 98:2) to give **9b** (124 mg, 85%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 2.01-2.11 (m, 1H), 2.17-2.26 (m, 1H), 2.35-2.44 (m, 1H), 2.74-2.82 (m, 1H), 2.86-2.97 (m, 2H), 3.15-3.26 (m, 4H), 3.28-3.30 (m, 1H), 3.71-3.80 (m, 4H), 3.98-4.04 (m, 1H), 4.11-4.17 (m, 1H), 7.03-7.07 (m, 1H), 7.09-7.13 (m, 2H), 7.21-7.23 (m, 2H), 7.30-7.32 (m, 1H), 7.36 (dd, J = 8.1, 8.1 Hz, 1H), 7.70-7.72 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 28.8, 30.7, 33.7, 35.5, 41.3, 41.9, 45.2, 48.8, 49.1, 109.6, 112.7, 116.5, 119.3, 119.5, 121.2, 122.0, 124.2, 129.7, 131.5, 132.1, 148.4, 151.1, 163.1, 171.0. IR(CCl₄) 2886, 1651, 1611, 1526, 1491, 1449, 1410, 1348, 1310, 1307, 1230, 1168, 1131, 1099, 1075 cm^{-1} . MS (CI+NH₃) m/z 443 (MH⁺).

3-(2,3-dihydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]imidazol-3-yl)-propionic acid 4-methoxybenzyl ester (9c). To a solution of **8c** (100 mg, 0.33 mmol) in 1 ml of triethylamine was added excess of 4-methoxybenzyl alcohol (1 ml). The resulting mixture was stirred for 24 hours, concentrated under reduced pressure and purified by flash column chromatography (silica gel, AcOEt-petroleum ether, 1:1) to give **9c** (99 mg, 86%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 1.99-2.09 (m, 1H), 2.18-2.36 (m, 2H), 2.60-2.79 (m, 2H), 2.80-2.89 (m, 1H), 3.25-3.33 (m, 1H), 3.79 (s, 3H), 3.94-4.01 (m, 1H), 4.06-4.14 (m, 1H), 5.03 (d, *J* = 12.0 Hz, 1H), 5.07 (d, *J* = 12.0 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 2H), 7.19-7.25 (m, 2H), 7.26-7.31 (m, 3H), 7.69-7.73 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 28.3, 32.1, 33.2, 35.4, 41.9, 55.3, 66.2, 109.6, 113.9, 119.7, 121.8, 122.0, 128.0, 130.2, 132.1, 148.5, 159.6, 162.8, 173.0. IR(CCl₄) 2954, 2835, 1734, 1614, 1530, 1515, 1450, 1410, 1380, 1298, 1275, 1218, 1160, 1040 cm⁻¹. MS (CI+NH₃) *m/z* 351 (MH⁺).