Supporting Information
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Supporting Information

Microwave-Promoted Michael Addition of Azaheterocycles to α,β-Unsaturated Esters and Acid under Solvent-Free Conditions

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General methods

All reactions were carried out under argon atmosphere, and were monitored by thinlayer chromatography with Merck 60F-254 precoated silica (0.2 mm) on glass. Flash chromatography was performed with Merck Kieselgel 60 (200–500 μm); the solvent systems were given v/v. $^1$HNMR (250 MHz) and $^{13}$C NMR (63 MHz) spectra were recorded on a Bruker ARX-250 spectrometer and $^1$HNMR (500 MHz) and $^{13}$C NMR (125 MHz) spectra were recorded on a Bruker AVANCEII-500 spectrometer. Chemical shifts (δ) are reported in ppm. $^{13}$C chemical attributions were assigned using $^1$H-decoupled spectra. The regioselectivity of the alkylated compounds 5a-c has been confirmed by 2D NMR experiments using heteronuclear correlations (HMBC). IR spectra were obtained with a Perkin-Elmer Spectrum One FT-IR spectrometer equipped with a MIRacleTM single reflection horizontal ATR unit (zirconium-selenium crystal). Mass spectra were recorded on a Thermo Finnigan LCD Advantage spectrometer. HRMS were carried out by the mass spectrometry services at Gif-sur-Yvette CNRS. Spectroscopic ($^1$H and $^{13}$C NMR, MS) and/or analytical data were obtained using chromatographically homogeneous samples. Microwave reactions were performed using a Microwave/Milestone START and standard Pyrex vessels in open mode, maintaining the temperature max 100 °C by power modulation.

General Procedure A: Michael addition of azaheterocycles

Synthesis of the propionate derivatives (5a-c, 7a-c, 8b-c, 9b-c). Compounds 1-3 (1 equiv), DABCO (1-5 equiv) and TBAB (0.2-1 equiv) were grounded until the obtention of a homogeneous mass before adding α,β-unsaturated esters (4a-c) (1.5 equiv). The reaction mixture was stirred using a dark magnetic bar for 30 min. When K$_2$CO$_3$ (4 equiv) and/or KOH (0.4-4 equiv) was added, the mixture was stirred for further 2 min just before irradiation in a microwave oven. Power, time and purification are given in each case.

General Procedure B: Amino cyclization of adenine

Synthesis of 1,N$^6$-etheno-adenine derivatives 6a-c. Compounds 5a-c (1 equiv) in 25 mM of aqueous solution of sodium acetate (1 N) was acidified to pH≈5 with a hydrochloric acid solution (1 N). The reaction mixture was heated at 45 °C for 10 min before adding chloroacetaldehyde (50% in water, 10-25 equiv) and stirring was maintained 48 h at this
room temperature. The solution was then evaporated under vacuum and the residue purified by column chromatography on silica gel (CH$_2$Cl$_2$/MeOH: 97/3 or 9/1).

**General Procedure C: Deprotection of $t$-butyl ester**

**Preparation of derivatives 5c and 9-c.** To $t$-butyl ester compound (1 mmol) in anhydrous CH$_2$Cl$_2$ (4 mL) was added TFA (1 mL) and stirring was maintained for 2 h at room temperature. Evaporation of the solvents to dryness and precipitation in Et$_2$O furnished the carboxylate compound.

**Procedures and Characterization of Products**

**9-(2-Ethoxycarbonylethyl)adenine (5a):**

Following the general procedure A, 1 (2.027 g, 15 mmol), DABCO (1.681 g, 15 mmol), TBAB (967 mg, 3 mmol) and 4a (2.45 mL, 22.5 mmol) were submitted to irradiation at 200 W for 8 min. The reaction mixture was then suspended in CHCl$_3$ (450 mL) and washed with water (3×250 mL). The organic layer was dried (MgSO$_4$), filtered and evaporated under reduced pressure to give 2.753 g (78%) of 5a as a white powder. Mp 161-163 °C [(lit. 164-166 °C)$^1$, (lit.165-167 °C)$^2$]; Rf=0.4 (CH$_2$Cl$_2$/MeOH: 9/1); $^1$H NMR (500 MHz, CDCl$_3$): $^\delta$ 8.33 (s, 1H, H-2), 7.91 (s, 1H, H-8), 6.03 (s, 2H, NH$_2$), 4.48 (t, J=6.2 Hz, 2H, CH$_2$N), 4.10 (q, J=7.0 Hz, 2H, CH$_2$CH$_3$), 2.90 (t, J=6.2 Hz, 2H, CH$_2$CO), 0.84 (t, J=7.0 Hz, 3H, CH$_3$); $^{13}$C NMR (500 MHz, DMSO): $^\delta$ 170.5 (CO), 155.9 (C-6), 152.4 (C-2), 149.4 (C-4), 140.9 (C-8), 118.7 (C-5), 60.2 (CH$_2$CH$_3$), 39.0 (CH$_2$N), 34.9 (CH$_2$CO), 13.8 (CH$_3$); IR (v, cm$^{-1}$) 3290 (NH$_2$), 1718 (CO); MS (ESI$^+$), m/z (%): [M+H]$^+$=236.1.
9-(2-tert-Butoxycarbonylethyl)adenine (5b):

\[
\begin{align*}
\text{Following the general procedure A, 1 (2.027 g, 15 mmol), DABCO (1.681 g, 15 mmol),} \\
\text{TBAB (967 mg, 3 mmol) and 4b (3.27 mL, 22.5 mmol), were submitted to irradiation at} \\
\text{200 W for 8 min. The reaction mixture was then suspended in CHCl\textsubscript{3} (450 mL) and} \\
\text{washed with water (3×250 mL). The organic layer was dried (MgSO\textsubscript{4}), filtered and} \\
\text{evaporated under reduced pressure to give 2.810 g (71%) of 5b as a white powder. Mp} \\
\text{182-184 °C (lit. 183-185 °C\textsuperscript{3}); Rf=0.6 (CH\textsubscript{2}Cl\textsubscript{2}/MeOH: 9/1); \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3})::} \\
\text{δ 8.14 (s, 1H, H-2), 8.09 (s, 1H, H-8), 7.16 (s, 2H, NH\textsubscript{2}), 4.34 (t, J=7.0 Hz, 2H, CH\textsubscript{2}N),} \\
\text{2.85 (t, J=7.0 Hz, 2H, CH\textsubscript{2}CO), 1.31 (s, 9H, CH\textsubscript{3}); \textsuperscript{13}C NMR (500 MHz, DMSO): δ 169.7} \\
\text{(CO), 155.9 (C-6), 152.3 (C-2), 149.4 (C-4), 140.9 (C-8), 118.7 (C-5), 80.4 (Cq-tBu), 39.0} \\
\text{(CH\textsubscript{2}N), 34.9 (CH\textsubscript{2}CO), 27.8 (CH\textsubscript{3}); IR (ν, cm\textsuperscript{-1}) 3292 (NH\textsubscript{2}), 1723 (CO); MS (ESI\textsuperscript{+}), m/z} \\
\text{(%) [M+H\textsuperscript{+}]=264.0 (100%); HRMS (ESI\textsuperscript{+}) calcd for [C\textsubscript{12}H\textsubscript{17}N\textsubscript{5}O\textsubscript{2} + H\textsuperscript{+}]: 264.1457; found:} \\
\text{264.1451.}
\end{align*}
\]

9-(2-Carboxyethyl)adenine (5c)

\[
\begin{align*}
\text{Following the general procedure A, 1 (2.027 g, 15 mmol), DABCO (1.681 g, 15 mmol),} \\
\text{TBAB (967 mg, 3 mmol) and 4c (1.54 mL, 22.5 mmol), were submitted to irradiation at} \\
\text{200 W for 8 min. The reaction mixture was then suspended in water (50 mL) and} \\
\text{filtered to remove the precipitate. The filtrate was then acidified to pH 3 with HCl (1 N) and} \\
\text{the precipitate was recovered by filtration and dried under reduced pressure for 48 h to give} \\
\text{2.17 g (72%) of 5c as a white powder. Mp 284-286 °C [(lit. 279-280 °C\textsuperscript{4}; (lit. 284-288} \\
\text{°C),\textsuperscript{2} (lit. 285-288 °C\textsuperscript{5}); Rf=0.1 (CH\textsubscript{2}Cl\textsubscript{2}/MeOH: 9/1); \textsuperscript{1}H NMR (500 MHz, DMSO): δ}
\end{align*}
\]
12.4 (s, 1H, CO₂H), 8.13 (s, 1H, H-2), 8.08 (s, 1H, H-8), 7.20 (s, 2H, NH₂), 4.33 (t, J=7.0 Hz, 2H, CH₂N), 2.87 (t, J=7.0 Hz, 2H, CH₂CO); ¹³C NMR (500 MHz, DMSO): δ 172.1 (CO), 155.8 (C-6), 152.2 (C-2), 149.4 (C-4), 142.9 (C-8), 120.6 (C-5), 40.1 (CH₂N), 35.5 (CH₂CO); IR (ν, cm⁻¹) 3170 (NH₂), 3065 (OH), 1706 (CO); MS (ESI⁺), m/z (%): [M+H]⁺=208.1 (100%); HRMS (ESI⁺) calcd for [C₈H₉N₅O₂ + H]⁺: 208.0833; found: 208.0825.

1-(2-Ethoxycarbonylethyl)indole (7a):

Following the general procedure A, 2 (1.771 g, 15 mmol), DABCO (2.020 g, 18 mmol), TBAB (967 mg, 3 mmol), 4a (2.45 mL, 22.5 mmol) and KOH (337 mg, 6 mmol), were submitted to irradiation at 200 W for 1.5 min. The reaction mixture was then suspended in CH₂Cl₂ (200 mL), washed with a solution of saturated NH₄Cl (200 mL) and brine (2×200 mL). The organic layer was dried (MgSO₄) and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (cyclohexane/EtOAc: 99/1) to give 1.815 g (56%) of 7a as brown oil. Rf=0.3 (cyclohexane/EtOAc: 9/1); ¹H NMR (500 MHz, CDCl₃): δ 7.67 (d, J=7.9 Hz, 1H, H-7), 7.38 (d, J=8.2 Hz, 1H, H-4), 7.28 (t, J=7.9 Hz, 1H, H-6), 7.22 (t, J=8.2 Hz, H-5), 7.16 (d, J=3.3 Hz, 1H, H-2), 6.42 (d, J=3.3 Hz, 1H, H-3), 4.48 (t, J=6.8 Hz, 2H, CH₂N), 4.14 (q, J=7.3 Hz, 2H, CH₂CH₃), 2.84 (t, J=6.8 Hz, 2H, CH₂CO), 1.09 (t, J=7.3 Hz, 3H, CH₃); ¹³C NMR (500 MHz, CDCl₃): δ 171.2 (CO), 135.8, 128.8 (Cq-Ar), 127.9 (C-4), 121.7 (C-5), 121.0 (C-7), 119.5 (C-6), 109.1 (C-2), 101.6 (C-3), 60.0 (CH₂CH₃), 41.8 (CH₂N), 35.0 (CH₂CO), 14.0 (CH₃); IR (ν, cm⁻¹) 1731 (CO); MS (ESI⁺), m/z (%): [M+H]⁺=218.1 (100%); HRMS (ESI⁺) calcd for [C₁₃H₁₅NO₂ + H]⁺: 218.1177; found: 218.1182.

1-(2-tert-Butoxycarbonylethyl)indole (7b).

Following the general procedure A, 2 (1.771 g, 15 mmol), DABCO (2.020 g, 18 mmol), TBAB (967 mg, 3 mmol), 4a (2.45 mL, 22.5 mmol) and KOH (337 mg, 6 mmol), were submitted to irradiation at 200 W for 1.5 min. The reaction mixture was then suspended in CH₂Cl₂ (200 mL), washed with a solution of saturated NH₄Cl (200 mL) and brine (2×200 mL). The organic layer was dried (MgSO₄) and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (cyclohexane/EtOAc: 99/1) to give 1.815 g (56%) of 7a as brown oil. Rf=0.3 (cyclohexane/EtOAc: 9/1); ¹H NMR (500 MHz, CDCl₃): δ 7.67 (d, J=7.9 Hz, 1H, H-7), 7.38 (d, J=8.2 Hz, 1H, H-4), 7.28 (t, J=7.9 Hz, 1H, H-6), 7.22 (t, J=8.2 Hz, H-5), 7.16 (d, J=3.3 Hz, 1H, H-2), 6.42 (d, J=3.3 Hz, 1H, H-3), 4.48 (t, J=6.8 Hz, 2H, CH₂N), 4.14 (q, J=7.3 Hz, 2H, CH₂CH₃), 2.84 (t, J=6.8 Hz, 2H, CH₂CO), 1.09 (t, J=7.3 Hz, 3H, CH₃); ¹³C NMR (500 MHz, CDCl₃): δ 171.2 (CO), 135.8, 128.8 (Cq-Ar), 127.9 (C-4), 121.7 (C-5), 121.0 (C-7), 119.5 (C-6), 109.1 (C-2), 101.6 (C-3), 60.0 (CH₂CH₃), 41.8 (CH₂N), 35.0 (CH₂CO), 14.0 (CH₃); IR (ν, cm⁻¹) 1731 (CO); MS (ESI⁺), m/z (%): [M+H]⁺=218.1 (100%); HRMS (ESI⁺) calcd for [C₁₃H₁₅NO₂ + H]⁺: 218.1177; found: 218.1182.
Following the general procedure A, 2 (1.771 g, 15 mmol), DABCO (2.020 g, 18 mmol), TBAB (967 mg, 3 mmol), 4b (3.27 mL, 22.5 mmol) and KOH (337 mg, 6 mmol), were submitted to irradiation at 200 W for 1 min. The reaction mixture was then suspended in CH₂Cl₂ (200 mL), washed with water (3×200 mL). The organic layer was dried (MgSO₄) and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (cyclohexane/EtOAc: 99/1) to give 3.060 g (83%) of 7b as brown oil. R_f=0.5 (cyclohexane/EtOAc: 9/1); ¹H NMR (500 MHz, DMSO): δ 7.56 (d, J=8.0 Hz, 1H, H-7), 7.50 (d, J=8.2 Hz, 1H, H-4), 7.35 (d, J=3.2 Hz 1H, H-2), 7.14 (t, J=8.0 Hz, 1H, H-6), 7.02 (t, J=8.2 Hz, H-5), 6.42 (d, J=3.2 Hz, 1H, H-3), 4.40 (t, J=6.7 Hz, 2H, CH₂N), 2.74 (t, J=6.7 Hz, 2H, CH₂CO), 1.32 (s, 9H, CH₃); ¹³C NMR (500 MHz, CDCl₃): δ 170.2 (CO), 135.7, 128.7 (Cq-Ar), 127.8 (C-4), 121.4 (C-5), 120.9 (C-7), 119.3 (C-6), 109.1 (C-2), 101.3 (C-3), 80.7 (Cq-tBu), 41.7 (CH₂N), 36.0 (CH₂CO), 27.8 (CH₃); IR (ν, cm⁻¹) 1726 (CO); MS (ESI⁺), m/z (%): [M+H⁺]+=246.1 (100%); HRMS (ESI⁺) calcd for [C₁₅H₁₉NO₂ + H⁺]: 246.1489; found: 246.1488.

3-(1H-Indol-3-yl)-4-[1-{2-carboxyethyl}indol-3-yl]-1-methyl-1H-pyrrole-2,5-dione (8c) and Bis-[1-(2-carboxyethyl)indol-3-yl]-1-methyl-1H-pyrrole-2,5-dione (9c).

Following the general procedure A, 3 (289 mg, 0.85 mmol), DABCO (477 mg, 4.25 mmol), TBAB (274 mg, 0.85 mmol) and 4c (175 µL, 2.55 mmol), were submitted to irradiation at 500 W for 20 min. The residue was purified by column chromatography on silica gel (eluent: CH₂Cl₂/MeOH/AcOH: 99/1 to 90/10/2) to give 95 mg (27%) of 8c as a red crystal and 123 mg (37%) of 9c as red foam.

8c: Mp 95-97 °C; R_f=0.46 (CH₂Cl₂/MeOH/AcOH: 9/1/0.5); ¹H RMN (500 MHz, DMSO): δ 10.27 (brs, 1H, CO₂H), 8.14 (d, J=2.5 Hz, 1H, H-Ar), 8.08 (s, 1H, H-Ar), 7.76 (t, J=8.5 Hz, 2H, H-Ar), 7.40 (t, J=7.5 Hz, 1H, H-Ar), 7.36 (t, J=7.5 Hz, 1H, H-Ar), 7.24 (t, J=8.5 Hz, 1H, H-Ar), 7.13 (d, J=8.5 Hz, 1H, H-Ar), 7.01 (m, 2H, H-Ar), 4.82 (t, J=6.5 Hz, 1H, H-Ar), 4.48 (t, J=7.0 Hz, 1H, H-Ar), 3.91 (t, J=7.0 Hz, 1H, H-Ar), 3.81 (t, J=7.0 Hz, 1H, H-Ar), 3.72 (t, J=7.0 Hz, 1H, H-Ar), 3.63 (t, J=7.0 Hz, 1H, H-Ar), 3.54 (t, J=7.0 Hz, 1H, H-Ar), 3.45 (t, J=7.0 Hz, 1H, H-Ar), 3.36 (t, J=7.0 Hz, 1H, H-Ar), 3.27 (t, J=7.0 Hz, 1H, H-Ar), 3.18 (t, J=7.0 Hz, 1H, H-Ar), 3.09 (t, J=7.0 Hz, 1H, H-Ar), 3.00 (t, J=7.0 Hz, 1H, H-Ar), 2.91 (t, J=7.0 Hz, 1H, H-Ar), 2.82 (t, J=7.0 Hz, 1H, H-Ar), 2.73 (t, J=7.0 Hz, 1H, H-Ar), 2.64 (t, J=7.0 Hz, 1H, H-Ar), 2.55 (t, J=7.0 Hz, 1H, H-Ar), 2.46 (t, J=7.0 Hz, 1H, H-Ar), 2.37 (t, J=7.0 Hz, 1H, H-Ar), 2.28 (t, J=7.0 Hz, 1H, H-Ar), 2.19 (t, J=7.0 Hz, 1H, H-Ar), 2.10 (t, J=7.0 Hz, 1H, H-Ar), 2.01 (t, J=7.0 Hz, 1H, H-Ar), 1.92 (t, J=7.0 Hz, 1H, H-Ar), 1.83 (t, J=7.0 Hz, 1H, H-Ar), 1.74 (t, J=7.0 Hz, 1H, H-Ar), 1.65 (t, J=7.0 Hz, 1H, H-Ar), 1.56 (t, J=7.0 Hz, 1H, H-Ar), 1.47 (t, J=7.0 Hz, 1H, H-Ar), 1.38 (t, J=7.0 Hz, 1H, H-Ar), 1.29 (t, J=7.0 Hz, 1H, H-Ar), 1.20 (t, J=7.0 Hz, 1H, H-Ar), 1.11 (t, J=7.0 Hz, 1H, H-Ar), 1.02 (t, J=7.0 Hz, 1H, H-Ar), 0.93 (t, J=7.0 Hz, 1H, H-Ar), 0.84 (t, J=7.0 Hz, 1H, H-Ar), 0.75 (t, J=7.0 Hz, 1H, H-Ar), 0.66 (t, J=7.0 Hz, 1H, H-Ar), 0.57 (t, J=7.0 Hz, 1H, H-Ar), 0.48 (t, J=7.0 Hz, 1H, H-Ar), 0.39 (t, J=7.0 Hz, 1H, H-Ar), 0.30 (t, J=7.0 Hz, 1H, H-Ar), 0.21 (t, J=7.0 Hz, 1H, H-Ar), 0.12 (t, J=7.0 Hz, 1H, H-Ar), 0.03 (t, J=7.0 Hz, 1H, H-Ar).
CH₂N), 3.44 (s, 3H, NCH₃), 3.15 (t, J=6.5 Hz, 2H, CH₂CO); ¹³C NMR (500 MHz, CDCl₃): δ 173.4 (CO₂H), 173.2, 173.1 (CO-Ar), 137.2, 136.9 (Cq-Ar), 132.8, 129.8 (CH-Ar), 129.0, 128.4, 127.7, 126.8 (Cq-Ar), 123.1, 123.0, 122.5, 122.3, 120.8, 120.7 (CH-Ar), 112.6, 111.0 (Cq-Ar), 107.5, 106.9 (CH-Ar), 43.2 (CH₂N), 35.5 (CHH₂CO), 24.5 (NCH₃); IR (ν, cm⁻¹) 2960 (OH), 1693 (CO); MS (ESI⁺), m/z (%): [M-H]⁺=412.0 (70%), [2M–H]⁺=824.9 (100%).

9c: Rf=0.18 (CH₂Cl₂/MeOH/AcOH: 9/1/0.5); ¹H RMN (500 MHz, CDCl₃): δ 11.01 (brs, CO₂H), 7.54 (s, 2H, H-Ar), 7.30 (m, 2H, H-Ar), 7.10 (m, 4H, H-Ar) 6.85 (m, 2H, H-Ar), 4.42 (m, 4H, CH₂N), 3.16 (s, 3H, NCH₃), 2.85 (m, 4H, CH₂CO); ¹³C NMR (500 MHz, CDCl₃): δ 172.8 (CO₂H), 170.9 (CO-Ar), 137.0 (Cq-Ar), 133.0 (CH-Ar), 128.0, 127.6 (Cq-Ar), 122.9, 122.8, 120.7 (CH-Ar), 110.8 (Cq-Ar), 107.2 (CH-Ar), 43.2 (CH₂N), 36.8 (CH₂CO), 24.5 (NCH₃); IR (ν, cm⁻¹) 3436 (OH), 1728, 1698 (CO); MS (ESI⁺), m/z (%): [M–H]⁺=483.9 (100%), [2M–H]⁺=968.7 (35%); HRMS (ESI⁺) calcd for [C₂₇H₂₃N₃O₆ – H]⁺: 484.1503; found: 484.1488.

Following the general procedure A, 3 (1.707 g, 5 mmol), DABCO (673 mg, 6 mmol), TBAB (322 mg, 1 mmol), 4b (725 µL, 5 mmol) and KOH (112 mg, 2 mmol), were submitted to irradiation at 200 W for 10 min. The residue was purified by column
chromatography on silica gel (elucent: CH₂Cl₂/EtOAc: 95/5) to give 160 mg (25%) of 9b and 84 mg (9%) of 8b as red foam. Rf=0.6 (cyclohexane/EtOAc: 1/1); ¹H RMN (500 MHz, CDCl₃): δ 7.70 (m, 2H, H-Ar), 7.29 (m, 2H, H-Ar), 7.05 (m, 2H, H-Ar), 6.92 (m, 1H, H-Ar), 6.71 (m, 2H, H-Ar), 4.40 (t, J=7.0 Hz, 2H, CH₂N), 3.15 (s, 3H, NCH₃), 2.73 (t, J=7.0 Hz, 2H, CH₂CO), 1.41 (s, 9H, CH₃-tBu). ¹³C NMR (500 MHz, CDCl₃): δ 172.7 (CO₂tBu), 172.6 (CO-Ar), 170.2 (CO-Ar), 136.1, 136.0 (Cq-Ar), 132.0, 131.8 (CH-Ar), 128.2, 127.9, 127.2, 126.6, (Cq-Ar), 122.8, 122.5, 122.4, 122.2, 120.5, 120.4 (CH-Ar), 111.3, 109.6 (Cq-Ar) 107.6, 106.5 (CH-Ar), 82.9 (Cq-tBu) 42.6 (CH₂N), 36.2 (CH₂CO), 28.3 (CH₃-tBu), 24.4 (NCH₃); IR (ν, cm⁻¹) 3383 (NH), 1723, 1697 (CO); MS (ESI⁺), m/z (%): [M+H]⁺=468.1 (100%).

Bis-[1-(2-tert-butoxycarbonyylethyl)indol-3-yl]-1-methyl-1H-pyrrole-2,5-dione (9b).

Following the general procedure A, 3 (1.707 g, 5 mmol), DABCO (1.346 g, 12 mmol), TBAB (322 mg, 1 mmol), 4b (1.74 mL, 12 mmol) and KOH (224 mg, 4 mmol), were submitted to irradiation at 200 W for 10 min. The residue was purified by column chromatography on silica gel (elucent: CH₂Cl₂/EtOAc: 95/5) to give 2.123 g (71%) of 9b as red crystal. Mp 71-72 °C; Rf=0.8 (cyclohexane/EtOAc: 1/1); ¹H RMN (500 MHz, CDCl₃): δ 7.68 (s, 2H, H-Ar), 7.28 (d, J=8.0 Hz, 2H, H-Ar), 7.08 (t, J=8.0 Hz, 2H, H-Ar), 6.88 (t, J=7.6 Hz, 2H, H-Ar), 6.70 (t, J=7.6 Hz, 2H, H-Ar), 4.40 (t, J=7.0 Hz, 4H, CH₂N), 3.15 (s, 3H, NCH₃), 2.74 (t, J=7.0 Hz, 4H, CH₂CO), 1.41 (s, 18H, CH₃-tBu). ¹³C NMR (500 MHz, CDCl₃): δ 175.1 (CO₂tBu), 170.2 (CO-Ar), 136.1 (Cq-Ar), 131.8 (CH-Ar), 127.2 (Cq-Ar), 126.6 (Cq-Ar), 122.5 (CH-Ar), 122.4 (CH-Ar), 120.3 (CH-Ar), 115.2 (CH-Ar), 109.6 (CH-Ar), 82.9 (Cq-tBu) 42.6 (CH₂N), 36.2 (CH₂CO), 28.3 (CH₃-tBu), 25.5 (NCH₃); IR (ν, cm⁻¹) 1723, 1697 (CO); MS (ESI⁺), m/z (%): [M+H]⁺=597.9 (100%); HRMS (ESI⁺) calcd for [C₃₅H₃₉N₃O₆+H]⁺: 598.2907; found: 598.2905.
3-(2-Ethoxycarbonylethyl)-3H-imidazo[2,1-i]purine (6a)

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\text{CO}_2\text{CH}_2\text{CH}_3
\]

From 5a (110 mg, 0.465 mmol), chloroacetaldehyde (2 ml, 12 mmol) 90 mg (75%) of 6a was obtained as a white powder. Rf=0.55 (CH$_2$Cl$_2$/MeOH: 95/5); $^1$H NMR (500 MHz, CDCl$_3$): δ 8.83 (s, 1H, H-5), 8.04 (s, 1H, H-2), 7.69 (d, J=1.5 Hz, 1H, H-7), 7.54 (d, J=1.5 Hz, 1H, H-8), 4.56 (t, J=6.0 Hz, 2H, CH$_2$N), 4.08 (q, J=7.0 Hz, 2H, CH$_2$CH$_3$), 2.92 (t, J=6.0 Hz, 2H, CH$_2$CO), 1.17 (t, J=7.0 Hz, 3H, CH$_3$); $^{13}$C NMR (500 MHz, CDCl$_3$): δ 170.7 (CO), 141.7 (C-2), 138.2 (Cq-Ar), 135.7 (C-5), 133.0 (C-8), 115.3 (Cq-Ar), 111.3 (C-7), 61.4 (CH$_2$CH$_3$), 40.4 (CH$_2$N), 34.6 (CH$_2$CO), 14.2 (CH$_3$).

3-(2-tert-Butoxycarbonylethyl)-3H-imidazo[2,1-i]purine (6b):

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\text{CO}_2\text{C(CH}_3)_3
\]

From 5b (1.316 g, 5 mmol), chloroacetaldehyde (7.85 ml, 50 mmol) 980 mg (68%) of 6b was obtained as a white powder. Mp 169 °C; Rf=0.3 (CH$_2$Cl$_2$/MeOH: 95/5); $^1$H NMR (500 MHz, CDCl$_3$): δ 8.82 (s, 1H, H-5), 8.02 (s, 1H, H-2), 7.68 (d, J=1.5 Hz, 1H, H-7), 7.57 (d, J=1.5 Hz, 1H, H-8), 4.52 (t, J=6.5 Hz, 2H, CH$_2$N), 2.82 (t, J=6.5 Hz, 2H, CH$_2$CO), 1.34 (s, 9H,CH$_3$); $^{13}$C NMR (500 MHz, DMSO): δ 169.6 (CO), 141.2 (C-2), 140.6 (Cq-Ar), 136.6 (C-5), 132.5 (C-8), 122.6 (Cq-Ar), 111.9 (C-7), 80.4 (Cq-tBu), 40.2 (CH$_2$N), 35.0 (CH$_2$CO), 27.5 (CH$_3$); IR (v, cm$^{-1}$) 1726 (CO); MS (ESI$^+$), m/z (%): [M+H]$^+$=288.0 (100%); HRMS (ESI$^+$) calcd for [C$_{14}$H$_{17}$N$_5$O$_2$ + H]$^+$: 288.1457; found: 288.1456.
3-(2-Carboxyethyl)-3H-imidazo[2,1-i]purine (6c):

![Chemical Structure](image)

From 5c (125 mg, 0.6 mmol), chloroacetaldehyde (2.4 ml, 30 mmol) 72 mg (52%) of 6c was obtained as a white powder. Mp 238 °C; Rf=0.1 (CH₂Cl₂/MeOH: 85/15) ¹H NMR (500 MHz, DMSO): δ 9.67 (s, 1H, H-5), 8.66 (s, 1H, H-2), 8.48 (s, 1H, H-7), 8.06 (s, 1H, H-8), 4.59 (t, J=6.5 Hz, 2H, CH₂N), 2.98 (t, J=6.5 Hz, 2H, CH₂CO). ¹³C NMR (500 MHz, DMSO): δ 171.7 (CO), 144.7 (C-2), 142.5 (Cq-Ar), 137.4 (C-5), 123.5 (C-8), 118.9 (Cq-Ar), 114.1 (C-7), 40.5 (CH₂N), 33.7 (CH₂CO); IR (ν, cm⁻¹) 3015 (OH), 1728 (CO); MS (ESI⁺), m/z (%): [M+H]+=232.1 (100%); HRMS (ESI⁺) calcd for [C₁₀H₉N₅O₂ + H]⁺: 232.0833; found: 232.0826.

Compound 6c was also obtained by acidic hydrolysis of 5b according to the procedure described by Karskela.⁶ To 6b (143.66 mg, 0.5 mmol) in anhydrous CH₂Cl₂ (3.75 mL) was added TFA (7.50 mL) and stirring was maintained for 3 h at room temperature. After evaporation of the solvents to dryness, the residue was suspended in water, solubilized in a saturated NaHCO₃ solution, precipitated by acidification to pH 2 with HCl (2 N) and left a night at 4 °C. The product was filtered and dried in vacuo to give 6c in 80% yield (93 mg).

References