

Supporting information

Iodine-mediated regioselective guanylation-amination of propargylamines towards the synthesis of diversely substituted 2-aminoimidazoles

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General Information

NMR spectra were recorded on a 300 MHz instrument using CDCl₃ as solvent unless and otherwise stated (s = singlet, d = doublet, t = triplet, m = multiplet). The ¹H and ¹³C chemical shifts are reported in parts per million relative to tetramethylsilane as an internal standard. For the Mass spectrometry, ion source temperature was 150-250°C, as required. High-resolution EI-mass spectra were performed with a resolution of 10,000. For chromatography, analytical TLC plates and 70-230 mesh silica gel were used. All the solvents and chemicals were purchased and used as available.

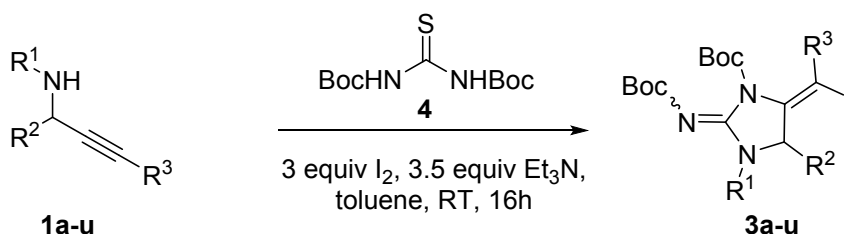
The microwave irradiation experiments were carried out in a dedicated CEM-Discover monomode microwave apparatus, operating at a frequency of 2.45 GHz with continuous irradiation power from 0 to 300 W and utilization of the standard absorbance level of 100 W. The reactions were carried out in 10 mL glass tubes, sealed with Teflon septum and placed in the microwave cavity. The reactions were irradiated at the required set temperature for the stipulated time and then cooled to ambient temperature with air jet cooling.

Experimental procedure

a) Synthesis of starting material

All propargylamines **1a-u** were synthesized according to the literature^[S1]

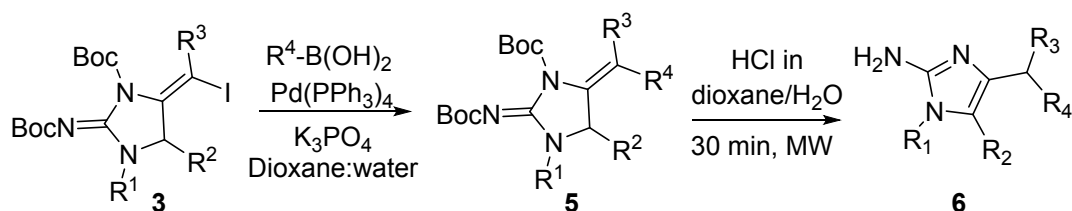
b) One-pot guanylation/iodocyclization procedure



Propargylamine **1a-u** (1 mmol) was dissolved in toluene (10 mL) followed by addition of N,N-diBoc-thiourea (427 mg, 1.5 mmol) and triethylamine (0.488 mL, 3.5 mmol). The mixture was flushed with nitrogen and cooled down to 0°C when iodine (761 mg, 3 mmol) was slowly added and the mixture was allowed to warm up to room temperature and stirred for 16 h. Thereafter the reaction was quenched by the addition of sodium bisulfite (aq. sat. solution 20 mL). The organic layer was separated, dissolved with diethyl ether (100 mL) and washed with water (3 x 50 mL). The solvent was evaporated by reduced pressure. The product was purified by column chromatography (heptane/ethyl acetate 10:1.5).

c) Suzuki/deprotection reaction procedure

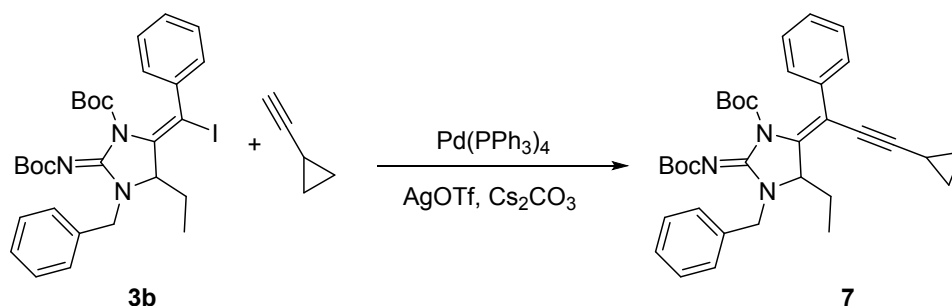
[S1] (a) J. Yoo, L. Zhao, C. -J. Li, *Aldrichimica Acta*, 2011, **44**, 43; (b) V. A. Peshkov, O. P. Pereshivko, E. V. Van der Eycken, *Chem. Soc. Rev.*, 2012, **41**, 3790; (c) C. Wei, Z. Li, C.-J. Li, *Synlett*, 2004, **9**, 1472.



Entry	R1	R2	R3	R4	Yield of 5 (%)	Yield of 6 from 5 (%)
1	Benzyl	Ethyl	Phenyl	Phenyl	85 [4b]	100% [5b]
2	Benzyl	<i>iso</i> -butyl	Butyl	4-Fluorophenyl	84 [4s]	100% [5s]
3	<i>iso</i> -butyl	Propyl	Phenyl	3,5-dimethylphenyl	62 [4h]	100% [5h]
4	<i>iso</i> -butyl	<i>iso</i> -Propyl	2-Fluorophenyl	3,5-dimethoxyphenyl	40 [4m]	100% [5m]

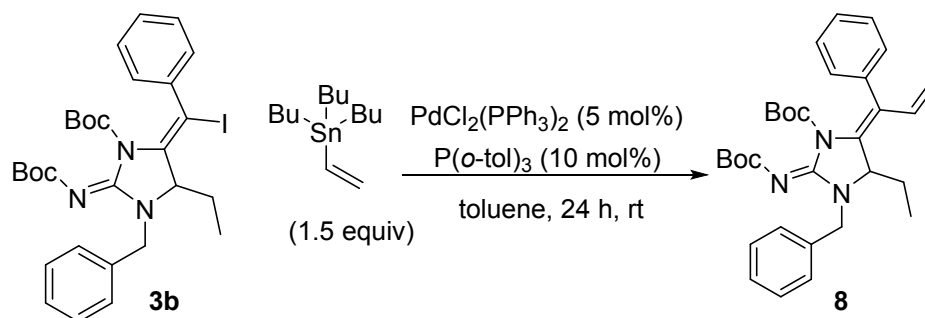
A mixture of the iodocyclized product (0.162 mmol), boronic acid (0.259 mmol), Pd(PPh₃)₄ (11.23 mg, 9.72 μmol) and potassium phosphate (68.7 mg, 0.324 mmol) in dioxane/water (9:1, 1 mL) was degassed and flushed with nitrogen and then allowed to stir at 85°C for 24 h. The reaction mixture was dissolved with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The organic phase was concentrated *in vacuo* and purified by preparative HPLC (MeCN/H₂O 50% to 100% in 20 min followed by 100% MeCN for 10 min). The purified product was concentrated, dissolved in dioxane and flushed with nitrogen followed by dropwise addition of hydrochloric acid (4N) in water/dioxane solution (50 equiv, 2 mL). The reaction vial was submitted to microwave irradiation for 30 min at 70°C and 150 W followed by concentration under reduced pressure to provide **6**.

d) Sonogashira reaction procedure



A degassed solution of **3b** (100 mg, 0.162 mmol), ethynylcyclopropane (0.046 mL, 0.486 mmol), Pd(PPh₃)₄ (9.36 mg, 8.10 μmol), silver triflate (4.16 mg, 0.016 mmol) and Cs₂CO₃ (106 mg, 0.324 mmol) in 1,4-dioxane (1 mL) was flushed with nitrogen and stirred for 24 h at 85°C. To the reaction mixture was added water (10 mL) and it was extracted with ethyl acetate (3 x 30 mL). The organic phase was concentrated *in vacuo* and purified by preparative HPLC (MeCN/H₂O 50% to 100% in 20 min followed by 100% MeCN for 10 min) to afford **7** (74.7 mg, 0.134 mmol, 83% yield).

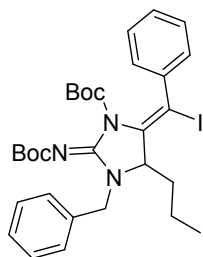
e) Stille reaction procedure



Compound **3b** (50 mg, 0.081 mmol) was dissolved in toluene (1 mL) in a 25 mL round-bottom flask. To the flask was added tributyl(vinyl)stannane (0.028 mL, 0.097 mmol), $\text{PdCl}_2(\text{PPh}_3)_2$ (0.909 mg, 4.05 μmol) and tri-*o*-tolylphosphane (2.464 mg, 8.10 μmol). The reaction mixture was degassed and flushed with nitrogen and heated in a sealed tube at 80°C for 24 h. After cooling to room temperature water (10 mL) was added to the flask and the organic phase was separated and washed with water (2 x 30 mL). The solvent was evaporated *in vacuo* and purified by preparative HPLC (MeCN/H₂O 50% to 100% in 20 min followed by 100% MeCN for 10 min) to afford **8** (31.0 mg, 0.060 mmol, 74% yield).

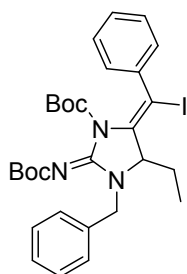
Spectral data of compounds

Tert-butyl (5E)-3-benzyl-2-((tert-butoxycarbonyl)imino)-5-(iodo(phenyl)methylene)-4-propylimidazolidine-1-carboxylate (3a)



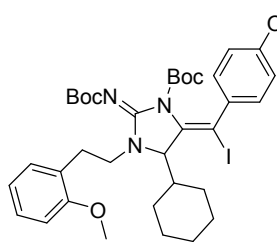
Orange solid, Yield 76%, mp: 175-177°C. ¹H NMR (300 MHz, CDCl₃) δ 7.70 (d, J = 8.3 Hz, 2H), 7.38 – 7.18 (m, 9H), 4.86 (d, J = 15.3 Hz, 1H), 4.49 (d, J = 15.3 Hz, 1H), 4.12 (t, J = 3.4 Hz, 1H), 1.98 – 1.81 (m, 1H), 1.55 (s, 9H), 1.28 – 1.13 (m, 3H), 1.01 (s, 9H), 0.75 (t, J = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 159.39, 151.88, 147.25, 140.58, 136.19, 135.50, 130.13, 128.80, 128.38, 128.13, 127.97, 127.83, 90.83, 83.59, 79.33, 77.49, 77.07, 76.64, 64.79, 47.54, 32.46, 28.20, 28.02, 27.37, 16.26, 13.92. HRMS *m/z* (ESI) Calculated for C₃₀H₃₉IN₃O₄[M+H]⁺: 632.1981, found 632.2006.

Tert-butyl (5E)-3-benzyl-2-((tert-butoxycarbonyl)imino)-4-ethyl-5-(iodo(phenyl)methylene)imidazolidine-1-carboxylate (3b)



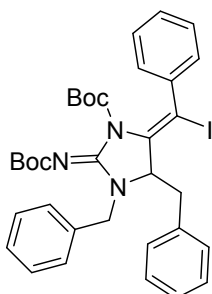
Yellow amorphous solid, Yield 78%, ¹H NMR (400 MHz, CDCl₃): δ 7.73 – 7.67 (m, 2H), 7.37 – 7.19 (m, 8H), 4.94 (d, J = 15.4 Hz, 1H), 4.40 (d, J = 15.4 Hz, 1H), 4.11 (t, J = 3.7 Hz, 1H), 2.07 – 1.91 (m, 1H), 1.55 (s, 9H), 1.01 (s, 9H), 0.78 (t, J = 7.5 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 159.31, 151.95, 147.11, 140.66, 136.05, 135.24, 130.11, 128.81, 128.38, 128.14, 127.97, 127.84, 90.84, 83.63, 79.31, 77.36, 77.04, 76.72, 65.08, 47.31, 28.22, 27.34, 23.09, 7.13. HRMS *m/z* (ESI) Calculated for C₂₉H₃₇IN₃O₄: 618.1825, found 618.1840.

Tert-butyl (5E)-2-((tert-butoxycarbonyl)imino)-4-cyclohexyl-5-(iodo(4-methoxyphenyl)methylene)-3-(2-methoxyphenethyl)imidazolidine-1-carboxylate (3c)



Orange amorphous solid, Yield 67%, ¹H NMR (300 MHz, CDCl₃) δ 7.81 (d, J = 8.7 Hz, 2H), 7.13 (t, J = 7.7 Hz, 1H), 6.91 (d, J = 8.8 Hz, 2H), 6.81 – 6.67 (m, 3H), 4.55 – 4.44 (m, 1H), 3.85 (s, 3H), 3.71 – 3.65 (m, 4H), 3.02 – 2.77 (m, 3H), 1.98 – 1.90 (m, 1H), 1.84 – 1.74 (m, 2H), 1.70 – 1.60 (m, 4H), 1.55 (s, 9H), 1.29 – 1.14 (m, 4H), 1.09 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 160.34, 159.74, 159.65, 148.68, 148.49, 140.80, 139.85, 131.15, 130.27, 129.64, 121.37, 114.41, 112.84, 112.36, 82.76, 80.19, 78.81, 75.73, 55.29, 55.10, 52.81, 43.66, 35.43, 34.07, 30.70, 30.00, 28.32, 27.63, 26.47, 26.03, 25.93. HRMS *m/z* (ESI) Calculated for C₃₆H₄₉IN₃O₆: 746.2662, found 746.2665.

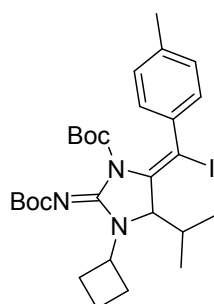
Tert-butyl (5E)-3,4-dibenzyl-2-((tert-butoxycarbonyl)imino)-5-(iodo(phenyl)methylene)imidazolidine-1-carboxylate (3d)



Orange solid, Yield 38%, mp: 175-176°C, ¹H NMR (300 MHz, CDCl₃) δ 7.67 (d, J = 7.6 Hz, 2H), 7.37 – 7.17 (m, 11H), 7.06 (d, J = 6.3 Hz, 2H), 5.07

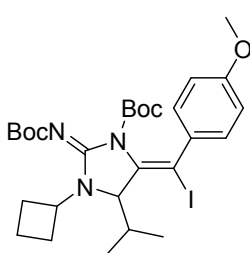
(d, $J = 15.3$ Hz, 1H), 4.18 (dd, $J = 7.5, 4.3$ Hz, 1H), 3.70 (d, $J = 15.4$ Hz, 1H), 3.09 (dd, $J = 13.8, 4.1$ Hz, 1H), 2.87 (dd, $J = 13.8, 7.7$ Hz, 1H), 1.54 (s, 9H), 0.99 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.14, 151.39, 147.19, 140.53, 135.86, 135.67, 134.80, 130.05, 129.66, 128.80, 128.78, 128.47, 128.21, 127.84, 127.24, 91.51, 83.65, 79.35, 77.46, 77.24, 77.04, 76.62, 65.15, 47.69, 37.51, 28.22, 28.01, 27.30. HRMS m/z (ESI) Calculated for $\text{C}_{34}\text{H}_{39}\text{IN}_3\text{O}_4$: 680.1981, found 680.2001.

Tert-butyl (5E)-2-((tert-butoxycarbonyl)imino)-3-cyclobutyl-5-(iodo(p-tolyl)methylene)-4-isopropylimidazolidine-1-carboxylate (3e)



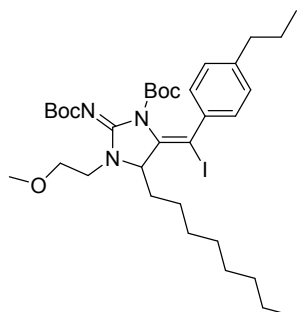
Yellowish solid, Yield 70%, mp: 148-150°C. ^1H NMR (300 MHz, CDCl_3) δ 7.55 (d, $J = 8.1$ Hz, 2H), 7.12 (d, $J = 8.1$ Hz, 2H), 4.37 – 4.24 (m, 1H), 4.21 (d, $J = 3.0$ Hz, 1H), 2.42 – 2.24 (m, 8H), 1.69 – 1.58 (m, 2H), 1.53 (s, 9H), 1.06 – 0.99 (m, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 159.03, 150.74, 147.06, 138.24, 138.22, 135.90, 129.87, 128.63, 91.53, 83.10, 78.92, 68.17, 50.65, 33.14, 30.95, 29.33, 28.57, 28.29, 28.01, 27.30, 21.14, 18.81, 18.24, 15.06. HRMS m/z (ESI) Calculated for $\text{C}_{28}\text{H}_{41}\text{IN}_3\text{O}_4$ $[\text{M}+\text{H}]^+$: 610.2137, found 610.2150.

Tert-butyl (5E)-2-((tert-butoxycarbonyl)imino)-3-cyclobutyl-5-(iodo(4-methoxyphenyl)methylene)-4-isopropylimidazolidine-1-carboxylate (3f)



Yellow amorphous solid, Yield 69%, ^1H NMR (300 MHz, CDCl_3) δ 7.62 (d, $J = 8.9$ Hz, 2H), 6.85 (d, $J = 8.9$ Hz, 2H), 4.39 – 4.25 (m, 1H), 4.21 (d, $J = 3.2$ Hz, 1H), 3.81 (s, 3H), 2.40 – 2.21 (m, 4H), 1.69 – 1.61 (m, 2H), 1.52 (s, 9H), 1.07 – 1.03 (m, 12H), 1.00 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.40, 150.86, 147.14, 135.46, 133.60, 131.40, 113.31, 91.50, 83.06, 78.94, 68.16, 55.46, 50.64, 33.16, 29.34, 28.60, 28.28, 27.40, 18.79, 18.31, 15.07. HRMS m/z (ESI) Calculated for $\text{C}_{28}\text{H}_{41}\text{IN}_3\text{O}_5$: 626.2087, found 626.2101.

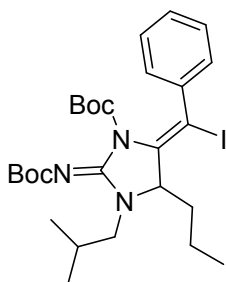
Tert-butyl (5E)-2-((tert-butoxycarbonyl)imino)-5-(iodo(4-propylphenyl)methylene)-3-(2-methoxyethyl)-4-octylimidazolidine-1-carboxylate (3g)



Dark-orange sticky liquid, Yield 76%, ^1H NMR (300 MHz, CDCl_3) δ 7.65 – 7.56 (m, 2H), 7.17 – 7.10 (m, 2H), 4.40 – 4.34 (m, 1H), 3.78 – 3.67 (m, 1H), 3.64 – 3.55 (m, 2H), 3.50 – 3.40 (m, 1H), 3.37 – 3.32 (m, 3H), 2.63 – 2.52 (m, 2H), 2.10 – 1.95 (m, 1H), 1.70 – 1.58 (m, 3H), 1.56 – 1.51 (m, 9H), 1.31 – 1.19 (m, 12H), 1.03 – 0.98 (m, 9H), 0.97 – 0.91 (m, 3H), 0.90 – 0.83 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.39, 151.49, 147.24, 143.16, 138.20, 135.18, 130.02, 128.12, 90.96, 83.26, 79.23, 70.73, 66.32, 58.88, 43.84, 37.75, 35.44, 32.73, 31.90, 31.84, 30.45, 29.84, 29.53, 29.34, 29.04, 28.21, 27.37, 26.45, 26.34, 24.60,

22.92, 22.82, 22.71, 22.64, 14.12, 13.84. HRMS m/z (ESI) Calculated for $C_{34}H_{55}IN_3O_5$: 712.3182, found 712.3196.

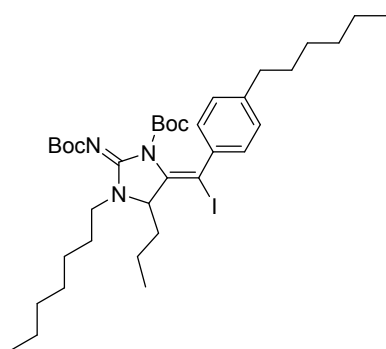
Tert-butyl (5E)-2-((tert-butoxycarbonyl)imino)-5-(iodo(phenyl)methylene)-3-isobutyl-4-propylimidazolidine-1-carboxylate, (3h)



Yellowish solid, Yield 81%, mp: 172-174°C. 1H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, J = 8.3 Hz, 2H), 7.33 (t, J = 7.7 Hz, 2H), 7.25 – 7.18 (m, 1H), 4.23 (t, J = 4.1 Hz, 1H), 3.70 (dd, J = 14.0, 9.1 Hz, 1H), 2.86 (dd, J = 14.0, 6.4 Hz, 1H), 2.14 – 1.89 (m, 2H), 1.67 – 1.60 (m, 1H), 1.52 (s, 9H), 1.39 – 1.21 (m, 2H), 1.01 (s, 9H), 0.99 – 0.89 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.36,

151.64, 147.21, 140.53, 135.89, 130.12, 128.36, 128.11, 90.80, 83.35, 79.01, 64.59, 50.12, 32.60, 28.26, 27.97, 27.36, 26.62, 20.09, 19.68, 16.78, 14.12. HRMS m/z (ESI) Calculated for $C_{27}H_{41}IN_3O_4$ $[M+H]^+$: 598.2137, found 598.2146.

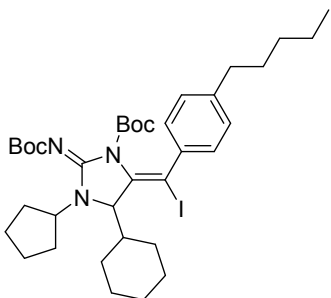
Tert-butyl (5E)-3-benzyl-2-((tert-butoxycarbonyl)imino)-5-(iodo(phenyl)methylene)-4-(p-tolyl)imidazolidine-1-carboxylate (3i)



Yellow sticky liquid, Yield 82%, 1H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, J = 8.3 Hz, 2H), 7.13 (d, J = 8.3 Hz, 2H), 4.21 (t, J = 4.0 Hz, 1H), 3.76 – 3.65 (m, 1H), 3.14 – 3.04 (m, 1H), 2.59 (t, J = 6.9 Hz, 1H), 2.07 – 1.94 (m, 1H), 1.57 – 1.52 (m, 14H), 1.35 – 1.25 (m, 16H), 1.00 (s, 9H), 0.93 – 0.85 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.68, 159.43, 151.25, 147.26, 143.42, 137.97,

135.13, 129.99, 129.04, 128.23, 128.08, 125.30, 91.17, 83.18, 79.00, 77.46, 77.03, 76.61, 64.68, 43.32, 35.59, 32.78, 31.73, 31.43, 28.99, 28.94, 28.23, 27.98, 27.56, 27.36, 26.72, 22.65, 22.58, 16.45, 14.12, 14.09. HRMS m/z (ESI) Calculated for $C_{36}H_{59}IN_3O_4$: 724.3546, found 724.3566.

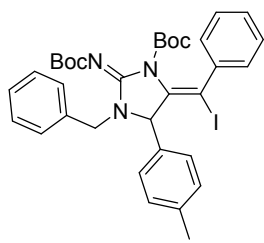
Tert-butyl (5E)-2-((tert-butoxycarbonyl)imino)-4-cyclohexyl-3-cyclopentyl-5-(iodo(4-pentylphenyl)methylene)imidazolidine-1-carboxylate (3j)



Yellowish solid, Yield 77%, mp: 142-143 °C, 1H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, J = 8.2 Hz, 2H), 7.13 (d, J = 8.2 Hz, 2H), 4.22 – 4.10 (m, 2H), 2.63 – 2.56 (m, 2H), 1.89 – 1.57 (m, 17H), 1.53 (s, 9H), 1.35 – 1.28 (m, 4H), 1.14 – 1.04 (m, 4H), 1.00 (s, 9H), 0.89 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.63, 151.40,

147.14, 143.27, 138.45, 136.14, 129.99, 127.97, 92.83, 82.75, 78.98, 67.83, 57.43, 44.23, 35.57, 31.44, 31.16, 30.67, 30.02, 29.22, 28.23, 27.91, 27.38, 26.58, 26.47, 26.25, 23.45, 23.27, 22.54, 14.03. HRMS m/z (ESI) Calculated for $C_{36}H_{55}IN_3O_4$: 720.3233, found 720.3271.

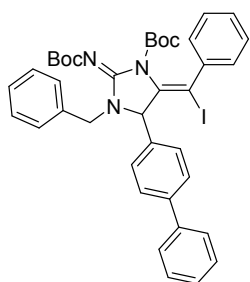
Tert-butyl (5E)-3-benzyl-2-((tert-butoxycarbonyl)imino)-5-(iodo(phenyl)methylene)-4-(p-tolyl)imidazolidine-1-carboxylate (3k)



Yellowish amorphous solid, Yield 45%, ^1H NMR (300 MHz, CDCl_3) δ 7.75 – 7.60 (m, 2H), 7.41 – 7.19 (m, 11H), 7.17 – 7.08 (m, 3H), 5.26 – 5.15 (m, 1H), 4.90 – 4.80 (m, 1H), 3.88 – 3.70 (m, 1H), 2.39 – 2.32 (m, 3H), 1.61 – 1.55 (m, 9H), 1.06 – 1.00 (m, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.27, 151.02, 147.59, 140.57, 140.52, 138.83, 135.57, 135.39, 135.31, 134.88, 132.47, 130.15, 129.50, 128.83, 128.44, 128.18, 128.14, 128.05, 127.82, 92.58, 83.84, 79.47, 79.41, 67.20, 66.97, 46.03, 45.81, 28.25, 28.02, 27.34, 21.26. HRMS m/z (ESI) Calculated for $\text{C}_{34}\text{H}_{39}\text{IN}_3\text{O}_4$: 680.1981, found 680.1996.

Tert-butyl

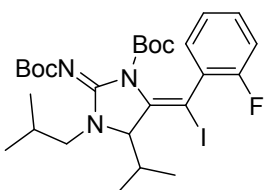
(5E)-4-([1,1'-biphenyl]-4-yl)-3-benzyl-2-((tert-butoxycarbonyl)imino)-5-iodo(phenyl)methylene)imidazolidine-1-carboxylate (3l)



Yellowish solid, Yield 41%, ^1H NMR (300 MHz, CDCl_3) δ 7.72 – 7.21 (m, 21H), 5.20 (dd, J = 15.4, 3.4 Hz, 1H), 4.89 (d, J = 14.7 Hz, 1H), 3.86 (dd, J = 20.6, 15.4 Hz, 1H), 1.60 – 1.56 (m, J = 2.3 Hz, 1H), 1.05 – 1.01 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.26, 151.04, 147.61, 141.75, 140.51, 140.25, 135.31, 134.69, 134.48, 130.17, 128.85, 128.52, 128.24, 128.18, 128.08, 127.86, 127.66, 127.46, 127.10, 92.87, 83.96, 79.52, 67.19, 67.00, 46.09, 28.24, 27.98, 27.36. HRMS m/z (ESI) Calculated for $\text{C}_{39}\text{H}_{41}\text{IN}_3\text{O}_4$: 742.2137, found 742.2144.

Tert-butyl

(5E)-2-((tert-butoxycarbonyl)imino)-5-((2-fluorophenyl)iodomethylene)-3-isobutyl-4-isopropylimidazolidine-1-carboxylate (3m)

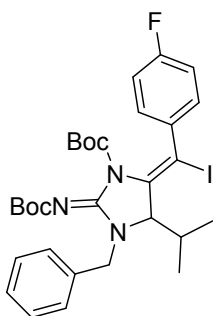


White solid, Yield 75%, mp: 142-143°C, ^1H NMR (300 MHz, CDCl_3) δ 7.52 (t, J = 7.5 Hz, 1H), 7.32 – 7.23 (m, 1H), 7.17 – 7.02 (m, 2H), 4.18 (d, J = 3.6 Hz, 1H), 3.85 (dd, J = 14.1, 9.0 Hz, 1H), 2.84 (dd, J = 14.1, 6.5 Hz, 1H), 2.34 – 2.23 (m, 1H), 2.21 – 2.08 (m, 1H), 1.48 (s, 9H), 1.13 – 1.06 (m, 12H), 1.01 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.6 Hz, 3H), 0.91 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 147.14, 130.34, 130.23, 129.06, 128.89, 123.90, 123.86, 116.33, 83.63, 80.11, 78.94, 77.45, 77.03, 76.60, 52.40, 32.27, 28.28, 27.41, 26.16, 19.95, 19.65, 19.48, 17.33. HRMS m/z (ESI) Calculated for $\text{C}_{27}\text{H}_{39}\text{FIN}_3\text{O}_4$: 616.2043, found 616.2070.

Tert-butyl

(5E)-3-benzyl-2-((tert-butoxycarbonyl)imino)-5-((4-fluorophenyl)iodomethylene)-4-isopropylimidazolidine-1-carboxylate

(3n)



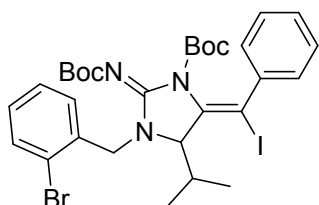
Yellow solid, Yield 68%, mp: 179-181°C, ^1H NMR (300 MHz, CDCl_3) δ 7.71 (dd, J = 8.7, 5.3 Hz, 2H), 7.39 – 7.23 (m, 5H), 7.05 (t, J = 8.6 Hz, 2H), 5.25 (d, J = 15.6 Hz, 1H), 4.23 (d, J = 15.6 Hz, 1H), 3.89 (d, J = 3.1 Hz, 1H), 2.35 – 2.22 (m, 1H), 1.54 (s, 9H), 1.06 (s, 9H), 1.01 (d, J = 7.1 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 162.29 (d, J = 249.3 Hz), 159.50, 152.84, 147.00, 136.93 (d, J = 3.4 Hz), 136.40, 135.95, 131.95 (d, J = 8.2 Hz), 128.92, 127.81,

127.53, 114.94 (d, $J = 21.7$ Hz), 89.99, 83.64, 79.46, 77.46, 77.03, 76.61, 68.32, 49.70, 31.92, 28.20, 27.43, 19.91, 16.79. HRMS m/z (ESI) Calculated for $C_{30}H_{38}FIN_3O_4$: 650.1887, found 650.1904.

Tert-butyl

(5E)-3-(2-bromobenzyl)-2-((tert-butoxycarbonyl)imino)-5-

(iodo(phenyl)methylene)-4-isopropylimidazolidine-1-carboxylate (3o)



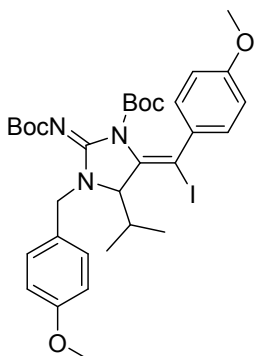
Brownish solid, Yield 66%, mp: 187-189°C, 1H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, $J = 7.6$ Hz, 2H), 7.57 (d, $J = 8.0$ Hz, 1H), 7.38 – 7.30 (m, 4H), 7.25 – 7.10 (m, 2H), 5.17 (d, $J = 16.2$ Hz, 1H), 4.51 (d, $J = 16.1$ Hz, 1H), 3.91 (d, $J = 3.2$ Hz, 1H), 2.38 – 2.26 (m, 1H), 1.53

(s, 9H), 1.03 – 0.95 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.05, 152.46, 147.08, 140.84, 136.14, 135.09, 133.08, 130.02, 129.42, 129.25, 128.40, 128.15, 127.92, 123.32, 91.68, 83.60, 79.39, 77.47, 77.04, 76.62, 69.13, 49.96, 31.98, 28.20, 28.01, 27.34, 19.60, 16.90. HRMS m/z (ESI) Calculated for $C_{30}H_{38}BrIN_3O_4$: 710.1087, found 710.1102.

Tert-butyl

(5E)-2-((tert-butoxycarbonyl)imino)-5-(iodo(4-methoxyphenyl)methylene)-4-

isopropyl-3-(4-methoxybenzyl)imidazolidine-1-carboxylate (3p)



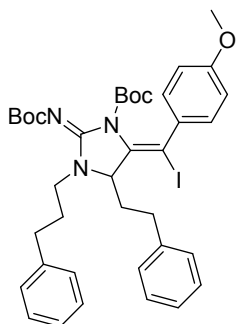
Yellowish solid, Yield 71%, mp: 159-161°C, 1H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, $J = 8.8$ Hz, 2H), 7.20 (d, $J = 8.6$ Hz, 2H), 6.87 (d, $J = 8.8$ Hz, 4H), 5.19 (d, $J = 15.3$ Hz, 1H), 4.15 (d, $J = 15.4$ Hz, 1H), 3.89 (d, $J = 3.1$ Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 2.33 – 2.22 (m, 1H), 1.55 (s, 9H), 1.05

(s, 9H), 1.01 (d, $J = 7.3$ Hz, 3H), 0.92 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.70, 159.51, 159.45, 159.22, 159.15, 152.86, 152.61, 149.57, 148.77, 147.16, 141.10, 135.18, 133.43, 131.44, 131.10, 130.36, 129.32, 128.93, 128.27, 128.11, 114.23, 113.35, 112.96, 91.53, 83.27, 83.03, 80.46, 79.24, 78.96, 73.11, 68.15, 55.47, 55.25, 53.25, 49.16, 33.86, 31.99, 28.31, 28.25, 27.59, 27.41, 20.56, 20.33, 19.97, 16.77. HRMS m/z (ESI) Calculated for $C_{32}H_{43}IN_3O_6$ $[M+H]^+$: 692.2192, found 692.2208.

Tert-butyl

(5E)-2-((tert-butoxycarbonyl)imino)-5-(iodo(4-methoxyphenyl)methylene)-4-

phenethyl-3-(3-phenylpropyl)imidazolidine-1-carboxylate (3q)

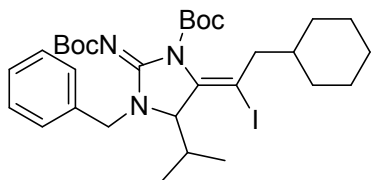


Yellow amorphous solid, Yield 48%, 1H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, $J = 8.8$ Hz, 2H), 7.31 – 7.12 (m, 10H), 6.92 (d, $J = 8.8$ Hz, 2H), 4.20 – 4.09 (m, 1H), 4.04 (t, $J = 7.1$ Hz, 1H), 3.84 (s, 3H), 2.98 – 2.88 (m, 1H), 2.84 – 2.76 (m, 1H), 2.60 (m, 2H), 2.11 – 1.96 (m, 2H), 1.94 – 1.82 (m, 2H), 1.56 (s, 9H), 1.08 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.82,

158.22, 148.68, 143.18, 141.55, 141.26, 140.65, 131.09, 130.97, 129.94, 128.57, 128.43, 128.39, 128.15, 126.28, 125.92, 113.02, 83.18, 79.98, 79.01, 68.93, 55.30,

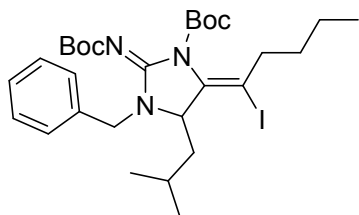
50.90, 48.96, 34.82, 32.73, 32.32, 29.70, 28.26, 27.58. HRMS m/z (ESI) Calculated for $C_{38}H_{47}IN_3O_5$: 752.2556, found 752.2551.

Tert-butyl (5E)-3-benzyl-2-((tert-butoxycarbonyl)imino)-5-(2-cyclohexyl-1-iodoethylidene)-4-isopropylimidazolidine-1-carboxylate (3r)



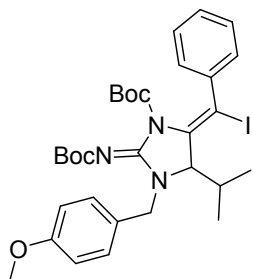
Orange amorphous solid, Yield 41%, 1H NMR (300 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 3H), 7.15 – 7.08 (m, 2H), 5.37 (d, J = 15.6 Hz, 1H), 4.00 (d, J = 15.7 Hz, 1H), 3.75 (d, J = 3.5 Hz, 1H), 2.43 – 2.31 (m, 1H), 2.27 – 2.14 (m, 2H), 1.76 – 1.61 (m, 5H), 1.52 – 1.50 (m, 9H), 1.50 – 1.48 (m, 9H), 1.27 – 1.17 (m, 6H), 1.02 (d, J = 7.0 Hz, 3H), 0.91 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.40, 152.62, 148.57, 136.15, 135.96, 128.70, 127.69, 127.34, 100.55, 83.98, 82.01, 79.02, 66.95, 49.41, 45.79, 38.01, 33.02, 31.47, 30.28, 28.51, 28.08, 28.04, 27.99, 26.38, 26.21, 26.03, 19.90, 16.90. HRMS m/z (ESI) Calculated for $C_{31}H_{47}IN_3O_4$: 652.2607, found 652.2618.

Tert-butyl (5E)-3-benzyl-2-((tert-butoxycarbonyl)imino)-5-(1-iodopentylidene)-4-isobutylimidazolidine-1-carboxylate (3s)



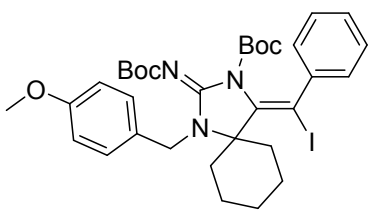
Brownish amorphous solid, Yield 77%, 1H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 3H), 7.19 – 7.13 (m, 2H), 5.19 (d, J = 15.6 Hz, 1H), 4.07 (d, J = 15.6 Hz, 1H), 3.96 – 3.84 (m, 1H), 2.65 – 2.50 (m, 1H), 2.37 – 2.25 (m, 1H), 1.74 – 1.61 (m, 2H), 1.52 (s, J = 8.4 Hz, 9H), 1.50 (s, 9H), 1.43 – 1.24 (m, 5H), 0.98 – 0.82 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.04, 152.46, 149.19, 135.95, 135.76, 128.85, 127.84, 127.58, 100.69, 83.95, 79.14, 61.62, 47.85, 40.56, 38.42, 31.81, 28.35, 28.11, 24.40, 23.97, 22.52, 21.47, 14.04. HRMS m/z (ESI) Calculated for $C_{29}H_{45}IN_3O_4$: 626.2450, found 626.2474.

Tert-Butyl (5E)-2-((tert-butoxycarbonyl)imino)-5-(iodo(phenyl)methylene)-4-isopropyl-3-(4-methoxybenzyl)imidazolidine-1-carboxylate (3t)



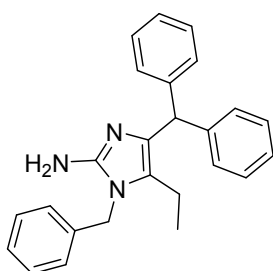
Yellowish solid, Yield 62%, mp: 177-178°C, 1H NMR (300 MHz, $CDCl_3$): δ 7.74-7.61 (m, 2H), 7.37-7.30 (m, 2H), 7.23-7.17 (m, 4H), 6.93-6.80 (m, 2H), 5.20 (d, J = 15.2 Hz, 1H), 4.15 (d, J = 15.3 Hz, 1H), 3.89 (d, J = 3.0 Hz, 1H), 3.79 (s, 3H), 2.37-2.23 (m, 1H), 1.55 (s, 9H), 1.06-0.97 (m, J = 7.5 Hz, 12H), 0.95-0.91 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.4, 159.2, 152.7, 147.1, 140.8, 136.3, 130.1, 128.9, 128.3, 128.1, 114.3, 91.3, 83.5, 79.3, 77.5, 77.1, 76.6, 68.1, 55.3, 49.2, 31.9, 28.2, 27.3, 20.0, 16.7. HRMS m/z (ESI) Calculated for $C_{31}H_{41}IN_3O_5$ $[M+H]^+$: 662.2087, found 662.2092.

Tert-butyl (4E)-2-((tert-butoxycarbonyl)imino)-4-(iodo(phenyl)methylene)-1-(4-methoxybenzyl)-1,3-diazaspiro[4.5]decane-3-carboxylate (3u)



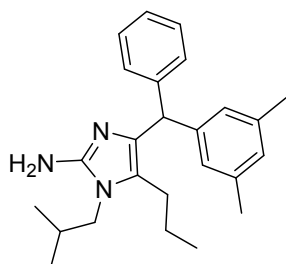
Orange amorphous solid, Yield 34%, ^1H NMR (300 MHz, CDCl_3) δ 7.75 – 7.70 (m, 2H), 7.38 – 7.31 (m, 2H), 7.25 – 7.16 (m, 3H), 6.89 – 6.84 (m, 2H), 4.92 (s, 2H), 3.79 (s, 3H), 2.84 – 2.71 (m, 2H), 1.75 – 1.64 (m, 6H), 1.52 – 1.43 (m, 11H), 1.11 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.48, 158.62, 151.41, 147.72, 142.26, 139.28, 131.00, 129.68, 128.18, 127.94, 127.68, 113.92, 85.11, 83.91, 79.00, 65.08, 55.24, 53.45, 47.03, 31.03, 28.18, 27.40, 23.52, 21.77. HRMS m/z (ESI) Calculated for $\text{C}_{33}\text{H}_{43}\text{N}_3\text{O}_5$: 688.2243, found 688.2271.

4-benzhydryl-1-benzyl-5-ethyl-1H-imidazol-2-amine (6b)



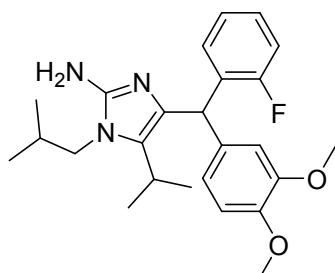
Yellow solid, Quantitative yield, ^1H NMR (300 MHz, MeOD) δ 7.38 – 7.27 (m, 9H), 7.19 – 7.15 (m, 4H), 7.12 – 7.08 (m, 2H), 5.59 (s, 1H), 5.14 (s, 2H), 2.32 (q, $J = 7.5$ Hz, 2H), 0.73 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (151 MHz, MeOD) δ 140.39, 134.69, 128.82, 128.55, 128.44, 127.86, 127.07, 126.58, 125.69, 46.19, 45.24, 15.36, 12.82. MS m/z (ESI) Calculated for $\text{C}_{25}\text{H}_{27}\text{N}_3$ $[\text{M}+\text{H}]^+$: 369.21, found 369.25.

4-((3,5-dimethylphenyl)(phenyl)methyl)-1-isobutyl-5-propyl-1H-imidazol-2-amine (6h)



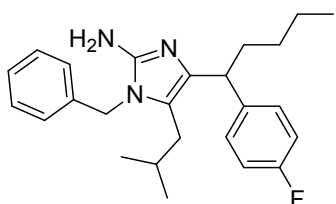
Yellow solid, Quantitative yield, ^1H NMR (300 MHz, MeOD) δ 7.39 – 7.24 (m, 3H), 7.14 (d, $J = 7.0$ Hz, 2H), 6.93 (s, 1H), 6.75 (s, 2H), 5.48 (s, 1H), 3.64 (t, $J = 4.0$ Hz, 1H), 2.38 – 2.30 (m, 2H), 2.25 (s, 6H), 1.43 – 1.26 (m, 3H), 0.95 (d, $J = 6.7$ Hz, 6H), 0.79 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (101 MHz, MeOD) δ 146.30, 140.59, 140.24, 138.22, 128.45, 128.40, 126.93, 126.20, 125.14, 123.52, 27.77, 24.00, 22.54, 19.98, 18.25, 12.55. MS m/z (ESI) Calculated for $\text{C}_{25}\text{H}_{34}\text{N}_3$ $[\text{M}+\text{H}]^+$: 376.27, found 376.25.

4-((3,4-dimethoxyphenyl)(2-fluorophenyl)methyl)-1-isobutyl-5-isopropyl-1H-imidazol-2-amine (6m)



Yellow solid, Quantitative yield, ^1H NMR (400 MHz, MeOD) δ 7.43 – 7.34 (m, 1H), 7.24 – 7.13 (m, 2H), 7.08 (t, $J = 7.9$ Hz, 1H), 6.96 (d, $J = 7.7$ Hz, 1H), 6.70 (s, 1H), 6.64 (d, $J = 7.9$ Hz, 1H), 5.94 (s, 1H), 3.84 (s, 3H), 3.74 (s, 3H), 3.10 – 2.97 (m, 3H), 2.16 – 2.03 (m, 1H), 1.28 (d, $J = 16.4$ Hz, 6H), 1.00 – 0.95 (m, 6H); ^{13}C NMR (101 MHz, MeOD) δ 161.71, 159.26, 149.51, 148.70, 146.04, 131.77, 129.98, 129.95, 129.46, 129.37, 129.32, 127.96, 127.82, 124.47, 124.43, 121.85, 120.47, 115.40, 115.18, 111.99, 111.81, 72.34, 72.18, 71.05, 62.91, 60.78, 55.12, 55.09, 42.34, 39.30, 39.27, 28.20, 24.01, 20.66, 20.29, 18.15, 18.13. MS m/z (ESI) Calculated for $\text{C}_{25}\text{H}_{35}\text{FN}_3\text{O}_2$ $[\text{M}+\text{H}]^+$: 426.25, found 426.24.

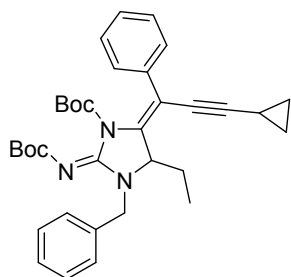
1-benzyl-4-(1-(4-fluorophenyl)pentyl)-5-isobutyl-1H-imidazol-2-amine (6s)



Yellow solid, Quantitative yield, ^1H NMR (400 MHz, MeOD) δ 7.42 – 7.31 (m, 5H), 7.13 – 7.05 (m, 4H), 5.16 (s, 2H), 4.05 (t, $J = 7.8$ Hz,

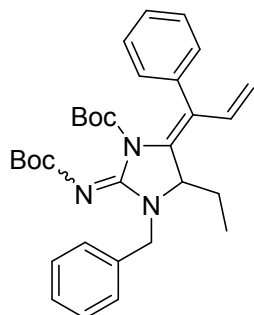
1H), 2.36 (d, $J = 7.2$ Hz, 1H), 2.11 – 1.94 (m, 2H), 1.65 – 1.58 (m, 1H), 1.45 – 1.37 (m, 2H), 1.33 – 1.26 (m, 2H), 0.93 (t, $J = 7.0$ Hz, 3H), 0.88 (d, $J = 6.1$ Hz, 3H), 0.76 (d, $J = 6.2$ Hz, 3H); ^{13}C NMR (101 MHz, MeOD) δ 162.97, 160.54, 147.06, 138.00, 137.96, 134.63, 128.86, 128.77, 127.83, 125.51, 125.39, 123.24, 115.18, 114.96, 45.54, 39.82, 34.01, 30.99, 29.81, 27.94, 22.11, 21.07, 21.03, 12.95. MS m/z (ESI) Calculated for $\text{C}_{25}\text{H}_{33}\text{FN}_3$ $[\text{M}+\text{H}]^+$: 394.26, found 394.23.

Tert-butyl (2Z,5E)-3-benzyl-2-((tert-butoxycarbonyl)imino)-5-(3-cyclopropyl-1-phenylprop-2-yn-1-ylidene)-4-ethylimidazolidine-1-carboxylate (7)



Yellow solid, Yield 83%, ^1H NMR (300 MHz, CDCl_3) δ 7.73 – 7.68 (m, 2H), 7.38 – 7.20 (m, 8H), 4.93 (d, $J = 15.4$ Hz, 1H), 4.41 (d, $J = 15.4$ Hz, 1H), 4.29 (t, $J = 3.8$ Hz, 1H), 1.99 – 1.89 (m, 1H), 1.57 (s, 9H), 1.43 – 1.33 (m, 1H), 1.00 – 0.96 (m, 9H), 0.86 – 0.80 (m, 2H), 0.76 (t, $J = 7.5$ Hz, 3H), 0.70 – 0.64 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.24, 151.82, 147.34, 137.67, 136.98, 135.86, 128.35, 127.83, 127.75, 127.70, 127.35, 127.22, 111.15, 99.70, 83.14, 78.92, 77.12, 76.69, 76.27, 72.65, 60.47, 46.59, 27.88, 26.91, 23.14, 8.52, 8.34, 6.82. MS m/z (ESI) Calculated for $\text{C}_{34}\text{H}_{41}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$: 556.32, found 556.37.

Tert-butyl (5Z)-3-benzyl-2-((tert-butoxycarbonyl)imino)-4-ethyl-5-(1-phenylallylidene)imidazolidine-1-carboxylate (8)



Yellow solid, 84% yield, ^1H NMR (300 MHz, CDCl_3) δ 7.51 – 7.45 (m, 2H), 7.43 – 7.24 (m, 8H), 6.46 (dd, $J = 16.9, 11.2$ Hz, 1H), 5.18 (dd, $J = 9.9, 1.2$ Hz, 1H), 5.17 (dd, $J = 18.2, 1.2$ Hz, 1H), 5.00 (d, $J = 15.4$ Hz, 1H), 4.31 (d, $J = 15.4$ Hz, 1H), 4.20 (t, $J = 4.2$ Hz, 1H), 1.69 – 1.63 (m, 1H), 1.58 – 1.51 (m, 9H), 1.07 – 1.00 (m, 9H), 0.87 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.33, 152.19, 147.86, 136.18, 135.96, 132.45, 132.05, 130.24, 128.79, 128.16, 127.95, 127.76, 127.44, 118.51, 83.16, 79.09, 58.29, 47.00, 28.25, 27.37, 24.73, 7.53. MS m/z (ESI) Calculated for $\text{C}_{31}\text{H}_{39}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$: 518.30, found 518.33.

^1H and ^{13}C spectra of compounds

