SUPPORTING INFORMATION

Highly Stereoselective and Catalyst-Free Synthesis of Annulated Tetrahydropyridines by Intramolecular Imino-Diels-Alder Reaction under Microwave Irradiation in Water

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**General Experiment**

All microwave reactions were performed in a Monowave 300, in sealed reaction vessels. The temperature was controlled using an IR sensor. TLC were performed on silica gel 60 F254 plates. GC-MS spectra were recorded on a Varian 450 GC triple quadrupole coupled to a Varian 320 MS mass spectrometer equipped with an electronic impact source (EI). HPLC-ESI-MS experiments were performed on an Exactive Plus Orbitrap MS Thermo Scientific. The accurate mass measurements were performed at a resolution of 140.000 in positive mode. 1H NMR (200 and 400 MHz) and 13C NMR (50 and 100 MHz) spectra were recorded on a Bruker Biospin GmbH NMR.

**General procedure for the preparations of imines (3a-c and 4a,b)**

5-Amino-1-(tert-butyl)-1H-pyrrole-3-carbonitrile (1 mmol, 1 eq.) or 5-amino-1-(phenyl)-pyrazole-3-methyl, were dissolved in methanol (60 mL) and the corresponding salicylaldehyde (1 mmol, 1 eq.) was added. The mixture was stirred at reflux for 6-8 hours and left overnight at room temperature. The crystals were filtered and washed with cold methanol and used without further purification.

**General procedure for the preparation of 5a-g and 6a-d**

The corresponding imine derivative (1 mmol, 1eq.) was dissolved in acetonitrile (20 mL) and K₂CO₃ (3 mmol, 3eq.) and the corresponding allyl bromide (1 mmol, 1eq.) was added. The mixture was refluxed for 8 hours. After cooling, the solvent was evaporated and the residue was dissolved in AcOEt (8mL), avoiding the undesirable dichloromethane for extractions.¹ Water (12mL) was added and the mixture stirred for 15 min at room temperature. The organic phase was separated and the aqueous layer was extracted with AcOEt (2x12mL). The combined organic phases were dried over Na₂SO₄ anhydrous, filtered and concentrated under reduce pressure, dissolved in 5mL of methanol or in a mixture of hexane/AcOet (4:1, 5mL) for crystallization and left overnight. The formed crystals were filtered to give the corresponding products. No other purification method was used (e.g column chromatography).

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General procedure for the preparation of 7a-k and 8a-d.

5a-g, 6a-d or 9 (0.5 mmol) and water (2-4 mL) were introduced in a microwave reaction vial which was sealed with a PTFE-coated silicone septum and closed with a PEEK cap. The solution was heated for 5 minutes at 200°C. After cooling the aqueous solution was sonicated to break the compact precipitated formed and left overnight. Method A: for compounds 7a-f and 8a-d (Figure 1) the formed precipitate was filtered and washed with water. Method B: for compounds 7h-k, the aqueous solution was extracted with 1 mL (x2) of ethyl acetate, dried over sodium sulfate concentrated and crystallized from methanol. No column chromatography was necessary for purification, except for compounds 7a’ and 7b’ for cis isomer isolation.

![Figure 1](image.png)

**Compound Characterisation**

(E)-5-(2-(Allyloxy)benzylideneamino)-1-tert-butyl-1H-pyrrole-3-carbonitrile (5a), (380 mg, 52%). mp 82.7-83.7°C (from MeOH). $^1$H (200 MHz, CDCl$_3$) $\delta$ 8.95 (1H, s, N=CH), 8.07 (1H, dd, $J_1 = 1.1$ Hz, $J_2 = 7.7$ Hz), 7.41 (1H, t, $J = 11.3$, 4.3 Hz), 7.25 (1H, d, $J = 1.9$ Hz), 7.03 (1H , t), 6.94 (1H, d, $J = 8.5$ Hz), 6.39 (1H, d, $J = 1.6$ Hz), 6.19 – 6.00 (1H, m), 5.45 (1H, d, $J = 17.3$ Hz), 5.34 (1H, d, $J = 10.5$ Hz), 4.64 (2H, d, $J = 5.1$ Hz), 1.71 (9H, s). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 158.53, 151.32, 132.78, 132.52, 128.88, 128.51, 127.10, 125.07, 124.68, 121.08, 117.95, 112.59, 98.22, 90.07, 69.24, 58.32, 30.14. MS(GC, 70eV): m/z(%) = 307.1 (M+,100%), 250.2(75). HRMS (ESI): Mass calculated for C$_{19}$H$_{21}$N$_3$O [M-H]$^-$ 307.1685. Found: 308.1757.
(E)-5-(2-(allyloxy)-3-methoxybenzylideneamino)-1-tert-butyl-1H-pyrrole-3-carbonitrile (5b), (487 mg, 60%). mp 139.7-141.5°C. \( ^1 \text{H NMR} \) (200 MHz, CDCl\(_3\)) \( \delta \) 8.82 (1H, s), 7.62 (1H, d, \( J = 7.82 \) Hz), 7.23 (1H, s), 7.10 (1H, t, \( J_1 = 8.80; J_2 = 7.82 \) Hz), 6.99 (1H, d, \( J = 3.91,7.82 \) Hz), 6.36 (1H, d, \( J = 1.22 \) Hz), 6.05 (1H, m, \( J=5.38, 6.11 \) Hz), 5.36 (1H, d), 5.26 (1H, d, \( J = 10.27 \) Hz), 4.58 (2H, d, \( J = 5.87 \) Hz), 3.87 (3H, s) 1.68 (9H, s). 13C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 153.04, 151.61, 148.78, 143.67, 133.51, 130.34, 124.86, 124.24, 118.50, 118.37, 117.22, 114.78, 98.41, 90.20, 74.98, 58.38, 55.94, 30.16. MS (GC, 70eV) m/z 337.1 (M\(^+\), 62%), 280.3 (33), 162 (100). HRMS (ESI): Mass calculated for C\(_{19}\)H\(_{21}\)N\(_3\)O [M-H]\(^+\) 337.1790. Found: 338.1864.

(E)-5-(2-(allyloxy)-5-bromobenzylideneamino)-1-tert-butyl-1H-pyrrole-3-carbonitrile (5c), (554 mg, 56%). mp 121.5-122.0°C. \( ^1 \text{H NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 8.89 (1H, s), 8.06 (1H, d, \( J = 2.2 \) Hz), 7.47 (1H, dd, \( J = 8.8, 2.4 \) Hz), 7.26 (1H, s), 6.83 (1H, d, \( J = 8.8 \) Hz), 6.41 (1H, s), 6.13 – 5.98 (1H, m), 5.43 (1H, d, \( J = 17.3 \) Hz), 5.36 (1H, d, \( J = 10.5 \) Hz), 4.62 (2H, d, \( J = 5.1 \) Hz), 1.71 (9H, s). 13C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 157.41, 149.68, 143.45, 134.81, 132.31, 129.59, 126.85, 125.07, 118.36, 117.10, 114.48, 113.78, 98.76, 90.29, 69.55, 58.44, 30.21. MS (GC, 70eV) m/z 385.1 (M\(^+\), 65%), 329.1 (63), 222.1 (100). HRMS (ESI): Mass calculated for C\(_{19}\)H\(_{20}\)BrN\(_3\)O [M-H]\(^+\) 385.0790. Found: 386.08863.

(E)-1-tert-butyl-5-(2-(3-methylbut-2-enyloxy)benzylideneamino)-1H-pyrrole-3-carbonitrile (5d), (480 mg, 48%). mp 115.2-116.3°C. \( ^1 \text{H NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 8.91 (1H, s), 8.06 (1H, dd, \( J = 7.6, 1.5 \) Hz), 7.40 (1H, t), 7.24 (1H, d, \( J = 1, 7 \) Hz), 7.01 (1H, t), 6.95 (1H, d, \( J = 8.3 \) Hz), 6.39 (1H, d, \( J = 1.9 \) Hz), 5.51 (1H, m) 4.61 (1H, d, \( J = 6.6 \) Hz), 1.82 (3H, s), 1.76 (3H, s), 1.70 (9H s). 13C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 159.00, 151.76, 144.19, 138.40, 132.62, 127.15, 125.15, 124.69, 120.89, 119.46, 117.44, 112.73, 98.31, 90.09, 65.57, 58.38, 30.23, 25.92, 18.41. MS (GC, 70eV) m/z 335.2 (M\(^+\), 55%), 264.0 (100), 172.1 (60).
(E)-1-tert-butyl-5-(3-methoxy-2-(3-methylbut-2-enyloxy)benzylideneamino)-1H-pyrrole-3-carbonitrile (Se), (492 mg, 60%). mp 92.1-93.5°C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.48 (1H, s) 7.65 (1H, d, $J$ = 7.8 Hz), 7.25 (1H, d, $J$ = 1.9 Hz), 7.12 (1H, t), 7.01 (1H, d, $J$ = 9.0 Hz), 6.38 (1H, d, 1.9 Hz), 5.54 (1H, m), 4.59 (2H, d, $J$ = 7.6 Hz), 3.91 (3H, s), 1.76 (3H, s), 1.71 (9H, s), 1.65 (3H, s). $^{13}$C NMR (101 MHz, DMSO) δ 153.35, 152.18, 149.07, 139.82, 130.79, 124.91, 124.23, 119.82, 118.41, 117.38, 114.79, 98.33, 90.26, 70.46, 58.48, 56.07, 30.26, 25.96, 18.09. MS (GC, 70eV): m/z 365.1(M+, 66%), 294(1200), 1662.1(68).

![Diagram of (E)-1-tert-butyl-5-(3-methoxy-2-(3-methylbut-2-enyloxy)benzylideneamino)-1H-pyrrole-3-carbonitrile (Se).]

(E)-5-(5-bromo-2-(3-methylbut-2-enyloxy)benzylideneamino)-1-tert-butyl-1H-pyrrole-3-carbonitrile (Sf), (376 mg, 55%). mp 122.3-123.5°C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.80 (1H, s) 8.10 (1H, d, $J$ = 2.7 Hz), 7.45 (1H, dd, $J$ = 8.8, 2.4 Hz), 7.26 (1H, s), 6.84 (1H, d, $J$ = 8.8 Hz), 6.41 (1H, d, $J$ = 1.7 Hz), 5.48 (1H, m), 4.60 (2H, d, $J$ = 6.6 Hz), 1.82 (3H, s), 1.76 (3H, s), 1.71 (9H, s). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 157.90, 150.15, 143.66, 138.95, 134.91, 129.64, 126.98, 125.11, 119.01, 117.27, 114.64, 113.57, 98.87, 90.33, 65.91, 58.53, 30.31, 25.93, 18.45. MS(GC, 70eV): m/z 413.1(M+, 52%), 342.1(100), 250.1(50).

![Diagram of (E)-5-(5-bromo-2-(3-methylbut-2-enyloxy)benzylideneamino)-1-tert-butyl-1H-pyrrole-3-carbonitrile (Sf).]

(E)-1-tert-butyl-5-(2-(prop-2-nyloxy)benzylideneamino)-1H-pyrrole-3-carbonitrile (Sg), (378 mg, 51%). mp 101.3-102.8°C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.82 (1H, s), 8.01 (1H, dd, $J$ = 8.07, 1.7 Hz), 7.39 – 7.33 (1H, m, $J$ =1.71, 8.3Hz), 7.17 (1H, d, $J$ = 1.9 Hz), 7.02 (1H, d, $J$ = 6.6 Hz), 6.99 (1H, d, $J$ = 8.07Hz), 6.34(1H, dd, $J$ =1.9 Hz), 4.74 (2H, dd, $J$ = 9.7, 2.4 Hz), 2.48 (1H, t, $J$ = 2.4 Hz), 1.63 (1H, s). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 157.52 (s), 151.11 (s), 143.93 (s), 132.51 (s), 127.31 (s), 125.63 (s), 124.87 (s), 122.00 (s), 117.36 (s), 113.07 (s), 98.52 (s), 90.22 (s), 78.15 (s), 76.30 (s), 58.44 (s), 56.53 (s), 30.25 (s).
(E)-N-(2-allyloxy)-3-methoxybenzylidene)-3-methyl-1-phenyl-1H-pyrazol-5-amine (6a), (64%, 498 mg). mp 96-97°C. 1H NMR (400 MHz, CDCl₃) δ 9.03 (1H, s), 7.65 (1H, d, J = 8.07 Hz), 7.65 (1H, d, J = 7.8 Hz), 7.43 (1H, t), 7.29 (1H, t), 7.09 (1H, t), 7.03 (1H, d, J = 7.8 Hz), 6.17 (1H, s), 6.08 (1H, m), 5.40 (1H, d), 5.29 (1H, d), 4.62 (1H, 5.9 Hz), 3.89 (3H, s), 2.37 (3H, s). 13C NMR (101 MHz, CDCl₃) δ 156.60, 152.88, 150.96, 149.19, 149.13, 139.53, 133.53, 129.96, 128.51, 126.35, 124.29, 124.12, 118.99, 118.53, 115.41, 93.38, 75.02, 55.94, 14.21.

(E)-N-(3-methoxy-2-(prop-2ynyloxy)benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5-amine (6b), (356 mg, 59%). mp 111-112°C. 1H NMR (400 MHz, CDCl₃) δ 9.12 (1H, s), 7.76 (1H, d, J = 7.9 Hz), 7.69 (1H, d, 7.8 Hz), 7.44 (1H, t), 7.30 (1H, t), 7.14 (1H, t), 7.03 (1H, 8.1 Hz), 6.23 (1H, s), 4.84 (2H, d), 3.89 (3H, s), 2.48 (1H, m), 2.37 (3H, s). 13C NMR (101 MHz, CDCl₃) δ 157.02, 152.67, 150.95, 149.20, 147.56, 139.54, 130.96, 128.50, 126.34, 124.99, 124.12, 118.91, 115.17, 93.60, 78.74, 78.41, 60.79, 55.92, 14.22.

(Z)-methyl 4-(2-((E)-(3-methyl-1-phenyl-1H-pyrazol-5-ylimino)methyl)phenoxy)but-2-enolate (6c), (364 mg, 58%). mp 115-116°C. 1H NMR (400 MHz, CDCl₃) δ 9.12 (1H, s), 8.09 (1H, dd, J = 1.7, J = 7.7 Hz), 7.75 (1H, d, J = 7.9 Hz), 7.44 (3H, m), 7.30 (1H, t), 7.13 (1H, dt), 7.03 (1H, t), 6.86 (1H, d, J = 8.4 Hz), 6.21 (2H, m), 4.81 (2H, dd, J = 1.7, 3.8 Hz), 3.87 (3H, s), 3.78 (3H, s), 2.38 (3H, s). 13C NMR (101 MHz, CDCl₃) δ 166.25, 158.15, 155.59, 151.07, 149.19, 142.02, 139.57, 133.24, 128.52, 128.00, 126.33, 124.73, 124.08, 122.14, 121.71, 112.23, 93.46, 66.99, 51.83, 14.21.
E-N-(2-{allyloxy})-3-methoxybenzylidene)-3-methyl-1-phenyl-1H-pyrazol-5-amine (6d), (280 mg, 62%), mp 110-111°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.99 (1H, s), 7.73 (1H, d, $J = 7.7$ Hz), 7.63 (1H, d, $J = 7.9$ Hz), 7.43 (2H, t), 7.29 (1H, t), 7.11 (1H, m), 7.03 (1H, d, $J = 7.9$ Hz), 6.28 (1H, td), 6.18 (1H, s), 4.74 (2H, dd, $J = 1.7, 6.2$ Hz), 3.87 (3H, s), 3.78 (3H, s), 2.36 (3H, s). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 166.55, 155.86, 152.63, 150.77, 149.24, 148.65, 143.01, 139.46, 129.66, 128.52, 126.42, 124.70, 124.15, 121.65, 119.15, 115.50, 93.50, 72.28, 55.97, 14.16.

10-({tert-butyl})-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7a), (106 mg, 87%), mp 202.5-203.5°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.60 (1H, d, $J = 7.6$ Hz), 7.22 (1H, t), 7.02 (1H, s), 6.96 (1H, t, $J = 7.5$ Hz), 6.87 (1H, d, $J = 8.1$ Hz), 4.42 (1H, dd, $J = 11.1, 3.0$ Hz), 4.00 (1H, t, $J = 10.5$ Hz), 3.90 (1H, t, $J = 9.2$ Hz), 2.81 (1H, dd, $J = 15.2, 5.1$ Hz), 2.58 (1H, d, $J = 10.5$ Hz), 2.29 (1H, t), 2.18 - 1.92 (1H, m), 1.65 (9H, s). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 164.88, 156.89, 153.82, 144.65, 128.83, 126.99, 123.45, 120.88, 116.52, 110.52, 109.75, 68.71, 59.46, 59.30, 34.76, 29.19, 25.88. MS(GC, 70eV) m/z 307.4(M$^+$, 100%), 251.3 (63.3), 157.1(28.7). HRMS (ESI): Mass calculated for C$_{19}$H$_{21}$N$_3$O [M-H]$^-$ 307.1685. Found: 308.1755.

A coupling constant of $J_{6a,11a} = 10.5$ Hz for the signal at $\delta = 3.96 - 4.01$ ppm can be measured. Interestingly a coupling constant of $J = 10.3$ Hz between the proton at C-11a and the nitrogen is observed.

10-({tert-butyl})-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7a’). (55mg, 30%). mp 186.2-188.3°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.78 (d, $J = 7.6$ Hz, 1H), 7.26 (s, 1H), 7.21 (t, 1H), 7.01 (t, $J = 7.5$ Hz, 1H), 6.85 (d, $J = 8.3$ Hz, 1H), 4.59 (d, $J = 10.5$ Hz, 1H), 4.36 (dd, $J = 11.1, 3.4$ Hz, 1H), 4.11 (t, $J = 11.0$ Hz, 1H), 3.15 (dd, $J = 17.6, 3.9$ Hz, 1H), 2.46 (dd, $J = 17.2, 14.2$ Hz, 1H), 2.33-2.27 (m, 1H), 1.71 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 164.87, 156.87, 153.81, 144.64, 128.81, 126.97, 123.43, 120.87, 116.51, 110.61, 109.73, 68.69, 59.44, 59.28, 34.75, 29.17.

The isolated cis isomer showed a signal at 4.38- 4.34 ppm with a coupling constant \( J_{6a,11a} = 3.4 \) Hz.

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\text{NMR (400 MHz, CDCl}_3 \text{): } \delta 7.22 \text{ (1H, d, } J = 7.8 \text{ Hz), } 7.01 \text{ (1H, s), } 6.95 \text{ (1H, t, } J = 7.8 \text{ Hz), } 6.85 \text{ (1H, d, } J = 7.82 \text{ Hz), } 4.57 \text{ (1H, dd, } J = 11.2, 3.6 \text{ Hz), } 4.00 \text{ (1H, t, } J = 10.5 \text{ Hz), } 3.94 \text{ (1H, t, } J = 11.25 \text{ Hz), } 3.89 \text{ (3H, s), } 2.83 \text{ (1H, d, } J = 7.8 \text{ Hz), } 2.30 \text{ (1H, t, } J = 4.9 \text{ Hz). NMR (1H, s).} \]

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\text{C NMR (101 MHz, CDCl}_3 \text{): } \delta 148.49, 144.39, 135.15, 123.88, 120.97, 119.03, 116.97, 110.83, 108.29, 88.81, 69.64, 68.60, 57.19, 56.11, 55.15, 34.50, 29.75, 22.76. \]

MS(GC, 70eV): m/z 337.3 (M⁺, 89.5 %), 280.3(28.6), 162.2(100). HRMS (ESI): Mass calculated for C₂₀H₂₃N₃O₂ [M-H]⁺ 337.1790. Found: 338.1860.

For the reaction carried out in p-xylene, the isolated cis isomer showed a signal at 3.95- 3.88 ppm with a coupling constant \( J_{6a,11a} = 5.8 \) Hz.
2-bromo-10-(tert-buty)l-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7c). (144 mg, 75%) mp 236.2-238.5°C. 1H NMR (400 MHz, DMSO) δ 7.62 (1H, s), 7.36 (1H, d, J = 2.0, 8.80 Hz), 7.33 (1H, s), 6.82 (1H, d, J = 8.8 Hz), 4.44 (1H, d, J = 4.1, 10.52 Hz), 4.41 (1H, d, J = 10.76 Hz), 3.92 (1H, d, J = 11.15 Hz), 3.87 (1H, t, J = 3.32, 6.60 Hz), 2.66 (1H, dd, J = 9.78, 5.4 Hz), 2.23 – 2.14 (1H, m), 2.02 (1H, dd, J = 10.8, 5.5 Hz), 1.60 (9H, s). 13C NMR (101 MHz, DMSO) δ 140.02, 136.54, 131.41, 129.77, 127.00, 126.96, 123.80, 122.05, 119.02, 112.18, 107.77, 87.63, 57.51, 54.50, 32.85, 29.89, 22.34. HRMS (ESI): Mass calculated for C19H20BrN3O [M-H]⁺ 385.0790. Found: 386.0862.

10-(tert-buty)l-7.7-dimethyl-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7d) (139 mg, 83%). mp 212.5-213.4°C. 1H NMR (400 MHz, CDCl3) δ 7.63 (1H, d, J = 7.6 Hz), 7.21 (1H, t, J = 7.6 Hz), 7.03 (1H, s), 6.98 (1H, t), 4.47 (1H, d, J = 11.0, 3.2 Hz), 4.15 (1H, t), 3.92 (1H, t), 2.52 (1H, d, J = 10.5 Hz), 1.88 – 1.78 (1H, m), 1.64 (9H, s), 1.56 (3H s), 1.21 (3H, s). 13C NMR (101 MHz, DMSO) δ 150.20, 128.61, 124.17, 122.50, 118.89, 117.48, 116.25, 114.01, 113.11, 112.13, 81.61, 60.85, 52.30, 46.65, 41.13, 28.01, 24.80, 22.43, 19.66. MS(GC, 70eV): m/z 335.3 (M⁺, 83%), 264.2(100), 172(41). HRMS (ESI): Mass calculated for C21H23N3O3 [M-H]⁺ 335.1998. Found: 336.2070.

10-(tert-buty)l-4.methoxy-7,7-dimethyl-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7e) (153 mg, 84%). mp 214.8-216.6°C. 1H NMR (400 MHz, CDCl3) δ 7.45 (1H, d, J = 9.4 Hz), 7.23 (1H, s), 7.15 (1H, d, J = 10.0, 5.8 Hz), 7.04 (1H, d, J = 8.0 Hz), 4.81 (1H, dd, J = 10.9, 2.7 Hz), 4.37 (1H, t, J = 10.7 Hz), 4.15 (1H, t, J = 11.3 Hz), 4.09 (2H, s), 3.92 (1H, q, J = 7.0 Hz), 2.71 (1H, d, J = 10.4 Hz), 1.83 (6H, s), 1.75 (2H, s, J = 5.9 Hz), 1.41 (1H, s). 13C NMR (101 MHz, CDCl3) δ 148.41, 144.48, 133.33, 124.37, 122.17, 120.66, 118.80, 117.84, 110.53, 110.50, 86.34, 66.01, 57.04, 55.99, 51.33, 45.72, 32.70, 29.61, 27.09, 24.50, 18.44. MS(GC, 70eV) m/z 365.4(M⁺, 83.5%), 294.3(99.7), 202.3(68.1), 162.2(100). HRMS (ESI): Mass calculated for C22H27N3O3 [M-H]⁺ 365.2103. Found: 366.2176.
2-bromo-10-(tert-butyl)-7,7-dimethyl-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7f), (173 mg, 84%). mp 266.4-267.1°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.89 (1H, s), 7.48 (1H, d, $J$ = 8.7 Hz), 7.23 (1H, s), 6.94 (1H, t, $J$ = 8.4 Hz), 4.66 (1H, dd, $J$ = 11.1, 2.8 Hz), 4.30 (1H, t, $J$ = 11.3 Hz), 3.90 (1H, q, $J$ = 7.0 Hz), 4.08 (1H, t, $J$ = 11.3 Hz), 3.90 (1H, q, $J$ = 7.0 Hz), 2.67 (1H, d, $J$ = 10.7 Hz), 1.83 (9H, s), 1.74 (3H, s), 1.38 (3H, s). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 154.16, 132.95, 131.88, 129.99, 125.68, 122.44, 118.88, 117.71, 113.13, 86.37, 65.76, 57.16, 51.31, 45.54, 32.75, 29.90, 27.18, 24.37, 18.44. MS(GC, 70eV) m/z 414(M+, 24.2%), 357.2(´46.5), 342.2(100). HRMS (ESI): Mass calculated for C$_{21}$H$_{24}$BrN$_3$O [M-H]$^-$ 413.1103. Found: 414.1176.

10-(tert-butyl)6,10-dihydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7g), (91 mg, 60%). mp 178.3-179.1°C. $^1$H NMR (400 MHz, DMSO) $\delta$ 8.47 (1H, s), 8.15 (1H, d, $J$ = 7.6, 1.2 Hz), 7.98 (1H, s), 7.38 – 7.30 (1H, m), 7.14 (1H, dd, $J$ = 9.5, 5.3 Hz), 7.00 (1H, dd, $J$ = 6.4 Hz), 5.34 (2H, s), 3.18 (1H, s, $J$ = 17.2 Hz), 1.81 (9H, s). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 156.62, 147.16, 144.02, 133.23, 131.08, 124.72, 123.71, 123.68, 122.30, 121.19, 120.48, 117.18, 115.48, 83.41, 77.33, 77.01, 76.70, 68.56, 58.68, 29.23. MS(GC, 70eV) m/z 303.3 (M$^+$, 58%), 246.2 (58). HRMS (ESI): Mass calculated for C$_{19}$H$_{17}$N$_3$O [M-H]$^-$ 303.1372. Found: 304.1454.

10-(tert-butyl)-4-methoxy-6,10-dihydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7h), (116 mg, 70%). mp 237.7-239.3°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.86 (1H, dd, $J$ = 7.9, 1.4 Hz), 7.80 (1H, s), 7.77 (1H, s), 7.04 (1H, dd, $J$ = 10.1, 5.8 Hz), 6.92 (1H, dd, $J$ = 8.0, 1.3 Hz), 5.37 (2H, s), 3.90 (3H, s), 1.85 (9H, s). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 148.79, 147.11, 145.98, 143.90, 133.31, 124.47, 123.72, 121.83, 121.06, 120.54, 116.64, 115.44, 113.07, 83.42, 68.94, 58.69, 56.19,

7i

methyl-10-(tert-butyl)-8-cyano-6,6a,7,10,11,11a-hexahydrochromenol[4,3-b]pyrrolo[3,2-e]pyridine-7-carboxylate (7i), (88 mg, 48%). mp 162.5-164.3°C. ¹H NMR (400 MHz, CDCl₃) δ 14.36 – 14.30 (1H, m), 7.58 (1H, d, J = 7.7 Hz), 7.23 (1H, t), 7.06 (1H, s), 7.00 (1H, t, J = 8.2, 6.1, 2.4 Hz), 6.88 (1H, dd, J = 8.2, 0.9 Hz), 4.48 (1H, dd), 4.12 – 4.06 (1H, m), 3.94 (1H, dd, J = 14.9, 7.7 Hz), 3.85 (3H, s), 3.51 (1H, dd, J = 10.9, 2.1 Hz), 2.67 (1H, dd, J = 10.6, 1.6 Hz), 2.41 – 2.33 (1H, m, J = 10.9, 7.2 Hz), 1.65 (9H, s). ¹³C NMR (101 MHz, CDCl₃) δ 172.97, 154.54, 135.65, 129.32, 126.27, 122.31, 121.09, 116.95, 106.25, 88.49, 67.63, 57.45, 54.36, 52.33, 41.53, 38.16, 29.64. MS(GC, 70eV) m/z 365.3 (M, 100%), 294.3(76) 202.3(39). HRMS (ESI): Mass calculated for C₂₁H₂₃N₃O₃ [M-H]⁺ 365.1739. Found: 366.1822.

7j

methyl-10-(tert-butyl)-8-cyano-4-methoxy-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-7-carboxylate (7j), (87 mg, 44%). mp 237.7-238.3°C. ¹H NMR (400 MHz, CDCl₃) δ 7.20 (1H, d, J = 7.8 Hz), 7.06 (1H, s), 6.96 (1H, t, J = 7.9 Hz), 6.86 (1H, d, J = 8.0 Hz), 4.62 (1H, dd, J = 11.1, 2.9 Hz), 4.09 (1H, t, J = 10.5 Hz), 3.98 (1H, t, J = 11.3 Hz), 3.89 (3H, s), 3.84 (3H, s), 3.76 – 3.66 (1H, m), 3.51 (1H, d, J = 10.8 Hz), 2.67 (1H, d, J = 10.5 Hz), 2.39 (1H, tt, J = 10.9, 5.5 Hz), 1.65 (9H s). ¹³C NMR (101 MHz, CDCl₃) δ 172.80, 148.39, 144.04, 135.63, 123.03, 122.30, 120.82, 117.84, 116.10, 111.02, 106.15, 88.53, 67.99, 57.43, 56.03, 54.28, 52.31, 41.43, 38.04, 29.62. MS(GC, 70eV): m/z 395.3(M+, 100%), 280.3(50), 232.3(32). HRMS (ESI): Mass calculated for C₂₂H₂₅N₃O₄ [M-H]⁺ 395.1845. Found: 396.1931.
methyl-2-bromo-10-(tert-butyl)-8-cyano-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-7-carboxylate (7k), (89 mg, 40%). mp 235.5-237.5°C. 1H NMR (400 MHz, CDCl3) δ 7.64 (1H, s), 7.30 (1H, d, J = 88 Hz), 7.06 (1H, s), 6.75 (1H, d, J = 8.5 Hz), 4.46 (1H, dd, J = 11.3, 2.2 Hz), 4.02 (1H, t, J = 10.5 Hz), 3.90 (1H, t, J = 10.8 Hz), 3.84 (3H, s), 3.48 (1H, d, J = 10.8, 2.1 Hz), 2.67 (1H, d, J = 10.8), 2.37-2.29 (1H, m), 1.65 (9H, s). 13C NMR (101 MHz, CDCl3) δ 172.77, 153.71, 135.29, 132.24, 129.05, 124.32, 122.52, 118.88, 113.23, 106.44, 88.50, 67.74, 57.56, 54.15, 41.38, 37.78, 29.71. MS(GC, 70eV): m/z 445.2 (M+, 100%), 280.1 (32.9). HRMS (ESI): Mass calculated for C21H22BrN3O3 [M-H]+ 443.0845. Found: 443.0841.

4-methoxy-8-methyl-10-phenyl-6,6a,7,10,11,11a-hexahydrochromeno[3,4-e]pyrazolo[3,4-b]pyridine (8a), (142 mg, 82%). mp 231-233°C. 1H NMR (400 MHz, CDCl3) δ 7.49 (1H, d, J = 7.8 Hz), 7.23 (1H, t), 7.06 (1H, t), 6.78 (1H, d, J = 7.8 Hz), 6.72 (1H, t), 6.70 (1H, t), 6.91 (1H, d, J = 7.8 Hz), 4.36 (1H, dd, J = 2.7, J = 11 Hz), 3.99 (1H, t, J = 8.8 Hz), 3.76 (1H, t, J = 10.7 Hz), 3.66 (3H, s), 3.42 (1H, dd, J = 6.1 Hz), 2.46 (1H, m), 2.02 (3H, s), 1.97 (2H, m). 13C NMR (101 MHz, CDCl3) δ 148.42, 146.95, 143.82, 143.65, 139.2, 129.39, 129.35, 126.03, 123.16, 121.69, 120.62, 117.21, 110.64, 100.49, 69.48, 55.97, 54.23, 34.24, 21.50, 12.23. HRMS (ESI): Mass calculated for C21H22BrN3O2 [M-H]+ 347.1634. Found: 347.1925.

4-methoxy-8-methyl-10-phenyl-6,10-dihydrochromeno[3,4-e]pyrazolo[3,4-b]pyridine (8b), (128 mg, 75%). mp 232-233°C. 1H NMR (400 MHz, CDCl3) δ 8.38 (1H, d, J = 7.8 Hz), 8.23 (1H, s), 7.87 (1H, s), 7.59 (2H, t), 7.32 (1H, t), 7.14 (2H, m), 5.358 (2H, s), 3.84 (3H, s), 2.60 (3H, s). 13C NMR (101 MHz, CDCl3) δ 150.72, 149.14, 148.54, 147.03, 145.51, 139.79, 129.70, 127.20, 125.73, 123.93, 122.44, 121.27, 120.18, 117.02, 116.35, 115.11, 68.35, 56.29, 12.67. HRMS (ESI): Mass calculated for C21H21N3O2 [M-H]+ 343.1321. Found: 344.1215.
Methyl 8-methyl-10-phenyl-6,6a,7,10,11,11a-hexahydrochromeno[3,4-e]pyrazolo[3,4-b]pyridine-7-carboxylate (8c), (166 mg, 89%). mp 185-187 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.77 (1H, d, \(J = 8.1\) Hz), 7.56 (1H, d, \(J = 7.6\) Hz), 7.48 (2H, t), 7.25 (1H, dt), 6.98 (1H, t), 6.84 (1H, d, \(J = 8.1\) Hz), 5.78 (1H, d), 4.34 (1H, dd, \(J = 3.7, 11.3\) Hz), 4.23 (1H, dd, \(J = 7.6, 10.6\) Hz), 4.06 (1H, t), 3.77 (3H, s), 3.53 (1H, m), 2.26 (1H, m), 2.02 (3H, s). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 173.70, 154.22, 145.85, 145.45, 139.74, 129.41, 128.99, 127.44, 125.87, 121.51, 121.09, 116.57, 100.42, 99.99, 67.17, 53.12, 52.58, 37.87, 12.89. HRMS (ESI): Mass calculated for \(\text{C}_{22}\text{H}_{21}\text{N}_3\text{O}_3\) [M-H]⁺ 375.1583.

Methyl-4-methoxy-8-methyl-10-phenyl-6,6a,7,10,11,11a-hexahydrochromeno[3,4-e]pyrazolo[3,4-b]pyridine-7-carboxylate (8d), (170 mg, 84%). mp 238-239°C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.77 (2H, d, \(J = 8.3\) Hz), 7.49 (2H, t), 7.28 (1H, t), 7.14 (1H, t), 6.92 (2H, 4.7 Hz), 5.7 (1H, d, \(J = 7.3\) Hz), 4.36 (1H, dd, \(J = 3.4, 11.0\) Hz), 4.22 (1H, dd, \(J = 7.2, 10.3\) Hz) 4.02 (1H, t), 3.07 (3H, s), 2.95 (3H, s), 3.54 (1H, d), 2.23 (1H, m), 2.02 (3H, s). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 173.70, 154.37, 145.85, 145.52, 143.94, 139.75, 129.46, 125.90, 123.71, 121.49, 120.68, 118.85, 111.58, 100.44, 67.04, 56.10, 56.10, 53.16, 52.61, 37.80, 12.90. HRMS (ESI): Mass calculated for \(\text{C}_{23}\text{H}_{23}\text{N}_3\text{O}_4\) [M-H]⁺ 405.1689. Found: 406.2223.

1-tert-butyl-4,4,7-trimethyl-4a,5,6,7,8,8a,9-octahydro-1H-pyrrolo[2,3-b]quinoline-3-carbonitrile (10), (97 mg, 65%). m.p 164.6-165.5°C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.23 (1H, s), 4.02 (1H, m), 2.25 (1H, d), 1.61 (9H, s), 1.61 (2H, m), 1.48 (1H, m), 1.44 (3H, s), 1.35 (3H, m), 1.27 (3H, s), 0.89 (3H, d). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 165.45, 156.02, 152.86, 111.85, 107.72, 58.85, 55.30, 45.34, 42.34, 36.77, 34.20, 29.18, 27.22, 26.53, 23.91, 22.65, 22.27. MS(GC, 70eV): \(m/z\) 298.2(M⁺, 100%), 258(41). HRMS (ESI): Mass calculated for \(\text{C}_{19}\text{H}_{23}\text{N}_3\) [M-H]+ 299.2361.
$\text{NC}_2\text{C}$

$\text{N} - \text{Bu}$

O

Br

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$5d$

![Chemical Structure](image1)

![Chemical Shift (ppm)](image2)
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