Cobalt-Porphyrin-Catalysed Intramolecular Ring-Closing C-H Amination of Aliphatic Azides: A Nitrene-Radical Approach to Saturated Heterocycles

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Supporting Information

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General information
All reactions involving air- or moisture sensitive compounds were carried out under nitrogen using standard Schlenk and vacuum line techniques. Toluene was distilled over sodium prior to use. All chemicals not listed below were purchased from Alfa Aesar, Acros, Fluka, Strem and Aldrich without purification before use. $^1$H NMR, $^{13}$F NMR and $^{13}$C NMR spectra were measured on a Bruker Avance II 300 MHz, Bruker Avance I 400 MHz, Bruker DRX 300 or a Bruker 500 MHz spectrometer. $^1$H-NMR chemical shifts are given in ppm, and were calibrated by using the residual non-deuterated solvent as internal reference (CHCl$_3$ (7.26 ppm)). $^{13}$C-NMR chemical shifts were recorded in ppm from the solvent peak employed as internal reference (CDCl$_3$ (77.0 ppm)). IR spectra were measured on a Bruker Alpha-P instrument as neat film. UV-vis spectra were measured on a Hewlett Packard 8453. High resolution mass spectra were recorded on a HRMS JEOL AccuTOF GCv4g JMS-T 100 GCV and HRMS AccuTOF LCplus JMS-T 100 LP. Chiral GC analysis was performed on a Finigan Focus GC with CP-Chirasil-dex CB column.

CAUTION: Azides are potentially explosive and should be handled with care! Although under the conditions and scale described here we did not encounter any problems, appropriate precautions should be taken when handling these compounds in general. All reactions were performed open to the nitrogen Schlenk line with an overpressure valve to avoid pressure build up or were performed behind a blast shield (high temperature reactions).

Synthesis of catalysts described in this study

1. **Synthesis of Cobalt(II) tetra(2,4,6-trimethylphenyl)porphyrin ([Co(TMP)], 3)**

   Tetra(2,4,6-trimethylphenyl)porphyrin (180 mg; 0.23 mmol) and anhydrous cobalt(II) chloride (0.20 g; 1.54 mmol) were dissolved in acetic acid (25 mL). After addition of sodium acetate (0.30 g; 3.64 mmol) the mixture was heated to reflux temperature. After 3 h of reaction the mixture was cooled to room temperature and solvent was removed under reduced pressure. The purple solid was washed with a saturated aqueous solution of sodium bicarbonate (50 mL) and water (2 x 50 mL). The product was collected with DCM (50 mL) and dried over magnesium sulfate. After filtration and removal of the solvent the product was obtained as a purple powder (71.6 mg, 85 µmol, 38%). Analysis was in agreement with previously reported data.\textsuperscript{14}

2. **Synthesis of 5,15-bis(2,6-dimethoxyphenyl)-10,20-dimesitylporphyrin (S1)**

   5-Mesityldipyromethene (0.54 g; 1.89 mmol) and 2,6-dimethoxybenzaldehyde (0.31 g, 1.89 mmol) were dissolved in CHCl\textsubscript{3} (500 mL) and degassed with N\textsubscript{2} for 20 minutes. BF\textsubscript{3}OEt\textsubscript{2} (0.12 mL, 0.14 g, 0.97 mmol) was added dropwise and the black mixture was stirred for 30 minutes. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (0.65 g, 2.86 mmol) was added and the mixture was stirred for one hour. Triethylamine (2.0 mL) was added, the mixture was filtered over silica and concentrated. The crude product was purified by column chromatography (SiO\textsubscript{2}, CHCl\textsubscript{3}) to yield the desired product S1 as a purple solid (0.25 g, 0.30 mmol, 32%). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): 8.68 (d, \textit{J} = 4.7 Hz, 4H), 8.58 (d, \textit{J} = 4.7 Hz, 4H), 7.71 (t, \textit{J} = 8.4 Hz, 2H), 7.24 (s, 4H), 7.00 (d, \textit{J}=8.5 Hz, 4H), 3.51 (s, 12H), 2.61 (s, 6H), 1.86 (s, 12H), 2.51 (s, 12H), 2.48 (s, 2H). \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): 160.8, 139.7, 138.9, 137.5, 130.2, 127.7, 120.2, 117.0, 111.4, 104.5, 56.3, 21.9, 21.6 (not all quaternary carbons were fully resolved). UV-Vis (λ\textsubscript{max}, nm): 419 (Soret), 514, 547, 591, 644 (Q-bands). CSI-ESI-MS; calculated (C\textsubscript{54}H\textsubscript{51}N\textsubscript{4}O\textsubscript{4}): 819.3910, experimental mass (m/z): 819.3949 [M+H]\textsuperscript{+}.

![Figure S1: \textsuperscript{1}H-NMR spectrum of porphyrin S1.](image-url)
3. **Synthesis of 5,15-bis(2,6-dihydroxyphenyl)-10,20-dimesitylporphyrin (S2)**

To a stirred solution of 5,15-bis(2,6-dimethoxyphenyl)-10,20-dimesitylporphyrin S1 (0.12 g, 0.15 mmol) in dry DCM (10 mL) under nitrogen was added dropwise boron tribromide (0.10 mL, 0.9 mmol). After 19 hours, the mixture was quenched with MeOH (5.0 mL) and transferred into a separatory funnel with EtOAc (50 mL). The mixture was washed with saturated aqueous sodium bicarbonate solution (2x 50 mL) and brine (50 mL). The organic layer was dried over MgSO\(_4\), filtered and the solvents were removed under reduced pressure (40 °C) to yield the product S2 as a purple solid (0.11 g, 0.15 mmol, quantitative).

**\(^{1}\)H NMR** (300 MHz, CDCl\(_3\)) \(\delta\) 8.91 (d, \(J = 4.8\) Hz, 4H), 8.78 (d, \(J = 4.8\) Hz, 4H), 7.64 (t, \(J = 8.2\) Hz, 2H), 7.29 (s, 4H), 6.99 (d, \(J = 8.3\) Hz, 4H), 4.68 (s, 6H), 2.63 (s, 6H), 1.82 (s, 12H), -2.62 (bs, 2H). **\(^{13}\)C NMR** (300 MHz, CDCl\(_3\)): 136.3, 139.4, 138.4, 137.5, 131.4, 128.1, 119.9, 115.4, 108.1, 105.0, 21.9, 21.6. (not all quaternary carbons were fully resolved). **UV-Vis** (\(\lambda_{\text{max}}\), nm) 418 (Soret), 513, 546, 588, 642 (Q-band), CSI-ESI-MS; calculated (C\(_{50}\)H\(_{43}\)N\(_4\)O\(_4\)): 763.3284, experimental mass: 763.3306 [M+H]\(^{+}\).
4. Synthesis of (1S)-(−)-camphanic-ester substituted porphyrin (S3)

A mixture of 5,15-bis(2,6-dihydroxyphenyl)-10,20-dimesitylporphyrin S2 (50 mg; 66 µmol) and (1S)-(−)-camphanic chloride (83 mg; 396 mmol; 6 eq) was placed under nitrogen and dissolved in dry THF (3.0 mL). Triethylamine (0.1 mL) was added and the mixture was stirred for 68 hours at room temperature. The mixture was transferred into a separatory funnel with DCM (20 mL) and washed with saturated aqueous sodium bicarbonate solution (3x 20 mL). The organic layer was dried over MgSO4, filtered and solvents were removed under reduced pressure. The crude product was washed with MeOH until a colorless filtrate was obtained and dried under vacuum to yield the product S3 as a purple solid (50 mg, 34 µmol, 51 %). 1H NMR (300 MHz, CDCl3): 8.77 (d, J = 4.6 Hz, 4H), 8.66 (d, J = 4.8Hz, 4H), 7.95 (t, J = 8.3 Hz, 2H), 7.53 (d, J = 8.3 Hz, 4H), 7.26 (s, 4H), 2.62 (s, 6H), 1.73 (s, 12H), 1.30-1.16 (m, 4H), 1.08-0.94 (m, 4H), 0.94-0.77 (m, 8H), 0.12 (s, 12H), -1.03 (s, 12H), -1.61 (bs, 12H), -2.84 (bs, 2H). 13C NMR (75 MHz, CDCl3): 176.6, 165.5,151.6, 138.8, 138.3, 137.7, 130.7, 128.8, 128.1, 121.0, 119.1, 107.3, 89.9, 53.9, 52.8, 29.9, 28.0, 21.6, 21.5, 14.6, 13.9, 9.1, 1.2 UV-Vis (λmax, nm): 415 (Soret band), 510, 541, 586, 640 (Q-bands). CSI-ESI-MS; calculated (C90H91N4O16): 1483.6430, found (m/z) 1483.6428 [M+H]+.
Figure S6: $^{13}$C-NMR spectrum of porphyrin S3

5. **Synthesis of cobalt(II)-5,15-bis(2,6-dihydroxyphenyl)-10,20-dimesitylporphyrin (S4)**

To a pressure tube was added under nitrogen 5,15-bis(2,6-dihydroxyphenyl)-10,20-dimesitylporphyrin S2 (30.0 mg, 39.3 µmol), anhydrous CoCl$_2$ (52 mg, 0.40 mmol, 10 equivalents) and 2,6-lutidine (10 µL, 9.3 mg, 86 µmol). The mixture was dissolved in dry THF (2.0 mL) and the solution was heated to 70 °C behind a blast shield. After 16 hours of reaction the mixture was cooled to room temperature, transferred into a separatory funnel with EtOAc (20 mL) and washed with water (3x 20 mL). The organic layer was dried over MgSO$_4$, filtered and solvents removed under reduced pressure (40 °C) to yield the product S4 as a dark red solid (40 mg, 49 µmol, 92%). UV-Vis ($\lambda_{\text{max}}$, nm): 410 (Soret), 526, 554 (Q-band). CSI-ESI-MS; calculated: 819.2382 (C$_{50}$H$_{40}$CoN$_4$O$_4$), found (m/z) 819.2364 [M$^+$].

6. **Synthesis of (1S)-(−)-camphanic-ester substituted cobalt(II)-porphyrin (19)**

To a dried Schlenk flask was added (subsequently, under dinitrogen) cobalt(II)-5,15-bis(2,6-dihydroxyphenyl)-10,20-dimesitylporphyrin S4 (40 mg, 48.8 µmol), (1S)-(−)-camphanic chloride (65 mg, 0.30 mmol) and triethylamine (0.1 mL, 71.6 µmol). The mixture was dissolved in dry THF (3.0 mL) and stirred for 64 hours at room temperature. The mixture was transferred in a separatory funnel with DCM (20 mL) and washed with a saturated aqueous sodium bicarbonate solution (3x 20 mL). The organic layer was dried over MgSO$_4$, filtered and solvents removed under reduced pressure to yield the product 19 as a dark red solid (46 mg, 30 µmol, 61%). UV-Vis ($\lambda_{\text{max}}$, nm): 406 (Soret) 523, 553 (Q-band). CSI-ESI-MS; calculated (C$_{90}$H$_{88}$CoN$_4$O$_{16}$): 1539.5527, found 1539.5483 [M$^+$], calculated (C$_{90}$H$_{88}$CoN$_4$NaO$_{16}$): 1563.544, experimental mass (m/z): 1563.546 [M+Na$^+$].
Synthesis of 2-benzylxy-2-methylpropyl tosylate (S5)

To solution of 2-benzylxy-2-methylpropanol (250 mg, 1.39 mmol) in DCM (3.0 mL) and pyridine (0.25 mL) at 0 °C was added p-toluenesulfonyl chloride (0.54 g, 2.8 mmol, 2.0 equiv.). After 24 hours of reaction demi-water (10 mL) was added and the products were extracted with DCM (3x20 mL). The combined organic fractions were washed with a saturated aqueous solution of sodium bicarbonate (30 mL) and brine (30 mL). The solution was dried over magnesium sulfate, filtered and solvent removed under reduced pressure. The crude product was purified by column chromatography (SiO₂, cyclohexane/Ethyl acetate 10:1, Rf = 0.2) to yield the desired product as a colorless oil (418 mg, 1.25 mmol, 90%).

**Figure S7:** ¹H-NMR of 2-benzylxy-2-methylpropyl tosylate (S5).

**Figure S8:** ¹³C-NMR of 2-benzylxy-2-methylpropyl tosylate (S5).
8. Synthesis of 2-(benzylxy)-2-methylpropyl azide (7a)

A mixture of 2-(benzylxy)-2-methylpropyl tosylate S5 (411 mg, 1.23 mmol) and sodium azide (160 mg, 2.46 mmol) in DMF (3 mL) was heated to 100 °C for three days. After cooling to room temperature the mixture was poured in water (20 mL) and extracted with diethyl ether (3x25 mL). The combined organic fractions were dried over magnesium sulfate, filtered and solvent removed under reduced pressure. The crude product was purified using column chromatography (SiO₂, cyclohexane/Ethyl acetate 10/1, Rf = 0.4) to yield the product as a light yellow oil (105 mg, 0.51 mmol, 42%) and the recovered starting material (Rf = 0.2, 117 mg, 0.34 mmol, 28%).

**¹H-NMR** (300 MHz, CDCl₃): 7.49-7.19 (m, 5H), 4.49 (s, 2H), 3.26 (s, 2H), 1.31 (s, 6H);

**¹³C-NMR** (300 MHz, CDCl₃): 139.0, 128.3, 127.3, 127.3, 75.9, 64.3, 60.0, 23.2. IR (neat, cm⁻¹): 2976, 2926, 2865, 2095 (N₃), 1298, 1160, 1060, 733, 695. FD-MS: Experimental mass (m/z): 204.1133, calculated mass (C₁₁H₁₄N₃O): 204.1137 ([M-H]⁺).

**Figure S9:** ¹H-NMR of 2-(benzylxy)-2-methylpropyl azide (7a).

**Figure S10:** ¹³C-NMR of 2-(benzylxy)-2-methylpropyl azide (7a).
9. Synthesis of 2-azido-N-(4-methylbenzyl)ethanamine (9a)

A solution of 4-methylbenzyl amine (0.248 g, 2.05 mmol) and 2-azidoethyl 4-methylbenzenesulfonate (0.202 g, 0.84 mmol) in acetonitrile was stirred at reflux temperature for 20 hours. The crude product was purified by column chromatography (SiO$_2$, PE40-60/EtOAc 2:1) to yield the desired product as a colorless oil (0.217 g, 1.14 mmol, 56%). $^1$H-NMR (400 MHz, CDCl$_3$): 7.23 (d, $J$ = 8.0 Hz, 2H), 7.13 (d, 7.9 Hz, 2H), 3.81 (s, 2H), 3.45 (t, $J$ = 5.6 Hz, 2H), 2.84 (t, $J$ = 5.7 Hz, 2H), 2.36 (s, 3H). $^{13}$C-NMR (100.6 MHz, CDCl$_3$): 136.7, 136.6, 129.0, 127.9, 53.2, 51.4, 47.8, 21.0. IR (neat, cm$^{-1}$): 2922, 2828, 2093 (N$_3$), 1514, 1448, 1287, 1119, 802. FD-MS; Experimental mass (m/z): 190.1221, calculated mass (C$_{10}$H$_{14}$N$_4$): 190.1218 ([M$^+$]).

Figure S11: $^1$H-NMR spectrum of 2-azido-N-(4-methylbenzyl)ethanamine (9a)

Figure S12: $^{13}$C-NMR spectrum of 2-azido-N-(4-methylbenzyl)ethanamine (9a)
10. Synthesis of 2-azido-N-(4-phenylbenzyl)ethanamine (10a)

To a solution of 2-azidoethyl 4-methylbenzenesulfonate (0.205 g, 0.850 mmol) in acetonitrile (5.0 mL) was added 4-phenylbenzylamine (0.365 g, 1.99 mmol). The stirred mixture was heated at reflux temperature for 16 hours. After cooling to room temperature solvent was removed at reduced pressure and the crude product was purified by column chromatography (SiO₂, hexanes/EtOAc, 2:1, Rf=0.15) to yield a very dense oil which solidified upon standing to a white solid (116 mg, 0.458 mmol, 54%). ¹H-NMR (300 MHz, CDCl₃): 7.64-7.53 (m, 4H), 7.50-7.29 (m, 5H), 3.87 (s, 2H), 3.46 (t, J = 5.6 Hz, 2H), 2.86 (t, J = 5.6 Hz, 2H). ¹³C-NMR (75.5 MHz, CDCl₃): 141.1, 140.2, 139.1, 128.9, 128.7, 127.4, 127.4, 127.2, 53.4, 51.6, 48.1. IR (neat, cm⁻¹): 3027, 2924, 2829, 2091 (N₃), 1487, 1285, 759, 697. FD-MS; Experimental mass (m/z): 252.1383, calculated mass (C₁₅H₁₆N₄): 252.1375 ([M]+).
11. Synthesis of 2-azido-N-(4-fluorobenzyl)ethanamine (11a)

To a round-bottom flask was added 4-fluorobenzyl amine (0.250 mg, 2.0 mmol) and 2-azidoethyl 4-methylbenzenesulfonate (0.196 mg, 0.81 mmol) and acetonitrile (5.0 mL). The mixture was stirred for 16 hours at reflux temperature. After removal of the solvent the crude product was purified by column chromatography (SiO₂, hexanes/EtOAc 2:1) to yield the desired product as a colorless oil (0.132 mg, 0.68 mmol, 84%). ¹H-NMR (300 MHz, CDCl₃): 7.35-7.25 (m, 2H), 7.02 (t, J = 7.0 Hz, 2H), 3.79 (s, 2H), 3.43 (t, J = 5.5 Hz, 2H), 2.81 (t, J = 5.5 Hz, 2H). ¹³C-NMR (75.5 MHz, CDCl₃): 162.0 (d, J=245 Hz), 135.6, 129.6 (d, J=8 Hz), 115.3 (d, J=21 Hz), 52.9, 51.5, 47.9. ¹⁹F-NMR (282.4 MHz, CDCl₃): 115.8. IR (neat, cm⁻¹): 2928, 2835, 2093 (N₃), 1603, 1508, 1218, 823. FD-MS; Experimental mass (m/z): 194.0959, calculated mass (C₉H₁₁FN₄): 194.0968 ([M]+).

Figure S15: ¹H-NMR spectrum of 2-azido-N-(4-fluorobenzyl)ethanamine (11a).

Figure S16: ¹³C-NMR spectrum of 2-azido-N-(4-fluorobenzyl)ethanamine (11a).
12. Synthesis of 2-azido-\(N\)-(4-chlorobenzyl)ethanamine (12a)

To a solution of 2-azidoethyl 4-methylbenzenesulfonate (0.194 g, 0.83 mmol) in acetonitrile (5 mL) was added 4-chlorobenzylamine (2.6 mL, 2.0 mmol, 2.4 equivalents) and the mixture was heated to reflux temperature. After 16 h of reaction a white precipitate had formed and the mixture was cooled to room temperature. After removal of the solvent under reduced pressure the product was purified with column chromatography (SiO\(_2\), Hexanes/Ethyl acetate 2/1, Rf = 0.3) to yield the desired product as a light yellow oil (0.149 g, 0.71 mmol, 85%). \(^1\)H-NMR (300 MHz, CDCl\(_3\)): 7.35-7.22 (m, 4H), 3.79 (s, 2H), 3.43 (t, \(J = 5.8\) Hz, 2H), 2.80 (t, \(J = 5.8\) Hz, 2H). \(^13\)C-NMR (75.5 MHz, CDCl\(_3\)): 138.4, 132.8, 129.4, 128.6, 52.9, 51.4, 47.9. IR (neat, cm\(^{-1}\)): 2925, 2832, 2091 (N\(_3\)), 1490, 1284, 1088, 1014, 802. FD-MS; Experimental mass (m/z): 210.0630, calculated mass (C\(_9\)H\(_{11}\)ClN\(_4\)): 210.0672 ([M]+).

**Figure S17**: \(^1\)H-NMR spectrum of 2-azido-\(N\)-(4-chlorobenzyl)ethanamine (12a).

**Figure S18**: \(^13\)C-NMR spectrum of 2-azido-\(N\)-(4-chlorobenzyl)ethanamine (12a).
13. Synthesis of 2-azido-N-(4-bromobenzyl)ethanamine (13a)

To a solution of 4-bromobenzyl amine (400 mg, 2.15 mmol) in acetonitrile (5.0 mL) was added 2-azidoethyl 4-methylbenzenesulfonate (206 mg, 0.85 mmol) and the mixture was stirred at reflux temperature for 16 hours. After removal of the solvent the mixture was redissolved in ethyl acetate (20 mL) and washed with aqueous sodium hydroxide (2M, 3x20 mL). The crude product was purified by column chromatography (SiO₂, hexane/EtOAc 4:1 → EtOAc gradient) to yield the desired product as a colorless oil (156 mg, 0.61 mmol, 72%).

\[ ^1H \text{-NMR (300 MHz, CDCl}_3 \]: 7.45 (d, J=8.4 Hz, 2H), 7.21 (d, J=8.3 Hz, 2H), 3.77 (s, 2H), 3.43 (t, J=5.8 Hz, 2H), 2.80 (t, J=5 Hz, 2H). \]

\[ ^13C \text{-NMR (75.5 MHz, CDCl}_3 \]: 138.9, 131.6, 129.8, 120.9, 52.9, 51.4, 47.9. \]

IR (neat, cm⁻¹): 2923, 2830, 2092 (N₃), 1486, 1285, 1262, 1070, 1010, 798. FD-MS: Experimental mass (m/z): 254.0166, calculated mass (C₁₀H₁₁BrN₄): 254.0167 (\([M]⁺\)).

Figure S19: \(^1H\)-NMR spectrum of 2-azido-N-(4-bromobenzyl)ethanamine (13a).

Figure S20: \(^13C\)-NMR spectrum of 2-azido-N-(4-bromobenzyl)ethanamine (13a).

\[
\begin{align*}
\text{Pd/C (10 wt\%)} & \quad \text{D}_2 \text{ (balloon)} & \quad \text{NaN}_3 \text{ (2 equiv.)} \\
\text{CD}_3\text{OD, 20 h} & \quad \text{DMF} & \quad 80 \degree \text{C, 24 h}
\end{align*}
\]

The regioselective benzylic deuteration was performed based on a modified literature procedure.\(^{[15]}\) A mixture of (4-bromobutyl)benzene (0.53 g, 2.5 mmol) and Pd/C (10 wt\%, 0.33 g, 60 mol\%) in CD\(_3\)OD (5 mL) was placed under nitrogen and equipped with a deuterium balloon. After 20h of reaction the mixture was filtered over celite and the product diluted with diethyl ether (20 mL). The solution was washed with water (20 mL) and a saturated aqueous solution of sodium bicarbonate (2 x 20 mL). The organic fraction was dried over magnesium sulfate filtered and solvent removed to yield 4-bromo-1,1-bisdeutero-1-phenylbutane as a colorless oil (0.40 g, 1.85 mmol, 74\%) which was used in the next step without additional purification.\(^{1}H\)-NMR (300 MHz, CDCl\(_3\)): 7.34-7.13 (m, 5H), 3.42 (t, J= 6.6 Hz, 2H), 1.97-1.68 (m, 4H). \(^{2}H\)-NMR (300 MHz, CDCl\(_3\)): 2.61. \(^{13}C\)-NMR (75.5 MHz, CDCl\(_3\)): 141.9, 128.5, 126.0, 33.8, 32.3, 29.8. IR (neat, cm\(^{-1}\)): 3059, 3023, 2960, 2929, 2862, 2194, 1495, 1447, 1253, 733, 698. FD-MS; Experimental mass (m/z): 214.032, 216.031, calculated mass (C\(_{10}\)H\(_{11}\)BrD\(_2\)): 214.033, 216.031.

Figure S21: \(^1H\)-NMR spectrum of 4-bromo-1,1-bisdeutero-1-phenylbutane.

Figure S22: \(^{13}C\)-NMR spectrum of 4-bromo-1,1-bisdeutero-1-phenylbutane.
The obtained 4-bromo-1,1-bisdeutero-1-phenylbutane (0.35 g, 1.6 mmol) was dissolved in DMF (10 mL) and sodium azide (0.30 g, 4.6 mmol) was added to the stirred solution. After heating at 80 °C for 16 hours the mixture was cooled to room temperature and water (20 mL) was added. The product was extracted with diethyl ether (20 mL) and the organic fraction was washed with water (5x30 mL), dried over MgSO₄, filtered and solvent removed to yield the desired product as a colorless oil (0.26 g, 1.46 mmol, 90%). ¹H-NMR (300 MHz, CDCl₃): 7.40-7.21 (m, 5H), 3.35 (t, J=6.5 Hz, 2H), 1.83-1.62 (m, 4H). ²H-NMR (300 MHz, CDCl₃): 2.67 (s). ¹³C-NMR (75.5 MHz, CDCl₃): 141.9, 128.5, 128.5, 126.1, 51.5, 28.5, 28.4. IR (neat, cm⁻¹): 3025, 2931, 2863, 2088 (N₃), 1495, 1448, 1258, 734, 698. GC-EI; Experimental mass (m/z): 148.1078, calculated mass: 148.1080 [C₁₀H₁₃N, M-N₂+H]+.
Intramolecular ring-closing C–H amination reactions

15. General C–H azidation procedure

To a dry Schlenk flask was added catalyst (12 µmol), substrate (0.30 mmol) and di-tert-butyldicarbonate (0.36 mmol) in dry toluene (3.0 mL). The stirred mixture was heated to 100 °C for 16 h. After cooling to room temperature the crude product was purified by flash chromatography (SiO₂, DCM/hexanes/TEA 50:50:1).

16. Synthesis of tert-butyl 2-phenylpyrrolidine-1-carboxylate (5b)

(4-azidobutyl)benzene 5a (50.5 mg, 0.288 mmol), di-tert-butyldicarbonate (65.1 mg, 0.298 mmol, 1.04 equivalents), [Co(TMP)] catalyst 3 (10.2 mg, 12.1 µmol, 4.2 mol%) and toluene (3.0 mL) were handled according to the general procedure to yield the desired product 5b as a light yellow oil (63.6 mg, 0.257 mmol, 89%, TON= 21). Analysis data were in agreement to previously published data. The ¹H NMR data of the crude reaction mixture and after purification are shown in Figure S25 and Figure S26 respectively.

Figure S25: Crude ¹H-NMR of tert-butyl-2-phenylpyrrolidine-1-carboxylate (5b).

Figure S26: ¹H-NMR of tert-butyl-2-phenylpyrrolidine-1-carboxylate (5b) after purification.
17. Synthesis of 2-phenylpyrrolidine (5c)

High catalyst loading: (4-azidobutyl)benzene 5a (15.2 mg, 0.087 mmol), [Co(TMP)] catalyst 3 (14.6 mg, 17 µmol, 20 mol%) and toluene (3.0 mL) were heated to 100 °C under N₂ for 16h. The reaction mixture was cooled to room temperature and Boc₂O (20.2 mg, 93 µmol) was added. After 1 the mixture was analyzed with ¹H-NMR with mesitylene (4.3 mg, 36 µmol) as standard to yield 2-phenylpyrrolidine 5c (15 µmol, 17%).

High temperature reaction in absence of Boc₂O: To a pressure tube was added (4-azidobutyl)benzene 5a (35.6 mg, 0.203 mmol) and the atmosphere was replaced with nitrogen. [Co(TMP)] catalyst 3 (6.9 mg, 8.2 µmol, 4.0 mol%) and degassed chlorobenzene (2.0 mL) were added subsequently. The pressure tube was closed and heated to 140 °C behind a blast shield. After 16h the solvent was removed and triphenylmethane (22.4 mg, 91.7 µmol) added as a standard. ¹H-NMR analysis showed complete conversion of the substrate to yield 19% of the desired product (54 µmol, TON =5) and several unknown byproducts as shown in Figure S27. Note: In absence of the catalyst no conversion of the azide was observed, not even at 140 °C.

Figure S27: Product mixture of (4-azidobutyl)benzene 5a cyclization without Boc₂O with Ph₃CH as external standard.

18. Synthesis of tert-butyl 2-phenyloxazolidine-3-carboxylate (6b)

2-(benzoyloxy)ethyl azide (58.2 mg, 0.329 mmol), di-tert-butyldicarbonate (89.5 mg, 0.410 mmol, 1.25 equivalents), [Co(TMP)] catalyst 3 (11.2 mg, 13.3 µmol, 4.1 mol%) and toluene (3.0 mL) were handled according to the general procedure to yield the desired product as a light yellow oil (76.1 mg, 0.305 mmol, 93%). ¹H-NMR (300 MHz, CDCl₃, 60 °C): 7.50-7.258 (m, 5H), 6.03 (bs, 1H), 4.15-3.95 (m, 2H), 3.90-3.75 (m, 1H), 3.63-3.47 (m, 1H), 1.37 (bs, 9H). ¹³C-NMR (75.5 MHz, CDCl₃, 60 °C): 153.2, 139.9, 128.4, 128.1, 126.6, 89.3, 80.3, 65.6, 45.0, 28.2. IR (neat, cm⁻¹): 2975, 2887, 1697, 1391, 1364, 1161, 1129, 1060, 902, 754, 697. FD-MS: Experimental mass (m/z): 249.1361, calculated mass (C₁₄H₁₉NO₃): 249.1365 ([M⁺]).
19. Synthesis of tert-Butyl 2-phenyloxazolidine-3-carboxylate (7b)

To a flame dried Schlenk flask 2-benzyloxy-2-methyl-1-propyl azide (49.2 mg, 0.24 mmol), Boc:O (66.8 mg, 0.31 mmol, 1.3 eq) and dry toluene (2.0 mL) were added under a nitrogen atmosphere. After addition of [Co(TMP)] catalyst 3 (8.2 mg, 0.98 µmol, 4.1 mol%) the stirred reaction mixture was heated at 100 °C for 16 h under a nitrogen atmosphere. The solvent was removed under reduced pressure and the crude product was purified using column chromatography (SiO₂, hexane:DCM:Et₃N; 50:50:1) to yield the product as a yellow oil (21.4 mg, 77 µmol, 32%, TON=8). ¹H-NMR (CDCl₃, 300MHz, RT) δ 7.50 – 7.26 (m, 5H), 6.06 (bs, 0.28H rotamer) 5.88 (bs, 0.82 rotamer), 3.74 (bs, 1H), 3.31 (bs, 1H), 1.43 (s, 3H), 1.33 (s, 3H), 1.23 (bs, 9H); ¹H-NMR (CDCl₃, 300MHz, 60 °C) δ 7.45 – 7.25 (m, 5H), 5.97 (s, 1H), 3.75 (d, J=10.1 Hz, 1H), 3.28 (d, J=10.2 Hz, 1H), 1.43 (s, 3H), 1.34 (s, 3H), 1.33 (bs, 9H); ¹³C-NMR (CDCl₃, 75MHz) 153.5, 140.8, 128.6, 128.3, 127.1, 88.9, 80.5, 79.9, 56.5, 28.5, 26.1, 25.0; IR (neat, cm⁻¹): 2975, 2932, 2882, 1697, 1364, 1149, 1027, 902, 753, 696; FD-MS; Experimental mass (m/z): 277.1662, calculated mass (C₁₆H₂₃NO₃): 277.1678 ([M]+).
Figure S30: $^1$H-NMR spectrum of tert-Butyl 2-phenyloxazolidine-3-carboxylate at room temperature (7b).

Figure S31: $^1$H-NMR spectrum of tert-Butyl 2-phenyloxazolidine-3-carboxylate (7b) at 60 °C.

Figure S32: $^{13}$C-NMR spectrum of tert-Butyl 2-phenyloxazolidine-3-carboxylate (7b).
20. Synthesis of di-tert-butyl 2-phenylimidazolidine-1,3-dicarboxylate (8b)

2-azido-N-benzylethanamine (27.0 mg, 0.15 mmol), di-tert-butyldicarbonate (87.5 mg, 0.40 mmol, 2.6 equiv), [Co(TMP)] catalyst 3 (5.0 mg, 6.0 µmol, 3.9 mol%) and toluene (1.0 mL) were handled according to the general procedure to yield the desired product as a light red oil (36.6 mg, 0.105 mmol, 69%). 1H-NMR (300 MHz, CDCl3, 60 °C): 7.43-7.24 (m, 5H), 6.15 (bs, 1H), 3.95-3.77 (m, 2H), 3.77-3.61 (m, 2H), 1.38 bs (18H). 13C-NMR (75.5 MHz, CDCl3, 60 °C): 152.9, 141.4, 128.0, 127.8, 126.6, 80.5, 72.6, 43.7, 28.2. IR (neat, cm⁻¹): 2975, 2931, 2894, 1692, 1365, 1160, 1106, 860, 697. FD-MS; Experimental mass (m/z): 348.2050, calculated mass (C19H28N2O4): 348.2049 ([M]+).

Figure S33: 1H-NMR spectrum (60 °C) of di-tert-butyl 2-phenylimidazolidine-1,3-dicarboxylate (8b).

Figure S34: 13C-NMR spectrum (60 °C) of di-tert-butyl 2-phenylimidazolidine-1,3-dicarboxylate (8b).

21. Synthesis of di-tert-butyl 2-phenylimidazolidine-1,3-dicarboxylate (8b) from tert-butyl (2-azidoethyI)benzyl)carbamate 8c.

A solution of tert-butyl (2-azidoethyl)(benzyl)carbamate 8c (27.8 mg, 0.101 mmol) in toluene (1.0 mL) was degassed for 15 minutes by bubbling nitrogen through the solution. Boc2O (29.7 mg, 0.136 mmol, 1.3 equivalents) and [Co(TMP)] catalyst 3 (3.5 mg, 4.2 µmol, 4.1 mol%) were added and the mixture was heated to 100 °C under nitrogen. After 16 hours of reaction the mixture was cooled to room temperature and purified by flash chromatography to yield the product 8b (23.6 mg, 67.8 µmol, 67%, TON = 16). Analysis data was in agreement with 8b.
22. Synthesis of di-tert-butyl 2-(p-tolyl)imidazolidine-1,3-dicarboxylate (9b)

2-azido-N-(4-methylbenzyl)ethanamine 9a (51.3 mg, 0.27 mmol), Boc₂O (137.7 mg, 0.63 mmol, 2.4 equivalents), [Co(TPP)] catalyst 1 (7.2 mg, 10.5 µmol, 4.0 mol%) and toluene (3.0 mL) were handled according to the general procedure described above and in the main text, to yield the desired product as a dark orange oil (96.9 mg, 0.26 mmol, 96%, TON =24). ^1H-NMR (300 MHz, CDCl₃): 7.23 (bs, 2H), 7.12 (d, J=7.8 Hz, 2H), 6.17 (rotamer bs, 0.65H), 5.92 (rotamer, bs 0.35H), 3.50-3.95 (m, 4H), 2.33 (s, 3H), 1.33 (bs, 9H). ^13C-NMR (75.5 MHz, CDCl₃, 60 °C): 152.9, 138.4, 137.5, 128.7, 126.5, 80.4, 72.3, 43.6, 28.3, 21.0. IR (neat, cm⁻¹): 2976, 2930, 1692, 1365, 1160, 1105, 731. FD-MS; Experimental mass (m/z): 362.2188, calculated mass (C₂₀H₃₀N₂O₄): 362.2206 ([M]+).

Figure S35: ^1H-NMR spectrum of di-tert-butyl 2-(p-tolyl)imidazolidine-1,3-dicarboxylate (9b).

Figure S36: ^13C-NMR spectrum of di-tert-butyl 2-(p-tolyl)imidazolidine-1,3-dicarboxylate (9b) at 60 °C.
23. Synthesis of di-tert-butyl 2-([1,1'-biphenyl]-4-yl)imidazolidine-1,3-dicarboxylate (10b)

2-azido-N-(4-phenylbenzyl)ethanamine 12a (44.1 mg, 0.175 mmol), Boc₂O (91.5 mg, 2.4 equivalents), [Co(TMP)] catalyst 3 (6.0 mg, 7.1 µmol, 4.1 mol%) and dry toluene (1.7 mL) were handled according to the general procedure to yield the desired product as an off-white solid (67.6 mg, 0.199 mmol, 91%, TON = 22). 

**¹H-NMR** (500 MHz, CDCl₃, 60 °C): 7.59 (d, J = 7.5 Hz, 2H), 7.56 (d, J = 8.1 Hz, 2H), 7.46-7.39 (m, 4H), 7.33 (t, J = 7.4 Hz, 1H), 6.19 (bs, 1H), 3.92-3.81 (m, 2H), 3.74-3.65 (m, 2H), 1.39 (bs, 18H).

**¹³C-NMR** (125.7 MHz, CDCl₃, 60 °C): 152.9, 140.9, 140.9, 140.4, 128.7, 127.2, 127.1, 127.0, 126.8, 80.6, 72.4, 43.7, 28.3. IR (neat, cm⁻¹): 2975, 2931, 2894, 1691, 1365, 1160, 1107, 763, 733. FD-MS; Experimental mass (m/z): 424.2342, calculated mass (C₂₅H₃₂N₂O₄): 424.2362 ([M]+).

![Image of NMR spectra](image-url)

**Figure S37:** ¹H-NMR spectrum of di-tert-butyl 2-([1,1'-biphenyl]-4-yl)imidazolidine-1,3-dicarboxylate (10b) at 60 °C.

**Figure S38:** ¹³C-NMR spectrum of di-tert-butyl 2-([1,1'-biphenyl]-4-yl)imidazolidine-1,3-dicarboxylate (10b) at 60 °C.
24. Synthesis of di-tert-butyl 2-(4-fluorophenyl)imidazolidine-1,3-dicarboxylate (11b)

2-azido-N-(4-fluorobenzyl)ethanamine 11a (53.4 mg, 0.27 mmol), di-tert-butyl dicarbonate (146.3 mg, 0.66 mmol, 2.4 equivalents), [Co(TPP)] catalyst 1 (7.5 mg, 10.9 µmol, 4.0 mol%) and dry toluene (3.0 mL) were handled according to the general procedure to yield the desired product 11b as a dark yellow oil (82.8 mg, 0.23 mmol, 84%, TON = 21). 1H-NMR (300 MHz, CDCl3): 7.42-7.23 (bs, 2H), 7.00 (t, J = 8.7 Hz, 2H), 6.12 (bs, 0.67H, rotamer), 5.90 (bs, 0.33H, rotamer), 3.90-3.75 (m, 2H), 3.75-3.56 (m, 2H), 1.32 (bs, 18H). 13C-NMR (75.5 MHz, CDCl3, 60 °C): 162.7 (d, J = 246 Hz), 153.0, 137.6, 128.6 (d, J = 8.2 Hz), 115.1 (d, J = 21.5 Hz), 80.9, 72.2, 43.9, 28.5. 19F-NMR (282.4 MHz, CDCl3): 114.2, 114.4. IR (neat, cm⁻¹): 2977, 2932, 2893, 1691, 1365, 1155, 800, 766, 733. FD-MS: Experimental mass (m/z): 366.1949, calculated mass (C₁₉H₂₇FN₂O₄): 366.1955 ([M]+).

Figure S39: 1H-NMR spectrum of di-tert-butyl 2-(4-fluorophenyl)imidazolidine-1,3-dicarboxylate (11b).

Figure S40: 13C-NMR spectrum of di-tert-butyl 2-(4-fluorophenyl)imidazolidine-1,3-dicarboxylate (11b) at 60 °C.
25. Synthesis of di-tert-butyl 2-(4-chlorophenyl)imidazolidine-1,3-dicarboxylate (12b)

2-azido-N-(4-chlorobenzyl)ethanamine 12a (65.3 mg, 0.310 mmol), di-tert-butyldicarbonate (158.7 mg, 0.744 mmol, 2.4 equivalents), [Co(TPP)] catalyst 1 (8.3 mg, 12.4 µmol, 4.0 mol%) and toluene (3.0 mL) were handled according to the general procedure to yield the desired product as a light yellow oil (103.1 mg, 0.269 mmol, 87%, TON = 22). 1H-NMR (300 MHz, CDCl3): 7.49-7.10 (m, 4H), 6.12 (bs, 0.63H rotamer), 5.90 (bs, 0.37H rotamer), 3.83 (bs, 2H), 3.67 (br s, 2H), 1.32 (br s, 18H). 13C-NMR (75.5 MHz, CDCl3): 152.8, 139.9, 133.8, 128.3, 128.1, 80.9, 71.9, 43.7, 28.3. IR (neat, cm⁻¹): 2977, 2932, 2893, 1691, 1365, 1159, 1107, 912, 730. FD-MS; Experimental mass (m/z): 382.1642, calculated mass (C₁₉H₂₇ClN₂O₄): 382.1659 ([M]+).
26. Synthesis of di-tert-butyl 2-(4-bromophenyl)imidazolidine-1,3-dicarboxylate (13b)

2-azido-N-(4-bromobenzyl)ethanamine 13a (73.8 mg, 0.29 mmol), [Co(TPP)] catalyst 1 (7.8 mg, 11.6 mmol, 4.0 mol%), di-tert-butyl dicarbonate (171.3 mg, 0.79 mmol, 2.7 equivalents) and degassed toluene (3.0 mL) were handled according to the general procedure to yield the desired product 13b as a yellowish oil (118 mg, 0.276 mmol, 95%, TON=24). \( ^1 \)H- NMR (300 MHz, CDCl\(_3\), 60 °C); 7.45 (d, J=8.0 Hz, 2H), 7.25 (d, J=8.0 Hz, 2H), 6.06 (s, 1H), 3.90-3.75 (m, 2H), 3.73-3.56 (m, 2H), 1.37 (s, 18H). \( ^{13} \)C-NMR (75.5 MHz, CDCl\(_3\), 60 °C): 153.0, 140.7, 131.4, 131.4, 128.6, 122.1, 81.0, 72.2, 43.9, 28.5. IR (neat, cm\(^{-1}\)): 2977, 2932, 2894, 1691, 1366, 1159, 1108, 910, 729. FD-MS; Experimental mass (m/z): 426.1175, calculated mass (C\(_{19}\)H\(_{27}\)BrN\(_2\)O\(_4\)): 426.1154 ([M\(^{+}\)]).
27. Synthesis of di-tert-butyl 2-(4-methoxyphenyl)imidazolidine-1,3-dicarboxylate (14b)

2-azido-N-(4-methoxybenzyl)ethanamine 14a (26.9 mg, 0.130 mmol), di-tert-butyl dicarbonate (72.0 mg, 0.330 mmol, 2.5 equivalents) [Co(TPP)] catalyst 1 (3.6 mg, 5.4 µmol, 4.1 mol%) and dry toluene (2.5 mL) were handled according to the general procedure to yield the desired product 14b as a dark yellow oil (40.1 mg, 0.106 mmol, 82%, TON=20). The product still contained minor amounts of the Boc-protected starting material S7. ¹H-NMR (300 MHz, CDCl₃): 7.35-7.10 (m, 2H), 6.84 (d, J = 8.7 Hz, 2H), 6.14 (bs, 0.62H, rotamer), 5.89 (bs, 0.38H, rotamer), 3.88-3.54 (m, 4H), 3.79 (s, 3H), 1.33 (bs, 18H). ¹³C-NMR (75.5 MHz, CDCl₃, 60 °C): 159.6, 153.1, 128.0, 114.3, 113.7, 80.6, 72.4, 55.4, 43.8, 28.5. IR (neat, cm⁻¹): 2975, 2933, 1691, 1365, 1245, 1161, 1105, 1031, 761, 731. FD-MS: Experimental mass (m/z): 378.2157, calculated mass (C₂₀H₃₀N₂O₅): 378.2155 ([M⁺]).

Figure S45: ¹H-NMR spectrum of di-tert-butyl 2-(4-methoxyphenyl)imidazolidine-1,3-dicarboxylate (14b). Signals marked with “x” correspond to the Boc-protected starting material (S7).

Figure S46: ¹³C-NMR spectrum (60 °C) of di-tert-butyl 2-(4-methoxyphenyl)imidazolidine-1,3-dicarboxylate (14b).
28. Synthesis of tert-butyl isoindoline-2-carboxylate (15b)

1-(azidomethyl)-2-methylbenzene 15a (45.4 mg, 0.308 mmol), Boc₂O (80.3 mg, 0.368 mmol, 1.2 equivalents), dry toluene (3.0 mL) and [Co(TMP)] catalyst (10.1 mg, 12.0 µmol, 3.9 mol%) were handled according to the general procedure to yield a mixture of tert-butyl isoindoline-2-carboxylate 15b\textsuperscript{[16]} (27%, TON= 7) and tert-butyl 2-methylbenzylcarbamate 15c\textsuperscript{[17]} (35%). The mass balance is incomplete due to the formation of oligomeric/polymeric material under the applied reaction conditions. In the absence of Boc₂O the reaction still leads to full conversion however the expected isoindolene product was not observed. The characteristic peak at 6.32 ppm of 2H-isooindole was however observed (Figure S47) which is known to readily polymerize\textsuperscript{[18]}.

![Figure S47: 1H-NMR spectrum of the mixture of tert-butyl isoindoline-2-carboxylate (15b) and tert-butyl 2-methylbenzylcarbamate (15c).](image1)

![Figure S48: 1H-NMR spectrum of the reaction of 1-(azidomethyl)-2-methylbenzene 15a in absence of Boc₂O.](image2)
29. Synthesis of 2-tert-Butoxycarbonyl-1,3-dihydro-1-methylisoindole (16b)

To a dry Schlenk flask was added under nitrogen 1-(azidomethyl)-2ethylbenzene (32.0 mg, 0.199 mmol), di-tert-butyldicarbonate (51.6 mg, 0.236 mmol, 1.19 equivalents) and [Co(TMP)] catalyst 3 (3.2 mg, 3.8 µmol, 1.9 mol%). After addition of dry toluene (1.0 mL) the mixture was heated to 100 °C under nitrogen. After 16 h of reaction the mixture was poured over a silica plug and eluted with DCM containing 1 vol% triethylamine. The mixture was purified by flash column chromatography (SiO2, DCM:TEA 99:1) to yield the product as a light yellow oil (43.6 mg, 0.187 mmol, 94%, TON=49). Analysis data was in accordance to previously reported spectra.[19]

Figure S49: 1H-NMR spectrum of 2-tert-Butoxycarbonyl-1,3-dihydro-1-methylisoindole after purification.

30. Synthesis of tert-butyl 3,4-dihydroisoquinoline-2-carboxylate (17b)

1-(2-azidoethyl)-2-methylbenzene 17a (53.4 mg, 0.331 mmol), di-tert-butyldicarbonate (92.0 mg, 0.422 mmol, 1.3 equivalents), [Co(TMP)] catalyst 3 (11.4 mg, 13.6 µmol, 4.1 mol%) and dry tolene (3.0 mL) were handled according to the general procedure to yield a mixture of tert-butyl 3,4-dihydroisoquinoline-2-carboxylate (17b, 28%, TON = 7),[20] tert-butyl 2-methylphenethylcarbamate (17c, 37%).[21] As previously described for substrate 15a when the reaction was performed in absence of Boc2O full conversion was observed however no products could be identified suggesting oligomer/polymer formation is a competing reaction for this cyclization.

Figure S50: 1H-NMR spectrum of the product mixture of 1-(2-azidoethyl)-2-methylbenzene 17a cyclization.
31. Synthesis of tert-butyl 2-phenylpiperidine-1-carboxylate (18b)

7-azidohept-1-ene (43.9 mg, 0.315 mmol), di-tert-butyl dicarbonate (73.7 mg, 0.338 mmol, 1.1 equivalents), [Co(TMP)] catalyst 3 (9.7 mg, 11.5 µmol, 3.7 mol%) and dry toluene (3.0 mL) were handled according to the general procedure to yield a mixture of tert-butyl 2-phenylpiperidine-1-carboxylate (18b, 38%, TON = 10) tert-butyl hept-6-en-1-yl carbamate (18c, 12%), starting material (18a, 37%) and some unidentified decomposition products. The product 18b could be isolated by column chromatography (38%). Analysis was in agreement with previously reported data.\cite{22}

32. Additional substrates used in the intramolecular C–H amination protocol.

To evaluate which C–H bonds react and which don’t in the ring-closing C–H bond amination reactions we examined several additional substrates containing less activated (or unactivated) C–H bonds (Table S1). Upon replacement of the phenyl ring with an ester the C–H bond dissociation energy (BDE) increases significantly (85 and 96 kcal mol\(^{-1}\), respectively). Using the substrate listed in entry 1 leads to formation of several unidentified side products in addition to the desired ring closing reaction. In a stoichiometric reaction it is possible to convert hexylazide. However, with this substrate a 1:1 mixture of tert-butyl hexyl carbamate\cite{23} and hexane-nitrile was obtained. The high BDE of the unactivated C–H bonds at the delta position apparently prevents ring-closure and the more reactive alpha C–H bond of the azide substrate reacts instead (entry 2). This likely involves an intermolecular HAT between the nitrene radical intermediate and an additional azide substrate molecule. Such pathways would also explain the formation of oligomers/polymer, as observed for some of the reactions shown in Scheme 1 in the main text.

**Table S1: Additional substrates studied in intramolecular C–H amination by [Co(TMP)] catalyst 3.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>BDE(^b)</th>
<th>Conversion(^c)</th>
<th>Products</th>
<th>Yield(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Chem" /></td>
<td>96</td>
<td>74%</td>
<td><img src="image2" alt="Chem" /></td>
<td>26%</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="Chem" /></td>
<td>98</td>
<td>72%(^d)</td>
<td><img src="image4" alt="Chem" /></td>
<td>A 1:1 mixture of the linear and the nitrile product was obtained(^d)</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="Chem" /></td>
<td>83</td>
<td>63%</td>
<td><img src="image6" alt="Chem" /></td>
<td>38% + 12%(^e)</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7" alt="Chem" /></td>
<td>85</td>
<td>&lt;10%</td>
<td><img src="image8" alt="Chem" /></td>
<td>Traces</td>
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<tr>
<td>5</td>
<td><img src="image9" alt="Chem" /></td>
<td>82</td>
<td>40%</td>
<td><img src="image10" alt="Chem" /></td>
<td>10% cyclic product + 15% linear product(^e)</td>
</tr>
</tbody>
</table>

\(^a\) Conditions: Substrate (0.3 mmol), Boc\(^2\)O (1.2 equivalent), [Co(TMP)] (4 mol%), and toluene (3.0 mL) were added and reacted for 16 h at 100 °C. \(^b\) Bond dissociation energy (kcal mol\(^{-1}\)) of the C–H bond for cyclization.\cite{21} \(^c\) Isolated yields unless stated otherwise. \(^d\) Stoichiometric reaction. \(^e\) Not isolated.

The allylic C–H bond of 7-azidohept-1-ene (83 kcal mol\(^{-1}\)) can be activated to form the pyrrolidinone product (entry 3). The formation of six-membered heterocycles is however more challenging and the increased ring-strain in formation of a six-membered ring leads to a higher barrier for HAT. This leads to incomplete conversion (63%) and a moderate yield (38%) of the ring product (entry 3).\cite{22} In addition, formation of the linear Boc-protected amine product was observed in the crude \(^1\)H-NMR spectrum when using this substrate. The benzyl hydrogen atom of the substrate shown in entry 4 has a slightly higher BDE (85 kcal mol\(^{-1}\)). This, in combination with the challenging formation of a six-membered ring product, again leads to low
conversion of the substrate (<10%). Apparently, competing intermolecular reactions also lead to enhanced catalyst deactivation. Activation of the benzylic C–H bond of the substrate shown in entry 5, which is further activated by the neighboring oxygen atom (BDE = 82 kcal mol⁻¹), does lead to the desired six-membered product, albeit in low yield (10%).

The results shown in Table S1 indicate that if the ring-closing step requires breaking of a stronger C–H bond (higher BDE), the reaction is partially driven to intermolecular HAT reactions, most likely involving the alpha position of another azide substrate. This is consistent with the formation of oligomeric/polymeric products (see main text), linear Boc protected amines as well as nitriles from substrates containing even stronger C–H bonds. In contrast, substrates with weaker benzylic C–H bonds at the delta position lead to selective formation of five-membered rings without indications for intermolecular HAT (see main text, Table 1 and Table 2).

Isotopic labeling studies

33. Intermolecular kinetic isotope effect

\[
\begin{align*}
\text{Ph} & \text{H} \quad \text{N}_3 + \text{D} \quad \text{H} \quad \text{N}_3 \\
& \text{Co(TMP) (1 mol%)} \\
& \text{tol, 100 °C} \\
& 16h, N_2 \\
& \text{Boc} \quad \text{Ph} \quad \text{H} \quad \text{D} \\
& \text{Boc} \quad \text{Ph} \quad \text{N} \quad \text{D} \\
\end{align*}
\]

A mixture of (4-azidobutyl)benzene 5a (27.2 mg, 0.155 mmol) and 4-azido-1,1-bisdeutero-1-phenylbutane (31.7 mg, 0.179 mmol) was analyzed by ¹H-NMR (CDCl₃, Figure S51) to show a H₂ to D₂ ratio of 1.00:1.00. The mixture was transferred quantitatively to a Schlenk flask and solvent was removed. The mixture was placed under nitrogen and Boc₂O (108.0 mg, 0.495 mmol, 1.5 equiv.) and [Co(TMP)] catalyst 3 (2.8 mg, 3.3µmol, 1.0 mol%) were added followed by dry toluene (3.0 mL). The mixture was heated to 100 °C for 16h and the crude product purified by column chromatography (SiO₂, Hexanes/DCM/TEA; 50/50/1) to yield a light yellow oil (12.5 mg, 51µmol, 15%). The k_H/k_D ratio was determined from the ratio of the methylene and methine protons at the 2- and 4-position in the ¹H-NMR spectrum. The reaction was performed in duplo resulting in a k_H/k_D ratio of 0.99, which corresponds to a KIE of 1 within the error-limits of NMR integrations. In Figure S52 a representative ¹H-NMR spectrum is shown.

Figure S51: ¹H-NMR spectrum of the ratio of starting materials for the intermolecular kinetic isotope effect.
Figure S52: Representative $^1$H-NMR spectrum of the product mixture after flash column chromatography.

34. Intramolecular kinetic isotope effect

(4-azido-1-deuterobutyl)benzene (8.2 mg, 47 µmol), BocO (12.9 mg, 59 µmol, 1.26 equiv.), [Co(TMP)] catalyst 3 (0.9 mg, 1.1µmol, 2.3 mol%) and dry toluene (0.5 mL) were handled according to the general procedure. The $k_H/k_D$ ratio was determined from the ratio of the methylene and methine protons at the 2- and 4-position in the $^1$H-NMR spectrum. The reaction was performed in duplo resulting in a $k_H/k_D$ ratio of 7.0 which corresponds to a KIE of 7. In Figure S53 a representative $^1$H-NMR spectrum is shown.

Figure S53: Representative $^1$H-NMR spectrum of the product mixture after flash column chromatography.
Enantioselective intramolecular ring-closing C-H amination

(4-azidobutyl)benzene 5a (30.0 mg, 0.171 mmol), di-tert-butyl dicarbonate (45.0 mg, 0.206 mmol, 1.2 equivalents), chiral porphyrin cobalt catalyst 19 (10.5 mg, 6.8 µmol, 4.0 mol%) and dry toluene (3.0 mL) were handled according to the general procedure (see main text) at 80 °C to yield the desired product 5b as a light yellow oil (9.4 mg, 38.0 µmol, 22%, TON = 6). The enantiomeric ratio was analyzed by chiral GC to yield the two enantiomers in a ratio of 73:27 (enantiomeric excess = 46%). The chromatogram is shown in Figure S54 (bottom). The signals were compared with a racemic sample of the product to verify the retention time of the two enantiomers (Figure S54, top).

Figure S54: Chiral GC chromatogram of racemic (top) and enantiomerically enriched (bottom) tert-butyl 2-phenylpyrrolidine-1-carboxylate (5b).
Boc-protected side products obtained in this study

35. Synthesis of tert-butyl (2-azidoethyl)(benzyl)carbamate (8c)

To a solution of 2-azido-N-benzylethanamine (92.1 mg; 0.5 mmol) in toluene (2 mL) was added di-tert-butyl dicarbonate (222 mg, 1.0 mmol). Upon addition gas evolution was observed and the progress of the reaction was monitored by TLC (SiO\textsubscript{2}; EtOAc). After 30 minutes the crude product was placed on a small silica column and washed extensively with hexane to remove all excess di-tert-butyl dicarbonate. The product was collected with EtOAc to yield a light yellow oil (76.8 mg, 0.28 mmol, 56%).

\(^1\)H-NMR (300 MHz, CDCl\textsubscript{3}): 7.38-7.24 (m, 5H), 4.52 (s, 2H), 3.50-3.26 (m, 4H), 1.48 (s, 9H). \(^1^3\)C-NMR (75.5 MHz, CDCl\textsubscript{3}, 60 °C): 155.5, 138.1, 128.5, 127.4, 127.3, 80.3, 51.4, 49.8, 46.1, 28.4. IR (neat, cm\textsuperscript{-1}): 2976, 2930, 2096 (N\textsubscript{3}), 1689, 1408, 1365, 1243, 1162, 1126, 699. FD-MS; Experimental mass (m/z): 276.15855, calculated mass (C\textsubscript{14}H\textsubscript{20}N\textsubscript{4}O\textsubscript{2}): 276.1586 ([M]+).

Figure S55: \(^1\)H-NMR spectrum of tert-butyl (2-azidoethyl)(benzyl)carbamate (8c).

Figure S56: \(^1^3\)C-NMR spectrum (60 °C) of tert-butyl (2-azidoethyl)(benzyl)carbamate (8c).
36. Synthesis of tert-butyl (2-azidoethyl)(4-methylbenzyl)carbamate (S6)

To a solution of 2-azido-N-(4-methylbenzyl)ethanamine 9a (34.5 mg, 0.181 mmol) in toluene (1.0 mL) was added Boc₂O (89.2 mg, 0.409 mmol) and the mixture was stirred for 16 hours. The crude product was purified by column chromatography (SiO₂: PE40-60/MeOH 19:1 → DCM/MeOH 19:1 gradient) to yield the desired product S6 as a light yellow oil (19.8 mg, 68.2 µmol, 38% yield). ¹H-NMR (300 MHz, CDCl₃): 7.13 (bs, 4H), 4.46 (s, 2H), 3.45-3.20 (m, 4H), 2.34 (s, 3H), 1.48 (bs, 9H). ¹³C-NMR (75.5 MHz, CDCl₃, 60 °C): 155.5, 137.0, 135.0, 129.2, 127.5, 80.3, 49.7, 45.9, 28.4, 20.94. One of the carbons resulted in a very broad signal around δ = 52 which was not clearly resolved. IR (neat, cm⁻¹): 2976, 2929, 2097 (N₃), 1690 (C=O), 1405, 1361, 1245, 1162, 1126, 773. FD-MS: Experimental mass (m/z): 290.1740, calculated mass (C₁₅H₂₁N₄O₂): 290.1743 ([M]+).

Figure S57: ¹H-NMR spectrum of tert-butyl (2-azidoethyl)(4-methylbenzyl)carbamate (S6)

Figure S58: ¹³C-NMR spectrum of tert-butyl (2-azidoethyl)(4-methylbenzyl)carbamate (S6) at 60 °C. Signals marked with “x” are from remaining Boc₂O.
37. Synthesis of tert-butyl (2-azidoethyl)(4-methoxybenzyl)carbamate (S7)

To a vial were added 2-azido-N-(4-phenylbenzyl)ethanamine 10a (7.3 mg, 28.9 µmol) toluene (1.0 mL) and Boc₂O (10.4 mg, 47.7 µmol). The mixture was stirred at room temperature for 1h after which full conversion was observed by TLC. The product was purified by gradient column chromatography (SiO₂, hexanes → hexanes/MeOH 19:1 → DCM/MeOH 19:1) to yield the desired product S7 as a white solid (8.4 mg, 23.8 µmol, 82%). ¹H-NMR (500 MHz, CDCl₃, 60 °C): 7.58 (t, J= 8.0 Hz, 4H), 7.43 (dd, J=8.4, 7.0 Hz, 2H), 7.34 (t, J=7.4 Hz, 1H), 7.31 (d, J=8.0 Hz, 2H), 4.55 (s, 2H), 3.41 (s, 4H), 1.51 (s, 9H). ¹³C-NMR (126 MHz, CDCl₃, 60 °C): 155.8, 141.1, 140.7, 137.4, 128.9, 128.1, 127.6, 127.5, 127.2, 80.7, 51.5, 50.1, 46.4, 28.6. IR (neat, cm⁻¹): 2975, 2930, 2097 (N₃), 1688 (C=O), 1404, 1365, 1163, 1129, 759, 698. FD-MS: Experimental mass (m/z): 352.1898, calculated mass (C₂₀H₂₄N₄O₂): 352.1899 ([M]+).

Figure S59: ¹H-NMR spectrum (60 °C) of tert-butyl (2-azidoethyl)(4-methoxybenzyl)carbamate (S7)

Figure S60: ¹³C-NMR spectrum (60 °C) of tert-butyl (2-azidoethyl)(4-methoxybenzyl)carbamate (S7).
38. Synthesis of tert-butyl (2-azidoethyl)(4-fluorobenzyl)carbamate (S8)

To a solution of Boc₂O (11.6 mg, 53.1 µmol) in toluene (1.0 mL) was added 2-azido-N-(4-fluorobenzyl)ethanamine 11a (9.6 mg, 49.4 µmol) and the mixture was stirred for 1h. Additional Boc₂O (8.0 mg, 36.6 mg) was added and after 3h the mixture was purified by column chromatography (SiO₂, toluene/MeOH 20:0 → 19:1) to obtain the product as a colorless oil (6.6 mg, 22.4 µmol, 45%). ¹H-NMR (500 MHz, CDCl₃, 60 °C): 7.21 (dd, J=8.5, 5.5 Hz, 2H), 7.02 (t, J = 8.7 Hz, 2H), 4.47 (s, 2H), 3.36 (bs, 4H), 1.49 (s, 9H). ¹³C-NMR (126 MHz, CDCl₃, 60 °C): 162.51 (d, J = 246 Hz), 155.7, 134.2, 129.3, 115.7 (d, 21.4 Hz), 80.8, 51.1, 50.1, 46.4, 28.6. IR (neat, cm⁻¹): 2977, 2931, 2097 (N₃), 1688 (C=O), 1458, 1406, 1220, 1155, 1095, 815. FD-MS; Experimental mass (m/z): 294.1496, calculated mass (C₁₄H₁₉FN₄O₂): 294.1492 ([M]+).
39. Synthesis of tert-butyl (2-azidoethyl)(4-chlorobenzyl)carbamate (S9)

To a solution of 2-azido-N-(4-chlorobenzyl)ethanamine 12a (23.7 mg, 0.113 mmol) in toluene was added di-tert-butyl dicarbonate (25.8 mg, 0.118 mmol, 1.05 equivalents). After 1 h of reaction solvent was removed under reduced pressure to obtain the desired product S9 as a light yellow oil (containing still 5% of Boc₂O which can be removed by the work-up described for 8c). ¹H-NMR (300 MHz, CDCl₃, 60 °C): 7.30 (d, J = 7.9 Hz, 2H), 7.17 (d, J = 7.9 Hz, 2H), 4.47 (s, 2H), 3.36 (bs, 4H), 1.48 (s, 9H). ¹³C-NMR (75.5 MHz, CDCl₃, 60 °C): 155.6, 136.9, 133.5, 129.0, 129.0, 80.8, 51.1, 50.1, 46.5, 28.6. IR (neat, cm⁻¹): 2977, 2932, 2098 (N₃), 1402, 1164, 1129, 798. FD-MS; Experimental mass (m/z): 310.1224, calculated mass (C₁₄H₁₉ClN₄O₂): 310.1197 ([M]⁺).

Figure S63: ¹H-NMR spectrum of tert-butyl (2-azidoethyl)(4-chlorobenzyl)carbamate (S9).

Figure S64: ¹³C-NMR spectrum of tert-butyl (2-azidoethyl)(4-chlorobenzyl)carbamate (S9). Signals marked with “x” correspond to small amounts of Boc₂O contaminant in the product.
40. Synthesis of tert-butyl (2-azidoethyl)(4-bromobenzyl)carbamate (S10)

To a vial was added 2-azido-N-(4-bromobenzyl)ethanamine 13a (13.3 mg, 52.1 µmol), Boc₂O (22.7 mg, 0.104 mmol) and toluene (1.0 mL). After 16 h of reaction the crude product was purified by column chromatography (SiO₂; PE40-60 → PE40-60/MeOH 19:1 → DCM/MeOH 19:1) to yield the desired product S10 as a colorless oil (17.1 mg, 48.1 µmol, 92%).

1H-NMR (300 MHz, CDCl₃): 7.46 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 4.45 (s, 2H), 3.36 (bs, 4H), 1.48 (s, 9H). 13C-NMR (75.5 MHz, CDCl₃, 60 °C): 155.4, 137.2, 131.7, 129.1, 121.2, 80.6, 51.1, 49.9, 46.3, 28.3. IR (neat, cm⁻¹): 2976, 2930, 2096 (N₃), 1688 (C=O), 1400, 1366, 1161, 1128, 1011, 824. FD-MS; Experimental mass (m/z): 354.0694, calculated mass (C₁₄H₁₉BrN₄O₂): 354.0691 ([M]+).

Figure S65: 1H-NMR spectrum of tert-butyl (2-azidoethyl)(4-bromobenzyl)carbamate (S10).

Figure S66: 13C-NMR spectrum of tert-butyl (2-azidoethyl)(4-bromobenzyl)carbamate (S10).
41. Synthesis of tert-butyl (2-azidoethyl)(4-methoxybenzyl)carbamate (S11)

To a solution of 2-azido-N-(4-methoxybenzyl)ethanamine 16a (13.1 mg, 63.5 µmol) in toluene (1.0 mL) was added di-tert-butyl dicarbonate (25.0 mg, 0.115 mmol) and the mixture was stirred at room temperature for 16 hours. The crude product was purified by column chromatography (SiO2, hexanes → hexanes/MeOH 19:1 → DCM/MeOH 19:1) to yield the product S11 as a colorless oil (14.0 mg, 45.7 µmol, 72%). 1H-NMR (500 MHz, CDCl3, 60 °C): 7.16 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 4.44 (s, 2H), 3.80 (s, 3H), 3.34 (bs, 4H), 1.50 (s, 9H). 13C-NMR (126 MHz, CDCl3, 60 °C): 159.4, 155.7, 130.5, 129.1, 114.4, 80.5, 55.5, 51.1, 50.0, 46.1, 28.6. IR (neat, cm⁻¹): 2975, 2933, 2097 (N₃), 1688 (C=O), 1512, 1407, 1243, 1161, 1126, 1034. FD-MS: Experimental mass (m/z): 306.1704, calculated mass (C₁₅H₂₂N₄O₃): 306.1692 ([M]+).

Figure S67: 1H-NMR spectrum (60 °C) of tert-butyl (2-azidoethyl)(4-methoxybenzyl)carbamate (S11).

Figure S68: 13C-NMR spectrum (60 °C) of tert-butyl (2-azidoethyl)(4-methoxybenzyl)carbamate (S11).
Kinetic studies

To a dried NMR pressure tube was added (4-azidobutyl)benzene (11.5 mg, 65.6 µmol) and Boc₂O (18.2 mg, 83.4 µmol, 1.3 equivalents). The tube was placed under nitrogen and [Co(TMP)] catalyst 3 was added (1.8 mol% (0.9 mg, 1.1 µmol), 3.2 mol% (1.8 mg, 2.1 µmol), or 6.5 mol% (3.6 mg, 4.3 µmol). After addition of toluene-<sup>d</sup>₈ (0.5 mL) and triphenylmethane (4.7 mg, 19.2 µmol) as internal standard the NMR tube was closed and heated in the NMR spectrometer at 100 °C. A <sup>1</sup>H-NMR spectrum was recorded every 10 minutes and the amount of substrate and product with respect to the standard was determined (Figure S69). Following the decrease of the substrate concentration ([A]<sub>t</sub>) in time using different catalyst loadings and plotting the data as ln[A]<sub>t</sub>-ln[A]<sub>0</sub> versus time plot reveal linear regression lines with R² values >0.99 showing first order kinetics in the [substrate] (Figure S70). The rate also increases linearly with the catalyst concentration (or loading), thus showing first order kinetics in [catalyst 3] (Figure S71). Following the decrease of the substrate concentration ([A]<sub>t</sub>) in time using different amounts of Boc₂O and plotting the observed rate K<sub>obs</sub> (h<sup>-1</sup>) versus the concentration of Boc₂O (Figure S72) shows zero order kinetics in [Boc₂O].
Figure S71: Reaction rate $k_{\text{obs}}$ as a function of catalyst concentration (with $k_{\text{obs}} = k[3]$).

Figure S72: Reaction rate $k_{\text{obs}}$ as a function of Boc$_2$O concentration.

**Empirical rate law:**

$$\text{Rate} = \frac{-d[\text{substrate}]}{dt} = k[\text{substrate}][\text{catalyst 3}]$$

with second order rate constant $k = 11.9 \text{ M}^{-1} \text{ h}^{-1}$
Arrhenius plot:

In order to determine the experimental activation energy ($E_a$) the reaction was monitored at 353K, 363K, 373K, 383K and 388K. The data from the various experiments are depicted in Table S2 and graphically represented in Figure S73.

**Table S2: Experimental $K$ values at varying temperatures.**

<table>
<thead>
<tr>
<th>Temperature (K)</th>
<th>$k_{obs}$ (h$^{-1}$)</th>
<th>[substrate] (M)</th>
<th>[catalyst] (M)</th>
<th>k (M$^{-1}$ h$^{-1}$)</th>
<th>1/T (K$^{-1}$)</th>
<th>Ln(k/T)</th>
<th>Ln(k)</th>
</tr>
</thead>
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<td>0.00238</td>
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<td>0.002755</td>
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<td>0.00214</td>
<td>31.638</td>
<td>0.002577</td>
<td>-2.506</td>
<td>3.4543</td>
</tr>
</tbody>
</table>

**Figure S73: Arrhenius plot of rate constants (k) versus temperature.**

Using the equation:

$$\ln(k) = -\frac{E_a}{RT} + \ln(A)$$

With $-E_a/R$ as the slope and $\ln(A)$ as the intercept with the y-axis results in:

$$E_a = +78.3 \pm 9.7 \text{ kJ mol}^{-1} = +18.7 \pm 2.3 \text{ kcal mol}^{-1}.$$
Eyring plot

The Eyring equation strictly only holds for single step reactions, and multistep reactions are most reliably analyzed with the Arrhenius equation.[51] However, substrate binding and subsequent azide activation can be approached as a one-step rate limiting process in evaluation of the activation parameters, and such the $\Delta H^\ddagger$, $\Delta S^\ddagger$ and $\Delta G^\ddagger$ values determined from an Eyring plot (using the rates shown in Table S2) still provide useful information about the transition state relative to the resting state.

\[ \ln\left(\frac{k}{T}\right) = \frac{-\Delta H^\ddagger}{RT} + \ln\left(\frac{k'}{h}\right) + \frac{\Delta S^\ddagger}{R} \]

Using the equation:

\[ \ln\left(\frac{k}{T}\right) = \frac{-\Delta H^\ddagger}{RT} + \ln\left(\frac{k'}{h}\right) + \frac{\Delta S^\ddagger}{R} \]

(k′ = Boltzmann constant, h = Planck constant, R = gas constant)

With $-\Delta H^\ddagger/R$ as the slope and $\ln(k'/h) + \Delta S^\ddagger/R$ as the intercept with the y-axis results in:

$\Delta H^\ddagger = 75.2 \pm 9.7$ kJ mol$^{-1} = +18.0 \pm 2.3$ kcal mol$^{-1}$.

$\Delta S^\ddagger = -92.1$ J mol$^{-1}$ K$^{-1} = -22.0 \pm 6.2$ cal mol$^{-1}$ K$^{-1}$.

$\Delta G^\ddagger_{373K} = \Delta H^\ddagger - T\Delta S^\ddagger = +109.6 \pm 26.1$ kJ mol$^{-1} = +26.2 \pm 4.6$ kcal mol$^{-1}$.
42. Determination of the binding constant for 2-phenylpyrrolidine (5c).

A stock solution [Co(TMP)] catalyst 3 (2.51 mg, 2.99 µmol) in dry toluene (25 mL) was prepared and diluted to obtain a concentration of 23.9 µM. 2-phenylpyrrolidine (5c, 57.8 mg, 0.393 mmol) was dissolved in the catalyst stock solution (1.0 mL) to obtain the titration stock solution. Under nitrogen the stock solution of the guest (5b) was titrated to the host solution (3) at 298K and the changes in absorption was monitored at 528 nm and 590 nm. The titration scheme is reported in Table S3 and the UV–vis spectra are shown in Figure S75.

Table S3: Titration data for binding of 2-phenylpyrrolidine (5c) to [Co(TMP)] catalyst 3.

<table>
<thead>
<tr>
<th>stock solution 5c (µL)</th>
<th>Concentration 5c (mM)</th>
<th>Equivalents 5c</th>
<th>Absorption (528 nm)</th>
<th>Absorption (590 nm)</th>
</tr>
</thead>
<tbody>
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</table>

Figure S75: UV–vis titration for 2-phenylpyrrolidine (5c) to [Co(TMP)] catalyst 3.
The decrease in absorption at 528 nm and the increase in absorption at 590 nm were fitted to a 1:2 binding model to obtain Figures S76 and S77 respectively.

\[
\text{[5c] M}^{-1}
\]

\begin{align*}
\Delta A (\text{a.u.}) & \quad \Delta A_{\text{obs}} \\
\Delta A_{\text{calc}} & \quad R^2 = 0.998
\end{align*}

**Figure S76**: Experimental and calculated absorption decrease at 528 nm with \( K_1 = 1303 \text{ M}^{-1} \), \( K_2 = 81 \text{ M}^{-1} \).

\begin{align*}
\Delta A (\text{a.u.}) & \quad \Delta A_{\text{obs}} \\
\Delta A_{\text{calc}} & \quad R^2 = 0.996
\end{align*}

**Figure S77**: Experimental and calculated absorption increase at 590 nm with \( K_1 = 1303 \text{ M}^{-1} \), \( K_2 = 81 \text{ M}^{-1} \).

Both wavelengths were fitted simultaneously to obtain \( K_1 = 1303 \text{ M}^{-1} \) for the 1:1 complex and \( K_2 = 81 \text{ M}^{-1} \) for a 1:2 complex with a low \( R^2 \) value for each wavelength (0.998 and 0.996 respectively).

The binding constant for the starting material (4-azidobutyl)benzene 5a could not be obtained due to the very low binding constant.\(^{[26]}\)
Computational details

The mechanism of the [Co(por)] catalyzed intramolecular C–H amination ring-closing reaction of 5a to 5b was explored computationally, using DFT. A simplified model porphyrin without meso-substituents was used to reduce computation time. Geometry optimizations were carried out with the Turbomole program package\(^1\) coupled to the PQS Baker optimizer\(^2\) via the BOpt package\(^3\). We used unrestricted ri-DFT-D3 calculations at the BP86 level\(^4\) in combination with the def2-TZVP basis set\(^5\) and a small (m4) grid size. Grimme’s dispersion corrections\(^6\) (version 3, disp3, ‘zero damping’) were used to include Van der Waals interactions. All minima (no imaginary frequencies) and transition states (one imaginary frequency) were characterized by calculating the Hessian matrix. ZPE and gas-phase thermal corrections (entropy and enthalpy, 373 K, 1 bar) from these analyses were calculated. The nature of the transition states was confirmed by following the intrinsic reaction coordinate. The relative free energies (\(\Delta G_{310K}\) in kcal mol\(^{-1}\)) obtained from these calculations are reported in the main text. A separate archive file containing an excel sheet containing the energies and entropies (\(\Delta G_{310K}, \Delta G_{298K}, \Delta H, \Delta S, \text{SCF+ZPE, SCF}\)) and negative eigenvalues of the transition states and all optimized geometries (.pdb and .xyz format) is provided.

DFT calculations without dispersion corrections strongly underestimate the metal-ligand interactions, as was clear from a series of test calculations. We therefore employed Grimme’s version 3 (disp3) dispersion corrections. Used as such, the computed dispersion corrected metal-ligand association/dissociation energies to/from the non-solvated [Co(por)] catalyst A are overestimated though. This is due to neglected dispersion interactions between the metal binding site of the catalyst and a solvent molecule in solution. We therefore used the Van der Waals π-complex between [Co(por)] catalyst A and a discrete toluene solvent molecule (interacting with catalyst at the metal binding site) as the energetic reference point in our calculations to prevent overestimation of the metal-ligand interactions as a result of such uncompensated dispersion forces. However, this approach also leads to an erroneous cancelation of all translational entropy contributions to the computed free energies. This is because the translational entropy contributions to substrate/product association/dissociation are fully counterbalanced by the translational entropy contributions resulting from dissociation/association of the involved solvent molecule in the DFT calculated thermodynamics (A-solv + L ↔ A-L + solv). This is not realistic in comparison to actual solution phase chemistry, for which the translational entropy contributions associated with substrate/product association/dissociation steps can of course not be neglected.\(^7\) Therefore we applied a translational entropy contribution of \(20\) cal mol\(^{-1}\) K\(^{-1}\) to the computed free energies of all substrate/product binding/dissociation steps in the catalytic cycle. This leads to realistic metal-ligand binding entropies comparable to those reported for related systems in toluene.\(^8\) See also the excel sheet in the separate archive file.

Detailed description of the DFT results

The mechanism of the metallo-radical catalysed ring-closing reaction of substrate 5a to product 5c by means of DFT (BP86, def2-TZVP, disp3). We anticipated that the initial steps of the mechanism might involve coordination of the aliphatic azide 5a to cobalt(II), followed by dinitrogen loss to produce a related nitrene radical intermediate (Table S4). This indeed is a plausible pathway. Azide coordination is slightly endergonic (+3.2 kcal mol\(^{-1}\)) and subsequent loss of dinitrogen via TS1 to produce the key nitrene-radical species C appears to be the rate limiting step. The relatively high computed barrier for TS1 (+24.5 kcal mol\(^{-1}\)) is in agreement with the fact that catalytic conversion of 5a requires heating (100 °C). Spin density plots of species C show 88% spin population at the nitrene moiety and only 6% at Co, thus confirming the nitrene-radical nature of these intermediates (inset Table S4). Subsequent hydrogen atom transfer (HAT) from the benzyl position of the activated substrate to the nitrene-radical moiety (TS2) to produce amido-benzyl radical intermediate D has a remarkably low barrier (+8.5 kcal mol\(^{-1}\)), and the following radical rebound step over TS3 to produce pyrrolidine adduct E is virtually barrierless. However, dissociation of amine product 5c from cobalt(II) species E is endergonic, resulting in product inhibition. This is in agreement with the experimental data, as an amine trapping agent (Boc\(_2\)O) is required for catalytic turnover. To further evaluate the effect of product inhibition on the reaction barriers, both unsaturated (5-coordinate cobalt) and saturated pathways (6-coordinate cobalt, having pyrrolidine 5c bound trans to the reactive site) were considered computationally. The azide activation barrier for the 5-coordinated analog is about 4 kcal mol\(^{-1}\) higher than with the corresponding 4-coordinated complex A. It is clear from these studies that product adduct E becomes the resting state if the unprotected amine product 5c is not removed from the reaction mixture, while azide adduct B is the resting state if 5c is trapped by an amine scavenger such as Boc\(_2\)O. The overall barrier from E to TS1 (rate limiting step in absence of Boc\(_2\)O) is much higher than the barrier from B to TS1 (rate limiting step in presence of Boc\(_2\)O) and as such, the computations are in good agreement with the experimental observations.
Table S4. DFT computed pathway (BP86, def2-TZVP, disp3) of Co(por) catalysed intramolecular C–H amination ring-closing reaction of 5a to 5b ($\Delta G^\circ_{373K}$ in kcal mol$^{-1}$).

<table>
<thead>
<tr>
<th>L</th>
<th>Barriers $^{[a]}$</th>
<th>Barriers $^{[b]}$</th>
<th>L = 5c Barriers $^{[a]}$</th>
<th>Barriers $^{[b]}$</th>
</tr>
</thead>
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<tr>
<td></td>
<td>unsaturated</td>
<td>saturated</td>
<td>unsaturated</td>
<td>saturated</td>
</tr>
<tr>
<td>A</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>+3.2</td>
<td>+7.4</td>
<td>+3.2</td>
<td>+7.4</td>
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<tr>
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<tr>
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<tr>
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<tr>
<td>D</td>
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<td>−11.3</td>
<td>−6.1</td>
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<tr>
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<tr>
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<tr>
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<tr>
<td>B + 5c</td>
<td>−45.7</td>
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</table>

$^{[a]}$ TS1 from B, unsaturated pathway, relevant in presence of Boc$_2$O.
$^{[b]}$ TS1 from E, saturated pathway, relevant in absence of Boc$_2$O.
IR spectra of prepared compounds
J. Am. Chem. Soc. toluene and related apolar solvents are in the range between entropy contributions as contributions to the toluene molecule association/dissociation steps. These are of little influence on the translational
TURBOMOLE Version 7.0.1 (TURBOMOLE GmbH, Karlsruhe, Germany).
In solution the catalyst is completely surrounded by solvent molecules, leading to small translational entropy contributions to the toluene molecule association/dissociation steps. These are of little influence on the translational entropy contributions associated with substrate/product association/dissociation. Hence, the latter are not canceled by the former in toluene solution.
Experimental binding entropies reported for association of a series of pyridine-type donors to Zn(porphor) complexes in toluene and related apolar solvents are in the range between −12 to −19 cal mol⁻¹ K⁻¹. See: F. A. Walker, M. Benson, J. Am. Chem. Soc. 1980, 102, 5530-5538.