Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O: Reaction Development, Synthetic Scope, and Mechanistic Studies

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List of Known Compounds/General Methods

All starting materials reported in the manuscript have been previously described in literature or prepared by the method reported previously. Imides were purchased from commercial suppliers or prepared by standard methods.\textsuperscript{1-9} Samarium(II) iodide was prepared by standard methods and titrated prior to use.\textsuperscript{10-14} All experiments involving SmI\textsubscript{2} were performed using standard techniques under argon or nitrogen atmosphere unless stated otherwise. All solvents were purchased at the highest commercial grade and used as received or after purification by passing through activated alumina columns or distillation from Na/benzophenone under nitrogen. All solvents were deoxygenated prior to use. All other chemicals were purchased at the highest commercial grade and used as received. Reaction glassware was oven-dried at 140 °C for at least 24 h or flame-dried prior to use, allowed to cool under vacuum and purged with argon (three cycles). All products were identified using \textsuperscript{1}H NMR, and/or GC-MS analysis and comparison with authentic samples. \textsuperscript{1}H NMR and \textsuperscript{13}C NMR spectra were recorded in CDCl\textsubscript{3} on Bruker and Varian spectrometers at 500 and 600 MHz (\textsuperscript{1}H NMR) and 125 and 150 MHz (\textsuperscript{13}C NMR). All shifts are reported in parts per million (ppm) relative to residual CHCl\textsubscript{3} peak (7.27 and 77.2 ppm, \textsuperscript{1}H NMR and \textsuperscript{13}C NMR, respectively). All coupling constants (J) are reported in hertz (Hz). Abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; br s, broad singlet. GC-MS chromatography was performed using Agilent HP6890 GC System and Agilent 5973A inert XL EI/CI MSD using helium as the carrier gas at a flow rate of 1 mL/min and an initial oven temperature of 50 °C. The injector temperature was 250 °C. The detector temperature was 250 °C. For runs with the initial oven temperature of 50 °C, temperature was increased with a 10 °C/min ramp after 50 °C hold for 3 min to a final temperature of 280 °C, then hold at 280 °C for 30 min (splitless mode of injection, total run time of 54.00 min). High-resolution mass spectra (HRMS) were measured on a 7T Bruker Daltonics FT-MS instrument. All flash chromatography was performed using silica gel, 60 Å, 300 mesh. TLC analysis was carried out on glass plates coated with silica gel 60 F254, 0.2 mm thickness. The plates were visualized using a 254 nm ultraviolet lamp or aqueous potassium permanganate solutions. \textsuperscript{1}H NMR and \textsuperscript{13}C NMR data are given for all compounds in the Supporting Experimental for characterization purposes. \textsuperscript{1}H NMR, \textsuperscript{13}C NMR and HRMS data are reported for all new compounds.
List of Known Compounds

The following compounds are known: tert-butyl 1-methyl-2,6-dioxopiperidine-3-carboxylate,\textsuperscript{15} tert-butyl 1-methyl-2,5-dioxopyrrolidine-3-carboxylate,\textsuperscript{15} ethyl 1-methyl-2,5-dioxopyrrolidine-3-carboxylate,\textsuperscript{16} 1-methyl-3-phenylpyrrolidine-2,5-dione.\textsuperscript{17} All olefins have been prepared following the procedure by Wong.\textsuperscript{18} All alkyl derivatives have been prepared following the procedure by Aubé.\textsuperscript{19,20} All other substrates have been prepared according to procedures outlined below.
Experimental Procedures and Characterization Data

General Procedure for Reductive Cyclization of Imides using SmI$_2$–H$_2$O. An oven-dried vial containing a stir bar was charged with a cyclic imide substrate (neat, 1 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF (typically, 2.0 mL) and water (typically, 600 equiv) were added, followed by a rapid injection of samarium(II) iodide (0.1 M, THF solution, typically 3 equiv) with vigorous stirring, which resulted in the formation of a characteristic burgundy-red color of the SmI$_2$(H$_2$O)$_n$ complex ($n > 5$ with respect to SmI$_2$), and the reaction mixture was stirred for the indicated time (typically, 15 min). The excess of Sm(II) was oxidized by bubbling air through the reaction mixture, and the reaction mixture was diluted with Et$_2$O (30 mL) and HCl (0.1 N, 20 mL). The aqueous layer was extracted with Et$_2$O (3 x 20 mL), organic layers were combined, dried over Na$_2$SO$_4$, filtered and concentrated. The sample was analyzed by $^1$H NMR (CDCl$_3$, C$_6$D$_6$ or CD$_3$C(O)CD$_3$) and/or GC-MS (neat) to determine product distribution and diastereoselectivity from the crude reaction mixture. The crude product was purified by chromatography on silica gel or crystallization, concentrated under reduced pressure and stored neat or as a solution in acetone. Note that reactions involving samarium(II) can typically be followed by visual observation of the color changes of the respective reaction mixtures. In the case of Sm(II)/H$_2$O complexes, the color changes from Sm$^{II}$ (burgundy red) to Sm$^{III}$ (white: oxidized, solvated; then yellow: fully oxidized, characteristic of SmI$_2$X).

Representative Procedure for the Large Scale Cyclization. An oven-dried 250 mL round-bottomed flask equipped with a stir bar was placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. The flask was charged with 3 (neat, 1.00 g, 2.68 mmol, 1.0 equiv), THF (25 mL), and H$_2$O (19.3 mL, 400 equiv). Samarium(II) iodide (53.6 mL, 2.0 equiv, THF solution, 0.10 M) was added with vigorous stirring, which resulted in the formation of a characteristic burgundy-red color of the SmI$_2$(H$_2$O)$_n$ complex ($n > 5$ with respect to SmI$_2$). The reaction mixture was stirred at room temperature for 5 min. The excess of SmI$_2$ was oxidized by bubbling air through the reaction mixture. The reaction mixture was diluted with Et$_2$O (100 mL) and HCl (50 mL, 1.0 N). The aqueous layer was extracted with Et$_2$O (2 x 100 mL), organic layers were combined, dried over Na$_2$SO$_4$, filtered and
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Note: Unless indicated otherwise, in all examples reported in the manuscript the observed cyclization/reduction selectivity was >95:5 (>78:22 in three examples as indicated below). Unless indicated otherwise, in all examples reported in the manuscript the observed diastereoselectivity was >95:5 with respect to all three stereocenters (analysis of crude reaction mixtures; 60:40-75:25 in two examples reacting via ‘olefin-first’ mechanism). All compounds have been prepared as racemates.
Characterization Data for Starting Materials

**General Alkylation Procedure.** A previously published procedure was followed.\textsuperscript{19,20} The following procedure is representative: A 25 mL round-bottomed flask was charged with NaH (60%, 1.1 equiv, typically 1.1 mmol, 0.044 g), THF (typically, 2.0 mL), HMPA (2.0 equiv, typically, 1.1 mmol, 0.2 mL), and the reaction mixture was stirred at room temperature for 10 min. The reaction mixture was cooled to 0 °C, a solution of imide substrate (1.0 equiv) in THF (2.0 mL) was added, and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was cooled to 0 °C, a solution of alkyl halide (2.0 equiv) in THF (3.0 mL) was added, and the reaction mixture was stirred at room temperature for 18 h. The reaction mixture cooled to room temperature, diluted with H\textsubscript{2}O (2 mL), extracted with Et\textsubscript{2}O (1 x 30 mL). The organic layers were combined, washed with water (1 x 10 mL), sodium thiosulfate (1 x 10 mL), and brine (1 x 10 mL), dried and concentrated. Purification by chromatography using EtOAc/hexane (6/1-3/1) afforded the title product. All products were obtained as single olefin isomers.

**tert-Butyl (E)-1-methyl-2,5-dioxo-3-(4-phenylbut-3-en-1-yl)pyrrolidine-3-carboxylate (1).**
White solid. Mp = 82-83 °C. Yield 64% (0.22 g). \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) δ 7.32-7.27 (m, 4 H), 7.21 (t, J = 7.0 Hz, 1 H), 6.37 (d, J = 15.7 Hz, 1 H), 6.12 (dt, J = 15.6, 5.9 Hz, 1 H), 3.13 (d, J = 18.1 Hz, 1 H), 2.95 (s, 3 H), 2.68 (d, J = 18.2 Hz, 1 H), 2.38-2.25 (m, 1 H), 2.16 (dddd, J = 19.2, 13.7, 9.3, 4.4 Hz, 3 H), 1.45 (s, 9 H). \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) δ 176.12, 175.43, 168.45, 137.24, 131.27, 128.69, 128.42, 127.42, 126.18, 83.47, 55.64, 37.77, 32.99, 28.28, 27.92, 25.42. HRMS calcd for C\textsubscript{20}H\textsubscript{25}NO\textsubscript{4}Na (M\textsuperscript{+} + Na) 366.1676, found 366.1687.
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tert-Butyl (E)-3-(4-(4-methoxyphenyl)but-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (3). White solid. Mp = 93-94 °C. Yield 76 % (1.25 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.24 (d, $J = 8.2$ Hz, 2 H), 6.83 (d, $J = 8.1$ Hz, 2 H), 6.31 (d, $J = 15.8$ Hz, 1 H), 5.97 (dt, $J = 13.4$, 6.1 Hz, 1 H), 3.80 (s, 3 H), 3.12 (d, $J = 18.2$ Hz, 1 H), 2.93 (s, 3 H), 2.68 (d, $J = 18.2$ Hz, 1 H), 2.32-2.09 (m, 4 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 176.18, 175.48, 168.50, 159.11, 130.65, 130.08, 127.30, 126.21, 114.11, 83.43, 55.66, 55.43, 37.71, 33.09, 28.28, 27.92, 25.42. HRMS calcd for C$_{21}$H$_{27}$NO$_5$Na (M$^+ +$ Na) 396.1781, found 396.1794.

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\text{CO}_2t-\text{Bu} \quad \text{4-CF}_3\text{C}_6\text{H}_4
\]

\[5\]

tert-Butyl (E)-1-methyl-2,5-dioxo-3-(4-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)pyrrolidine-3-carboxylate (5). White solid. Mp = 88-89 °C. Yield 45% (0.095 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.54 (d, $J = 8.1$ Hz, 2 H), 7.40 (d, $J = 8.1$ Hz, 2 H), 6.41 (d, $J = 15.8$ Hz, 1 H), 6.24 (dt, $J = 15.8$, 6.2 Hz, 1 H), 3.13 (d, $J = 18.2$ Hz, 1 H), 2.96 (s, 3 H), 2.67 (d, $J = 18.1$ Hz, 1 H), 2.36-2.30 (m, 1 H), 2.22-2.12 (m, 3 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 176.02, 175.28, 168.35, 140.73, 131.35, 130.04, 129.28 (q, $J^F = 32.2$ Hz), 126.32, 125.67 (q, $J^F = 3.8$ Hz), 124.34 (q, $J^F = 270.1$ Hz), 83.60, 55.57, 37.89, 32.82, 28.26, 27.92, 25.43. $^{19}$F NMR (470 MHz, CDCl$_3$) δ -62.47. HRMS calcd for C$_{21}$H$_{24}$F$_3$NO$_4$Na (M$^+ +$ Na) 434.1550, found 434.1564.

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\text{CO}_2t-\text{Bu} \quad \text{4-Br-C}_6\text{H}_4
\]

\[7\]

tert-Butyl (E)-3-(4-(4-bromophenyl)but-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (7). White solid. Mp = 87-88 °C. Yield 76% (0.16 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.43 (d, $J = 8.3$ Hz, 2 H), 7.19 (d, $J = 8.4$ Hz, 2 H), 6.33 (d, $J = 15.8$ Hz, 1 H), 6.19-6.10 (m, 1 H), 3.14 (d, $J = 18.2$ Hz, 1 H), 2.97 (s, 3 H), 2.69 (d, $J = 18.2$ Hz, 1 H), 2.36-2.27 (m, 1 H), 2.22-
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2.11 (m, 3 H), 1.47 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 176.06, 175.34, 168.38, 136.18, 131.78, 130.11, 129.35, 127.71, 121.13, 83.53, 55.56, 37.79, 32.83, 28.24, 27.91, 25.43. HRMS calcd for C$_{20}$H$_{24}$BrNO$_4$Na (M$^+$ + Na) 444.0781, found 444.0793.

**tert-Butyl (E)-3-(4-(3,5-dichlorophenyl)but-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (9).** White solid. Mp = 101-103 °C. Yield 46% (0.092 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.24-7.07 (m, 3 H), 6.27 (d, $J = 15.8$ Hz, 1 H), 6.17 (dt, $J = 15.8$, 5.9 Hz, 1 H), 3.13 (d, $J = 18.2$ Hz, 1 H), 2.98 (s, 3 H), 2.64 (d, $J = 18.1$ Hz, 1 H), 2.35-2.27 (m, 1 H), 2.19-2.09 (m, 3 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 175.94, 175.25, 168.29, 140.28, 135.24, 131.72, 128.87, 127.20, 124.56, 83.63, 55.53, 37.93, 32.82, 28.16, 27.92, 25.47. HRMS calcd for C$_{20}$H$_{23}$Cl$_2$NO$_4$Na (M$^+$ + Na) 434.0896, found 434.0910.

**tert-Butyl (E)-1-methyl-3-(4-(naphthalen-2-yl)but-3-en-1-yl)-2,5-dioxopyrrolidine-3-carboxylate (11).** White solid. Mp = 117-118 °C. Yield 61% (0.18 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.82-7.73 (m, 3 H), 7.65 (s, 1 H), 7.53 (d, $J = 8.5$ Hz, 1 H), 7.43 (p, $J = 6.7$ Hz, 2 H), 6.54 (d, $J = 15.7$ Hz, 1 H), 6.25 (dt, $J = 15.7$, 6.3 Hz, 1 H), 3.14 (d, $J = 18.1$ Hz, 1 H), 2.94 (s, 3 H), 2.71 (d, $J = 18.1$ Hz, 1 H), 2.41-2.31 (m, 1 H), 2.27-2.14 (m, 3 H), 1.46 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 176.12, 175.41, 168.45, 134.69, 133.72, 132.95, 131.35, 128.86, 128.31, 128.03, 127.76, 126.35, 125.86, 125.84, 123.51, 83.46, 55.63, 37.74, 32.98, 28.40, 27.91, 25.42. HRMS calcd for C$_{24}$H$_{27}$NO$_4$Na (M$^+$ + Na) 416.1832, found 416.1846.
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**tert-Butyl 3-(but-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (13).** Colorless oil. Yield 45% (0.21 g). $^{1}$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.75 (ddt, $J = 16.5, 10.3, 6.1$ Hz, 1 H), 5.02 (d, $J = 17.1$ Hz, 1 H), 4.98 (d, $J = 10.1$ Hz, 1 H), 3.11 (d, $J = 18.2$ Hz, 1 H), 2.99 (s, 3 H), 2.62 (d, $J = 18.2$ Hz, 1 H), 2.14-2.07 (m, 2 H), 2.04-1.93 (m, 2 H), 1.44 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 176.06, 175.46, 168.41, 136.80, 115.92, 83.41, 55.67, 37.90, 32.80, 28.88, 25.36. HRMS calcd for C$_{14}$H$_{21}$NO$_4$Na (M$^+$ + Na) 290.1363, found 290.1371.

**Ethyl 3-(but-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (15).** Colorless oil. Yield 59% (0.10 g). $^{1}$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.75 (ddt, $J = 16.7, 10.3, 6.3$ Hz, 1 H), 5.03 (d, $J = 17.0$ Hz, 1 H), 4.99 (d, $J = 10.3$ Hz, 1 H), 4.22 (q, $J = 7.2$ Hz, 2 H), 3.20 (d, $J = 18.2$ Hz, 1 H), 3.01 (s, 3 H), 2.65 (d, $J = 18.2$ Hz, 1 H), 2.21-1.96 (m, 4 H), 1.27 (t, $J = 7.2$ Hz, 3 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 175.67, 175.18, 169.40, 136.56, 116.09, 62.66, 54.97, 37.81, 33.11, 28.85, 25.48, 14.15. HRMS calcd for C$_{12}$H$_{17}$NO$_4$Na (M$^+$ + Na) 262.1050, found 262.1057.

**(E)-3-(4-(4-Methoxyphenyl)but-3-en-1-yl)-1-methyl-3-phenylpyrrolidine-2,5-dione  (17).** White solid. Mp = 81-82 °C. Yield 60% (0.21 g). $^{1}$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.46 (d, $J = 7.8$ Hz, 2 H), 7.37 (t, $J = 7.6$ Hz, 2 H), 7.29 (t, $J = 7.4$ Hz, 1 H), 7.22 (d, $J = 8.2$ Hz, 2 H), 6.82 (d, $J = 8.7$ Hz, 2 H), 6.29 (d, $J = 15.7$ Hz, 1 H), 5.96 (dt, $J = 15.9, 6.0$ Hz, 1 H), 3.79 (s, 3 H), 3.16 (d,
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$J = 18.2$ Hz, 1 H), 3.00 (s, 3 H), 2.92 (d, $J = 18.2$ Hz, 1 H), 2.27-2.04 (m, 4 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 180.18, 175.60, 159.00, 140.61, 130.37, 130.12, 129.01, 127.66, 127.19, 126.37, 126.20, 114.04, 55.36, 51.74, 41.49, 39.30, 28.49, 25.13. HRMS calcd for C$_{22}$H$_{23}$NO$_3$Na (M$^+$ + Na) 372.1570, found 372.1580.

![Chemical structure](image)

(E)-3-(4-(Bromophenyl)but-3-en-1-yl)-1-methyl-3-phenylpyrrolidine-2,5-dione (19).

Colorless oil. Yield 40% (0.050 g). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.45 (d, $J = 7.8$ Hz, 2 H), 7.39 (d, $J = 8.4$ Hz, 2 H), 7.38 (t, $J = 8.0$ Hz, 2 H), 7.30 (t, $J = 7.3$ Hz, 1 H), 7.14 (d, $J = 8.4$ Hz, 2 H), 6.27 (d, $J = 15.7$ Hz, 1 H), 6.09 (ddd, $J = 15.9$, 8.0, 4.6 Hz, 1 H), 3.17 (d, $J = 18.2$ Hz, 1 H), 3.00 (s, 3 H), 2.98 (d, $J = 18.3$ Hz, 1 H), 2.28-2.15 (m, 3 H), 2.08 (tdd, $J = 13.3$, 12.0, 5.8, 3.6 Hz, 1 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 180.14, 175.55, 140.45, 136.27, 131.75, 129.91, 129.55, 129.11, 127.80, 127.66, 126.23, 121.04, 51.74, 41.63, 39.13, 28.53, 25.21. HRMS calcd for C$_{21}$H$_{20}$BrNO$_2$Na (M$^+$ + Na) 420.0570, found 420.0582.

![Chemical structure](image)

**tert-Butyl 1-methyl-2,5-dioxo-3-(4-phenylbut-3-yn-1-yl)pyrrolidine-3-carboxylate** (21).

Colorless oil. Yield 34% (0.045 g). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.39-7.33 (m, 2 H), 7.28 (m, 3 H), 3.14 (d, $J = 18.2$ Hz, 1 H), 2.98 (s, 3 H), 2.93 (d, $J = 18.2$ Hz, 1 H), 2.62-2.45 (m, 2 H), 2.32 (dtd, $J = 21.9$, 14.1, 6.9 Hz, 2 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 175.79, 175.40, 168.20, 131.66, 128.40, 128.11, 123.30, 87.75, 83.68, 82.29, 55.60, 37.99, 31.79, 27.90, 25.49, 15.34. HRMS calcd for C$_{20}$H$_{22}$NO$_4$Na (M$^+$ + Na) 364.1519, found 364.1530.
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**tert-Butyl (E)-1-methyl-2,6-dioxo-3-(4-phenylbut-3-en-1-yl)piperidine-3-carboxylate (33).**

Colorless oil. Yield 55% (0.195 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.33 (d, $J$ = 7.2 Hz, 2 H), 7.29 (t, $J$ = 7.6 Hz, 2 H), 7.20 (t, $J$ = 7.1 Hz, 1 H), 6.42 (d, $J$ = 15.8 Hz, 1 H), 6.19 (dt, $J$ = 15.8, 6.7 Hz, 1 H), 3.17 (s, 3 H), 2.76 (ddd, $J$ = 18.1, 5.0, 3.3 Hz, 1 H), 2.64 (ddd, $J$ = 18.1, 12.7, 5.5 Hz, 1 H), 2.47-2.38 (m, 1 H), 2.27-2.11 (m, 3 H), 2.10-1.96 (m, 2 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 171.92, 171.66, 169.99, 137.55, 130.80, 129.42, 128.65, 127.23, 126.12, 83.50, 55.17, 34.81, 30.11, 28.35, 27.99, 27.19, 25.89. HRMS calcd for C$_{21}$H$_{27}$NO$_4$Na (M$^+$ + Na) 380.1832, found 380.1842.

**tert-Butyl (E)-3-(4-(4-methoxyphenyl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (35).**

Colorless oil. Yield 88% (0.51 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.25 (d, $J$ = 5.4 Hz, 2 H), 6.83 (d, $J$ = 8.3 Hz, 2 H), 6.35 (d, $J$ = 15.9 Hz, 1 H), 6.04 (d, $J$ = 15.8 Hz, 1 H), 3.80 (s, 3 H), 3.16 (s, 3 H), 2.75 (dt, $J$ = 18.4, 3.9 Hz, 1 H), 2.69-2.59 (m, 1 H), 2.27-2.21 (m, 1 H), 2.20-2.10 (m, 2 H), 2.09-1.94 (m, 3 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 171.92, 171.66, 169.99, 137.55, 130.80, 129.42, 128.65, 127.23, 126.12, 83.50, 55.17, 34.81, 30.11, 28.35, 27.99, 27.19, 25.86. HRMS calcd for C$_{22}$H$_{29}$NO$_5$Na (M$^+$ + Na) 410.1938, found 410.1950.

**tert-Butyl (E)-1-methyl-2,6-dioxo-3-(4-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)piperidine-3-carboxylate (37).**

Colorless oil. Yield 42% (0.18 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.53 (d, $J$ = 5.5 Hz, 1 H), 7.00 (t, $J$ = 7.6 Hz, 1 H), 6.75 (d, $J$ = 15.8 Hz, 1 H), 6.19 (dt, $J$ = 15.8, 6.7 Hz, 1 H), 3.17 (s, 3 H), 2.76 (ddd, $J$ = 18.1, 5.0, 3.3 Hz, 1 H), 2.64 (ddd, $J$ = 18.1, 12.7, 5.5 Hz, 1 H), 2.47-2.38 (m, 1 H), 2.27-2.11 (m, 3 H), 2.10-1.96 (m, 2 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 171.92, 171.66, 169.99, 137.55, 130.80, 129.42, 128.65, 127.23, 126.12, 83.50, 55.17, 34.81, 30.11, 28.35, 27.99, 27.19, 25.86. HRMS calcd for C$_{24}$H$_{31}$FNO$_5$Na (M$^+$ + Na) 439.1938, found 439.1950.
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= 8.1 Hz, 2 H), 7.41 (d, $J = 8.1$ Hz, 2 H), 6.45 (d, $J = 15.9$ Hz, 1 H), 6.30 (dt, $J = 15.7$, 6.7 Hz, 1 H), 3.17 (s, 3 H), 2.80-2.72 (m, 1 H), 2.68-2.59 (m, 1 H), 2.52-2.42 (m, 1 H), 2.27-2.12 (m, 3 H), 2.10-1.96 (m, 2 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 171.83, 171.64, 169.92, 141.00, 132.28, 129.46, 128.90 (q, $J^F = 32.1$ Hz), 126.18, 125.49 (q, $J^F = 3.6$ Hz), 124.31 (q, $J^F = 270.0$ Hz), 83.64, 55.11, 34.61, 30.09, 28.38, 27.99, 27.20, 26.02. $^{19}$F NMR (470 MHz, CDCl$_3$) δ -62.44. HRMS calcd for C$_{22}$H$_{26}$F$_3$NO$_4$Na (M$^+$ + Na) 448.1706, found 448.1718.

**tert-Butyl (E)-3-(4-(4-bromophenyl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (39).** Colorless oil. Yield 45% (0.090 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.40 (d, $J = 8.5$ Hz, 2 H), 7.19 (d, $J = 8.5$ Hz, 2 H), 6.35 (d, $J = 15.8$ Hz, 1 H), 6.18 (dt, $J = 15.8$, 6.7 Hz, 1 H), 3.16 (s, 3 H), 2.75 (ddd, $J = 18.1$, 4.9, 3.2 Hz, 1 H), 2.64 (ddd, $J = 18.1$, 12.7, 5.5 Hz, 1 H), 2.42 (tt, $J = 12.9$, 6.1 Hz, 1 H), 2.24 (ddd, $J = 13.7$, 5.4, 3.2 Hz, 1 H), 2.21-2.09 (m, 2 H), 2.08-1.95 (m, 2 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 171.87, 171.65, 169.95, 136.50, 131.73, 130.32, 129.67, 127.67, 120.90, 83.58, 55.13, 34.69, 30.10, 28.34, 28.00, 27.20, 25.96. HRMS calcd for C$_{21}$H$_{26}$BrNO$_4$Na (M$^+$ + Na) 458.0937, found 458.0951.

![Diagram](image_url)

**tert-Butyl (E)-3-(4-(3,5-dichlorophenyl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (41).** Colorless oil. Yield 20% (0.036 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.18-7.17 (m, 3 H), 6.30 (d, $J = 16.0$ Hz, 1 H), 6.26-6.19 (m, 1 H), 3.17 (s, 3 H), 2.80-2.71 (m, 1 H), 2.71-2.57 (m, 1 H), 2.44 (dd, $J = 13.1$, 6.8 Hz, 1 H), 2.27-2.09 (m, 3 H), 2.08-1.93 (m, 2 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 171.79, 171.59, 169.87, 140.61, 135.18, 132.71, 128.44, 126.99, 124.53, 83.66, 55.09, 34.59, 30.09, 28.29, 28.00, 27.21, 26.07. HRMS calcd for C$_{21}$H$_{25}$Cl$_2$NO$_4$Na (M$^+$ + Na) 448.1053, found 448.1066.

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Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

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**tert-Butyl (E)-3-(4-(3,4-difluorophenyl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (43).** Colorless oil. Yield 29\% (0.057 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.13 (ddd, $J$ = 11.6, 7.6, 2.1 Hz, 1 H), 7.10-7.03 (m, 1 H), 7.03-6.95 (m, 1 H), 6.32 (d, $J$ = 15.7 Hz, 1 H), 6.12 (td, $J$ = 15.6, 13.2, 5.6 Hz, 1 H), 3.17 (s, 3 H), 2.76 (ddd, $J$ = 18.2, 5.2, 3.1 Hz, 1 H), 2.63 (ddd, $J$ = 18.2, 12.7, 5.5 Hz, 1 H), 2.42 (ddt, $J$ = 16.9, 12.7, 5.9 Hz, 1 H), 2.26-2.20 (m, 1 H), 2.20-2.09 (m, 2 H), 2.07-1.95 (m, 2 H), 1.45 (s, 9 H). 13C NMR (125 MHz, CDCl$_3$) δ 171.84, 171.64, 169.92, 150.81 (dd, $J^F = 120.4$, 12.6 Hz), 151.05 (d, $J^F = 121.0$ Hz), 134.84, 130.63 (d, $J^F = 1.9$ Hz), 128.85, 122.22 (q, $J^F = 3.5$ Hz), 117.33 (d, $J^F = 17.3$ Hz), 114.42 (d, $J^F = 17.5.0$ Hz), 83.62, 55.11, 30.09, 28.21, 28.06, 27.20, 26.00. 19F NMR (470 MHz, CDCl$_3$) δ -138.16 (d, $J = 20.9$ Hz), -139.97 (d, $J = 20.9$ Hz). HRMS calcd for C$_{21}$H$_{25}$F$_2$NO$_4$Na (M$^+$ + Na) 416.1644, found 416.1655.

**tert-Butyl (E)-3-(4-mesitylbut-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (45).** Colorless oil. Yield 51\% (0.102 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 6.85 (s, 2 H), 6.34 (d, $J = 16.0$ Hz, 1 H), 5.63 (dt, $J = 16.0$, 6.8 Hz, 1 H), 3.19 (s, 3 H), 2.76 (ddd, $J = 18.1$, 5.2, 3.3 Hz, 1 H), 2.70-2.61 (m, 1 H), 2.46-2.39 (m, 1 H), 2.26 (s, 3 H), 2.24 (s, 6 H), 2.15-1.99 (m, 3 H), 1.46 (s, 9 H). 13C NMR (125 MHz, CDCl$_3$) δ 171.96, 171.73, 170.03, 135.97, 135.93, 134.31, 133.97, 128.58, 128.36, 83.51, 55.22, 35.12, 30.11, 28.85, 28.01, 27.20, 25.98, 21.02. HRMS calcd for C$_{24}$H$_{33}$NO$_4$Na (M$^+$ + Na) 422.2302, found 422.2346.
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-14

**tert-Butyl (E)-3-(4-(2-fluorophenyl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (47).** Colorless oil. Yield 29% (0.055 g). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.43-7.38 (m, 1 H), 7.20-7.13 (m, 1 H), 7.07 (t, $J=7.5$ Hz, 1 H), 7.04-6.97 (m, 1 H), 6.56 (d, $J=15.9$ Hz, 1 H), 6.31-6.23 (m, 1 H), 3.17 (s, 3 H), 2.76 (ddd, $J=18.1$, 5.2, 3.2 Hz, 1 H), 2.64 (ddd, $J=18.1$, 12.6, 5.5 Hz, 1 H), 2.51-2.40 (m, 1 H), 2.29-2.12 (m, 3 H), 2.11-1.97 (m, 2 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 171.90, 171.65, 169.96, 160.10 (d, $J_F=248.7$ Hz), 132.16 (d, $J_F=4.4$ Hz), 128.44 (d, $J_F=8.3$ Hz), 127.23 (d, $J_F=4.0$ Hz), 125.28 (d, $J_F=12.5$ Hz), 124.16 (d, $J_F=3.5$ Hz), 123.25 (d, $J_F=3.9$ Hz), 115.78 (d, $J_F=22.3$ Hz), 83.55, 55.17, 34.69, 30.11, 28.77, 28.00, 27.19, 25.93. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -118.74. HRMS calcd for C$_{21}$H$_{26}$FNO$_4$Na (M$^+$ + Na) 398.1738, found 398.1751.

![Chemical Structure](image1.png)

**tert-Butyl (E)-3-(4-(benzo[d][1,3]dioxol-5-yl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (49).** Colorless oil. Yield 71% (0.285 g). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.87 (s, 1 H), 6.82-6.64 (m, 2 H), 6.32 (d, $J=15.7$, 1 H), 6.01 (dt, $J=13.8$, 6.8 Hz, 1 H), 5.93 (s, 2 H), 3.16 (s, 3 H), 2.75 (ddd, $J=18.1$, 5.2, 3.1 Hz, 1 H), 2.69-2.59 (m, 1 H), 2.45-2.31 (m, 1 H), 2.27-2.21 (m, 1 H), 2.19-2.09 (m, 2 H), 2.09-1.95 (m, 2 H), 1.44 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 171.91, 171.65, 169.97, 148.08, 146.92, 132.08, 130.34, 127.65, 120.52, 108.36, 105.54, 101.09, 83.48, 55.16, 34.89, 30.10, 28.22, 27.99, 27.18, 25.87. HRMS calcd for C$_{22}$H$_{27}$NO$_5$Na (M$^+$ + Na) 424.1730, found 424.1744.

SI-14
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI₂·H₂O

Shi, Lalancette, Szostak

tert-Butyl (E)-1-methyl-3-(4-(naphthalen-2-yl)but-3-en-1-yl)-2,6-dioxopiperidine-3-carboxylate (51). Colorless oil. Yield 44% (0.089 g). ¹H NMR (500 MHz, CDCl₃) δ 7.77 (t, J = 9.0 Hz, 3 H), 7.67 (s, 1 H), 7.56 (d, J = 8.6 Hz, 1 H), 7.48-7.38 (m, 2 H), 6.58 (d, J = 15.8 Hz, 1 H), 6.33 (dt, J = 15.7, 6.8 Hz, 1 H), 3.18 (s, 3 H), 2.77 (ddd, J = 18.0, 4.9, 3.3 Hz, 1 H), 2.65 (ddd, J = 18.1, 12.7, 5.5 Hz, 1 H), 2.48 (tt, J = 13.6, 6.6 Hz, 1 H), 2.32-2.16 (m, 3 H), 2.10 (ddd, J = 13.7, 11.3, 4.6 Hz, 1 H), 2.02 (td, J = 13.2, 5.2 Hz, 1 H), 1.46 (s, 9 H). ¹³C NMR (125 MHz, CDCl₃) δ 171.92, 171.68, 171.68, 135.02, 133.78, 132.90, 129.90, 128.26, 128.00, 127.76, 126.31, 125.74, 125.72, 123.59, 83.53, 55.19, 34.84, 30.12, 28.47, 28.00, 27.20, 25.92. HRMS calcd for C₂₅H₂₉NO₄Na (M⁺ + Na) 430.1988, found 430.2000.

tert-Butyl 3-(4,4-diphenylbut-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (53). Colorless oil. Yield 65% (0.282 g). ¹H NMR (500 MHz, CDCl₃) δ 7.36 (t, J = 7.3 Hz, 2 H), 7.30 (d, J = 7.3 Hz, 1 H), 7.25 (d, J = 9.5 Hz, 2 H), 7.21 (td, J = 6.5, 3.3 Hz, 3 H), 7.18-7.09 (m, 2 H), 6.06 (td, J = 7.2, 2.2 Hz, 1 H), 3.12 (s, 3 H), 2.68-2.52 (m, 2 H), 2.35-2.24 (m, 1 H), 2.16-2.03 (m, 4 H), 1.78 (td, J = 13.6, 13.0, 6.3 Hz, 1 H), 1.36 (s, 9 H). ¹³C NMR (125 MHz, CDCl₃) δ 171.92, 171.60, 169.88, 142.55, 142.47, 139.94, 129.90, 128.41, 128.26, 128.25, 127.33, 127.24, 127.18, 83.39, 55.11, 35.00, 29.99, 27.90, 27.18, 25.45, 25.21. HRMS calcd for C₂₇H₃₁NO₄Na (M⁺ + Na) 456.0145, found 456.0148.

SI-15
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI₂–H₂O

Shi, Lalancette, Szostak

**tert-Butyl 1-methyl-2,6-dioxo-3-((3E,5E)-6-phenylhexa-3,5-dien-1-yl)piperidine-3-carboxylate (55).** Colorless oil. Yield 61% (0.254 g). ¹H NMR (500 MHz, CDCl₃) δ 7.37 (d, J = 7.7 Hz, 2 H), 7.30 (t, J = 7.7 Hz, 2 H), 7.20 (t, J = 7.5 Hz, 1 H), 6.73 (dd, J = 15.7, 10.4 Hz, 1 H), 6.46 (d, J = 15.7 Hz, 1 H), 6.24 (dd, J = 15.1, 10.5 Hz, 1 H), 5.79 (dt, J = 14.6, 6.9 Hz, 1 H), 3.17 (s, 3 H), 2.76-2.71 (m, 1 H), 2.69-2.63 (m, 1 H), 2.37-2.33 (m, 1 H), 2.25-2.21 (m, 1 H), 2.16-2.09 (m, 2 H), 2.05-1.97 (m, 2 H), 1.45 (s, 9 H). ¹³C NMR (125 MHz, CDCl₃) δ 171.92, 171.64, 169.96, 137.58, 133.86, 131.49, 130.98, 129.05, 128.70, 127.41, 126.34, 83.51, 55.16, 50.15, 34.77, 30.10, 28.00, 27.21, 25.93. HRMS calcd for C₂₃H₂₉NO₄Na (M⁺ + Na) 406.1989, found 406.1999.

![](image_url)

**tert-Butyl (E)-3-(5-butoxy-5-oxopent-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (65).** Oil. Yield 76% (0.025 g). ¹H NMR (500 MHz, CDCl₃) δ 6.88 (dt, J = 15.6, 6.3 Hz, 1 H), 5.82 (d, J = 15.6 Hz, 1 H), 4.11 (t, J = 6.7 Hz, 2 H), 3.10 (d, J = 18.1 Hz, 1 H), 2.99 (s, 3 H), 2.57 (d, J = 18.1 Hz, 1 H), 2.32-2.24 (m, 1 H), 2.18-2.10 (m, 2 H), 2.06-2.00 (m, 1 H), 1.63-1.57 (m, 2 H), 1.43 (s, 9 H), 1.38 (dd, J = 15.0, 7.4 Hz, 2 H), 0.92 (t, J = 7.4 Hz, 3 H). ¹³C NMR (125 MHz, CDCl₃) δ 175.64, 175.02, 168.07, 168.07, 166.38, 146.40, 122.57, 83.72, 64.39, 55.40, 38.14, 32.03, 30.81, 27.87, 27.28, 25.42, 19.27, 13.82. HRMS calcd for C₁₉H₂₉NO₆Na (M⁺ + Na) 390.1887, found 390.1897.

![](image_url)

**tert-Butyl (E)-3-(5-butoxy-5-oxopent-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (67).** Oil. Yield 68% (0.065 g). ¹H NMR (500 MHz, CDCl₃) δ 6.92 (dt, J = 15.3, 6.7 Hz, 1 H), 5.84 (d, J = 15.7 Hz, 1 H), 4.11 (t, J = 6.7 Hz, 2 H), 3.15 (s, 3 H), 2.73 (ddd, J = 18.3, 5.3, 3.1 Hz, 1 H), 2.60 (ddd, J = 18.2, 12.8, 5.5 Hz, 1 H), 2.50-2.39 (m, 1 H), 2.18 (tdd, J = 18.1, 8.5, 4.6 Hz,
2 H), 2.04 (dq, $J = 25.5$, 13.7, 4.8 Hz, 2 H), 1.93 (td, $J = 13.2$, 5.2 Hz, 1 H), 1.62 (p, $J = 6.9$ Hz, 2 H), 1.42 (s, 9 H), 1.41-1.34 (m, 2 H), 0.92 (t, $J = 7.4$ Hz, 3 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 171.66, 171.42, 169.66, 166.60, 147.43, 122.09, 83.73, 64.30, 54.90, 33.52, 30.81, 29.98, 27.93, 27.47, 27.15, 26.17, 19.26, 13.82. HRMS calcd for C$_{20}$H$_{31}$NO$_6$Na ($M^+ +$ Na) 404.2044, found 404.2052.
Reductive Cyclization of Cyclic Imides using SmI₂–H₂O

**tert-Butyl (3aR,6R,6aR)-6-benzyl-6a-hydroxy-1-methyl-2-oxohexahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (Chart 1, 2)**

According to the general procedure, the reaction of 1 (0.10 mmol), samarium(II) iodide (0.30 mmol, 3.0 equiv, 3.0 mL, 0.10 M) and H₂O (1.08 mL, 600 equiv) in THF (2.0 mL) for 15 min afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 94% yield (32.4 mg). Recrystallization from CH₂Cl₂/hexanes. White solid. Mp = 134-135 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ¹H NMR (500 MHz, CDCl₃) δ 7.29 (t, J = 7.4 Hz, 2 H), 7.20 (t, J = 7.4 Hz, 1 H), 7.16 (d, J = 7.1 Hz, 2 H), 4.07 (s, 1 H), 3.15 (dd, J = 12.1, 2.6 Hz, 1 H), 2.95 (d, J = 17.3 Hz, 4 H), 2.42-2.26 (m, 3 H), 2.18 (td, J = 12.7, 6.5 Hz, 1 H), 1.74-1.67 (m, 1 H), 1.65-1.60 (m, 1 H), 1.48 (s, 9 H), 1.26 (tq, J = 12.1, 6.2 Hz, 1 H). ¹³C NMR (125 MHz, CDCl₃) δ 174.13, 173.17, 140.42, 128.84, 128.63, 126.36, 100.25, 83.19, 56.79, 54.03, 42.47, 36.20, 34.15, 28.14, 27.89, 27.55. HRMS calcd for C₂₀H₂₇NO₄Na (M⁺ + Na) 368.1832, found 368.1842.

**tert-Butyl (3aR,6R,6aR)-6a-hydroxy-6-(4-methoxybenzyl)-1-methyl-2-oxohexahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (Chart 1, 4)**

According to the general procedure, the reaction of 3 (0.10 mmol), samarium(II) iodide (0.30 mmol, 3.0 equiv, 3.0 mL, 0.10 M) and H₂O (1.08 mL, 600 equiv) in THF (2.0 mL) for 15 min afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 93% yield (35.0 mg).
Recrystallization from CH$_2$Cl$_2$/hexanes. White solid. Mp = 149-151 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. $^1$H NMR (500 MHz, CD$_3$C(O)CD$_3$) δ 7.15 (d, $J = 8.5$ Hz, 2 H), 6.85 (d, $J = 8.6$ Hz, 2 H), 5.05 (s, 1 H), 3.76 (s, 3 H), 3.13-3.05 (m, 2 H), 2.85 (s, 3 H), 2.47 (tdd, $J = 11.8$, 5.7, 2.9 Hz, 1 H), 2.43-2.32 (m, 2 H), 2.18 (d, $J = 17.4$ Hz, 1 H), 1.60 (dtt, $J = 12.8$, 6.9, 3.8 Hz, 2 H), 1.45 (s, 9 H), 1.32 (qd, $J = 11.6$, 7.3 Hz, 1 H). $^{13}$C NMR (125 MHz, CD$_3$C(O)CD$_3$) δ 172.96, 171.83, 158.02, 133.05, 129.42, 113.56, 100.70, 80.58, 57.48, 54.41, 53.33, 40.62, 34.49, 34.06, 27.62, 27.13, 26.81. HRMS calcd for C$_{21}$H$_{29}$NO$_5$Na (M$^+$ + Na) 398.1938, found 398.1950.

terr-Butyl (3aR,6R,6aR)-6a-hydroxy-1-methyl-2-oxo-6-(4-(trifluoromethyl)benzyl)hexahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (Chart 1, 6)

According to the general procedure, the reaction of 5 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H$_2$O (0.54 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et$_2$O/HCl (1.0 N) the title compound in 93% yield (19.2 mg). Recrystallization from CH$_2$Cl$_2$/hexanes. White solid. Mp = 160-162 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.54 (d, $J = 7.9$ Hz, 2 H), 7.28 (d, $J = 8.0$ Hz, 2 H), 4.22 (s, 1 H), 3.21 (d, $J = 9.1$ Hz, 1H), 3.02-2.88 (m, 4 H), 2.45-2.30 (m, 3 H), 2.19 (td, $J = 12.7$, 6.5 Hz, 1 H), 1.71 (dd, $J = 13.2$, 5.8 Hz, 1 H), 1.60-1.54 (m, 1 H), 1.48 (s, 9 H), 1.26 (dq, $J = 11.5$, 5.8 Hz, 1 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 173.99, 173.23, 144.57, 129.13, 128.80 (q, $J^{CF} = 32.2$ Hz), 125.57 (q, $J^{CF} = 3.6$ Hz), 124.36 (q, $J^{CF} = 271.6$ Hz), 100.11, 83.28, 56.66, 53.67, 42.35, 36.04, 34.10, 28.11, 27.89, 27.40. $^{19}$F NMR (470 MHz, CDCl$_3$) δ -62.38. HRMS calcd for C$_{23}$H$_{26}$F$_3$NO$_4$Na (M$^+$ + Na) 436.1706, found 436.1715.
**tert-Butyl (3aR,6R,6aR)-6-(4-bromobenzyl)-6a-hydroxy-1-methyl-2-oxohexahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (Chart 1, 8)**

According to the general procedure, the reaction of 7 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H₂O (0.54 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 75% yield (16.0 mg). Recrystallization from CH₂Cl₂/hexanes. White solid. Mp = 179-180 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by X-ray analysis.¹H NMR (500 MHz, CD₃C(O)CD₃) δ 7.47 (d, J = 8.1 Hz, 2 H), 7.22 (d, J = 8.0 Hz, 2 H), 5.11 (s, 1 H), 3.14 (d, J = 11.1 Hz, 1 H), 3.08 (d, J = 17.4 Hz, 1 H), 2.85 (s, 3 H), 2.53-2.36 (m, 3 H), 2.19 (d, J = 17.4 Hz, 1 H), 1.63-1.56 (m, 2 H), 1.45 (s, 9 H), 1.39-1.31 (m, 1 H).¹³C NMR (125 MHz, CD₃C(O)CD₃) δ 174.00, 172.74, 141.72, 132.17, 131.70, 120.11, 101.64, 81.63, 58.39, 53.85, 41.53, 35.74, 35.04, 28.44, 28.13, 27.79. HRMS calcd for C₂₀H₂₆BrNO₄Na (M⁺ + Na) 446.0937, found 446.0938.

**tert-Butyl (3aR,6R,6aR)-6-(3,5-dichlorobenzyl)-6a-hydroxy-1-methyl-2-oxohexahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (Chart 1, 10)**

According to the general procedure, the reaction of 9 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H₂O (0.54 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 90% yield (18.7 mg).
Recrystallization from CH$_2$Cl$_2$/hexanes. White solid. Mp = 189-190 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.21 (s, 1 H), 7.06 (s, 2 H), 3.11 (d, J = 10.7 Hz, 1 H), 2.94 (d, J = 17.5 Hz, 1 H), 2.93 (s, 3 H), 2.37 (d, J = 17.9 Hz, 1 H), 2.33-2.12 (m, 3 H), 1.73 (dd, J = 13.4, 6.1 Hz, 1 H), 1.62 (dt, J = 11.6, 5.6 Hz, 1 H), 1.48 (s, 9 H), 1.23 (dq, J = 12.1, 5.8 Hz, 1 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 173.99, 173.14, 137.77, 133.54, 132.12, 128.14, 127.63, 127.45, 127.17, 127.00, 126.10, 125.43, 100.19, 83.08, 56.68, 53.83, 42.32, 36.21, 34.01, 28.00, 27.83, 27.48. HRMS calcd for C$_{20}$H$_{25}$Cl$_2$NO$_4$Na (M$^+$ + Na) 436.1053, found 436.1068.

tert-Butyl (3aR,6R,6aR)-6a-hydroxy-1-methyl-6-(naphthalen-2-ylmethyl)-2-oxohexahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (Chart 1, 12)

According to the general procedure, the reaction of 11 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H$_2$O (0.54 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et$_2$O/HCl (1.0 N) the title compound in 93% yield (18.3 mg). Recrystallization from CH$_2$Cl$_2$/hexanes. White solid. Mp = 193-195 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.84-7.74 (m, 3 H), 7.61 (s, 1 H), 7.45 (p, J = 7.0 Hz, 2 H), 7.30 (d, J = 8.4 Hz, 1 H), 4.14 (s, 1 H), 3.32 (d, J = 8.4 Hz, 1 H), 3.01 (s, 3 H), 2.70 (d, J = 18.0 Hz, 1 H), 2.56-2.43 (m, 2 H), 2.41 (d, J = 18.0 Hz, 1 H), 2.18 (td, J = 12.7, 6.6 Hz, 1 H), 1.71 (dd, J = 13.4, 6.1 Hz, 1 H), 1.64-1.58 (m, 1 H), 1.49 (s, 9 H), 1.36-1.25 (m, 1 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 173.99, 173.14, 137.77, 133.54, 132.12, 128.14, 127.63, 127.45, 127.17, 127.00, 126.10, 125.43, 100.19, 83.08, 56.68, 53.83, 42.32, 36.21, 34.01, 28.00, 27.83, 27.48. HRMS calcd for C$_{24}$H$_{29}$NO$_4$Na (M$^+$ + Na) 418.1989, found 418.2002.
**Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI₂–H₂O**

**Shi, Lalancette, Szostak**

**tert-Butyl (3aR,6S,6aR)-6a-hydroxy-1,6-dimethyl-2-oxohexahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (Chart 1, 14)**

![Diagram](image)

According to the general procedure, the reaction of 13 (0.1 mmol), samarium(II) iodide (0.80 mmol, 8.0 equiv, 8.0 mL, 0.10 M) and H₂O (2.16 mL, 1200 equiv) in THF (1.0 mL) for 1 h afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 77% yield (20.7 mg). Recrystallization from CH₂Cl₂/hexanes. White solid. Dr >95:5. Cyclization/reduction selectivity = 91:9. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ¹H NMR (500 MHz, CDCl₃) δ 3.88 (s, 1 H), 2.95 (d, J = 17.8 Hz, 1 H), 2.91 (s, 3 H), 2.39-2.33 (m, 2 H), 2.23 (dt, J = 11.7, 6.6 Hz, 1 H), 1.86 (dtd, J = 12.3, 6.2, 2.4 Hz, 1 H), 1.75 (ddd, J = 13.0, 5.9, 2.3 Hz, 1 H), 1.50 (s, 9 H), 1.46 (d, J = 4.7 Hz, 1 H), 1.07 (d, J = 7.1 Hz, 3 H). ¹³C NMR (125 MHz, CDCl₃) δ 174.06, 173.01, 100.89, 83.03, 56.87, 46.31, 42.59, 34.25, 30.65, 28.14, 27.62, 14.73. HRMS calcd for C₁₄H₂₃NO₄Na (M⁺ + Na) 292.1519, found 292.1527.

**Ethyl (3aR,6S,6aR)-6a-hydroxy-1,6-dimethyl-2-oxohexahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (Chart 1, 16)**

![Diagram](image)

According to the general procedure, the reaction of 15 (0.1 mmol), samarium(II) iodide (0.80 mmol, 8.0 equiv, 8.0 mL, 0.10 M) and H₂O (2.16 mL, 1200 equiv) in THF (1.0 mL) for 1 h afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 55% yield (13.3 mg). Recrystallization from CH₂Cl₂/hexanes. White solid. Dr >95:5. Cyclization/reduction selectivity = 92:8. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ¹H NMR (500 MHz, CDCl₃) δ 4.23 (q, J = 7.1 Hz, 2 H), 3.56 (s, 1 H),
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using \( \text{SmI}_2 \cdot \text{H}_2\text{O} \)
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3.00 (d, \( J = 17.8 \text{ Hz}, 1 \text{ H} \)), 2.89 (s, 3 H), 2.41 (dt, \( J = 12.7, 6.1 \text{ Hz}, 1 \text{ H} \)), 2.35 (d, \( J = 17.7 \text{ Hz}, 1 \text{ H} \)), 2.21 (tt, \( J = 12.8, 6.6 \text{ Hz}, 1 \text{ H} \)), 1.86 (dttd, \( J = 12.6, 6.4, 2.5 \text{ Hz}, 1 \text{ H} \)), 1.75 (dddt, \( J = 12.7, 5.7, 2.0 \text{ Hz}, 1 \text{ H} \)), 1.37-1.31 (m, 1 H), 1.30 (t, \( J = 7.0 \text{ Hz}, 3 \text{ H} \)), 1.06 (d, \( J = 7.0 \text{ Hz}, 3 \text{ H} \)). \(^{13}\text{C NMR} \ (125 \text{ MHz, CDCl}_3) \delta 174.67, 172.93, 101.03, 62.02, 56.58, 46.21, 42.42, 34.23, 30.75, 27.74, 14.66, 14.28. \) HRMS calcd for \( \text{C}_{12}\text{H}_{19}\text{NO}_4\text{Na} \ (M^+ + \text{Na}) \) 264.1206, found 264.1227.

\((3aS,6R,6aR)-6a\text{-Hydroxy-6-(4-methoxybenzyl)-1-methyl-3a-phenylhexahydrocyclopenta[b]pyrrol-2(1H)-one} \) (Chart 1, 18)

According to the general procedure, the reaction of 17 (0.1 mmol), samarium(II) iodide (0.80 mmol, 8.0 equiv, 8.0 mL, 0.10 M) and \( \text{H}_2\text{O} \) (2.16 mL, 1200 equiv) in THF (1.0 mL) for 1 h afforded after work-up with \( \text{Et}_2\text{O}/\text{HCl} \) (1.0 N) the title compound in 92% yield (32.5 mg). Recrystallization from \( \text{CH}_2\text{Cl}_2/\text{hexanes} \). White solid. \( \text{Mp} = 142-144 \text{ °C} \). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. \(^1\text{H NMR} \ (500 \text{ MHz, CDCl}_3) \delta 7.41 \ (t, \( J = 7.6 \text{ Hz}, 2 \text{ H} \)), 7.32 \ (t, \( J = 7.5 \text{ Hz}, 1 \text{ H} \)), 7.27 \ (d, \( J = 7.8 \text{ Hz}, 2 \text{ H} \)), 7.09 \ (d, \( J = 8.2 \text{ Hz}, 2 \text{ H} \)), 6.83 \ (d, \( J = 8.2 \text{ Hz}, 2 \text{ H} \)), 3.79 \ (s, 3 \text{ H} \)), 3.09-3.03 \ (m, 1 \text{ H} \)), 2.96 \ (s, 3 \text{ H} \)), 2.90 \ (d, \( J = 18.0 \text{ Hz}, 1 \text{ H} \)), 2.71 \ (d, \( J = 18.0 \text{ Hz}, 1 \text{ H} \)), 2.47-2.34 \ (m, 2 \text{ H} \)), 2.33-2.25 \ (m, 1 \text{ H} \)), 1.94-1.73 \ (m, 3 \text{ H} \)), 1.48 \ (dp, \( J = 17.3, 6.2, 5.7 \text{ Hz}, 1 \text{ H} \)). \(^{13}\text{C NMR} \ (125 \text{ MHz, CDCl}_3) \delta 173.95, 158.15, 142.20, 132.38, 129.73, 129.46, 127.82, 126.53, 113.99, 100.85, 56.26, 55.38, 54.31, 46.00, 35.73, 34.10, 28.56, 27.71. \) HRMS calcd for \( \text{C}_{22}\text{H}_{25}\text{NO}_3\text{Na} \ (M^+ + \text{Na}) \) 374.1727, found 374.1738.

\((3aS,6R,6aR)-6-(4\text{-Bromobenzyl)-6a-hydroxy-1-methyl-3a-phenylhexahydrocyclopenta[b]pyrrol-2(1H)-one} \) (Chart 1, 20)

SI-23
According to the general procedure, the reaction of 19 (0.1 mmol), samarium(II) iodide (0.80 mmol, 8.0 equiv, 8.0 mL, 0.10 M) and H₂O (2.16 mL, 1200 equiv) in THF (1.0 mL) for 1 h afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 89% yield (35.5 mg). Recrystallization from CH₂Cl₂/hexanes. White solid. Mp = 137-139 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2D NMR experiments and confirmed by an X-ray analysis of a derivative. 

\[
\begin{align*}
\text{1H NMR (500 MHz, CD}_3\text{C(O)CD}_3\text{)} & \delta 7.47 (d, J = 8.3 Hz, 2 H), 7.39 - 7.27 (m, 4 H), 7.24 (d, J = 8.5 Hz, 2 H), 7.22 (t, J = 6.5 Hz, 1 H), 4.22 (s, 1 H), 3.16 (dd, J = 12.4, 2.8 Hz, 1 H), 2.91 (s, 3 H), 2.75 (d, J = 17.6 Hz, 1 H), 2.60 (d, J = 17.5 Hz, 1 H), 2.49 (t, J = 12.2 Hz, 1 H), 2.43-2.33 (m, 2 H), 1.88 (ddd, J = 13.0, 6.6, 1.9 Hz, 1 H), 1.68 (dtd, J = 12.9, 6.5, 2.0 Hz, 1 H), 1.54 (ddt, J = 18.4, 11.6, 6.7 Hz, 1 H). \\
\text{13C NMR (126 MHz, CD}_3\text{C(O)CD}_3\text{)} & \delta 173.87, 144.61, 141.67, 132.14, 131.80, 128.87, 128.12, 127.20, 120.07, 101.31, 55.89, 54.92, 46.13, 36.42, 36.32, 28.25, 27.75. HRMS calcd for C₂₁H₂₂BrNO₂Na (M⁺ + Na) 422.0726, found 422.0732.
\end{align*}
\]

**tert-Butyl (3aR,6aR)-6-((E)-benzylidene)-6a-hydroxy-1-methyl-2-oxohexahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (Chart 1, 22)**

According to the general procedure, the reaction of 21 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H₂O (0.54 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 65% yield (11.2 mg). Colorless oil. Dr >95:5. Cyclization/reduction selectivity = 75:25. E/Z >95:5. Stereochemistry determined by 2D NMR experiments and confirmed by an X-ray analysis of a derivative. 

\[
\begin{align*}
\text{1H NMR (500 MHz, CD}_3\text{C(O)CD}_3\text{)} & \delta 7.47 (d, J = 8.3 Hz, 2 H), 7.39 - 7.27 (m, 4 H), 7.24 (d, J = 8.5 Hz, 2 H), 7.22 (t, J = 6.5 Hz, 1 H), 4.22 (s, 1 H), 3.16 (dd, J = 12.4, 2.8 Hz, 1 H), 2.91 (s, 3 H), 2.75 (d, J = 17.6 Hz, 1 H), 2.60 (d, J = 17.5 Hz, 1 H), 2.49 (t, J = 12.2 Hz, 1 H), 2.43-2.33 (m, 2 H), 1.88 (ddd, J = 13.0, 6.6, 1.9 Hz, 1 H), 1.68 (dtd, J = 12.9, 6.5, 2.0 Hz, 1 H), 1.54 (ddt, J = 18.4, 11.6, 6.7 Hz, 1 H). \\
\text{13C NMR (126 MHz, CD}_3\text{C(O)CD}_3\text{)} & \delta 173.87, 144.61, 141.67, 132.14, 131.80, 128.87, 128.12, 127.20, 120.07, 101.31, 55.89, 54.92, 46.13, 36.42, 36.32, 28.25, 27.75. HRMS calcd for C₂₁H₂₂BrNO₂Na (M⁺ + Na) 422.0726, found 422.0732.
\end{align*}
\]
NMR (500 MHz, CDCl₃) δ 7.44-7.37 (m, 4 H), 7.28 (m, 1 H), 6.78 (s, 1 H), 3.70 (s, 1 H), 3.08 (d, J = 17.3 Hz, 1 H), 2.94-2.87 (m, 1 H), 2.80 (s, 3 H), 2.66-2.58 (m, 1 H), 2.44 (d, J = 17.3 Hz, 1 H), 2.37 (dd, J = 14.4, 9.0, 5.9 Hz, 1 H), 1.86-1.78 (m, 1 H), 1.45 (s, 9 H). ¹³C NMR (125 MHz, CDCl₃) δ 172.95, 172.53, 140.62, 136.50, 129.05, 128.59, 127.58, 125.89, 98.76, 82.87, 55.25, 39.59, 34.39, 28.10, 27.63, 24.49. HRMS calcd for C₂₀H₂₅NO₄Na (M⁺ + Na) 366.1676, found 366.1684.

**tert-Butyl (4aR,7R,7aR)-7-benzyl-7a-hydroxy-1-methyl-2-oxo-octahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 34)**

According to the general procedure, the reaction of 33 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H₂O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 86% yield (15.5 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ¹H NMR (500 MHz, CDCl₃) δ 7.36 (t, J = 7.3 Hz, 1 H), 7.20 (t, J = 7.4 Hz, 2 H), 7.16 (d, J = 7.1 Hz, 2 H) 5.57 (s, 1 H), 3.04 (s, 3 H), 2.78 (d, J = 6.4 Hz, 1 H), 2.47 (dd, J = 7.3, 4.3 Hz, 1 H), 2.40-2.35 (m, 2 H), 2.29-2.23 (m, 2 H), 2.08-2.05 (m, 2 H), 1.94-1.82 (m, 3 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl 7-benzyl-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (34") using TsOH (1.0 equiv) in CH₂Cl₂ (1.0 mL) at room temperature for 3 h. Colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 7.30 (t, J = 7.4 Hz, 2 H), 7.26-7.17 (m, 3 H), 3.74 (d, J = 16.0 Hz, 1 H), 3.52 (d, J = 16.0 Hz, 1 H), 3.28 (s, 3 H), 2.53 (ddt, J = 17.7, 14.8, 9.3 Hz, 3 H), 2.39 (ddd, J = 12.9, 6.5, 4.3 Hz, 1 H), 2.28 (dd, J = 12.9, 8.4 Hz, 1 H), 2.14 (dd, J = 15.5, 9.1 Hz, 1 H), 1.80-1.69 (m, 2 H), 1.46 (s, 9 H). ¹³C NMR (125 MHz, 500 MHz, CDCl₃) δ 173.95, 170.43, 138.92, 137.58, 128.58, 128.26, 126.31, 121.76, 81.27, 57.19, 34.75, 34.21, 34.12, 31.40, 30.44, 28.08. HRMS calcd for C₂₁H₂₅NO₄Na (M⁺ + Na) 364.1883, found 364.1894.
**Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI₂–H₂O**  
Shi, Lalancette, Szostak

**tert-Butyl (4aR,7R,7aR)-7a-hydroxy-7-(4-methoxybenzyl)-1-methyl-2-oxooctahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 36)**

According to the general procedure, the reaction of 35 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H₂O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 85% yield (16.5 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2D NMR experiments and confirmed by an X-ray analysis of a derivative. 

1H NMR (500 MHz, CDCl₃) δ 7.04 (d, J = 7.9 Hz, 2 H), 6.81 (d, J = 8.2 Hz, 2 H), 5.54 (s, 1 H), 3.77 (s, 3 H), 3.02 (s, 3 H), 2.75 (d, J = 12.8 Hz, 1 H), 2.56-2.47 (m, 2 H), 2.32 (dd, J = 18.6, 9.2 Hz, 1 H), 2.23-2.14 (m, 2 H), 2.05 (d, J = 7.4 Hz, 2 H), 1.92-1.81 (m, 3 H), 1.46 (s, 9 H). The title compound has been fully characterized after dehydration to tert-butyl 7-(4-methoxybenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (36") using TsOH (1.0 equiv) in CH₂Cl₂ (1.0 mL) at room temperature for 3 h. Colorless oil. 1H NMR (500 MHz, CDCl₃) δ 7.10 (d, J = 8.2 Hz, 2 H), 6.83 (d, J = 8.2 Hz, 2 H), 3.79 (s, 3 H), 3.66 (d, J = 15.9 Hz, 1 H), 3.45 (d, J = 15.8 Hz, 1 H), 3.27 (s, 3 H), 2.54 (dd, J = 16.4, 8.0 Hz, 3 H), 2.42-2.33 (m, 1 H), 2.30-2.22 (m, 1 H), 2.13 (dd, J = 15.1, 9.3 Hz, 1 H), 1.73 (tt, J = 18.9, 9.4 Hz, 2 H), 1.45 (s, 9 H). 13C NMR (125 MHz, CDCl₃) δ 174.06, 170.53, 158.23, 137.36, 130.93, 129.27, 122.37, 114.09, 81.34, 57.29, 55.42, 34.32, 34.21, 34.15, 33.96, 31.51, 30.55, 28.17. HRMS calcd for C₂₂H₂₉NO₄Na (M⁺ + Na) 394.1989, found 394.1998.

**tert-Butyl (4aR,7R,7aR)-7a-hydroxy-1-methyl-2-oxo-7-(4-(trifluoromethyl)benzyl)octahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 38)**
According to the general procedure, the reaction of 37 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et2O/HCl (1.0 N) the title compound in 86% yield (18.5 mg). Recrystallization from CH2Cl2/hexanes. White solid. Mp = 185-187 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.54 (d, $J$ = 7.9 Hz, 2 H), 7.25 (d, $J$ = 7.6 Hz, 2 H), 5.60 (s, 1 H), 3.04 (s, 3 H), 2.87 (dd, $J$ = 13.8, 3.5 Hz, 1 H), 2.63-2.51 (m, 2 H), 2.36-2.22 (m, 3 H), 2.20-1.99 (m, 3 H), 1.90 (tdd, $J$ = 21.1, 9.1, 4.4 Hz, 2 H), 1.48 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 175.46, 169.46, 144.17, 129.09, 125.60 (q, $J_{CF}$ = 3.7 Hz), 124.35 (q, $J_{CF}$ = 272.2 Hz), 96.20, 83.30, 54.91, 50.12, 40.03, 33.30, 29.11, 28.08, 28.04, 26.91, 26.83. $^{19}$F NMR (470 MHz, CDCl$_3$) δ -62.40. HRMS calcld for C$_{22}$H$_{28}$F$_3$NO$_4$Na (M$^+$ + Na) 450.1863, found 450.1872.

**tert-Butyl (4aR,7R,7aR)-7-(4-bromobenzyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 40)**

According to the general procedure, the reaction of 39 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et2O/HCl (1.0 N) the title compound in 76% yield (16.7 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.39 (d, $J$ = 8.0 Hz, 2 H), 7.01 (d, $J$ = 7.5 Hz, 2 H), 5.57 (s, 1 H), 3.02 (s, 3 H), 2.76 (d, $J$ = 11.6 Hz, 2 H), 2.20 (tdd, $J$ = 21.1, 9.1, 4.4 Hz, 2 H), 1.48 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 175.46, 169.46, 144.17, 129.15 (q, $J_{CF}$ = 32.7 Hz), 129.09, 125.60 (q, $J_{CF}$ = 3.7 Hz), 124.35 (q, $J_{CF}$ = 272.2 Hz), 96.20, 83.30, 54.91, 50.12, 40.03, 33.30, 29.11, 28.08, 28.04, 26.91, 26.83. $^{19}$F NMR (470 MHz, CDCl$_3$) δ -62.40. HRMS calcld for C$_{22}$H$_{28}$F$_3$NO$_4$Na (M$^+$ + Na) 450.1863, found 450.1872.
Hz, 1 H), 2.59-2.52 (m, 2 H), 2.36-2.27 (m, 3 H), 2.07-2.00 (m, 2 H), 1.95-1.85 (m, 3 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to tert-butyl 7-(4-bromobenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (40") using TsOH (1.0 equiv) in CH2Cl2 (1.0 mL) at room temperature for 3 h. Colorless oil. 1H NMR (500 MHz, CDCl3) δ 7.41 (d, J = 8.0 Hz, 2 H), 7.08 (d, J = 8.0 Hz, 2 H), 3.68 (d, J = 16.2 Hz, 1 H), 3.46 (d, J = 16.2 Hz, 1 H), 3.25 (s, 3 H), 2.52 (dt, J = 17.2, 9.8 Hz, 3 H), 2.43-2.34 (m, 1 H), 2.27 (dd, J = 12.4, 8.8 Hz, 1 H), 2.11 (dd, J = 15.2, 9.2 Hz, 1 H), 1.73 (dt, J = 21.9, 9.6 Hz, 2 H), 1.45 (s, 9 H). 13C NMR (125 MHz, 500 MHz, CDCl3) δ 173.86, 170.44, 138.07, 138.04, 131.76, 130.09, 120.86, 120.23, 81.49, 57.30, 34.32, 34.23, 34.17, 34.14, 31.41, 30.49, 28.18. HRMS calcd for C21H26BrNO3Na (M+ + Na) 442.0988, found 442.0999.

**tert-Butyl (4aR,7R,7aR)-7-(3,5-dichlorobenzyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 42)**

According to the general procedure, the reaction of 41 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et2O/HCl (1.0 N) the title compound in 71% yield (15.2 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. 1H NMR (500 MHz, CDCl3) δ 7.20 (s, 1 H), 7.03 (s, 2 H), 5.58 (s, 1 H), 3.03 (s, 3 H), 2.77 (d, J = 13.7 Hz, 1 H), 2.52 (dd, J = 17.6, 5.2 Hz, 2 H), 2.35-2.16 (m, 3 H), 2.27 (d, J = 17.6 Hz, 1 H) 2.10-2.04 (m, 1 H), 2.03-1.90 (m, 2 H), 1.88-1.82 (m, 1 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to tert-butyl 7-(3,5-dichlorobenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b] pyridine-4a-carboxylate (42") using TsOH (1.0 equiv) in CH2Cl2 (1.0 mL) at room temperature for 3 h. Colorless oil. 1H NMR (500 MHz, CDCl3) δ 7.23 (s, 1 H), 7.08 (s, 2 H), 3.73 (d, J = 16.3 Hz, 1 H), 3.46 (d, J = 16.3 Hz, 1 H), 3.25 (s, 3 H), 2.59-2.48 (m, 3 H), 2.39 (ddd, SI-28
\[ J = 13.3, 6.6, 4.1 \text{ Hz}, 1 \text{ H}], 2.31 (dd, J = 13.1, 8.3 \text{ Hz}, 1 \text{ H}), 2.12 (dd, J = 15.5, 9.1 \text{ Hz}, 1 \text{ H}), 1.80-1.71 (m, 2 \text{ H}), 1.47 (s, 9 \text{ H}). \]^1^C NMR (125 MHz, CDCl\textsubscript{3}) \( \delta \) 173.77, 170.40, 142.57, 138.98, 135.33, 126.87, 126.81, 119.40, 81.72, 57.32, 34.45, 34.34, 34.18, 34.14, 31.42, 30.46, 28.21. HRMS calcd for C\textsubscript{21}H\textsubscript{25}Cl\textsubscript{2}NO\textsubscript{3}Na (M\textsuperscript{+} + Na) 432.1104, found 432.1115.

**tert-Butyl** (4a\text{R}, 7R, 7a\text{R})-7-(3,4-difluorobenzyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 44)

According to the general procedure, the reaction of 43 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H\textsubscript{2}O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et\textsubscript{2}O/HCl (1.0 \( N \)) the title compound in 87\% yield (17.2 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. \(^1^H\) NMR (500 MHz, CDCl\textsubscript{3}) \( \delta \) 7.05 (ddt, \( J = 10.6, 8.2, 2.5 \text{ Hz}, 1 \text{ H})), 6.99-6.91 (m, 1 H), 6.89-6.79 (m, 1 H), 5.57 (d, \( J = 2.4 \text{ Hz}, 1 \text{ H})), 3.02 (s, 3 H), 2.77 (d, \( J = 13.9 \text{ Hz}, 1 \text{ H})), 2.57-2.46 (m, 2 H), 2.37-2.16 (m, 4 H), 2.10-1.98 (m, 2 H), 1.94-1.81 (m, 2 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to **tert**-butyl 7-(3,4-difluorobenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (44") using TsOH (1.0 equiv) in CH\textsubscript{2}Cl\textsubscript{2} (1.0 mL) at room temperature for 3 h. Colorless oil. \(^1^H\) NMR (500 MHz, CDCl\textsubscript{3}) \( \delta \) 7.08 (q, \( J = 8.5 \text{ Hz}, 1 \text{ H})), 7.04-6.98 (m, 1 H), 6.92 (s, 1 H), 3.71 (d, \( J = 16.2 \text{ Hz}, 1 \text{ H})), 3.46 (d, \( J = 16.3 \text{ Hz}, 1 \text{ H})), 3.25 (s, 3 H), 2.52 (tt, \( J = 9.9, 5.4 \text{ Hz}, 3 \text{ H})), 2.40 (ddd, \( J = 13.4, 6.8, 3.9 \text{ Hz}, 1 \text{ H})), 2.28 (dd, \( J = 13.2, 8.5 \text{ Hz}, 1 \text{ H})), 2.12 (dd, \( J = 15.4, 9.2 \text{ Hz}, 1 \text{ H})), 1.75 (dddd, \( J = 15.8, 13.0, 8.1, 5.0 \text{ Hz}, 2 \text{ H})), 1.46 (s, 9 H). \(^1^C\) NMR (125 MHz, CDCl\textsubscript{3}) \( \delta \) 173.81, 171.43, 151.10 (d, \( J^F = 192.0 \text{ Hz})), 148.80 (dd, \( J^F = 178.2, 12.6 \text{ Hz})), 138.40, 136.02 (d, \( J^F = 4.3 \text{ Hz})), 124.13 (q, \( J^F = 3.8 \text{ Hz})), 120.33, 117.42 (d, \( J^F = 17.1 \text{ Hz})), 117.16 (d, \( J^F = 17.3 \text{ Hz})), 81.64, 57.33, 34.18, 34.17, 34.16, 34.06, 31.39, 30.46, 28.17. \(^1^9^F\) NMR (470 MHz, CDCl\textsubscript{3}) \( \delta \) -137.63 (d, \( J = 21.0 \text{ Hz})), -141.32 (d, \( J = 21.4 \text{ Hz})). HRMS calcd for C\textsubscript{21}H\textsubscript{25}F\textsubscript{2}NO\textsubscript{3}Na (M\textsuperscript{+} + Na) 400.1695, found 400.1704.
**Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI₂–H₂O**

Shi, Lalancette, Szostak

**tert-Butyl (4aR,7R,7aR)-7a-hydroxy-1-methyl-2-oxo-7-(2,4,6-trimethylbenzyl)octahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 46)**

![Chemical structure](image)

According to the general procedure, the reaction of **45** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H₂O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 62% yield (12.4 mg). Dr >95:5. Cyclization/reduction selectivity = 78:22. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **1**H NMR (500 MHz, CDCl₃) δ 6.82 (s, 2 H), 5.52 (s, 1 H), 3.09 (s, 3 H), 2.66-2.59 (m, 2 H), 2.65-2.51 (m, 2 H), 2.38-2.34 (m, 1 H), 2.25 (s, 3 H), 2.23 (s, 6 H), 2.15-2.10 (m, 2 H), 1.86 (ddt, J = 10.7, 6.8, 3.3 Hz, 2 H), 1.72 (dt, J = 9.6, 4.4 Hz, 2 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to tert-butyl 1-methyl-2-oxo-7-(2,4,6-trimethylbenzyl)-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (46") using TsOH (1.0 equiv) in CH₂Cl₂ (1.0 mL) at room temperature for 3 h. White solid. Mp = 87-89 °C. **1**H NMR (500 MHz, CDCl₃) δ 6.82 (s, 2 H), 3.64 (d, J = 15.7 Hz, 1 H), 3.52 (d, J = 15.7 Hz, 1 H), 3.38 (s, 3 H), 2.54-2.40 (m, 2 H), 2.34-2.26 (m, 3 H), 2.25 (s, 3 H), 2.21 (s, 6 H), 1.83 (dd, J = 14.0, 8.8 Hz, 1 H), 1.70 (dt, J = 13.4, 8.1 Hz, 1 H), 1.53 (dd, J = 9.0, 3.8 Hz, 1 H), 1.43 (s, 9 H). **13**C NMR (125 MHz, CDCl₃) δ 174.12, 171.03, 136.62, 136.46, 135.80, 132.60, 129.08, 124.13, 81.25, 57.22, 35.27, 34.06, 31.89, 31.64, 30.76, 28.69, 28.15, 20.97, 20.26. HRMS calcd for C₂₄H₃₃NO₃Na (M⁺ + Na) 406.2353, found 406.2363.

**tert-Butyl (4aR,7R,7aR)-7-(2-fluorobenzyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 48)**
According to the general procedure, the reaction of 47 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et2O/HCl (1.0 N) the title compound in 67% yield (12.7 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2D NMR experiments and confirmed by an X-ray analysis of a derivative. 1H NMR (500 MHz, CDCl3) δ 7.21-7.16 (m, 1 H), 7.14 (t, J = 6.9 Hz, 1 H), 7.06 (d, J = 7.3 Hz, 1 H), 7.04-6.96 (m, 1 H), 5.55 (s, 1 H), 3.05 (s, 3 H), 2.76 (d, J = 13.5 Hz, 1 H), 2.61-2.48 (m, 2 H), 2.41-2.21 (m, 4 H), 2.08 (d, J = 10.2 Hz, 2 H), 1.91-1.82 (m, 2 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to tert-butyl 7-(2-fluorobenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (48") using TsOH (1.0 equiv) in CH2Cl2 (1.0 mL) at room temperature for 3 h. Colorless oil. 1H NMR (500 MHz, CDCl3) δ 7.24-7.17 (m, 2 H), 7.07 (t, J = 7.5 Hz, 1 H), 7.03 (t, J = 9.1 Hz, 1 H), 3.69 (d, J = 16.4 Hz, 1 H), 3.56 (d, J = 16.4 Hz, 1 H), 3.27 (s, 3 H), 2.58-2.47 (m, 3 H), 2.38 (ddd, J = 13.3, 6.7, 4.2 Hz, 1 H), 2.28 (ddd, J = 13.1, 8.2, 1.7 Hz, 1 H), 2.14 (dd, J = 15.6, 9.1 Hz, 1 H), 1.80-1.69 (m, 2 H), 1.45 (s, 9 H). 13C NMR (125 MHz, CDCl3) δ 173.96, 170.53, 162.20 (d, JF = 246.0 Hz), 138.06, 130.03 (d, JF = 4.5 Hz), 128.20 (d, JF = 7.9 Hz), 125.95 (d, JF = 16.0 Hz), 124.23 (d, JF = 3.6 Hz), 120.51, 115.38 (d, JF = 21.4 Hz), 81.43, 57.35, 34.15, 34.10, 31.44, 30.52, 28.17, 28.02, 27.99. 19F NMR (470 MHz, CDCl3) δ -117.42. HRMS calcd for C21H26FNO3Na (M+ + Na) 382.1789, found 382.1798.

**tert-Butyl (4aR,7R,7aR)-7-(benzo[d][1,3]dioxol-5-ylmethyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 50)**
According to the general procedure, the reaction of 49 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H₂O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 70% yield (14.1 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. 

**1H NMR (500 MHz, CDCl₃)** δ 6.71 (d, J = 7.9 Hz, 1 H), 6.62 (s, 1 H), 6.57 (d, J = 8.0 Hz, 1 H), 5.91 (s, 2 H), 5.54 (s, 1 H), 3.02 (s, 3 H), 2.73 (dd, J = 13.7, 3.7 Hz, 1 H), 2.51 (d, J = 17.0 Hz, 2 H), 2.35-2.20 (m, 3 H), 2.15 (t, J = 13.0 Hz, 1 H), 2.08-2.00 (m, 2 H), 1.92-1.80 (m, 2 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to tert-butyl 7-(benzo[d][1,3]dioxol-5-ylmethyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (50") using TsOH (1.0 equiv) in CH₂Cl₂ (1.0 mL) at room temperature for 3 h. Colorless oil. 

**1H NMR (500 MHz, CDCl₃)** δ 6.74 (d, J = 7.9 Hz, 1 H), 6.68 (s, 1 H), 6.65 (d, J = 7.9 Hz, 1 H), 5.93 (s, 2 H), 3.65 (d, J = 15.9 Hz, 1 H), 3.43 (d, J = 16.0 Hz, 1 H), 3.27 (s, 3 H), 2.60-2.47 (m, 3 H), 2.38 (ddd, J = 13.2, 6.7, 4.2 Hz, 1 H), 2.31-2.25 (m, 1 H), 2.14 (dd, J = 15.6, 9.0 Hz, 1 H), 1.78-1.69 (m, 2 H), 1.46 (s, 9 H). 

**13C NMR (125 MHz, CDCl₃)** δ 174.03, 170.53, 148.05, 146.17, 137.63, 132.77, 121.94, 121.14, 108.78, 108.41, 101.08, 81.48, 75.32, 34.50, 34.27, 34.23, 34.16, 31.50, 30.54, 28.20. HRMS calcd for C₂₂H₂₇NO₅Na (M⁺ + Na) 408.1781, found 408.1791.

**tert-Butyl (4aR,7R,7aR)-7a-hydroxy-1-methyl-7-(naphthalen-2-ylmethyl)-2-oxooctahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 52)**

According to the general procedure, the reaction of 51 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H₂O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 71% yield (14.6 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. 

**1H NMR (500 MHz, CDCl₃)** δ 7.78 (dd, J = 14.4, 8.0 Hz, 3 H), 7.57 (s, 1 H), 7.44 (dq, J = 14.7, 6.8 Hz, 2 H), 7.28 (d, J = 8.4 Hz, 1 H).
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

The title compound has been fully characterized after dehydration to tert-butyl 1-methyl-7-(naphthalen-2-ylmethyl)-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (52") using TsOH (1.0 equiv) in CH$_2$Cl$_2$ (1.0 mL) at room temperature for 3 h. Colorless oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.86-7.74 (m, 3 H), 7.63 (s, 1 H), 7.46 (t, $J$ = 7.3 Hz, 2 H), 7.33 (d, $J$ = 8.2 Hz, 1 H), 3.88 (d, $J$ = 16.0 Hz, 1 H), 3.70 (d, $J$ = 15.9 Hz, 1 H), 3.33 (s, 3 H), 2.63-2.50 (m, 3 H), 2.44-2.36 (m, 1 H), 2.35-2.27 (m, 1 H), 2.18 (dd, $J$ = 15.2, 9.1 Hz, 1 H), 1.84-1.70 (m, 2 H), 1.49 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 173.92, 170.46, 137.72, 136.49, 133.62, 132.19, 128.24, 127.68, 127.45, 126.88, 126.44, 126.19, 125.52, 121.81, 81.27, 57.23, 35.02, 34.12, 34.06, 31.45, 30.11. HRMS calcld for C$_{25}$H$_{29}$NO$_3$Na (M$^+$ + Na) 414.2040, found 414.2044.

tert-Butyl (4aR,7R,7aR)-7-benzhydryl-7a-hydroxy-1-methyl-2-oxooctahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 54)

According to the general procedure, the reaction of 53 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H$_2$O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et$_2$O/HCl (1.0 N) the title compound in 98% yield (21.3 mg). Recrystallization from CH$_2$Cl$_2$/hexanes. Colorless solid. Mp = 195-196 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry of the major diastereoisomer determined by 2 D NMR experiments and confirmed by X-ray analysis. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.29 (d, $J$ = 7.2 Hz, 3 H), 7.25-7.19 (m, 5 H), 7.12 (q, $J$ = 7.2 Hz, 2 H), 5.52 (s, 1 H), 3.75 (d, $J$ = 10.8 Hz, 1 H), 3.36 (q, $J$ = 9.9 Hz, 1 H), 2.60 (d, $J$ = 17.3 Hz, 1 H), 2.37 (dt, $J$ = 18.9, 10.6 Hz, 1 H), 2.18 (q, $J$ = 10.9 Hz, 1 H), 2.08-1.98 (m, 3 H), 2.03 (s, 3 H), 1.70-1.64 (m, 1 H), 1.54-1.48 (m, 1 H), 1.44 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 175.42, 168.88, 144.73, 144.36, 128.94, 128.76, 128.35, 127.95, 126.54, 126.47, 96.16, 83.12, 56.94, 55.18, 52.68, 32.45, 29.11
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

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28.90, 28.07, 27.42, 24.71. HRMS calcd for C$_{27}$H$_{33}$NO$_4$Na (M$^+$ + Na) 458.2302, found 458.2312.

tert-Butyl (4aR,7R,7aR)-7a-hydroxy-1-methyl-2-oxo-7-((E)-3-phenylprop-1-en-1-yl)octahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 2, 56)

According to the general procedure, the reaction of 55 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H$_2$O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et$_2$O/HCl (1.0 N) the title compound in 94% yield (18.1 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.29-7.26 (m, 2 H), 7.18 (t, $J$ = 7.3 Hz, 1 H), 7.11 (d, $J$ = 7.2 Hz, 2 H), 5.61 (dt, $J$ = 14.3, 6.7 Hz, 1 H), 5.48 (s, 1 H), 5.29 (dd, $J$ = 15.1, 8.7 Hz, 1 H), 3.30 (d, $J$ = 6.8 Hz, 2 H), 2.87 (s, 3 H), 2.44 (d, $J$ = 17.9 Hz, 1 H), 2.32-2.23 (m, 2 H), 2.23-2.19 (m, 1 H), 2.16 (d, $J$ = 5.4 Hz, 1 H), 1.98-1.93 (m, 2 H), 1.85-1.78 (m, 1 H), 1.71-1.64 (m, 1 H), 1.46 (s, 9 H). The title compound has been fully characterized after dehydration to tert-butyl (E)-1-methyl-2-oxo-7-((3-phenylprop-1-en-1-yl)-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (56") using TsOH (1.0 equiv) in CH$_2$Cl$_2$ (1.0 mL) at room temperature for 3 h. Colorless oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.30 (t, $J$ = 7.4 Hz, 2 H), 7.22 (d, $J$ = 7.1 Hz, 1 H), 7.19 (d, $J$ = 7.5 Hz, 2 H), 6.45 (d, $J$ = 15.4 Hz, 1 H), 5.74 (dt, $J$ = 14.3, 6.8 Hz, 1 H), 3.48 (d, $J$ = 6.9 Hz, 2 H), 3.28 (s, 3 H), 2.65-2.57 (m, 1 H), 2.53-2.43 (m, 3 H), 2.39-2.29 (m, 2 H), 1.76-1.67 (m, 2 H), 1.41 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 173.72, 170.45, 140.09, 137.38, 131.41, 128.78, 128.66, 126.40, 125.02, 121.34, 81.45, 57.17, 39.78, 35.86, 33.85, 31.55, 30.99, 30.39, 28.10. HRMS calcd for C$_{23}$H$_{29}$NO$_3$Na (M$^+$ + Na) 390.2040, found 390.2050.

tert-Butyl (3aR,6aR)-6-(2-butoxy-2-oxoethyl)-6a-hydroxy-1-methyl-2-oxohexahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (Chart 3, 66)
According to the general procedure, the reaction of 65 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and t-BuOH (24 equiv) in THF (1.0 mL) for 2 h afforded after work-up with Et₂O/HCl (1.0 N) the title compound in 91% yield (16.8 mg). Dr = 75:25 (2 diastereoisomers). Cyclization/reduction selectivity >95:5. Stereochemistry of the major diastereoisomer determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. Stereochemistry of the minor diastereoisomer not assigned. ¹H NMR (500 MHz, CDCl₃) (Major diastereoisomer) δ 4.82 (s, 1 H), 4.11 (t, J = 5.5 Hz, 2 H), 3.10 (d, J = 17.5 Hz, 1 H), 2.82 (s, 3 H), 2.65-2.59 (m, 2 H), 2.52-2.39 (m, 2 H), 2.27 (d, J = 17.0 Hz, 1 H), 1.96-1.85 (m, 3 H), 1.47 (s, 9 H), 1.62 (t, J = 7.5 Hz, 2 H), 1.37 (q, J = 7.5 Hz, 2 H), 0.93 (t, J = 7.5 Hz, 3 H). (Minor diastereoisomer) δ 4.48 (s, 1 H), 4.12 (m, 2 H), 2.86 (s, 3 H), 2.76-2.71 (m, 2 H), 2.52-2.39 (m, 2 H), 2.34-2.31 (m, 2 H), 2.17-2.08 (m, 2 H), 1.97-1.93 (m, 1 H), 1.46 (s, 9 H), 1.62 (t, J = 7.5 Hz, 2 H), 1.37 (q, J = 7.5 Hz, 2 H), 0.93 (t, J = 7.5 Hz, 3 H). ¹³C NMR (125 MHz, CDCl₃) (Major diastereoisomer) δ 174.18, 173.76, 172.76, 100.48, 82.60, 65.28, 57.13, 47.49, 41.73, 34.69, 34.56, 30.68, 28.77, 28.12, 27.45, 19.22, 13.77. (Minor diastereoisomer) δ 174.39, 171.12, 169.53, 89.05, 81.87, 65.35, 56.31, 49.72, 40.09, 36.03, 29.83, 28.11, 27.99, 27.88, 26.00, 19.21, 13.79. HRMS calcld for C₁₉H₃₁NO₆Na (M⁺ + Na) 392.2044, found 392.2054.

**tert-Butyl (4aR,7aR)-7-(2-butoxy-2-oxoethyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (Chart 3, 68)**

According to the general procedure, the reaction of 67 (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and t-BuOH (24 equiv) in THF (1.0 mL) for 2 h afforded after
work-up with Et₂O/HCl (1.0 N) the title compound in 87% yield (16.7 mg). Dr = 60:40 (2 diastereoisomers). Cyclization/reduction selectivity >95:5. Stereochemistry of the major diastereoisomer determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. Stereochemistry of the minor diastereoisomer not assigned. The title compound has been fully characterized after dehydration to tert-butyl 7-(2-butoxy-2-oxoethyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (68''). Colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 4.10 (t, J = 6.6 Hz, 2 H), 3.35 (s, 1 H), 3.31 (s, 3 H), 3.18 (d, J = 15.7 Hz, 1 H), 2.65 (dt, J = 16.8, 8.6 Hz, 1 H), 2.50 (dp, J = 18.0, 6.5 Hz, 2 H), 2.39-2.26 (m, 2 H), 1.78-1.69 (m, 2 H), 1.64-1.58 (m, 3 H), 1.42 (s, 9 H), 1.40-1.34 (m, 2 H), 0.93 (t, J = 7.4 Hz, 3 H). ¹³C NMR (125 MHz, CDCl₃) δ 173.61, 170.59, 170.42, 138.97, 116.01, 81.40, 64.99, 57.10, 35.22, 34.65, 34.35, 34.15, 31.31, 30.78, 30.41, 28.08, 19.26, 13.82. C₂₀H₃₁NO₅Na (M⁺ + Na) 388.2094, found 388.2103.
**General Dehydration Procedure.** To a solution of 2-azabicycle in CH$_2$Cl$_2$ (1.0 mL) p-TsOH monohydrate (1 equiv) (Method A) or BF$_3$•Et$_2$O (3 equiv) (Method B) was added at room temperature (Method A) or at -78 °C (Method B) and the reaction mixture was stirred at the indicated temperature for 3 h. The reaction mixture was extracted with CH$_2$Cl$_2$, organic layers were combined, dried and concentrated. A sample was analyzed by $^1$H NMR (CDCl$_3$, 500 MHz) and GC-MS to obtain selectivity, conversion and yield using internal standard. Purification by chromatography on silica gel afforded the title product.

![Diagram](image)

**tert-Butyl 7-benzyl-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (71).** General procedure A. Yield 94% (27.6 mg). Oil. $^1$H NMR (500 MHz, CDCl$_3$) δ 4.23 (q, $J = 7.1$ Hz, 2 H), 3.56 (s, 1 H), 3.00 (d, $J = 17.8$ Hz, 1 H), 2.89 (s, 3 H), 2.41 (dt, $J = 12.7$, 6.1 Hz, 1 H), 2.35 (d, $J = 17.7$ Hz, 1 H), 2.21 (tt, $J = 12.8$, 6.6 Hz, 1 H), 1.86 (ddt, $J = 12.6$, 6.4, 2.5 Hz, 1 H), 1.75 (ddd, $J = 12.7$, 5.7, 2.0 Hz, 1 H), 1.37-1.31 (m, 1 H), 1.30 (t, $J = 7.0$ Hz, 3 H), 1.06 (d, $J = 7.0$ Hz, 3 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 174.67, 172.93, 101.03, 62.02, 56.58, 46.21, 42.42, 34.23, 30.75, 27.74, 14.66, 14.28. HRMS calcd for C$_{12}$H$_{19}$NO$_4$Na (M$^+$ + Na) 264.1206, found 264.1227. Note: the title compound was obtained in 65% yield according to the general procedure B.

![Diagram](image)

**tert-Butyl 7-(4-methoxybenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (72).** General procedure A. Yield 97% (30.5 mg). Oil. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.10 (d, $J = 8.2$ Hz, 2 H), 6.83 (d, $J = 8.2$ Hz, 2 H), 3.79 (s, 3 H), 3.66 (d, $J = 15.9$ Hz, 1 H), 3.45 (d, $J = 15.8$ Hz, 1 H), 3.27 (s, 3 H), 2.54 (dd, $J = 16.4$, 8.0 Hz, 3 H), 2.42-2.33 (m, 1 H), 2.30-2.22 (m, 1 H), 2.13 (dd, $J = 15.1$, 9.3 Hz, 1 H), 1.73 (tt, $J = 18.9$, 8.9 Hz, 1 H).
9.4 Hz, 2 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, 500 MHz, CDCl$_3$) $\delta$ 174.06, 170.53, 158.23, 137.36, 130.93, 129.27, 122.37, 114.09, 81.34, 57.29, 55.42, 34.32, 34.21, 34.15, 33.96, 31.96, 30.55, 28.17. HRMS calcd for C$_{22}$H$_{29}$NO$_4$Na (M$^+$ + Na) 394.1989, found 394.1998.

**tert-Butyl 7-(4-bromobenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4-carboxylate (73).** General procedure A. Yield 74% (23.5 mg). Oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.41 (d, $J$ = 8.0 Hz, 2 H), 7.08 (d, $J$ = 8.0 Hz, 2 H), 3.68 (d, $J$ = 16.2 Hz, 1 H), 3.46 (d, $J$ = 16.2 Hz, 1 H), 3.25 (s, 3 H), 2.52 (dd, $J$ = 17.2, 9.8 Hz, 3 H), 2.43-2.34 (m, 1 H), 2.27 (dd, $J$ = 12.4, 8.8 Hz, 1 H), 2.11 (dd, $J$ = 15.2, 9.2 Hz, 1 H), 1.73 (dt, $J$ = 21.9, 9.6 Hz, 2 H), 1.45 (s, 9 H). $^{13}$C NMR (125 MHz, 500 MHz, CDCl$_3$) $\delta$ 173.86, 170.44, 138.07, 138.04, 131.76, 130.09, 120.86, 120.23, 81.49, 57.30, 34.32, 34.23, 34.17, 34.14, 31.41, 30.49, 28.18. HRMS calcd for C$_{21}$H$_{26}$BrNO$_3$Na (M$^+$ + Na) 442.0988, found 442.0999.

**tert-Butyl 7-(3,4-difluorobenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4-carboxylate (74).** General procedure A. Yield 74% (24.2 mg). Oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.08 (q, $J$ = 8.5 Hz, 1 H), 7.04-6.98 (m, 1 H), 6.92 (s, 1 H), 3.71 (d, $J$ = 16.2 Hz, 1 H), 3.46 (d, $J$ = 16.3 Hz, 1 H), 3.25 (s, 3 H), 2.52 (tt, $J$ = 9.9, 5.4 Hz, 3 H), 2.40 (ddd, $J$ = 13.4, 6.8, 3.9 Hz, 1 H), 2.28 (dd, $J$ = 13.2, 8.5 Hz, 1 H), 2.12 (dd, $J$ = 15.4, 9.2 Hz, 1 H), 1.75 (dddd, $J$ = 15.8, 13.0, 8.1, 5.0 Hz, 2 H), 1.46 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 173.81, 171.43, 151.10 (d, $J^F$ = 192.0 Hz), 148.80 (dd, $J^F$ = 178.2, 12.6 Hz), 138.40, 136.02 (d, $J^F$ = 4.3 Hz), 124.13 (q, $J^F$ = 3.8 Hz), 120.33, 117.42 (d, $J^F$ = 17.1 Hz), 117.16 (d, $J^F$ = 17.3 Hz), 81.64, 57.33, 34.18, 34.17, 34.16, 34.06, 31.39, 30.46, 28.17. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$  -
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137.63 (d, $J = 21.0$ Hz), -141.32 (d, $J = 21.4$ Hz). HRMS calcd for C$_{21}$H$_{25}$F$_2$NO$_3$Na (M$^+$ + Na) 400.1695, found 400.1704.

**tert-Butyl 1-methyl-2-oxo-7-(2,4,6-trimethylbenzyl)-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (75).** General procedure A. Yield 71% (16.9 mg). Solid.

Mp = 87-89 °C.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.82 (s, 2 H), 3.64 (d, $J = 15.7$ Hz, 1 H), 3.52 (d, $J = 15.7$ Hz, 1 H), 3.38 (s, 3 H), 2.54-2.40 (m, 2 H), 2.34-2.26 (m, 3 H), 2.25 (s, 3 H), 2.21 (s, 6 H), 1.83 (dd, $J = 14.0, 8.8$ Hz, 1 H), 1.70 (dt, $J = 13.4, 8.1$ Hz, 1 H), 1.53 (dd, $J = 9.0, 3.8$ Hz, 1 H), 1.43 (s, 9 H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 174.12, 171.03, 136.62, 136.46, 135.80, 132.60, 129.08, 124.13, 81.25, 57.22, 35.27, 34.06, 31.89, 31.64, 30.76, 28.69, 28.15, 20.97, 20.26.

HRMS calcd for C$_{24}$H$_{33}$NO$_3$Na (M$^+$ + Na) 406.2353, found 406.2363.

**tert-Butyl 7-(2-fluorobenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (76).** General procedure A. Yield 64% (15.5 mg). Oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.24-7.17 (m, 2 H), 7.07 (t, $J = 7.5$ Hz, 1 H), 7.03 (t, $J = 9.1$ Hz, 1 H), 3.69 (d, $J = 16.4$ Hz, 1 H), 3.56 (d, $J = 16.4$ Hz, 1 H), 3.27 (s, 3 H), 2.58-2.47 (m, 3 H), 2.38 (ddd, $J = 13.3, 6.7, 4.2$ Hz, 1 H), 2.28 (ddd, $J = 13.1, 8.2, 1.7$ Hz, 1 H), 2.14 (dd, $J = 15.6, 9.1$ Hz, 1 H), 1.80-1.69 (m, 2 H), 1.45 (s, 9 H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 173.96, 170.53, 162.20 (d, $J_F = 246.0$ Hz), 138.06, 130.03 (d, $J_F = 4.5$ Hz), 128.20 (d, $J_F = 7.9$ Hz), 125.95 (d, $J_F = 16.0$ Hz), 124.23 (d, $J_F = 3.6$ Hz), 120.51, 115.38 (d, $J_F = 21.4$ Hz), 81.43, 57.35, 34.15, 34.10, 31.44, 30.52, 28.17, 28.02, 27.99. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -117.42. HRMS calcd for C$_{21}$H$_{26}$FNO$_3$Na (M$^+$ + Na) 382.1789, found 382.1798.
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**tert-Butyl 7-(benzo[d][1,3]dioxol-5-ylmethyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (77).** General procedure A. Yield 79% (21.2 mg). Oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.74 (d, $J = 7.9$ Hz, 1 H), 6.68 (s, 1 H), 6.65 (d, $J = 7.9$ Hz, 1 H), 5.93 (s, 2 H), 3.65 (d, $J = 15.9$ Hz, 1 H), 3.43 (d, $J = 16.0$ Hz, 1 H), 3.27 (s, 3 H), 2.60-2.47 (m, 3 H), 2.38 (ddd, $J = 13.2$, 6.7, 4.2 Hz, 1 H), 2.31-2.25 (m, 1 H), 2.14 (dd, $J = 15.6$, 9.0 Hz, 1 H), 1.78-1.69 (m, 2 H), 1.46 (s, 9 H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 174.03, 170.53, 148.05, 146.17, 137.63, 132.77, 121.94, 121.14, 108.78, 108.41, 101.08, 81.48, 57.32, 34.50, 34.08, 34.04, 31.50, 30.54, 28.20. HRMS calcd for C$_{22}$H$_{27}$NO$_5$Na (M$^+$ + Na) 408.1781, found 408.1791.

**tert-Butyl 1-methyl-7-(naphthalen-2-ylmethyl)-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (78).** General procedure A. Yield 94% (26.2 mg). Oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.86-7.74 (m, 3 H), 7.63 (s, 1 H), 7.46 (t, $J = 7.3$ Hz, 2 H), 7.33 (d, $J = 8.2$ Hz, 1 H), 3.88 (d, $J = 16.0$ Hz, 1 H), 3.70 (d, $J = 15.9$ Hz, 1 H), 3.33 (s, 3 H), 2.63-2.50 (m, 3 H), 2.44-2.36 (m, 1 H), 2.35-2.27 (m, 1 H), 2.18 (dd, $J = 15.2$, 9.1 Hz, 1 H), 1.84-1.70 (m, 2 H), 1.49 (s, 9 H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 173.92, 170.46, 137.72, 136.49, 133.62, 132.19, 128.24, 127.68, 127.45, 126.88, 126.44, 126.19, 125.52, 121.81, 81.27, 57.23, 35.02, 34.36, 34.12, 34.06, 31.45, 30.49, 28.11. HRMS calcd for C$_{25}$H$_{29}$NO$_3$Na (M$^+$ + Na) 414.2040, found 414.2044.
**General Procedure for Selectivity Studies.** An oven-dried vial containing a stir bar was placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. A solution of two substrates (each 0.10 mmol, 1.0 equiv) in THF (2.0 mL) was added followed by H\textsubscript{2}O (0.18 mL, 200 equiv) and samarium(II) iodide (THF solution, 0.10 mmol, 1.0 equiv, 0.10 M) with vigorous stirring, which resulted in the formation of a characteristic burgundy-red color of the SmI\textsubscript{2}(H\textsubscript{2}O)\textsubscript{n} complex (n > 5 with respect to SmI\textsubscript{2}). The reaction mixture was stirred until decolorization to white had occurred. The reaction mixture was diluted with Et\textsubscript{2}O (30 mL) and HCl (1 N, 30 mL). The aqueous layer was extracted with Et\textsubscript{2}O (3 x 30 mL), and the organic layers were combined, dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated. The sample was analyzed by \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples.

**General Procedure for Determination of the Effect of Concentration of SmI\textsubscript{2} on the Rate of Reduction.** According to the general procedure, a cyclic imide (0.05 mmol) was reacted with samarium(II) iodide (8 equiv), and H\textsubscript{2}O (1200 equiv) in THF for 2 h at room temperature. After the standard work-up, the reaction mixture was diluted with Et\textsubscript{2}O (30 mL) and HCl (1 N, 30 mL). The aqueous layer was extracted with Et\textsubscript{2}O (3 x 30 mL), and the organic layers were combined, dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated. The sample was analyzed by \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples.

**General Procedure for Determination of Deuterium Incorporation.** According to the general procedure, a cyclic imide (0.05 mmol) was reacted with samarium(II) iodide (3-8 equiv), and D\textsubscript{2}O (600-1200 equiv) in THF (2.0 mL) for the indicated time at room temperature. After the standard work-up as described above, the reaction mixture was diluted with Et\textsubscript{2}O (30 mL) and HCl (1 N, 30 mL). The aqueous layer was extracted with Et\textsubscript{2}O (3 x 30 mL), and the organic layers were combined, dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated. The sample was analyzed by \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz) and ESI-MS to obtain deuterium incorporation.

**General Procedure for Determination of Kinetic Isotope Effect.** According to the general procedure, a cyclic imide (0.05 mmol) was reacted with samarium(II) iodide (3-8 equiv), and
H$_2$O/D$_2$O (1:1, 600-1200 equiv) in THF (2.0 mL) for the indicated time at room temperature. After the standard work-up as described above, the reaction mixture was diluted with Et$_2$O (30 mL) and HCl (1 N, 30 mL). The aqueous layer was extracted with Et$_2$O (3 x 30 mL), and the organic layers were combined, dried over Na$_2$SO$_4$, filtered, and concentrated. The sample was analyzed by $^1$H NMR (CDCl$_3$, 500 MHz) and ESI-MS to obtain deuterium incorporation.

terr-Butyl (3aR,6R,6aR)-6a-hydroxy-6-((4-methoxyphenyl)methyl-d)-1-methyl-2-oxooctahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (4-D'). Dr = 50:50 (benzylic position). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ (mixture of $D'$ diastereoisomers) 7.07 (d, $J$ = 8.2 Hz, 2 H), 6.82 (d, $J$ = 8.2 Hz, 2 H), 4.08 (s, 1 H), 3.78 (s, 3 H), 3.07 (s, 1 H), 2.95 (d, $J$ = 17.5 Hz, 1 H), 2.37 (d, $J$ = 17.9 Hz, 1 H), 2.30 (dd, $J$ = 11.0, 5.2 Hz, 1 H), 2.17 (dd, $J$ = 12.5, 6.4 Hz, 1 H), 1.74-1.58 (m, 3 H), 1.48 (s, 9 H), 1.24 (dt, $J$ = 12.4, 6.3 Hz, 1 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 174.08, 173.21, 158.18, 132.40, 129.70, 114.01, 100.28, 83.12, 56.86, 55.39, 54.11, 42.43, 34.13, 28.12, 27.56, 27.88, 27.55. HRMS calcd for C$_{21}$H$_{28}$DNO$_5$Na (M$^+$ + Na) 399.2001, found 399.2008.

terr-Butyl (4aR,7R,7aR)-7a-hydroxy-7-((4-methoxyphenyl)methyl-d)-1-methyl-2-oxooctahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (36'-D'). Dr = 50:50 (benzylic position). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.04 (d, $J$ = 8.0 Hz, 2 H), 6.81 (d, $J$ = 8.2 Hz, 2 H), 5.54 (s, 1 H), 3.77 (s, 3 H), 3.02 (s, 3 H), 2.73 (s, 0.5 H), 2.51 (d, $J$ = 16.8 Hz, 2 H), 2.34 (d, $J$ = 9.4 Hz, 0.5 H), 2.28-2.14 (m, 2 H), 2.05 (d, $J$ = 7.4 Hz, 2 H), 1.92-1.81 (m, 3 H), 1.46 (s, 9 H). The title compound has been fully characterized after dehydration to terr-butyl 7-((4-methoxyphenyl)methyl-d)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4aH-cyclopenta[b]pyridine-4a-carboxylate (36''-D') using TsOH (1.0 equiv) in CH$_2$Cl$_2$ (1.0 mL) at room temperature for 3 h. Colorless oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.11 (d, $J$ = 8.1 Hz, 2 H), 6.84 (d, $J$ = 8.1 Hz, 2 H), 3.79 (s, 3 H), 3.63 (s, 0.5 H), 3.43 (s, 0.5 H), 3.27 (s, 3 H), 2.52 (pd, $J$ = 10.1, 3.2 Hz, 3 H), 2.43-2.33 (m, 1 H), 2.27 (dd, $J$ = 12.5, 6.6 Hz, 1 H), 2.13 (dd, $J$ = 15.1, 9.1 Hz, 1 H), 1.73 (dq, $J$ = 16.9, 9.4 Hz, 2 H), 1.46 (s, 9 H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 174.08, 170.55, 158.25, 137.36, 130.91, 129.29, 122.33, 114.10, 81.36, 57.30, 55.43, 34.31, 34.23, 34.15, 34.11, 31.52, 30.56, 28.18. HRMS calcd for C$_{22}$H$_{28}$DNO$_5$Na (M$^+$ + Na) 395.2052, found 395.2062.
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**tert-Butyl**

(3aR,6S,6aR)-6a-hydroxy-1-methyl-6-(methyl-d)-2-oxohexahydrocyclopenta[b]pyrrole-3a(1H)-carboxylate (14-D$^t$). $^1$H-NMR (500 MHz, CDCl$_3$) δ 3.85 (s, 1 H), 2.92 (d, $J$ = 17.7 Hz, 1 H), 2.88 (s, 3 H), 2.37-2.27 (m, 2 H), 2.20 (dq, $J$ = 12.9, 6.4 Hz, 1 H), 1.83 (dtd, $J$ = 12.1, 6.1, 2.3 Hz, 1 H), 1.74-1.69 (m, 1 H), 1.48 (s, 9 H), 1.30-1.26 (m, 1 H), 1.03 (d, $J$ = 6.7 Hz, 2 H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 174.05, 173.01, 100.89, 83.02, 56.87, 46.22, 42.58, 34.26, 30.61, 28.13, 27.61, 14.29 (t, $J$ = 19.5 Hz). HRMS calcd for C$_{14}$H$_{22}$DNO$_4$Na (M$^+$ + Na) 293.1582, found 293.1592.
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Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

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Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$ – H$_2$O

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Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

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Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-52
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI₂–H₂O

Shi, Lalancette, Szostak

13

CO₂t-Bu

O

N

Me
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

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Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

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Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-57
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

$\text{CO}_2\text{-Bu}$

$\text{Me}$

33
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using $\text{SmI}_2$–$\text{H}_2\text{O}$

Shi, Lalancette, Szostak

SI-59
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using \(\text{SmI}_2-H_2O\)

Shi, Lalancette, Szostak

SI-60
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-61
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

$\text{CO}_2\text{t-Bu}$

$\text{Br}$

$\text{N}$

Me

39
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-63
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-64
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-65
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-66
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

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SI-67
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-68
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI₂–H₂O

Shi, Lalancette, Szostak

SI-69
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-70
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI₂–H₂O

Shi, Lalancette, Szostak

SI-71
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

\[
\text{CO}_2\text{t-Bu}
\]

55
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-74
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-76
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI₂-H₂O

Shi, Lalancette, Szostak

\[
\begin{align*}
\text{CO}_2\text{t-Bu} & \quad \text{Me'} \quad \text{OH} \\
\text{N} & \quad \text{C} & \quad \text{CF}_3
\end{align*}
\]
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-79
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using \textit{SmI}_2–\textit{H}_2O

Shi, Lalancette, Szostak

\[ \text{Me} \quad \text{CO}_2\text{f-Bu} \]

\[ \text{OH} \quad \text{Cl} \]

\[ \text{Cl} \]

10

\[ \text{N} \]

SI-80
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-81
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using \( \text{SmI}_2 - \text{H}_2\text{O} \)

Shi, Lalancette, Szostak

SI-82
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

\[ \text{CO}_2\text{Et} \]

\[ \text{Me} \]

\[ \text{OH} \]

\[ \text{Me} \]

\[ \text{16} \]
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-85
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$-H$_2$O

Shi, Lalancette, Szostak

SI-86
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-88
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SnI₂–H₂O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI₂–H₂O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-91
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-93
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-94
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-96
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-97
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-98
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

54

CO$_2$-Bu

N
Me

O

O

SI-100
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI₂–H₂O

Shi, Lalancette, Szostak

66
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-103
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

36''-D$^f$
Cyclization of Imides to 2-Azabicycles via Aminoketyl Radicals using SmI$_2$–H$_2$O

Shi, Lalancette, Szostak

SI-106