Selective Reduction of Barbituric Acids Using SmI$_2$/H$_2$O: Synthesis, Reactivity, and Structural Analysis of Tetrahedral Adducts**

Michal Szostak,* Brice Sautier, Malcolm Spain, Maike Behlendorf, and David J. Procter*

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Corresponding Author:
Dr. Michal Szostak
Professor David J. Procter
School of Chemistry
University of Manchester
Oxford Road
Manchester, M13 9PL
United Kingdom
General Methods

All experiments involving SmI$_2$ were performed using standard Schlenk or glovebox 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 sodium/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). Samarium(II) iodide was prepared by standard methods and titrated prior to use.\textsuperscript{1-5} $^1$H NMR and $^{13}$C NMR spectra were recorded in CDCl$_3$ on Bruker spectrometers at 300, 400 and 500 MHz ($^1$H NMR) and 75, 100 and 125 MHz ($^{13}$C NMR). All shifts are reported in parts per million (ppm) relative to residual CHCl$_3$ peak (7.27 and 77.2 ppm, $^1$H NMR and $^{13}$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.

All flash chromatography was performed using silica gel, 60 Å, 230–400 mesh. TLC analysis was carried out on aluminium sheets 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.

List of Known Compounds

The following compounds are known: barbituric acids $^{1a}$, $^{1b}$, $^{1c}$, $^{1d}$, $^{1i}$, $^{1m}$, $^{3e}$.\textsuperscript{12} The following barbituric acids and derivatives have been prepared according to the known procedures: $^{1a}$, $^{1b}$, $^{1d}$, $^{1i}$, $^{1m}$, SI-5.\textsuperscript{17} (E)-(4-Bromobut-1-en-1-yl)benzene, (E)-1-(4-bromobut-1-en-1-yl)-4-methoxybenzene have been prepared following the procedure by Wong.\textsuperscript{18} The intermediate in the synthesis of barbituric acid $^{3d}$, 5-(cyclohexylmethyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione, have been previously reported.\textsuperscript{19} All other substrates have been prepared according to the procedures outlined below. $^1$H NMR and $^{13}$C NMR data are given for all compounds in the Supporting Experimental for characterization purposes. $^1$H NMR, $^{13}$C NMR, IR and HRMS data are reported for all new compounds.
Preparation of Starting Materials

5-Isobutyl-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (1a). A 100 mL round-bottomed flask was charged with 1,3-dimethylbarbituric acid (4.68 g, 30 mmol, 1.0 equiv), CH₂Cl₂ (60 mL), isovaleraldehyde (6.48 g, 90 mmol, 3.0 equiv) and BF₃•Et₂O (1.8 mL, 15 mmol, 0.5 equiv), and stirred at room temperature for 18 h. The reaction mixture was diluted with CH₂Cl₂ (200 mL), washed with NaOH (2 N, 2 x 50 mL), dried and concentrated to give 1,3-dimethyl-5-(2-methylpropylidene)pyrimidine-2,4,6(1H,3H,5H)-trione which was used in the next step without further purification. To the intermediate α,β-unsaturated barbituric acid (30 mmol) dissolved in absolute EtOH (50 mL), NaBH₄ (1.14 g, 30 mmol, 1.0 equiv) was added in portions over 5 minutes at room temperature, and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was concentrated to dryness under reduced pressure, the residue was taken in H₂O (100 mL) and extracted with CH₂Cl₂ (3 x 100 mL). The aqueous layer was acidified using HCl (conc., 20 mL), extracted with CH₂Cl₂ (3 x 100 mL), the organic layer was dried and concentrated to give the title product as a yellow solid (Mp = 48-50 °C). Yield 84% (5.33 g, 2 steps). ¹H NMR (400 MHz, CDCl₃) δ 0.86 (d, J = 6.4 Hz, 6 H), 1.70-1.81 (m, 1 H), 1.87 (t, J = 6.4 Hz, 2 H), 3.23 (s, 6 H), 3.41 (t, J = 6.4 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 22.2, 25.7, 28.6, 40.5, 47.8, 151.7, 169.0. Spectroscopic data matched literature values.

5-Decyl-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (1b). A solution of decanoyl chloride (prepared from decanoic acid (1.72 g, 10 mmol, 1.0 equiv) and SOCl₂ (15 mL) under reflux for 1 h, followed by removal of SOCl₂ under vacuum) was added neat to a solution of 1,3-dimethylbarbituric acid (3.12 g, 20 mmol, 2.0 equiv) in pyridine (25 mL). The resulting mixture was stirred at room temperature for 18 h, acidified with HCl (conc., 25 mL), filtered, washed with water and dried to give 5-decanoyl-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-
trione which was used in the next step without further purification. To the intermediate α,β-unsaturated barbituric acid (10 mmol) dissolved in acetic acid (15 mL), NaCNBH₃ (1.25 g, 20 mmol, 2.0 equiv) was added in portions over two minutes. The reaction mixture was stirred at room temperature for 2 h, diluted with H₂O (50 mL) and quenched with HCl (conc., 2 mL). After careful removal of HCN by bubbling N₂ through the solution, the reaction mixture was placed at 4 °C overnight, filtered, washed with water and dried in air to give the title compound as a solid (Mp = 53-55 °C). Yield 80% (2.36 g, 2 steps). ᵃH NMR (300 MHz, CDCl₃) δ 0.86 (t, J = 6.6 Hz, 3 H), 1.10-1.35 (m, 16 H), 2.02-2.16 (m, 2 H), 3.30 (s, 6 H), 3.48 (t, J = 5.1 Hz, 1 H); ᵧC NMR (75 MHz, CDCl₃) δ 14.1, 22.6, 26.0, 28.5, 29.2, 29.2, 29.4, 29.5, 31.5, 31.9, 49.1, 151.7, 168.8. Spectroscopic data matched literature values. Caution! Note that HCN is formed during the reaction and during the work-up. The above procedure should be performed in a well-ventilated fume-cupboard and appropriate precautions should be taken.

5-Isopentyl-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (1c). Prepared according to the procedure described below for 1d from 1,3-dimethylbarbituric acid (1.56 g, 10 mmol, 1.0 equiv), isovaleric acid (1.8 mL, 15 mmol, 1.5 equiv), DMAP (0.61 g, 5 mmol, 0.5 equiv), DCC (2.27 g, 11 mmol, 1.1 equiv) in CH₂Cl₂ (10 mL) to give the intermediate 5-(1-hydroxy-3-methylbutylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (2.74 g), which was converted directly (2.0 g) into the title compound using NaCNBH₃ (1.57 g, 19.7 mmol, 3 equiv) in AcOH (10 mL) for 2 h at room temperature. Colorless oil. Yield 92% (1.7 g, 2 steps). ᵃH NMR (400 MHz, CDCl₃) δ 0.86 (d, J = 6.6 Hz, 6 H), 1.08 - 1.17 (m, 2 H), 1.46 - 1.58 (m, 1 H), 2.07 - 2.16 (m, 2 H), 3.30 (s, 6 H), 3.48 (t, J = 5.3 Hz, 1 H); ᵧC NMR (100 MHz, CDCl₃) δ 22.2, 27.9, 28.5, 29.3, 34.6, 49.0, 151.6, 168.7. IR (neat) 755, 994, 1087, 1149, 1274, 1320, 1375, 1422, 1446, 1673, 2868, 2954. HRMS calcd for C₁₁H₁₉N₂O₃ (M⁺ + H) 227.1390, found 227.1384.
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1,3-Dimethyl-5-phenethylpyrimidine-2,4,6(1H,3H,5H)-trione (1d). A 100 mL round-bottomed flask was charged with 1,3-dimethylbarbituric acid (5.0 g, 32 mmol, 1.0 equiv), phenylacetic acid (6.53 g, 48 mmol, 1.5 equiv), DMAP (1.95 g, 16 mmol, 0.5 equiv) and CH$_2$Cl$_2$ (60 mL), and cooled to 0 °C. DCC (7.26 g, 35 mmol, 1.1 equiv) was added in portions over 5 minutes and the reaction mixture was stirred for 18 h at room temperature. The reaction mixture was filtered and the precipitated solid was washed with CH$_2$Cl$_2$ (1 x 150 mL). The organic layers were combined, washed with HCl (2 N, 2 x 40 mL), dried and concentrated. Recrystallization from MeOH gave the intermediate 1,3-dimethyl-5-(2-phenylacetyl)pyrimidine-2,4,6(1H,3H,5H)-trione as a white solid which was used in the next step without further purification. The intermediate α,β-unsaturated barbituric acid (2.74 g, 10 mmol, 1.0 equiv) was reduced according to the procedure described above using NaCNBH$_3$ (1.89 g, 30 mmol, 3.0 equiv) in acetic acid (15 mL) to give the title product as a white solid (Mp = 87-89 °C). Yield 92% (2.29 g, 2 steps). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 2.49-2.55 (m, 2 H), 2.72 (t, $J = 7.2$ Hz, 2 H), 3.24 (s, 6 H), 3.49 (t, $J = 5.4$ Hz, 1 H), 7.13-7.32 (m, 5 H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 28.5, 31.5, 32.1, 47.9, 126.6, 128.5, 128.7, 139.4, 151.4, 168.4. Spectroscopic data matched literature values.

1,3-Dimethyl-5-(2-phenylpropyl)pyrimidine-2,4,6(1H,3H,5H)-trione (1e). Prepared according to the procedure described for 1a from 1,3-dimethylbarbituric acid (2.34 g, 15 mmol, 1.0 equiv), 2-phenylpropionaldehyde (2.12 g, 15 mmol, 1.05 equiv) and BF$_3$•Et$_2$O (0.90 mL, 7.5 mmol, 0.5 equiv) in CH$_2$Cl$_2$ (30 mL) to give the intermediate 1,3-dimethyl-5-(2-phenylpropylidene)pyrimidine-2,4,6(1H,3H,5H)-trione which was converted without further purification into the title compound using NaBH$_4$ (1.14 g, 30 mmol, 2.0 equiv) in EtOH (50 mL). Yellow solid (Mp = 45-46 °C). Yield 77% (3.15 g, 2 steps). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.27 (d, $J = 6.6$ Hz, 3 H), 2.38-2.60 (m, 2 H), 2.88 (s, 3 H), 2.89-2.98 (m, 1
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H), 3.29 (s, 3 H), 3.35 (dd, $J = 3.0$, 7.2 Hz, 1 H), 7.08-7.30 (m, 5 H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 23.3, 28.3, 28.4, 37.4, 37.9, 47.1, 127.0, 127.6, 128.6, 143.8, 151.2, 168.5. IR (neat) 3028, 2960, 1667, 1435, 1418, 1373, 1278, 1127, 1083, 1024, 963, 913, 754 cm$^{-1}$. HRMS calcd for C$_{15}$H$_{19}$N$_2$O$_3$ (M$^+$ + H) 275.1391, found 275.1389.

5-(4-Methoxyphenethyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (1f). Prepared according to the procedure described above from 1,3-dimethylbarbituric acid (1.56 g, 10 mmol, 1.0 equiv), 4-methoxyphenylacetic acid (2.49 g, 15 mmol, 1.5 equiv), DMAP (0.61 g, 5 mmol, 0.5 equiv), DCC (2.27 g, 11 mmol, 1.1 equiv) in CH$_2$Cl$_2$ (10 mL) to give 5-(1-hydroxy-2-(4-methoxyphenyl)ethylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (2.79 g), which was converted directly (2.0 g) into the title compound using NaCNBH$_3$ (1.24 g, 19.7 mmol, 3 equiv) in AcOH (10 mL). Colorless oil. Yield 92% (1.9 g, 2 steps). $^1$H NMR (500 MHz, CDCl$_3$) δ 2.47 (dt, $J = 6.1$, 8.2 Hz, 2 H), 2.61 - 2.68 (m, 2 H), 3.22 (s, 6 H), 3.46 (t, $J = 5.4$ Hz, 1 H), 3.77 (s, 3 H), 6.80 (d, $J = 8.7$ Hz, 2 H), 7.05 (d, $J = 8.7$ Hz, 2 H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 28.4, 31.1, 31.7, 47.7, 55.2, 113.8, 129.7, 131.2, 151.3, 158.1, 168.3. IR (neat) 754, 815, 1034, 1098, 1181, 1245, 1286, 1378, 1421, 1446, 1511, 1676, 2837, 2950, 3206. HRMS calcd for C$_{15}$H$_{19}$N$_2$O$_3$ (M$^+$ + H) 291.1340, found 291.1348.

1,3-Dimethyl-5-(4-(trifluoromethyl)phenethyl)pyrimidine-2,4,6(1H,3H,5H)-trione (1g). Prepared according to the procedure described above from 1,3-dimethylbarbituric acid (1.56 g, 10 mmol, 1.0 equiv), 4-(trifluoromethyl)phenylacetic acid (3.06 g, 15 mmol, 1.5 equiv), DMAP (0.61 g, 5 mmol, 0.5 equiv), DCC (2.27 g, 11 mmol, 1.1 equiv) in CH$_2$Cl$_2$ (10 mL) to give the intermediate 5-(1-hydroxy-2-(4-(trifluoromethyl)phenyl)ethylidene)-1,3-dimethyl pyrimidine-2,4,6(1H,3H,5H)-trione (2.48 g), which was converted directly (2.0 g) into the title compound using NaCNBH$_3$ (1.10 g, 17.5 mmol, 3 equiv) in AcOH (10 mL). White solid.
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5-(4-Bromophenethyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (1h). Prepared according to the procedure described above from 1,3-dimethylbarbituric acid (1.56 g, 10 mmol, 1.0 equiv), 4-bromophenylacetic acid (3.23 g, 15 mmol, 1.5 equiv), DMAP (0.61 g, 5 mmol, 0.5 equiv), DCC (2.27 g, 11 mmol, 1.1 equiv) in CH$_2$Cl$_2$ (10 mL) to give 5-(1-hydroxy-2-(4-bromophenyl)ethylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (3.31 g), which was converted directly (3.0 g) into the title compound using NaCNBH$_3$ (1.60 g, 25.5 mmol, 3 equiv) in AcOH (10 mL). White solid (Mp = 52-54 °C). Yield 87% (2.7 g, 2 steps). $^1$H NMR (500 MHz, CDCl$_3$) δ 2.42 - 2.49 (m, 2 H), 2.63 - 2.70 (m, 2 H), 3.25 (s, 6 H), 3.46 (t, J = 5.4 Hz, 1 H), 7.05 (d, J = 8.4 Hz, 2 H), 7.39 (d, J = 8.4 Hz, 2 H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 28.5, 31.2, 31.6, 47.7, 120.3, 130.4, 131.5, 138.5, 151.3, 168.1. IR (neat) 635, 709, 755, 817, 1201, 1230, 1315, 1385, 1513, 1681. $^{19}$F NMR (470 MHz, CDCl$_3$) δ -62.5. HRMS calcd for C$_{14}$H$_{15}$N$_2$O$_3$BrNa (M$^+$ + Na) 361.0158, found 361.0143.
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room temperature, diluted with H₂O (50 mL) and extracted with Et₂O (3 x 50 mL). The organic layers were combined, washed with NaOH (2 N, 2 x 50 mL), dried and concentrated to give the title compound as a yellow solid (Mp = 51-51 °C). Yield 60% (0.61 g). ¹H NMR (300 MHz, CDCl₃) δ 0.79 (t, J = 6.6 Hz, 3 H), 0.93-1.06 (m, 2 H), 1.06-1.28 (m, 14 H), 1.44 (s, 3 H), 1.85-1.91 (m, 2 H), 3.24 (s, 6 H); ¹³C NMR (75 MHz, CDCl₃) δ 14.0, 22.6, 24.4, 25.2, 28.5, 29.1, 29.2, 29.3, 29.4, 31.8, 40.3, 51.6, 151.2, 172.3. IR (neat) 2924, 2854, 1674, 1444, 1380, 1278, 1068, 913, 755, 731 cm⁻¹. HRMS calcd for C₁₇H₃₀N₂O₃Na (M⁺ + Na) 333.2149, found 333.2153.

5-Isobutyl-1,3,5-trimethylpyrimidine-2,4,6(1H,3H,5H)-trione (1j). Prepared according to the procedure described above for 1i using 5-isobutyl-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (0.70 g, 3.30 mmol, 1.0 equiv), iodomethane (2 mL, 30 mmol, 10 equiv) and K₂CO₃ (2.0 g, 15 mmol, 4.5 equiv) in acetone (5 mL) at 50 °C for 18 h to give the title compound as a low melting solid (mp = 38-39 °C). Yield 85% (0.63 g). ¹H NMR (300 MHz, CDCl₃) δ 0.81 (d, J = 6.9 Hz, 6 H), 1.54 (s, 3 H), 1.45-1.56 (m, 1 H), 2.02 (d, J = 6.9 Hz, 2 H), 3.34 (s, 6 H); ¹³C NMR (75 MHz, CDCl₃) δ 23.0, 25.5, 26.8, 28.5, 48.1, 50.5, 151.1, 172.3. IR (neat) 1681, 1448, 1381, 1357, 1287, 1199, 1096, 1067, 978, 754 cm⁻¹. HRMS calcd for C₁₁H₁₀N₂O₃ (M⁺ + H) 227.1390, found 227.1387.

2,4-Dimethyl-2,4-diazaspiro[5.6]dodec-9-ene-1,3,5-trione (1k). A 100 mL flask was charged with 5,5-di(but-3-en-1-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (0.5 g, 1.9 mmol, 1 equiv), Grubbs I catalyst (156 mg, 0.2 mmol, 0.1 equiv) and toluene (60 mL) and stirred for 24 h at 90 °C to give after purification by chromatography using EtOAc/hexanes (10/90) the title compound as a white solid (Mp = 118-120 °C). Yield 70% (0.31 g). ¹H NMR (400 MHz, CDCl₃) δ 2.22 - 2.31 (m, 4 H), 2.41 - 2.51 (m, 4 H), 3.29 (s, 6 H), 5.65 (t, J = 2.6 Hz, 2 H); ¹³C NMR (100 MHz, CDCl₃) δ 24.9, 28.9, 34.6, 53.8, 129.9, 151.3, 172.6. IR (neat)
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631, 707, 756, 931, 1023, 1065, 1109, 1236, 1271, 1371, 1420, 1455, 2856, 2926, 3017. HRMS calcd for C$_{12}$H$_{16}$N$_2$O$_3$ (M$^+$) 236.1155, found 236.1157.

5-(1-Hydroxy-2-phenylethylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (1l). Pre pared according to the procedure described above from 1,3-dimethylbarbituric acid (5.0 g, 32 mmol, 1.0 equiv), phenylacetic acid (6.53 g, 48 mmol, 1.5 equiv), DMAP (1.95 g, 16 mmol, 0.5 equiv) and DCC (7.26 g, 35 mmol, 1.1 equiv) in CH$_2$Cl$_2$ (60 mL) for 18 h at room temperature to give the title compound as a white solid (Mp = 82-84 °C). Yield 75% (6.58 g). $^1$H NMR (300 MHz, CDCl$_3$) δ 3.39 (s, 6 H), 4.50 (s, 2 H), 7.22-7.35 (m, 3 H), 7.37-7.42 (m, 2 H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 27.9, 28.1, 41.8, 95.3, 127.3, 128.6, 129.7, 134.5, 150.2, 160.8, 169.9, 196.2. Spectroscopic data matched literature values.

1,3-Dimethyl-5-(2-methylpropylidene)pyrimidine-2,4,6(1H,3H,5H)-trione (1m). Prepared according to the procedure described above from 1,3-dimethylbarbituric acid (4.68 g, 30 mmol, 1.0 equiv), isovaleraldehyde (6.48 g, 90 mmol, 3.0 equiv) and BF$_3$•Et$_2$O (1.8 mL, 15 mmol, 0.5 equiv) in CH$_2$Cl$_2$ (60 mL) at room temperature for 18 h to give the title compound as white solid (mp = 39-40 °C). Yield 99% (6.2 g). $^1$H NMR (400 MHz, CDCl$_3$) δ 1.08 (d, J = 6.4 Hz, 6 H), 3.28 (s, 3 H), 3.29 (s, 3 H), 3.85-3.97 (m, 1 H), 7.69 (d, J = 10.0 Hz, 1 H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 21.4, 28.1, 28.7, 29.1, 118.4, 151.3, 160.9, 161.7, 173.7. Spectroscopic data matched literature values.
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5-(But-3-en-1-yl)-5-isobutyl-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (3a).

Prepared according to the procedure described above for 1i from 5-isobutyl-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (0.77 g, 3.6 mmol, 1.0 equiv), 4-bromobut-1-ene (0.73 g, 5.4 mmol, 1.5 equiv) and K$_2$CO$_3$ (1.0 g, 7.2 mmol, 2.0 equiv) in acetone (20 mL) for 24 h at 60 °C to give after purification by chromatography using EtOAc/hexanes (1/99-10/90) the title compound as a colorless oil. Yield 51% (0.49 g). R$_f$ (20% EtOAc/hexanes) = 0.73.

$^1$H NMR (400 MHz, CDCl$_3$) δ 0.71 (d, $J$ = 6.8 Hz, 6 H), 1.32-1.44 (m, 1 H), 1.82 (q, $J$ = 6.8 Hz, 2 H), 1.92 (d, $J$ = 6.8 Hz, 2 H), 2.02 (t, $J$ = 7.6 Hz, 2 H), 3.24 (s, 6 H), 4.80-4.87 (m, 2 H), 5.49-5.61 (m, 1 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 23.1, 25.5, 28.4, 29.6, 40.8, 48.8, 55.0, 115.6, 136.5, 151.1, 171.9. IR (neat) 2960, 2932, 1674, 1444, 1417, 1379, 1349, 1318, 1083, 917, 787 cm$^{-1}$. HRMS calcd for C$_{14}$H$_{22}$N$_2$O$_3$Na (M$^+$ + Na) 289.1523, found 289.1516.

(E)-5-Isobutyl-1,3-dimethyl-5-(4-phenylbut-3-en-1-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (3b). Prepared according to the procedure described above for 1i using 5-isobutyl-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (0.50 g, 2.4 mmol, 1.0 equiv), (E)-(4-bromobut-1-en-1-yl)benzene (0.60 g, 2.8 mmol, 1.2 equiv, prepared according to the procedure described by Wong$^{18}$) and K$_2$CO$_3$ (0.65 g, 4.7 mmol, 2.0 equiv) in acetone (5 mL) for 18 h at 60 °C to give after purification by chromatography using EtOAc/hexanes (2/98-10/90) the title compound as a colorless oil. Yield 53% (0.43 g). R$_f$ (10% EtOAc/hexanes) = 0.43. $^1$H NMR (300 MHz, CDCl$_3$) δ 0.79 (d, $J$ = 6.9 Hz, 6 H), 1.39-1.53 (m, 1 H), 2.00 (d, $J$ = 6.6 Hz, 2 H), 2.10 (q, $J$ = 6.6 Hz, 2 H), 2.18-2.25 (m, 2 H), 3.24 (s, 6 H), 6.02 (dt, $J$ = 6.9, 15.6 Hz, 1 H), 6.25 (d, $J$ = 15.9 Hz, 1 H), 7.18-7.34 (m, 5 H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 23.2, 25.5, 28.5, 29.2, 40.6, 49.5, 55.1, 126.1, 127.4, 128.2, 128.6, 131.3, 136.8, 151.1, 172.1. IR (neat) 2960, 2932, 2873, 1672, 1495, 1438, 1417, 1378, 1352, 1316, 1276, 1119, 1078, 967, 745, 692 cm$^{-1}$. HRMS calcd for C$_{20}$H$_{27}$N$_2$O$_3$ (M$^+$ + H) 343.2016, found 343.2018.
(E)-5-Isobutyl-5-(4-(4-methoxyphenyl)but-3-en-1-yl)-1,3-dimethylpyrimidine-2,4,6 (1H,3H,5H)-trione (3c). Prepared according to the procedure described above for 1i using 5-isobutyl-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (0.30 g, 1.4 mmol, 1.0 equiv), (E)-1-(4-bromobut-1-en-1-yl)-4-methoxybenzene (0.41 g, 1.7 mmol, 1.2 equiv, prepared according to the procedure described by Wong18) and K2CO3 (0.39 g, 2.8 mmol, 2.0 equiv) in acetone (5 mL) for 18 h at 60 °C to give after purification by chromatography using EtOAc/hexanes (2/98-10/90) the title compound as a colorless oil. Yield 71% (0.37 g). Rf (10% EtOAc/hexanes) = 0.26. 1H NMR (300 MHz, CDCl3) δ 0.78 (d, J = 6.9 Hz, 6 H), 1.38-1.52 (m, 1 H), 2.00 (d, J = 6.6 Hz, 2 H), 2.08 (q, J = 6.9 Hz, 2 H), 2.20 (t, J = 6.6 Hz, 2 H), 3.23 (s, 6 H), 3.81 (s, 3 H), 5.86 (dt, J = 6.9, 15.6 Hz, 1 H), 6.17 (d, J = 15.9 Hz, 1 H), 6.82 (d, J = 8.7 Hz, 2 H), 7.21 (d, J = 8.7 Hz, 2 H); 13C NMR (75 MHz, CDCl3) δ 23.2, 25.5, 28.5, 29.3, 40.8, 49.5, 55.1, 55.3, 114.0, 126.0, 127.2, 129.6, 130.6, 151.1, 159.1, 172.1. IR (neat) 2959, 2932, 1672, 1510, 1439, 1379, 1351, 1244, 1174, 1033, 967, 837, 755 cm⁻¹. HRMS calcd for C21H29N2O4 (M+ + H) 373.2122, found 373.2129.

(E)-5-(Cyclohexylmethyl)-1,3-dimethyl-5-(4-phenylbut-3-en-1-yl)pyrimidine-2,4,6 (1H,3H,5H)-trione (3d). Prepared according to the procedure described above for 1i using 5-(cyclohexylmethyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (0.50 g, 2.0 mmol, 1.0 equiv (prepared from 1,3-dimethylbarbituric acid and cyclohexanecarboxaldehyde as described above in 73% yield, 5.48 g, 2 steps, solid, mp = 85-87 °C).19 1H NMR (300 MHz, CDCl3) δ 0.88 (qd, J = 3.0, 11.7 Hz, 2 H), 1.03-1.26 (m, 3 H), 1.35-1.51 (m, 1 H), 1.53-1.72 (m, 5 H), 1.89 (t, J = 6.9 Hz, 2 H), 3.24 (s, 6 H), 3.46 (t, J = 6.3 Hz, 1 H); 13C NMR (75 MHz, CDCl3) δ 25.9, 26.2, 28.5, 32.8, 34.8, 38.9, 47.0, 151.7, 169.0. Spectroscopic data matched literature values), (E)-(4-bromobut-1-en-1-yl)benzene (0.63 g, 3.0 mmol, 1.5 equiv, prepared according to the procedure described by Wong18) in acetone (5 mL) for 18 h at 60 °C to give after purification by chromatography using EtOAc/hexanes (15/75) the title
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Compound as a white solid (mp = 98-99 °C). Yield 66% (0.48 g). \( R_f \) (15% EtOAc/hexanes) = 0.48. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 0.81 (qd, \( J = 3.0, 12.0 \text{ Hz}, 2 \text{ H} \)), 0.93-1.09 (m, 4 H), 1.32 (d, \( J = 12.5 \text{ Hz}, 2 \text{ H} \)), 1.45-1.56 (m, 3 H), 1.90 (d, \( J = 6.5 \text{ Hz}, 2 \text{ H} \)), 2.00 (q, \( J = 7.0 \text{ Hz}, 2 \text{ H} \)), 2.11 (t, \( J = 7.5 \text{ Hz}, 2 \text{ H} \)), 3.16 (s, 6 H), 5.93 (dt, \( J = 7.0, 15.5 \text{ Hz}, 1 \text{ H} \)), 6.15 (d, \( J = 15.5 \text{ Hz}, 1 \text{ H} \)), 7.10-7.14 (m, 1 H), 7.17-7.23 (m, 4 H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 25.9, 26.0, 28.5, 29.2, 33.7, 34.8, 40.7, 48.0, 54.8, 126.1, 127.4, 128.2, 128.6, 131.2, 136.8, 151.4, 172.1. IR (neat) 2997, 2945, 2850, 1669, 1492, 1411, 1261, 1240, 1200, 1054, 987, 954, 753, 744, 693 cm\(^{-1}\). HRMS calcd for C\(_{23}\)H\(_{31}\)N\(_3\)O\(_3\) (M\(^+\) + H) 383.2330, found 383.2321.

**5,5-Di(but-3-en-1-yl)-1,3-dimethylpyrimidine-2,4,6(1\(H\),3\(H\),5\(H\))-trione (3e).** A 50 mL flask was charged with 5,5-di(but-3-en-1-yl)-1,3-dimethylpyrimidine-2,4,6(1\(H\),3\(H\),5\(H\))-trione (1.6 g, 10 mmol, 1 equiv), 4-bromo-1-butene (1.2 mL, 12 mmol, 0.6 equiv), tetrabutylammonium bisulfate (34 mg, 0.1 mmol, 0.01 equiv), K\(_2\)CO\(_3\) (1.8 g, 20 mmol, 2 equiv) and DMF (25 mL) and stirred at 80 °C for 18 h. The organic layer was separated by filtration, concentrated and purified by chromatography to give the title compound as a white solid (Mp 43-45 °C). Yield 78% (1.2 g). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 1.85 - 1.95 (m, 4 H), 2.07 - 2.15 (m, 4 H), 3.28 (s, 6 H), 4.85 - 4.93 (m, 4 H), 5.55 - 5.68 (m, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 28.3, 29.8, 39.3, 55.4, 115.7, 136.5, 151.0, 171.7. IR (neat) 639, 753, 973, 999, 1036, 1083, 1171, 1258, 1281, 1334, 1382, 1416, 1445, 2928, 2955. HRMS calcd for C\(_{14}\)H\(_{20}\)N\(_2\)O\(_3\) (M\(^+\)) 264.1468, found 264.1461.

**5-(But-3-yn-1-yl)-5-isobutyl-1,3-dimethylpyrimidine-2,4,6(1\(H\),3\(H\),5\(H\))-trione (3f).** Prepared according to the procedure described above for 1i using 5-isobutyl-1,3-dimethylpyrimidine-2,4,6(1\(H\),3\(H\),5\(H\))-trione (0.64 g, 3.0 mmol, 1.0 equiv), 4-bromo-1-butyn (0.42 mL, 4.5 mmol, 1.5 equiv) and K\(_2\)CO\(_3\) (0.83 g, 6.0 mmol, 2.0 equiv) in acetone (15 mL) for 21 h at 60 °C to give after purification by chromatography using EtOAc/hexanes (10/90)
the title compound as a colorless oil. Yield 46% (0.31 g). $^1$H NMR (400 MHz, CDCl$_3$) δ 0.77 (d, $J = 6.8$ Hz, 6 H), 1.40 - 1.52 (m, 1 H), 1.91 (t, $J = 2.5$ Hz, 1 H), 1.95 (d, $J = 6.8$ Hz, 2 H), 2.11 (td, $J = 2.5$, 6.3 Hz, 2 H), 2.17 - 2.24 (m, 2 H), 3.30 (s, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 14.5, 23.2, 25.3, 28.5, 38.8, 49.3, 54.6, 69.8, 81.4, 151.1, 171.5. IR (neat) 645, 755, 1052, 1089, 1119, 1159, 1219, 1291, 1352, 1380, 1442, 1676, 2872, 2960, 3275. HRMS calcd for C$_{14}$H$_{21}$N$_2$O$_3$ (M$^+$ + H) 265.1547, found 265.1543.

5-Isobutyl-1,3-dimethyl-5-(4-(trimethylsilyl)but-3-yn-1-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (3g). Prepared according to the procedure described above for 1i using 5-isobutyl-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (0.64 g, 3.0 mmol, 1.0 equiv), (4-bromobut-1-yn-1-yl)trimethylsilane (1.0 g, 4.5 mmol, 1.5 equiv) and K$_2$CO$_3$ (0.83 g, 6.0 mmol, 2.0 equiv) in acetone (15 mL) for 21 h at 60 °C to give after purification by chromatography using EtOAc/hexanes (5/95) the title compound as a white solid (Mp 58-60 °C). Yield 19% (0.17 g). $^1$H NMR (500 MHz, CDCl$_3$) δ 0.11 (s, 9 H), 0.78 (d, $J = 6.9$ Hz, 6 H), 1.42 - 1.51 (m, 1 H), 1.96 (d, $J = 6.9$ Hz, 2 H), 2.11 - 2.16 (m, 2 H), 2.18 - 2.24 (m, 2 H), 3.33 (s, 6 H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 0.0, 15.9, 23.2, 25.4, 28.6, 39.0, 49.0, 54.7, 86.2, 103.9, 151.1, 171.4. IR (neat) 641, 700, 757, 842, 1048, 1088, 1159, 1252, 1277, 1351, 1379, 1443, 2959. HRMS calcd for C$_{17}$H$_{29}$N$_2$O$_3$Si (M$^+$ + H) 337.1942, found 337.1953.

5-Isobutyl-1,3-dimethyl-5-(4-phenylbut-3-yn-1-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (3h). A 10 mL vial was charged with 3f (106 mg, 0.4 mmol, 1 equiv), iodobenzene (0.1 mL, 0.8 mmol, 2 equiv), tetrakis(triphenylphosphine)palladium(0) (9 mg, 8 μmol, 0.02 equiv), copper(I) iodide (1 mg, 4 μmol, 0.01 equiv), diisopropylamine (0.4 mL) and THF (1 mL), and stirred at 60 °C for 8 h. The reaction mixture was cooled down to room temperature, filtered through celite and purified by chromatography to give the title compound as a colorless oil. Yield 91% (123 mg). $^1$H NMR (400 MHz, CDCl$_3$) δ 0.83 (d, $J = 6.6$ Hz, 6 H), 1.43 (d, $J = 6.6$ Hz, 3 H), 1.56 (d, $J = 6.6$ Hz, 3 H), 1.95 (d, $J = 6.6$ Hz, 3 H), 2.15 (d, $J = 6.6$ Hz, 3 H), 2.19 (d, $J = 6.6$ Hz, 3 H), 3.32 (s, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 14.7, 23.2, 25.3, 28.6, 38.8, 49.3, 54.7, 69.8, 81.4, 151.1, 171.4. IR (neat) 645, 755, 1052, 1089, 1119, 1159, 1219, 1291, 1352, 1380, 1442, 1676, 2872, 2960, 3275. HRMS calcd for C$_{14}$H$_{21}$N$_2$O$_3$ (M$^+$ + H) 265.1547, found 265.1543. 
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1.45 - 1.57 (m, 1 H), 2.03 (d, J = 6.6 Hz, 2 H), 2.28 - 2.44 (m, 4 H), 3.28 (s, 6 H), 7.29 - 7.33 (m, 3 H), 7.34 - 7.38 (m, 2 H); ¹³C NMR (100 MHz, CDCl₃) δ 15.6, 23.3, 25.4, 28.6, 38.9, 49.7, 54.8, 82.4, 86.8, 122.9, 128.1, 128.3, 131.7, 151.2, 171.7. IR (neat) 692, 755, 916, 1054, 1088, 1157, 1295, 1351, 1379, 1440, 1676, 2959. HRMS calcd for C₂₀H₂₅N₂O₃ (M⁺ + H) 341.1860, found 341.1871.

5,5-Di(but-3-yn-1-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (3i). Prepared according to the procedure described above for 3e using 5,5-di(but-3-en-1-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (1.6 g, 10 mmol, 1 equiv), 4-bromo-1-butyne (1.1 mL, 12 mmol, 0.6 equiv), tetrabutylammonium bisulfate (34 mg, 0.1 mmol, 0.01 equiv) and K₂CO₃ (1.8 g, 20 mmol, 2 equiv) in DMF (25 mL) to give after purification by chromatography the title compound as a white solid (Mp 67-69 °C). Yield 42% (0.7 g). ¹H NMR (400 MHz, CDCl₃) δ 1.93 (t, J = 2.8 Hz, 2 H), 2.11 - 2.20 (m, 4 H), 2.21 - 2.30 (m, 4 H), 3.31 (s, 6 H); ¹³C NMR (100 MHz, CDCl₃) δ 14.5, 28.5, 37.9, 54.4, 70.0, 81.3, 151.0, 170.9. IR (neat) 642, 753, 913, 1062, 1127, 1284, 1348, 1382, 1440, 1671, 2947, 3278. HRMS calcd for C₁₄H₁₇O₃N₂ (M⁺ + H) 261.1234, found 261.1229.
Selective Monoreduction of Cyclic 1,3-Diimides using SmI$_2$–H$_2$O

**General procedure for monoreduction of cyclic 1,3-diimides using SmI$_2$–H$_2$O.** An oven-dried vial containing a stir bar was charged with a cyclic 1,3-diimide (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, 1000 equiv, ca. 1:1 THF/H$_2$O v/v) were added, followed by a rapid injection of SmI$_2$ (in THF, typically 4 equiv) with vigorous stirring. After the specified time (typically, 10-60 s), the reaction was quenched by bubbling air through the reaction mixture, diluted with CH$_2$Cl$_2$ (30 mL) and HCl (0.1 N, 20 mL), H$_2$O (20 mL) or NaHCO$_3$ (2% in H$_2$O, 20 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (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 the product distribution and diastereoselectivity from the crude reaction mixture. The crude product was purified by chromatography on silica gel, concentrated under reduced pressure and stored neat or as a solution in acetone. All compounds have been prepared as racemates.

(5$S$,6$R$)-6-Hydroxy-5-isobutyl-1,3-dimethylidihydropyrimidine-2,4(1$H$,3$H$)-dione (2a).

According to the general procedure, the reaction of 1a (0.10 mmol), SmI$_2$ (0.30 mmol, 3 equiv, 5.5 mL, 0.055 M) and H$_2$O (1.8 mL, 1000 equiv) for 10 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 83%. Dr = 88:12 (crude), 88:12 (purified). Stereochemistry of the major diastereoisomer was determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. Rf (50% EtOAc/hexanes) = 0.53. $^1$H NMR (500 MHz, C$_6$D$_6$) $\delta$ (major diastereoisomer) 0.88 (d, $J = 6.5$ Hz, 3 H), 0.96 (d, $J = 6.5$ Hz, 3 H), 1.54-1.60 (m, 1 H), 1.69-1.78 (m, 1 H), 2.85-2.14 (m, 1 H), 2.23-2.27 (m, 1 H), 2.87 (s, 3 H), 3.20 (d, $J = 6.0$ Hz, 1 H), 3.32 (s, 3 H), 4.25 (dd, $J = 4.5$, 5.0 Hz, 1 H); (minor, diagnostic peaks only) 0.82 (d, $J = 6.5$ Hz, 3 H), 0.92 (d, $J = 6.5$ Hz, 3 H), 2.93 (s, 3 H), 3.31 (s, 3 H), 3.53 (d, $J = 4.5$ Hz, 1 H), 4.19 (d, $J = 2.0$ Hz, 1 H); $^{13}$C NMR (75 MHz, C$_6$D$_6$) $\delta$ (major diastereoisomer) 21.9, 23.3, 25.3, 27.7, 34.3, 34.8, 44.3,
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80.5, 153.6, 170.4; (minor, diagnostic peaks only) 22.2, 22.4, 25.7, 27.5, 34.6, 39.0, 47.6, 82.6, 171.6. IR (neat) 3392, 2956, 2871, 1710, 1650, 1468, 1421, 1295, 1143, 1094, 1055, 1031, 1000, 911, 793 cm$^{-1}$. HRMS calcd for C$_{10}$H$_{18}$N$_2$O$_3$Na (M$^+$ + Na) 237.1210, found 237.1217.

$\text{(5S,6R)-5-Decyl-6-hydroxy-1,3-dimethyldihydropyrimidine-2,4(1H,3H)-dione (2b).}$

According to the general procedure, the reaction of 1b (0.10 mmol), SmI$_2$ (0.30 mmol, 3 equiv, 6.7 mL, 0.045 M) and H$_2$O (1.8 mL, 1000 equiv) for 10 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 56%. Dr = 86:14 (crude), 92:8 (after purification). Stereochemistry of the major diastereoisomer was determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. Rf (50% EtOAc/hexanes) = 0.47. $^1$H NMR (500 MHz, CD$_3$C(O)CD$_3$) $\delta$ (major diastereoisomer) 0.82 (t, $J$ = 7.0 Hz, 3 H), 1.18-1.31 (m, 14 H), 1.36-1.43 (m, 2 H), 1.45-1.53 (m, 1 H), 1.89-1.97 (m, 1 H), 2.67-2.71 (m, 1 H), 2.99 (s, 3 H), 3.00 (s, 3 H), 4.94 (dd, $J$ = 3.5, 5.0 Hz, 1 H), 5.44 (dd, $J$ = 1.0, 5.5 Hz, 1 H); (minor, diagnostic peaks only) 2.59 (td, $J$ = 2.0, 7.5 Hz, 1 H), 3.00 (s, 3 H), 3.00 (s, 3 H), 4.82 (dd, $J$ = 1.5, 4.5 Hz, 1 H), 5.51 (d, $J$ = 5.0 Hz, 1 H); $^{13}$C NMR (75 MHz, CD$_3$C(O)CD$_3$) $\delta$ (major diastereoisomer) 14.4, 23.3, 26.4, 27.5, 27.5, 30.1, 30.3, 30.4, 30.5, 32.6, 34.4, 47.0, 80.5, 154.2, 171.5; (minor, diagnostic peaks only) 34.7, 50.2, 80.4, 172.1. IR (neat) 3310, 1920, 2851, 1709, 1652, 1494, 1469, 1418, 1301, 1219, 1156, 1090, 1003, 914, 763 cm$^{-1}$. HRMS calcd for C$_{16}$H$_{29}$N$_2$O$_2$ (M$^+$ + H – H$_2$O) 281.2224, found 281.2222.

$\text{(5S,6R)-6-Hydroxy-5-isopentyl-1,3-dimethyldihydropyrimidine-2,4(1H,3H)-dione (2c).}$

According to the general procedure, the reaction of 1c (0.10 mmol), SmI$_2$ (0.30 mmol, 3
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equiv, 5.5 mL, 0.055 M) and H$_2$O (1.8 mL, 1000 equiv) for 10 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a white solid (Mp 117-119 °C). Yield 80% (1H NMR analysis vs. internal standard). Analytical sample was purified for characterization purposes. Dr = 91:9 (crude), 94:6 (purified). Stereochemistry of the major diastereoisomer was determined by 2D NMR experiments and confirmed by an X-ray analysis of a derivative. 1H NMR (500 MHz, CD$_3$C(O)CD$_3$) δ (major diastereoisomer) 0.90 (d, J = 6.6 Hz, 3 H), 0.92 (d, J = 6.6 Hz, 3 H), 1.27 - 1.38 (m, 2 H), 1.49 - 1.62 (m, 2 H), 1.97 - 2.04 (m, 1 H), 2.71 (td, J = 3.6, 8.8 Hz, 1 H), 3.05 (s, 3 H), 3.06 (s, 3 H), 4.99 (dd, J = 3.6, 5.5 Hz, 1 H), 5.45 (dd, J = 0.8, 5.5 Hz, 1 H); (minor, diagnostic peaks only) δ 0.86 (d, J = 6.5 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H), 2.61 (td, J = 1.9, 7.4 Hz, 1 H), 3.05 (s, 3 H), 3.06 (s, 3 H), 4.88 (dd, J = 1.9, 4.7 Hz, 1 H), 5.51 (d, J = 4.7 Hz, 1 H); 13C NMR (125 MHz, CD$_3$C(O)CD$_3$) δ (major diastereoisomer) 22.8, 23.1, 24.4, 27.6, 29.0, 34.4, 36.7, 47.3, 80.5, 154.2, 171.6; (minor, diagnostic peaks only) δ 22.7, 27.4, 28.6, 34.7, 36.8, 50.4, 82.7, 155.1, 172.2. IR (neat) 762, 903, 969, 1004, 1055, 1095, 1146, 1222, 1296, 1379, 1423, 1483, 1653, 1710, 2870, 2954, 3393. HRMS calcd for C$_{11}$H$_{20}$N$_2$O$_3$Na (M$^+$ + Na) 251.1366, found 251.1369.

According to the general procedure, the reaction of 1d (0.10 mmol), SmI$_2$ (0.30 mmol, 3 equiv, 3.5 mL, 0.087 M) and H$_2$O (1.8 mL, 1000 equiv) for 10 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 75%. Dr = 88:12 (crude), 89:11 (after purification). Rf (60% EtOAc/hexanes) = 0.46. 1H NMR (300 MHz, CD$_3$C(O)CD$_3$) δ (major diastereoisomer) 1.80-1.98 (m, 1 H), 2.26-2.45 (m, 1 H), 2.68-2.87 (m, 3 H), 3.06 (s, 3 H), 3.08 (s, 3 H), 5.09 (dd, J = 3.6, 4.8 Hz, 1 H), 5.60 (d, J = 5.1 Hz, 1 H), 7.16-7.34 (m, 5 H); (minor, diagnostic peaks only) 3.06 (s, 3 H), 3.10 (s, 3 H), 3.92 (dd, J = 1.8, 4.2 Hz, 1 H); 13C NMR (75 MHz, CD$_3$C(O)CD$_3$) δ (major diastereoisomer) 27.5, 28.6, 33.6, 34.4, 46.2, 80.6, 126.7, 129.2, 129.3, 143.0, 154.1, 171.4; (minor, diagnostic peaks only) 46.2, 80.5, 126.9, 129.4, 142.2. IR (neat) 3391, 1943, 1712, 1652, 1486, 1454, 1295, 1117, 1079, 752 cm$^{-1}$. HRMS calcd for C$_{14}$H$_{18}$N$_2$O$_3$Na (M$^+$ + Na) 285.1210, found 285.1204.
(5S,6R)-6-Hydroxy-1,3-dimethyl-5-(2-phenylpropyl)dihydropyrimidine-2,4(1H,3H)-dione (2e). According to the general procedure, the reaction of 1e (0.10 mmol), SmI$_2$ (0.40 mmol, 4 equiv, 4.6 mL, 0.087 M) and H$_2$O (1.8 mL, 1000 equiv) for 60 s afforded after purification by chromatography (EtOAc) the title compound as colorless oil. Yield 78%. Dr = 58:42 (at the Me) (83:17 major, 86:14 minor; total 85:15) (crude); dr = 53:47 (at the Me) (89:11 major, 86:14 minor, total 88:12) (purified). Rf (60% EtOAc/hexanes) = 0.50. $^1$H NMR (500 MHz, CD$_3$C(O)CD$_3$) $\delta$ (major diastereoisomers) 1.14 (d, $J$ = 6.5 Hz, 3 H), 1.15 (d, $J$ = 7.0 Hz, 3 H), 1.61-1.68 (m, 1 H), 1.71-1.77 (m, 1 H), 2.10-2.17 (m, 1 H), 2.22-2.26 (m, 1 H), 2.27-2.32 (m, 1 H), 2.50-2.54 (m, 1 H), 2.82 (s, 3 H), 2.82-2.85 (m, 1 H), 2.86 (s, 3 H), 2.89 (s, 3 H), 2.93 (s, 3 H), 2.95-3.00 (m, 1 H), 4.64 (dd, $J$ = 3.5, 5.0 Hz, 1 H), 4.89 (dd, $J$ = 3.0, 5.0 Hz, 1 H), 5.41 (dd, $J$ = 1.0, 5.5 Hz, 1 H), 5.46 (dd, $J$ = 1.0, 5.5 Hz, 1 H), 7.03-7.19 (m, 5 H); (minor, diagnostic peaks only) 1.10 (d, $J$ = 6.5 Hz, 3 H), 2.83 (s, 3 H), 2.90 (s, 3 H), 2.92 (s, 3 H), 4.52 (dd, $J$ = 2.0, 4.5 Hz, 1 H), 4.82 (dd, $J$ = 2.0, 5.0 Hz, 1 H), 5.31 (d, $J$ = 4.0 Hz, 1 H); $^{13}$C NMR (75 MHz, CD$_3$C(O)CD$_3$) $\delta$ (major diastereoisomers) 22.5, 23.7, 27.5, 27.6, 34.1, 34.3, 34.5, 35.6, 37.1, 38.2, 45.1, 45.3, 80.1, 81.2, 127.0, 127.2, 127.8, 127.9, 129.4, 129.5, 147.1, 148.0, 153.9, 154.0, 171.3, 171.6. IR (neat) 3392, 2960, 1715, 1657, 1487, 1423, 1297, 1196, 1053, 992, 763 cm$^{-1}$. HRMS calcd for C$_{15}$H$_{20}$N$_2$O$_3$Na (M$^+$ + Na) 299.1366, found 299.1380.

(5S,6R)-6-Hydroxy-5-(4-methoxyphenethyl)-1,3-dimethylidihydropyrimidine-2,4(1H,3H)-dione (2f). According to the general procedure, the reaction of 1f (0.10 mmol), SmI$_2$ (0.30 mmol, 3 equiv, 5.5 mL, 0.055 M) and H$_2$O (1.8 mL, 1000 equiv) for 10 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a white solid (Mp 123-125 °C). Yield 80% ($^1$H NMR analysis vs. internal standard). Analytical
sample was purified for characterization purposes. Dr = 88:12 (crude), 88:12 (purified). Stereochemistry of the major diastereoisomer determined by an X-ray analysis (recrystallization from acetone). $^1$H NMR (500 MHz, CD$_3$C(O)CD$_3$) $\delta$ 1.77 - 1.87 (m, 1 H), 2.24 - 2.33 (m, 1 H), 2.70 - 2.79 (m, 3 H), 3.04 (s, 3 H), 3.06 (s, 3 H), 3.75 (s, 3 H), 5.05 (dd, $J$ = 3.8, 5.4 Hz, 1 H), 5.57 (dd, $J$ = 0.9, 5.4 Hz, 1 H), 6.85 (d, $J$ = 8.6 Hz, 2 H), 7.16 (d, $J$ = 8.6 Hz, 2 H); $^{13}$C NMR (125 MHz, CD$_3$C(O)CD$_3$) $\delta$ 27.6, 28.8, 32.7, 34.4, 46.3, 55.5, 80.6, 114.7, 130.2, 134.8, 154.1, 159.0, 171.5. IR (neat) 761, 827, 1033, 1120, 1178, 1244, 1296, 1424, 1484, 1510, 1657, 1711, 2850, 2926, 3373. HRMS calcd for C$_{15}$H$_{21}$N$_2$O$_4$ (M$^+$ + H) 293.1496, found 293.1501.

(5S,6R)-6-Hydroxy-1,3-dimethyl-5-(4-(trifluoromethyl)phenethyl)dihydropyrimidine-2,4(1H,3H)-dione (2g). According to the general procedure, the reaction of 1g (0.10 mmol), SmI$_2$ (0.30 mmol, 3 equiv, 5.5 mL, 0.055 M) and H$_2$O (1.8 mL, 1000 equiv) for 10 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 76% ($^1$H NMR analysis vs. internal standard). Analytical sample was for purified for characterization purposes. Dr = 85:15 (crude), 76:24 (purified). $^1$H NMR (500 MHz, CD$_3$C(O)CD$_3$) $\delta$ 1.84 - 1.93 (m, 1 H), 2.29 - 2.39 (m, 1 H), 2.81 - 2.85 (m, 1 H), 2.93 (t, $J$ = 8.2 Hz, 2 H), 3.05 (s, 3 H), 3.07 (s, 3 H), 5.10 (dd, $J$ = 3.8, 5.4 Hz, 1 H), 5.61 (dd, $J$ = 0.6, 5.4 Hz, 1 H), 7.50 (d, $J$ = 7.9 Hz, 2 H), 7.64 (d, $J$ = 7.9 Hz, 2 H); $^{13}$C NMR (125 MHz, CD$_3$C(O)CD$_3$) $\delta$ 27.7, 28.5, 33.5, 34.4, 46.4, 80.6, 125.6 (q, $J^\text{C,F}$ = 272.5 Hz), 126.2 (q, $J^\text{C,F}$ = 3.6 Hz), 128.6 (q, $J^\text{C,F}$ = 32.7 Hz), 130.1, 148.0, 154.0, 171.3. $^{19}$F NMR (470 MHz, CD$_3$C(O)CD$_3$) $\delta$ -62.4. IR (neat) 763, 830, 1017, 1066, 1120, 1163, 1325, 1423, 1485, 1660, 1713, 2856, 2927, 3391. HRMS calcd for C$_{15}$H$_{17}$O$_3$N$_2$F$_3$Na (M$^+$ + Na) 353.1083, found 353.1083.
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(5S,6R)-5-(4-Bromophenethyl)-6-hydroxy-1,3-dimethylidihydropyrimidine-2,4(1H,3H)-dione (2h). According to the general procedure, the reaction of 1h (0.10 mmol), SmI$_2$ (0.30 mmol, 3 equiv, 5.5 mL, 0.055 M) and H$_2$O (1.8 mL, 1000 equiv) for 10 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a white solid (Mp 116-118 °C). Yield 67%. Dr = 87:13 (crude), 87:13 (purified). $^1$H NMR (400 MHz, CD$_3$C(O)CD$_3$) $\delta$ 1.65 - 1.77 (m, 1 H), 2.11 - 2.22 (m, 1 H), 2.64 - 2.71 (m, 3 H), 2.91 (s, 3 H), 2.93 (s, 3 H), 4.94 (dd, $J$ = 3.8, 5.3 Hz, 1 H), 5.43 - 5.48 (m, 1 H), 7.10 (d, $J$ = 8.5 Hz, 2 H), 7.33 (d, $J$ = 8.5 Hz, 2 H); $^{13}$C NMR (100 MHz, CD$_3$C(O)CD$_3$) $\delta$ 27.6, 28.5, 33.0, 34.4, 46.3, 80.6, 120.0, 131.4, 132.3, 142.4, 153.9, 171.3. IR (neat) 762, 817, 1011, 1067, 1120, 1296, 1425, 1485, 1658, 1710, 2851, 2962, 3363. HRMS calcd for C$_{14}$H$_{18}$N$_2$O$_3$Br (M$^+$ + H) 341.0495, found 341.0505.

(5S,6R)-5-Decyl-6-hydroxy-1,3,5-trimethylidihydropyrimidine-2,4(1H,3H)-dione (2i). According to the general procedure, the reaction of 1i (0.10 mmol), SmI$_2$ (0.40 mmol, 4 equiv, 13.3 mL, 0.033 M) and H$_2$O (1.8 mL, 1000 equiv) for 60 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 71%. Dr = 77:23 (crude), >95:5 (after purification). The major diastereoisomer can be partially separated by chromatography on silica gel. Stereochemistry of the major diastereoisomer was determined by 2D NMR experiments and subsequently confirmed by an X-ray analysis of a derivative. Rf (50% EtOAc/hexanes) = 0.60. $^1$H NMR (500 MHz, C$_6$D$_6$) $\delta$ (major diastereoisomer) 0.97 (s, 3 H), 1.04 (t, $J$ = 7.0 Hz, 3 H), 1.27-1.48 (m, 16 H), 2.03 (td, $J$ = 5.0, 12.5 Hz, 1 H), 2.13 (td, $J$ = 4.0, 12.5 Hz, 1 H), 2.91 (s, 3 H), 3.17 (d, $J$ = 5.0 Hz, 1 H), 3.36 (s, 3 H), 4.09 (d, $J$ = 5.0 Hz, 1 H); $^{13}$C NMR (125 MHz, C$_6$D$_6$) $\delta$ (major diastereoisomer) 14.4, 20.7, 23.1, 23.1, 27.9, 29.9, 30.1, 30.2, 30.7, 32.3, 32.9, 34.6, 46.2, 85.2, 153.2, 174.5.
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IR (neat) 3446, 3014, 1923, 1739, 1652, 1365, 1295, 1228, 1216, 1205, 1050, 898, 765 cm$^{-1}$. HRMS caleed for C$_{17}$H$_{31}$N$_2$O$_2$ (M$^+$ + H – H$_2$O) 295.2381, found 295.2380.

(5S,6S)-5-Decyl-6-hydroxy(6-D$^1$)-1,3,5-trimethyldihydropyrimidine-2,4(1H,3H)-dione (2i-D$^1$). According to the above procedure reaction of 1i (0.10 mmol), SmI$_2$ (0.40 mmol, 3 equiv, 2.7 mL, 0.11 M) and D$_2$O (1.8 mL, 1000 equiv) for 60 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound with >98% $D_1$ incorporation as a colorless oil. Yield 57%. Dr = 77:23 (crude), >95:5 (after purification). The major diastereoisomer can be partially separated by chromatography on silica gel. $^1$H NMR (500 MHz, CD$_3$C(O)CD$_3$) δ (major diastereoisomer) 0.88 (t, $J = 6.9$ Hz, 3 H), 1.15 (s, 3 H), 1.22 - 1.36 (m, 15 H), 1.36 - 1.46 (m, 2 H), 1.70 - 1.82 (m, 2 H), 3.05 (s, 3 H), 5.48 (s, 1 H); (minor, diagnostic peaks only) 0.87 (t, $J = 6.9$ Hz, 3 H), 1.23 (s, 3 H), 1.42 - 1.50 (m, 1 H), 1.50 - 1.58 (m, 1 H), 5.47 (s, 1 H); $^{13}$C NMR (125 MHz, CD$_3$C(O)CD$_3$) δ (major diastereoisomer) 14.4, 21.1, 23.3, 23.4, 27.7, 30.1, 30.2, 30.4, 31.2, 32.7, 33.5, 34.6, 46.6, 84.8 (t, $J = 23.6$ Hz), 153.7, 175.6; (minor, diagnostic peaks only) 14.4, 17.8, 23.4, 24.7, 27.7, 32.7, 34.6, 37.5, 48.0, 153.7, 174.4. IR (neat) 764, 847, 965, 1064, 1316, 1384, 1417, 1469, 1656, 1711, 2854, 2924, 3398. HRMS caleed for C$_{17}$H$_{30}$DN$_2$O$_2$ (M$^+$–OH) 296.2443, found 296.2432. Kinetic isotope effect was determined by reacting 1i (0.10 mmol), SmI$_2$ (0.40 mmol, 3 equiv, 2.7 mL, 0.11 M) and D$_2$O/H$_2$O (1:1, 1.8 mL, 1000 equiv) for 60 s at rt, followed by standard work-up to give the title compound with 40.1% $D^i$ incorporation as determined by $^1$H NMR (500 MHz) analysis ($k_H/k_D = 1.49±0.1$).

(5S,6R)-6-Hydroxy-5-isobutyl-1,3,5-trimethyldihydropyrimidine-2,4(1H,3H)-dione (2j). According to the general procedure, the reaction of 1j (0.10 mmol), SmI$_2$ (0.40 mmol, 4 equiv, 13.3 mL, 0.033 M) and H$_2$O (1.8 mL, 1000 equiv) for 60 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 50%. Dr = 87:13 (crude), >95:5 (after purification). The major diastereoisomer can be partially separated by chromatography on silica gel. Stereochemistry of the major diastereoisomer was determined by 2 D NMR experiments. Rf (50% EtOAc/hexanes) = 0.40. $^1$H NMR (500 MHz, CD$_3$C(O)CD$_3$) δ (major diastereoisomer) 0.71 (t, $J = 7.0$ Hz, 3 H), 1.00 - 1.10 (m, 14 H), 2.01 - 2.28 (m, 4 H), 2.30 (s, 3 H), 2.32 (s, 3 H), 5.50 (s, 1 H); (minor, diagnostic peaks only) 0.70 (t, $J = 7.0$ Hz, 3 H), 1.00 - 1.10 (m, 15 H), 2.01 - 2.28 (m, 4 H), 2.30 (s, 3 H), 2.32 (s, 3 H), 5.50 (s, 1 H); $^{13}$C NMR (125 MHz, CD$_3$C(O)CD$_3$) δ (major diastereoisomer) 14.3, 21.1, 23.4, 23.6, 27.7, 30.1, 30.2, 30.4, 31.2, 32.7, 33.6, 34.6, 46.6, 84.8 (t, $J = 23.7$ Hz), 153.7, 175.6; (minor, diagnostic peaks only) 14.3, 17.8, 23.4, 24.7, 27.7, 32.7, 34.6, 37.5, 48.0, 153.7, 174.4. IR (neat) 764, 847, 965, 1064, 1316, 1384, 1417, 1469, 1656, 1711, 2854, 2924, 3398. HRMS caleed for C$_{17}$H$_{30}$DN$_2$O$_2$ (M$^+$–OH) 296.2443, found 296.2432. Kinetic isotope effect was determined by reacting 1j (0.10 mmol), SmI$_2$ (0.40 mmol, 4 equiv, 13.3 mL, 0.033 M) and H$_2$O (1.8 mL, 1000 equiv) for 60 s at rt, followed by standard work-up to give the title compound with 40.1% $D^i$ incorporation as determined by $^1$H NMR (500 MHz) analysis ($k_H/k_D = 1.49±0.1$).
5-Hydroxy-2,4-dimethyl-2,4-diazaspiro[5.6]dodec-9-ene-1,3-dione (2k). According to the general procedure, the reaction of 1k (0.10 mmol), Sml₂ (0.30 mmol, 3 equiv, 5.5 mL, 0.055 M) and H₂O (1.8 mL, 1000 equiv) for 10 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a white solid (Mp 136-138 °C). Yield 55% (¹H NMR analysis vs. internal standard). Analytical sample was purified for characterization purposes. ¹H NMR (500 MHz, CDCl₃(CO)CD₃) δ 1.75 (br. dd, J = 9.0, 14.3 Hz, 1 H), 1.84 - 1.92 (m, 1 H), 1.92 - 1.98 (m, 1 H), 2.05 - 2.13 (m, 1 H), 2.18 - 2.29 (m, 3 H), 2.34 - 2.40 (m, 1 H), 3.05 (s, 3 H), 3.07 (s, 3 H), 4.88 (d, J = 5.4 Hz, 1 H), 5.58 (d, J = 5.4 Hz, 1 H), 5.59 - 5.63 (m, 1 H), 5.63 - 5.68 (m, 1 H); ¹³C NMR (125 MHz, CD₂(CO)CD₃) δ 14.3, 14.6, 17.9, 19.3, 24.9, 24.9, 40.7, 84.7, 120.9, 122.1, 143.5, 165.1. IR (neat) 736, 763, 859, 928, 1030, 1062, 1109,
(5S, 6R)-6-Hydroxy-1,3-dimethyl-5-phenethyldihydropyrimidine-2,4(1H, 3H)-dione (2d). According to the general procedure using preformed SmI$_2$–H$_2$O system, the reaction of 1l (0.10 mmol), SmI$_2$ (0.80 mmol, 8 equiv, 8.0 mL, 0.10 M) and H$_2$O (1.8 mL, 1000 equiv) for 10 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 76%. Dr = 87:13 (crude), 88:12 (after purification). R$_f$ (60% EtOAc/hexanes) = 0.46. Spectroscopic properties matched those described above for 2d.

(5S, 6R)-6-Hydroxy-5-isobutyl-1,3-dimethyldihydropyrimidine-2,4(1H, 3H)-dione (2a). According to the general procedure using preformed SmI$_2$–H$_2$O system, the reaction of 1m (0.10 mmol), SmI$_2$ (0.60 mmol, 6 equiv, 6.0 mL, 0.10 M) and H$_2$O (1.8 mL, 1000 equiv) for 10 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 58%. Dr = 88:12 (crude), 88:12 (purified). R$_f$ (50% EtOAc/hexanes) = 0.53. Spectroscopic properties matched those described above for 2a.
Reductive Cyclization of Cyclic 1,3-Diimides using SmI$_2$–H$_2$O

**General procedure for reductive cyclization of cyclic 1,3-diimides using SmI$_2$–H$_2$O.** An oven-dried vial containing a stir bar was charged with a cyclic 1,3-diimide (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, 200 equiv) were added, followed by a rapid injection of SmI$_2$ (in THF, typically 6 equiv) with vigorous stirring. After the specified time (typically, 15 min), the reaction was quenched by bubbling air through the reaction mixture, diluted with CH$_2$Cl$_2$ (30 mL) and HCl (0.1 N, 20 mL), H$_2$O (20 mL) or NaHCO$_3$ (2% in H$_2$O, 20 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 20 mL), organic layers were combined, dried over Na$_2$SO$_4$, filtered and concentrated. The sample was analysed 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, concentrated under reduced pressure and stored neat or as a solution in acetone. All compounds have been prepared as racemates.

(4aS,7S,7aR)-7a-Hydroxy-4a-isobutyl-1,3,7-trimethyltetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4a). According to the general procedure, the reaction of 3a (0.10 mmol), SmI$_2$ (0.60 mmol, 6 equiv, 7.5 mL, 0.080 M) and H$_2$O (0.36 mL, 200 equiv) for 15 min afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a white solid. Mp = 112-114 °C. Yield 74%. Dr > 95:5 (crude), > 95:5 (purified). Stereochemistry of the major diastereoisomer was determined by X-ray analysis (re-crystallization from EtOAc). Rf (50% EtOAc/hexanes) = 0.41. $^1$H NMR (400 MHz, CDCl$_3$) δ 0.56 (d, $J = 7.6$ Hz, 3 H), 0.69 (d, $J = 6.8$ Hz, 3 H), 0.77 (d, $J = 6.4$ Hz, 3 H), 1.07-1.16 (m, 1 H), 1.26 (dd, $J = 8.4$, 12.8 Hz, 1 H), 1.30-1.41 (m, 1 H), 1.44-1.53 (m, 2 H), 1.85-1.95 (m, 1 H), 2.09 (s, 1 H), 2.08-2.17 (m, 1 H), 2.58-2.66 (m, 1 H), 2.91 (s, 3 H), 3.02 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 17.4, 23.4, 24.7, 25.0, 28.4, 28.6, 29.4, 31.5, 42.8, 54.9, 95.3, 152.7, 172.8. IR (neat) 3418, 2957, 1704, 1644, 1455, 1414, 1385, 1326, 1122, 1086, 1044, 913, 754 cm$^{-1}$. HRMS calcd for C$_{14}$H$_{23}$N$_2$O$_3$ (M$^+$ + H) 269.1860, found 269.1864.
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(4aS,7R,7aR)-7-Benzyl-7a-hydroxy-4a-isobutyl-1,3-dimethyltetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4b). According to the general procedure, the reaction of 3b (0.05 mmol), SmI$_2$ (0.30 mmol, 6 equiv, 3.75 mL, 0.080 M) and H$_2$O (2.16 mL, 2400 equiv) for 60 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a white solid. Mp = 131-132 °C. Yield 58%. Dr > 95:5 (crude), > 95:5 (purified). Stereochemistry of the major diastereoisomer was determined by analogy to 4a and further confirmed by 2D NMR experiments. Rf (50% EtOAc/hexanes) = 0.77. $^1$H NMR (400 MHz, CDCl$_3$) δ 0.79 (d, $J$ = 6.4 Hz, 3 H), 0.87 (d, $J$ = 6.4 Hz, 3 H), 1.30-1.41 (m, 2 H), 1.42-1.51 (m, 1 H), 1.56-1.65 (m, 2 H), 1.71-1.80 (m, 1 H), 1.89 (t, $J$ = 13.2 Hz, 1 H), 2.36-2.46 (m, 3 H), 2.70-2.78 (m, 1 H), 3.00 (s, 3 H), 3.17 (s, 3 H), 6.99 (d, $J$ = 7.2 Hz, 2 H), 7.11 (t, $J$ = 7.2 Hz, 1 H), 7.19 (t, $J$ = 7.6 Hz, 2 H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 23.4, 24.7, 25.1, 26.0, 28.6, 29.5, 31.3, 37.5, 42.8, 50.1, 55.3, 94.8, 126.4, 128.5, 128.8, 139.1, 152.6, 172.9. IR (neat) 3321, 2952, 2926, 2868, 1699, 1638, 1457, 1413, 1379, 1327, 1080, 1057, 1034, 756 cm$^{-1}$. HRMS calcd for C$_{20}$H$_{29}$N$_2$O$_3$ (M$^+$ + H) 345.2173, found 345.2183.

(4aS,7R,7aR)-7a-Hydroxy-4a-isobutyl-7-(4-methoxybenzyl)-1,3-dimethyltetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4c). According to the general procedure, the reaction of 3c (0.05 mmol), SmI$_2$ (0.30 mmol, 6 equiv, 3.75 mL, 0.080 M) and H$_2$O (2.16 mL, 2400 equiv) for 60 s afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a white solid. Mp = 133-134 °C. Yield 59%. Dr > 95:5 (crude), > 95:5 (purified). Stereochemistry of the major diastereoisomer was determined by analogy to 4a and further confirmed by 2D NMR experiments. Rf (50% EtOAc/hexanes) = 0.53. $^1$H NMR (400 MHz, CDCl$_3$) δ 0.79 (d, $J$ = 6.8 Hz, 3 H), 0.87 (d, $J$ = 6.4 Hz, 3 H), 1.28-1.38 (m, 2 H), 1.41-1.48 (m, 1 H), 1.55-1.64 (m, 2 H), 1.69-1.88 (m, 2 H), 2.08 (s, 1 H), 2.32-2.41 (m, 2 H), 2.70-2.78 (m, 1 H), 3.00 (s, 3 H), 3.16 (s, 3 H), 6.93 (d, $J$ = 7.2 Hz, 2 H), 7.11 (t, $J$ = 7.2 Hz, 1 H), 7.19 (t, $J$ = 7.6 Hz, 2 H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 23.4, 24.7, 25.1, 26.0, 28.6, 29.5, 31.3, 37.5, 42.8, 50.1, 55.3, 94.8, 126.4, 128.5, 128.8, 139.1, 152.6, 172.9. IR (neat) 3321, 2952, 2926, 2868, 1699, 1638, 1457, 1413, 1379, 1327, 1080, 1057, 1034, 756 cm$^{-1}$. HRMS calcd for C$_{20}$H$_{29}$N$_2$O$_3$ (M$^+$ + H) 345.2173, found 345.2183.
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2.70-2.77 (m, 1 H), 3.00 (s, 3 H), 3.17 (s, 3 H), 3.71 (s, 3 H), 6.73 (d, $J = 8.8$ Hz, 2 H), 6.90 (d, $J = 8.8$ Hz, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 23.4, 24.7, 25.1, 26.0, 28.6, 29.5, 31.2, 36.6, 42.8, 50.2, 55.2, 55.3, 94.8, 113.9, 129.7, 131.0, 152.5, 158.1, 172.8. IR (neat) 3439, 2953, 1704, 1651, 1511, 1456, 1418, 1364, 1329, 1246, 1177, 1034, 820, 754 cm$^{-1}$. HRMS calcd for C$_{21}$H$_{31}$N$_2$O$_4$ (M$^+$ + H) 375.2279, found 375.2267.

(4aS,7R,7aR)-7-Benzyl-4a-(cyclohexylmethyl)-7a-hydroxy-1,3-dimethyltetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4c). According to the general procedure, the reaction of 3d (0.05 mmol), SmI$_2$ (0.30 mmol, 6 equiv, 10.0 mL, 0.030 M) and H$_2$O (2.16 mL, 2400 equiv) for 5 min afforded after purification by chromatography (1/2 EtOAc/hexanes) the title compound as a white solid. Mp = 144-145 °C. Yield 64%. Dr > 95:5 (crude), > 95:5 (purified). Stereochemistry of the major diastereoisomer was determined by analogy to 4a and further confirmed by 2D NMR experiments. Rf (20% EtOAc/hexanes) = 0.31. $^1$H NMR (500 MHz, CDCl$_3$) δ 0.75-0.85 (m, 2 H), 0.96-1.06 (m, 1 H), 1.10-1.19 (m, 3 H), 1.29-1.36 (m, 1 H), 1.38-1.44 (m, 2 H), 1.47-1.62 (m, 5 H), 1.70-1.79 (m, 2 H), 1.89 (t, $J = 13.5$ Hz, 1 H), 2.35 (s, 1 H), 2.38-2.45 (m, 2 H), 2.68-2.74 (m, 1 H), 2.99 (s, 3 H), 3.16 (s, 3 H), 6.99 (d, $J = 7.0$ Hz, 2 H), 7.11 (tt, $J = 1.0$, 7.0 Hz, 1 H), 7.19 (t, $J = 8.0$ Hz, 2 H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 26.0, 26.1, 28.6, 29.5, 31.3, 34.1, 34.2, 35.0, 37.5, 41.5, 50.1, 55.0, 94.8, 126.3, 128.5, 128.8, 139.1, 152.6, 172.9. IR (neat) 3371, 2921, 2851, 1717, 1664, 1449, 1414, 1377, 1328, 1282, 1110, 1072, 1030, 912, 754, 731, 699 cm$^{-1}$. HRMS calcd for C$_{23}$H$_{33}$N$_2$O$_3$ (M$^+$ + H) 385.2486, found 385.2491.

(4aS,7S,7aR)-4a-(Cyclohexylmethyl)-7a-hydroxy-7-(D$^1$-(phenyl)methyl)-1,3-dimethyltetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4d-D$^1$). According to the general procedure, the reaction of 3d (0.05 mmol), SmI$_2$ (0.15 mmol, 3 equiv, 1.7 mL, 0.087 M) and D$_2$O (0.90 mL, 1000 equiv) for 5 min at rt afforded after purification by chromatography (40/60 EtOAc/hexanes) the title compound with >98% D$^1$ incorporation. Yield 54%. Dr > 95:5 (crude), > 95:5 (purified). Dr at benzylic position 1:1 (crude), 1:1 (purified). $^1$H NMR (500 MHz, CD$_3$C(O)CD$_3$) δ (mixture of D$^1$ diastereoisomers) 0.66 (qd, $J$
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$^1$H NMR (500 MHz, CD$_3$C(O)CD$_3$) $\delta$ 0.70 (d, $J = 7.3$ Hz, 3 H), 1.16 (dtt, $J = 4.7, 8.5, 13.0$ Hz, 1 H), 1.64 (ddd, $J = 8.5, 9.8, 12.9$ Hz, 1 H), 1.70 - 1.83 (m, 2 H), 1.84 - 1.94 (m, 1 H), 1.94 - 2.08 (m, 2 H), 2.38 - 2.46 (m, 1 H), 2.57 (ddd, $J = 4.1, 8.5, 12.9$ Hz, 1 H), 3.02 (s, 3 H), 3.08 (s, 3 H), 4.88 (ddt, $J = 1.5, 2.2, 10.4$ Hz, 1 H), 4.96 (d, $J = 1.5, 17.1$ Hz, 1 H), 5.12 (s, 1 H), 5.75 (ddt, $J = 6.5, 10.4, 17.1$ Hz, 1 H); $^{13}$C NMR (125 MHz, CD$_3$C(O)CD$_3$) $\delta$ 17.9, 28.3, 29.3, 29.3, 29.9, 32.0, 34.4, 45.3, 56.1, 94.3, 114.9, 139.3, 152.9, 173.7. IR (neat) 648, 755, 913, 1047, 1089, 1121, 1332, 1385, 1411, 1456, 1649, 1702, 2874, 2930, 2960, 3401. HRMS calcd for C$_{14}$H$_21$N$_2$O$_2$ (M$^+$ – OH) 249.1598, found 249.1601.

(4aR,7S,7aR)-4a-(But-3-en-1-yl)-7a-hydroxy-1,3,7-trimethyltetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4e). According to the general procedure, the reaction of 3e (0.10 mmol), SmI$_2$ (0.60 mmol, 6 equiv, 7.1 mL, 0.085 M) and H$_2$O (0.36 mL, 200 equiv) for 15 min afforded after purification by chromatography (1:1 EtOAc/hexanes) the title compound as a colorless oil. Yield 55%. Dr > 95:5 (crude), > 95:5 (purified). Stereochemistry of the major diastereoisomer 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$_3$) $\delta$ 0.70 (d, $J = 7.3$ Hz, 3 H), 1.16 (dtt, $J = 4.7, 8.5, 13.0$ Hz, 1 H), 1.64 (ddd, $J = 8.5, 9.8, 12.9$ Hz, 1 H), 1.70 - 1.83 (m, 2 H), 1.84 - 1.94 (m, 1 H), 1.94 - 2.08 (m, 2 H), 2.38 - 2.46 (m, 1 H), 2.57 (ddd, $J = 4.1, 8.5, 12.9$ Hz, 1 H), 3.02 (s, 3 H), 3.08 (s, 3 H), 4.88 (ddt, $J = 1.5, 2.2, 10.4$ Hz, 1 H), 4.96 (d, $J = 1.5, 17.1$ Hz, 1 H), 5.12 (s, 1 H), 5.75 (ddt, $J = 6.5, 10.4, 17.1$ Hz, 1 H); $^{13}$C NMR (125 MHz, CD$_3$C(O)CD$_3$) $\delta$ 17.9, 28.3, 29.3, 29.3, 29.9, 32.0, 34.4, 45.3, 56.1, 94.3, 114.9, 139.3, 152.9, 173.7. IR (neat) 648, 755, 913, 1047, 1089, 1121, 1332, 1385, 1411, 1456, 1649, 1702, 2874, 2930, 2960, 3401. HRMS calcd for C$_{14}$H$_21$N$_2$O$_2$ (M$^+$ – OH) 249.1598, found 249.1601.
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(4aS,7aR)-7a-Hydroxy-4a-isobutyl-1,3-dimethyl-7-methylenetetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4f). According to the general procedure, the reaction of 3f (0.10 mmol), SmI$_2$ (0.60 mmol, 6 equiv, 7.1 mL, 0.085 M) and H$_2$O (0.36 mL, 200 equiv) for 15 min afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 63%. Dr > 95:5 (crude), > 95:5 (purified). Stereochemistry of the major diastereoisomer determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. $^1$H NMR (400 MHz, CD$_3$C(O)CD$_3$) $\delta$ 0.86 (d, $J = 6.6$ Hz, 3 H), 0.90 (d, $J = 6.6$ Hz, 3 H), 1.53 (dd, $J = 7.6$, 14.3 Hz, 1H), 1.62 (dd, $J = 4.5$, 14.3 Hz, 1 H), 1.66 - 1.75 (m, 1 H), 1.78 - 1.88 (m, 1 H), 2.19 - 2.31 (m, 1 H), 2.36 - 2.49 (m, 2 H), 3.04 (s, 3 H), 3.12 (s, 3 H), 4.99 (t, $J = 2.3$ Hz, 1 H), 5.15 (t, $J = 2.3$ Hz, 1 H), 5.56 (s, 1 H); $^{13}$C NMR (100 MHz, CD$_3$C(O)CD$_3$) $\delta$ 24.5, 25.2, 25.7, 28.4, 29.7, 30.9, 41.1, 56.5, 91.6, 109.6, 151.9, 152.8, 173.4. IR (neat) 759, 809, 847, 902, 1025, 1067, 1109, 1205, 1324, 1386, 1414, 1454, 1647, 1705, 2865, 2955, 3363. HRMS calcd for C$_{14}$H$_{21}$N$_2$O$_2$ (M$^+$–OH) 249.1598, found 249.1605.

(4aS,7aS)-7a-hydroxy-4a-isobutyl-1,3-dimethyl-7-(D$^1$-methylene)tetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4f-D$^1$). According to the general procedure, reaction of 3f (0.10 mmol), SmI$_2$ (0.60 mmol, 6 equiv, 7.1 mL, 0.085 M) and D$_2$O (0.36 mL, 200 equiv) for 15 min afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound with >98% deuterium incorporation as a colorless oil. Yield 67%. Dr (at the hemiaminal carbon) > 95:5 (crude), > 95:5 (purified). Dr (at the vinylic position) = 66:34. (major diastereoisomer) $^1$H NMR (400 MHz, CD$_3$C(O)CD$_3$) $\delta$ 0.86 (d, $J = 6.6$ Hz, 0 H), 0.89 (d, $J = 6.6$ Hz, 3 H), 1.53 (dd, $J = 7.6$, 14.4 Hz, 1 H), 1.62 (dd, $J = 4.3$, 14.4 Hz, 1 H), 1.66 - 1.74 (m, 1 H), 1.78 - 1.87 (m, 1 H), 2.19 - 2.29 (m, 1 H), 2.36 - 2.49 (m, 2 H), 3.04 (s, 3 H), 3.11 (s, 3 H), 5.13 (t, $J = 2.5$ Hz, 1 H); (minor, diagnostic peaks only) 4.97 (t, $J = 2.1$ Hz, 1 H); $^{13}$C NMR (100 MHz, CD$_3$C(O)CD$_3$) $\delta$ 24.5, 25.2, 25.7, 28.4, 29.7, 30.8, 41.0, 56.4, 91.6, 109.1, 152.9, 154.3, 173.4; IR (neat) 757, 810, 847, 902, 974, 1025, 1067, 1109, 1205, 1324, 1386, 1414, 1454, 1647, 1705, 2865, 2955, 3363; HRMS calcd for C$_{14}$H$_{20}$DN$_2$O$_2$ (M$^+$–OH) 249.1660, found 250.1665. Kinetic isotope
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Effect was determined by reacting 3f (0.10 mmol), SmI$_2$ (0.60 mmol, 6 equiv, 7.1 mL, 0.085 M) and D$_2$O/H$_2$O (1:1, 0.36 mL, 200 equiv) for 15 min at rt, followed by standard work-up to give the title compound with 36.4% $D^1$ incorporation as determined by $^1$H NMR (500 MHz) analysis ($k_{H}/k_{D} = 1.75\pm0.1$).

$^{(4aS,7aS,E)}$-7a-Hydroxy-4a-isobutyl-1,3-dimethyl-7-((trimethylsilyl)methylene) tetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4g). According to the general procedure, the reaction of 3e (0.10 mmol), SmI$_2$ (0.60 mmol, 6 equiv, 7.1 mL, 0.085 M) and H$_2$O (0.36 mL, 200 equiv) for 15 min afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless solid (mp 156-158 °C). Yield 66%. Dr > 95:5 (crude), > 95:5 (purified). Stereochemistry of the major diastereoisomer determined by 2D NMR experiments and confirmed by an X-ray analysis. $^1$H NMR (400 MHz, CD$_3$C(O)CD$_3$) $\delta$ 0.09 (s, 9 H), 0.88 (d, $J = 6.6$ Hz, 3 H), 0.90 (d, $J = 6.6$ Hz, 3 H), 1.47 (dd, $J = 7.3$, 14.6 Hz, 1 H), 1.60 (dd, $J = 4.3$, 14.6 Hz, 1 H), 1.70 - 1.80 (m, 1 H), 1.85 - 1.92 (m, 1 H), 2.26 - 2.38 (m, 2 H), 2.44 - 2.53 (m, 1 H), 3.03 (s, 3 H), 3.07 (s, 3 H), 5.51 (s, 1 H), 5.72 (t, $J = 2.3$ Hz, 1 H); $^{13}$C NMR (100 MHz, CD$_3$C(O)CD$_3$) $\delta$ -0.6, 24.7, 25.3, 25.7, 26.8, 28.3, 29.8, 30.8, 40.8, 55.6, 92.7, 123.0, 153.0, 159.3, 173.6. IR (neat) 760, 846, 1024, 1063, 1103, 1249, 1324, 1385, 1414, 1462, 1652, 1707, 2955, 3390. HRMS calcd for C$_{17}$H$_{31}$N$_2$O$_3$Si (M$^+$ + H) 339.2098, found 339.2113.

$^{(4aS,7aS,E)}$-7a-Hydroxy-4a-isobutyl-1,3-dimethyl-7-($D^1$-(trimethylsilyl)methylene) tetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4g-$D^1$). According to the general procedure, the reaction of 3e (0.10 mmol), SmI$_2$ (0.60 mmol, 6 equiv, 5.5 mL, 0.110 M) and D$_2$O (0.36 mL, 200 equiv) for 15 min afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless solid (mp 156-158 °C) with >98% deuterium incorporation. Yield 78%. Dr > 95:5 (crude), > 95:5 (purified). Stereochemistry of the major diastereoisomer determined by 2D NMR experiments and confirmed by an X-ray analysis of a derivative. $^1$H NMR (400 MHz, CD$_3$C(O)CD$_3$) $\delta$ 0.09 (s, 9 H), 0.87 (d, $J = 6.7$ Hz, 3 H), 0.90 (d, $J = 6.7$ Hz, 3 H), 1.47 (dd, $J = 7.3$, 14.4 Hz, 1 H), 1.60 (dd, $J = 4.3$, 14.4 Hz, 3 H), 5.51 (s, 1 H), 5.72 (t, $J = 2.3$ Hz, 1 H); $^{13}$C NMR (100 MHz, CD$_3$C(O)CD$_3$) $\delta$ -0.6, 24.7, 25.3, 25.7, 26.8, 28.3, 29.8, 30.8, 40.8, 55.6, 92.7, 123.0, 153.0, 159.3, 173.6. IR (neat) 760, 846, 1024, 1063, 1103, 1249, 1324, 1385, 1414, 1462, 1652, 1707, 2955, 3390. HRMS calcd for C$_{17}$H$_{31}$N$_2$O$_3$Si (M$^+$ + H) 339.2098, found 339.2113.
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$\delta$ -0.6, 24.7, 25.3, 25.7, 26.7, 28.3, 29.8, 30.8, 40.8, 55.6, 92.6, 122.6 (d, $J = 20.3$ Hz), 153.0, 159.1, 173.6; IR(neat) 649, 690, 759, 837, 999, 1054, 1111, 1207, 1248, 1322, 1386, 1413, 1457, 1648, 1705, 2867, 2954, 3364; HRMS calcd for C$_{17}$H$_{30}$DN$_2$O$_3$Si (M$^+$ + H) 340.2161, found 340.2165. Kinetic isotope effect was determined by reacting 3e (0.10 mmol), SmI$_2$ (0.60 mmol, 6 equiv, 7.1 mL, 0.085 M) and D$_2$O/H$_2$O (1:1, 0.36 mL, 200 equiv) for 15 min at rt, followed by standard work-up to give the title compound with 39.4% $D^1$ incorporation as determined by $^1$H NMR (500 MHz) analysis ($k_H/k_D = 1.54\pm0.1$).

(4aS,7aR,E)-7-Benzylidene-7a-hydroxy-4a-isobutyl-1,3-dimethyltetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4h). According to the general procedure, the reaction of 3h (0.10 mmol), SmI$_2$ (0.60 mmol, 6 equiv, 5.5 mL, 0.110 M) and H$_2$O (0.36 mL, 200 equiv) for 15 min afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 90%. $E/Z = 37:63$. Stereochemistry of the major diastereoisomer was determined by 2D NMR experiments. $^1$H NMR (500 MHz, CD$_3$C(O)CD$_3$) $\delta$ (major diastereoisomer) 0.87 (d, $J = 6.6$ Hz, 3 H), 0.90 (d, $J = 6.6$ Hz, 3 H), 1.51 - 1.67 (m, 2 H), 1.69 - 1.76 (m, 1 H), 1.91 - 1.99 (m, 1 H), 2.50 - 2.56 (m, 2 H), 2.69 - 2.76 (m, 1 H), 3.04 (s, 3 H), 3.23 (s, 3 H), 5.72 (s, 1 H), 6.56 (t, $J = 2.4$ Hz, 1 H), 7.24 - 7.31 (1 H, m, 1 H), 7.34 - 7.39 (m, 4 H); (minor, diagnostic peaks only) 0.80 (d, $J = 6.6$ Hz, 3 H), 0.89 (d, $J = 6.6$ Hz, 3 H), 1.47 (dd, $J = 4.7$, 14.2 Hz, 1 H), 1.80 (ddd, $J = 7.9$, 10.4, 12.0 Hz, 1 H), 2.29 (s, 3 H), 2.39 (ddd, $J = 1.9$, 7.9, 9.8, 17.1 Hz, 1 H), 2.60 (dd, $J = 2.5$, 10.4, 17.1 Hz, 1 H), 3.07 (s, 3 H), 5.65 (s, 1 H), 6.53 (br. s, 1 H), 7.04 - 7.08 (m, 2 H), 7.18 - 7.23 (m, 1 H); $^{13}$C NMR (125 MHz, CD$_3$C(O)CD$_3$) $\delta$ (major diastereoisomer) 24.6, 25.2, 25.7, 26.3, 28.4, 30.0, 31.5, 40.8, 55.9, 93.1, 124.6, 128.2, 129.3, 129.9, 137.3, 144.1, 152.9, 173.3; (minor, diagnostic peaks only) 24.4, 25.0, 25.6, 28.4, 28.8, 29.5, 29.5, 40.3, 58.2, 91.1, 127.1, 127.5, 128.9, 129.1, 129.3, 138.2, 144.0, 152.0, 173.2. IR (neat) 699, 756, 1029, 1069, 1104, 1234, 1383, 1454, 1653, 2869, 2955, 3360. HRMS calcd for C$_{20}$H$_{27}$N$_2$O$_3$ (M$^+$ + H) 343.2016, found 343.2014.

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(4aS,7aR,E)-7a-Hydroxy-4a-isobutyl-1,3-dimethyl-7-(D₁-(phenyl)methylene)tetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4h-D₁). According to the general procedure, the reaction of 3h (0.06 mmol), SmI₂ (0.36 mmol, 6 equiv, 3.3 mL, 0.110 M) and D₂O (0.05 mL, 50 equiv) for 15 min afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil with >98% deuterium incorporation. Yield 65%. E:Z = 1.5:1. Stereochemistry of the major diastereoisomer determined by 2D NMR experiments. ¹H NMR (400 MHz, CD₃C(O)CD₃) δ (major diastereoisomer) 0.87 (d, J = 6.6 Hz, 3 H), 0.89 (d, J = 6.6 Hz, 3 H), 1.56 (dd, J = 7.3, 14.3 Hz, 1 H), 1.65 (dd, J = 4.5, 14.3 Hz, 1 H), 1.68 - 1.77 (m, 1 H), 1.92 - 2.00 (m, 1 H), 2.47 - 2.58 (m, 2 H), 2.65 - 2.79 (m, 1 H), 3.04 (s, 3 H), 3.23 (s, 3 H), 5.72 (s, 1 H), 7.14 - 7.31 (m, 1 H), 7.32 - 7.41 (m, 4 H); (minor, diagnostic peaks only) 0.80 (d, J = 6.6 Hz, 3 H), 0.90 (d, J = 6.6 Hz, 3 H), 1.44 - 1.52 (m, 1 H), 1.62 - 1.68 (m, 1 H), 1.80 (dt, J = 2.2, 10.0 Hz, 1 H), 2.30 (s, 3 H), 2.33 - 2.44 (m, 1 H), 2.59 - 2.65 (m, 1 H), 3.07 (s, 3 H), 5.65 (s, 1 H), 7.04 - 7.10 (m, 2 H); ¹³C NMR (100 MHz, CD₃C(O)CD₃) δ (major diastereoisomer) 24.6, 25.2, 25.7, 26.3, 28.3, 29.9, 31.6, 40.8, 55.9, 93.1, 124.3, 128.2, 129.3, 129.9, 137.3, 144.1, 152.9, 173.3; (minor, diagnostic peaks only) 24.4, 25.0, 25.6, 28.3, 28.7, 29.3, 29.5, 40.3, 58.2, 93.0, 124.0, 127.5, 128.9, 129.1, 137.5, 143.9, 152.0, 173.2. IR (neat) 698, 759, 1000, 1029, 1066, 1110, 1323, 1380, 1414, 1450, 1650, 1704, 2870, 2954, 3363. HRMS calcd for C₂₀H₂₄DN₂O₂ (M⁺–OH) 326.1973, found 326.1979.

(4aR,7aR)-4a-(But-3-yn-1-yl)-7a-hydroxy-1,3-dimethyl-7-methylenetetrahydro-1H-cyclopenta[d]pyrimidine-2,4(3H,4aH)-dione (4i). According to the general procedure, the reaction of 3i (0.10 mmol), SmI₂ (0.60 mmol, 6 equiv, 7.1 mL, 0.085 M) and H₂O (0.36 mL, 200 equiv) for 15 min afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 82%. Dr > 95:5 (crude), > 95:5 (purified). ¹H NMR (500 MHz, CD₃C(O)CD₃) δ 1.85 - 1.99 (m, 3 H), 2.06 - 2.12 (m, 1 H), 2.25 - 2.32 (m, 1 H), 2.33 (t, J = 2.5 Hz, 1 H), 2.34 - 2.43 (m, 1 H), 2.45 - 2.52 (m, 1 H), 2.51 - 2.59 (m, 1 H), 2.99 (s, 3 H), 3.07 (s, 3 H), 5.20 (t, J = 2.4 Hz, 1 H), 5.37 (t, J = 2.4 Hz, 1 H), 5.62 (s, 1
$^{13}$C NMR (125 MHz, CD$_3$C(O)CD$_3$) δ 15.2, 26.2, 28.2, 29.6, 31.3, 32.6, 54.4, 69.8, 85.2, 92.4, 111.8, 150.6, 152.9, 173.0. IR (neat) 759, 913, 1054, 1136, 1220, 1334, 1385, 1415, 1459, 1649, 1704, 2855, 2925, 3298. HRMS calcd for C$_{14}$H$_{19}$N$_2$O$_3$ (M$^+$ + H) 263.1390, found 263.1386.
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Transformations of Cyclic alpa-Hydroxy Carboxamides

$\text{(5R,6R)-5-Decyl-6-methoxy-1,3,5-trimethyldihydropyrimidine-2,4(1H,3H)-dione (5a)}$. A 10 mL vial was charged with $\text{2i}$ (0.032 mmol, 1.0 equiv), MeOH (1 mL) and HCl (0.2 mL, 2.0 $N$ in Et$_2$O), and stirred at room temperature for 3 h. Removal of solvent under reduced pressure afforded the title compound in 99% yield (1$H$ NMR analysis). Dr = 71:39. Note that the title compound is unstable and should be used immediately after preparation. 1$H$ NMR (400 MHz, CD$_3$C(O)CD$_3$) $\delta$ 0.82 (t, $J = 6.6$ Hz, 3 H), 1.18 (s, 3 H), 1.19 - 1.45 (m, 16 H), 1.45 - 1.55 (m, 1 H), 1.60 - 1.76 (m, 1 H), 3.00 (s, 3 H), 3.00 (s, 3 H), 3.13 - 3.17 (m, 3 H), 4.59 (br. s, 1 H); 13$C$ NMR (100 MHz, CD$_3$C(O)CD$_3$) $\delta$ ppm 14.3, 17.7, 23.3, 24.6, 27.6, 29.9, 30.0, 30.2, 30.6, 31.1, 32.5, 33.3, 34.7, 37.4, 48.0, 86.1, 153.6, 174.3. IR (neat) 722, 764, 930, 1040, 1074, 1184, 1293, 1380, 1421, 1467, 1487, 1657, 1713, 2854, 2924. HRMS calcd for C$_{17}$H$_{31}$N$_2$O$_2$ (M$^+$ − OCH$_3$) 295.2380, found 295.2392.

5-Decyl-1,3,5-trimethyldihydropyrimidine-2,4(1H,3H)-dione (5b). To a 10 mL vial charged with $\text{2i}$ (0.032 mmol, 1.0 equiv) and CH$_2$Cl$_2$ (1 mL), triethylsilane (0.05 mL, 0.32 mmol, 10 equiv) was added at -78 °C followed by BF$_3$$\cdot$OEt$_2$ (0.02 mL, 0.16 mmol, 5 equiv). After stirring for 5 min at -78 °C, the reaction mixture was warmed up to room temperature over 3 h, quenched with NH$_4$Cl (aq, sat., 1 mL) and extracted with CH$_2$Cl$_2$ (3 × 2 mL). Purification by chromatography using EtOAc/hexanes (30%) afforded the title compound as a colorless oil. Yield 96%. 1$H$ NMR (500 MHz, CD$_3$C(O)CD$_3$) $\delta$ 0.87 (t, $J = 6.9$ Hz, 3 H), 1.14 (s, 3 H), 1.22 - 1.34 (m, 16 H), 1.49 - 1.62 (m, 2 H), 3.00 (s, 3 H), 3.03 (s, 3 H), 3.21 (d, $J = 12.5$ Hz, 1 H), 3.25 (d, $J = 12.5$ Hz, 1 H); 13$C$ NMR (125 MHz, CD$_3$C(O)CD$_3$) $\delta$ ppm 14.4, 20.9, 23.4, 24.5, 28.0, 30.0, 30.1, 30.2, 30.3, 30.9, 32.7, 35.9, 36.8, 42.1, 54.0, 154.3, 175.3. IR (neat) 757, 1062, 1184, 1285, 1377, 1416, 1447, 1491, 1673, 1712, 2854, 2924. HRMS calcd for C$_{17}$H$_{33}$N$_2$O$_2$ (M$^+$ + H) 297.2537, found 297.2536.
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**(5R,6R)-5-Decyl-1,3,5,6-tetramethyldihydropyrimidine-2,4(1H,3H)-dione (5c).** To a 10 mL vial charged with 2i (0.032 mmol, 1.0 equiv) and CH$_2$Cl$_2$ (1 mL), trimethylaluminium (2.0 M in hexane, 0.32 mmol, 10 equiv), followed by BF$_3$•OEt$_2$ (0.02 mL, 0.16 mmol, 5 equiv) were added, the reaction mixture stirred at room temperature for 3 h, quenched with NH$_4$Cl (aq, sat., 1 mL) and extracted with CH$_2$Cl$_2$ (3 x 2 mL). Purification by chromatography using EtOAc/hexanes (30%) afforded the title compound as a colorless oil. Yield 78%. Dr = 91:9. $^1$H NMR (400 MHz, CD$_3$C(O)CD$_3$) $\delta$ (major diastereoisomer) 0.87 (t, $J$ = 6.8 Hz, 3 H), 1.07 (d, $J$ = 6.6 Hz, 3 H), 1.10 (s, 3 H), 1.11 - 1.17 (m, 1 H), 1.21 - 1.36 (m, 14 H), 1.36 - 1.42 (m, 1 H), 1.46 (ddd, $J$ = 4.4, 12.2, 13.4 Hz, 1 H), 1.61 (ddd, $J$ = 4.4, 12.2, 13.4 Hz, 1 H), 3.00 (s, 3 H), 3.04 (s, 3 H), 3.27 (q, $J$ = 6.6 Hz, 1 H); (minor, diagnostic peaks only) 0.88 (t, $J$ = 6.8 Hz, 3 H), 1.06 (d, $J$ = 6.6 Hz, 3 H), 1.19 (s, 3 H), 1.42 - 1.51 (m, 1 H), 1.81 (dd, $J$ = 10.1, 13.1 Hz, 1 H), 3.01 (s, 3 H), 3.04 (s, 3 H), 3.26 (q, $J$ = 6.6 Hz, 1 H); $^{13}$C NMR (100 MHz, CD$_3$C(O)CD$_3$) $\delta$ (major diastereoisomer) 14.2, 14.4, 18.3, 23.4, 24.6, 27.8, 30.1, 30.2, 30.4, 30.7, 32.7, 34.6, 37.7, 46.4, 59.0, 153.1, 174.7; (minor, diagnostic peaks only) 13.8, 21.7, 23.1, 31.1, 33.7, 58.8, 153.4, 174.9. IR (neat) 722, 758, 1055, 1109, 1185, 1285, 1415, 1459, 1670, 1710, 2855, 2924. HRMS calcd for C$_{18}$H$_{34}$N$_2$O$_2$Na (M$^+$ + Na) 333.2512, found 333.2504.

**(5R,6R)-6-Allyl-5-decyl-1,3,5-trimethyldihydropyrimidine-2,4(1H,3H)-dione (5d).** To a solution of 2i (0.032 mmol) and allyltrimethylsilane (10 equiv) in CH$_2$Cl$_2$ (1.0 mL), BF$_3$•Et$_2$O (3 equiv) was added dropwise at rt and the reaction was stirred at rt for 2 h. The reaction was diluted with CH$_2$Cl$_2$ (20 mL) and HCl (0.1 N, 20 mL), extracted with CH$_2$Cl$_2$ (2 x 20 mL), dried and concentrated. Purification by chromatography (1/1 EtOAc/hexanes) afforded the title compound as a colorless oil. Yield 86%. Rf (50% EtOAc/hexanes) = 0.76. Dr > 95:5 (crude), > 95:5 (purified). Stereochemistry of the major diastereoisomer was
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Determined by 2D NMR experiments. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 0.81 (t, $J$ = 7.0 Hz, 3 H), 0.99-1.08 (m, 1 H), 1.13 (s, 3 H), 1.14-1.26 (m, 15 H), 1.33 (td, $J$ = 4.0, 12.0 Hz, 1 H), 1.53 (td, $J$ = 4.5, 13.0 Hz, 1 H), 2.11-2.17 (m, 1 H), 2.30-2.36 (m, 1 H), 3.00 (s, 3 H), 3.02 (dd, $J$ = 4.5, 7.5 Hz, 1 H), 3.05 (s, 3 H), 4.98-5.03 (m, 2 H), 5.55-5.65 (m, 1 H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 14.1, 18.1, 22.7, 23.8, 27.7, 29.3, 29.4, 29.5, 29.9, 31.9, 34.3, 36.7, 37.7, 44.9, 63.1, 119.1, 132.6, 153.1, 174.5. IR (neat) 2924, 2854, 1669, 1467, 1417, 1381, 1366, 1283, 1217, 1083, 917, 757 cm$^{-1}$. HRMS calcd for C$_{20}$H$_{37}$N$_2$O$_2$ (M$^+$ + H) 337.2850, found 337.2852.

Reactivity of $\alpha$-Hydroxy Carboxamides – Additional Example

5-Ethyl-1,3-dimethyl-6-phenylhydropyrimidine-2,4(1H,3H)-dione (2-SI). According to the general procedure 1-SI (0.10 mmol) was reacted with SmI$_2$ (0.80 mmol, 8 equiv, 10.0 mL, 0.080 M) and H$_2$O (1.8 mL, 1000 equiv) for an extended period of 30 min at rt, followed by work-up with CH$_2$Cl$_2$/HCl (1.0 N) as described above to give after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 84%. Dr = 72:28 (crude), 71:29 (purified). Rf (50% EtOAc/hexanes) = 0.44. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ (major diastereoisomer) 0.85 (t, $J$ = 8.0 Hz, 3 H), 1.82-1.91 (m, 1 H), 2.11-2.20 (m, 1 H), 2.72 (s, 3 H), 2.85 (s, 3 H), 2.99-3.03 (m, 1 H), 3.92 (d, $J$ = 3.5 Hz, 1 H), 7.05 (dd, $J$ = 1.5, 7.0 Hz, 2 H), 7.13-7.24 (m, 3 H); (minor) 0.82 (t, $J$ = 7.0 Hz, 3 H), 1.82-1.91 (m, 2 H), 2.68 (s, 3 H), 2.96 (s, 3 H), 3.05-3.09 (m, 1 H), 3.93 (d, $J$ = 3.0 Hz, 1 H), 7.10 (dd, $J$ = 1.0, 7.0 Hz, 2 H), 7.13-7.23 (m, 3 H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ (major diastereoisomer) 12.5, 22.6, 24.5, 28.3, 47.4, 66.0, 127.5, 128.2, 128.5, 137.9, 156.6, 172.0; (minor) 12.5, 24.6, 25.0, 30.6, 49.5, 66.5, 127.5, 128.4, 128.6, 137.6, 157.2, 172.2. IR (neat) 2965, 2876, 1767, 1705, 1452, 1421, 1396, 1273, 1216, 1023, 757, 703 cm$^{-1}$. HRMS calcd for C$_{14}$H$_{18}$N$_2$O$_2$Na (M$^+$ + Na) 269.1260, found 269.1255. Full details of this rearrangement will be reported separately.
# Mechanistic Studies

## A) Effect of Additives and Optimization Studies

**Table SI-1. Effect of Additives on the Reduction of Cyclic 1,3-Diimides using SmI₂.**

| entry | SmI₂ (equiv) | additive | additive (equiv) | time⁴ | conv.⁵,⁶ (%) | yield⁵ (%) | dr⁵ |
|-------|--------------|----------|------------------|-------|--------------|------------|-----|
| 1     | 6            | -        | -                | 24 h  | <5 (83 SM)   | -          | -   |
| 2     | 6            | MeOH     | 4/1 v/v          | 2 h   | <5 (81 SM)   | -          | -   |
| 3     | 4            | t-BuOH   | 24               | 2 h   | <5 (85 SM)   | -          | -   |
| 4     | 4            | H₂O      | 1000             | 10 s  | 93 (7 SM)    | 84         | 86:14 |
| 5e    | 4            | H₂O      | 1000             | 1 h   | <5 (95 SM)   | -          | -   |
| 6     | 4            | HMPA     | 24               | 2 h   | >95 (<5 SM)  | -          | -   |
| 7     | 4            | LiCl     | 48               | 2 h   | 27 (73 SM)   | 8.6        | 81:19 |
| 8     | 4            | HO(CH₂)₂OH | 24             | 2 h   | >95 (<5 SM)  | 11         | 81:19 |
| 9     | 2            | Et₃N-MeOH | 12-18            | 2 h   | <5 (69 SM)   | <2         | -   |
| 10    | 2            | Et₃N-H₂O | 12-18            | <30 s | 49 (51 SM)   | 7.2        | 86:14 |

⁴All reactions carried out using standard Schlenk techniques. ⁵Quenched with air after the indicated time. ⁶Determined by ¹H NMR. ⁷Conversion to desired product is shown. The remaining starting material is shown in parentheses. ⁸The corresponding cyclic 1,3-malonamide 5-SI was used. See below for details. In all entries, SmI₂ prepared from Sm metal and ICH₂CH₂I was used.
Table SI-2. Effect of Addition Sequence and Work-up Conditions on the Reduction of Cyclic 1,3-Diimides using SmI₂.α

| entry | SmI₂ (equiv) | H₂O (equiv) | timeb | conv. c  | yieldc | drd  | addition/work-up |
|-------|--------------|-------------|--------|--------|--------|------|-----------------|
| 1     | 3            | 1000        | 5 min  | 91     | 81     | 88:12 | Conditions A    |
| 2     | 3            | 1000        | 5 min  | 92     | 80     | 88:12 | Conditions B    |
| 3     | 6            | 1000        | 3 min  | >95    | 52     | 77:23 | Conditions C    |

αAll reactions carried out using standard Schlenk techniques. βQuenched with air after the indicated time. γDetermined by 1H NMR. δAddition and work-up conditions: A) Cyclic 1,3-diimide, followed by H₂O and SmI₂; work-up using 0.1 M HCl. B) SmI₂, followed by H₂O and cyclic 1,3-diimide; work-up using 0.1 M HCl. C) Cyclic 1,3-diimide, followed by SmI₂ and H₂O work-up using 1.0 M HCl. In all entries, SmI₂ prepared from Sm metal and ICH₂CH₂I was used.

Table SI-3. Effect of SmI₂ Stoichiometry on the Reduction of Cyclic 1,3-Diimides using SmI₂.α

| entry | SmI₂ (equiv) | H₂O (equiv) | time | conv. | yield | dr   |
|-------|--------------|-------------|------|-------|-------|------|
| 1     | 3            | 1000        | 60 s | 91    | 76    | 88:12|
| 2     | 6            | 1000        | 10 s | >95   | 82    | 88:12|
| 3     | 12           | 1000        | 15 min | >95 | 49    | 86:14|

αAll reactions carried out using standard Schlenk techniques. βQuenched with air after the indicated time. γDetermined by 1H NMR. Conditions: 1,3-Diimide, followed by H₂O and SmI₂; work-up using 0.1 M HCl. In all entries, SmI₂ prepared from Sm metal and ICH₂CH₂I was used.
Table SI-4. Effect of H$_2$O Stoichiometry on the Reduction of Cyclic 1,3-Diimides using SmI$_2$.$^a$

![Chemical structure image]

| entry | SmI$_2$ (equiv) | H$_2$O (equiv) | time$^b$ | conv.$^c$ (%) | yield$^c$ (%) | dr$^c$ |
|-------|----------------|----------------|---------|--------------|--------------|-------|
| 1     | 6              | -              | 24 h    | <5           | <5           | -     |
| 2     | 4              | 10             | 2 h     | 24           | <5           | -     |
| 3     | 4              | 50             | 10 s    | 79           | <5           | -     |
| 4     | 4              | 200            | 10 s    | 84           | 57           | 82:18 |
| 5     | 4              | 1000           | 10 s    | 93           | 82           | 86:14 |
| 6     | 4              | 2500           | 10 s    | 66           | 49           | 88:12 |

$^a$All reactions carried out using standard Schlenk techniques. $^b$Quenched with air after the indicated time. $^c$Determined by $^1$H NMR. Conditions: 1,3-Diimide, followed by H$_2$O and SmI$_2$; work-up using 0.1 M HCl.

B) Studies on Mechanism of Reductive Cyclizations

Table SI-5. Effect of Additives on the Reductive Cyclization of Cyclic 1,3-Diimides.$^a$

![Chemical structure image]

| entry | SmI$_2$ (equiv) | additive | additive (equiv) | time$^b$ | conv.$^c$ (%) | yield$^c$ (%) | dr$^c$ |
|-------|----------------|----------|-----------------|---------|--------------|--------------|-------|
| 1     | 6              | -        | -               | 2 h     | <5           | <5           | -     |
| 2     | 6              | H$_2$O   | 10              | 2 h     | <5           | <5           | -     |
| 3     | 6              | H$_2$O   | 200             | 15 min  | >95          | 78           | -     |
| 4     | 6              | MeOH     | 4/1 v/v         | 2 h     | <5           | <5           | -     |
| 5     | 6              | HO(CH$_2$)$_2$OH | 36       | 15 min | 30           | 16$^d$     | >95:5 |
| 6     | 6              | LiCl     | 72              | 2 h     | >95          | 25           | 69:31 |
| 7     | 6              | HMPA     | 24              | 1 h     | >95          | <5           | -     |

$^a$All reactions carried out using standard Schlenk techniques. $^b$Quenched with air after the indicated time. $^c$Determined by $^1$H NMR. $^d$Reduction product formed in 8% yield corresponding to 67:33 ratio of cyclization to reduction. In other entries reduction was not observed. SmI$_2$ prepared from Sm metal and ICH$_2$CH$_2$I was used.
C) Selectivity of Monoreduction and Cyclization of Cyclic 1,3-Diimides

**General Procedure.** 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. Samarium(II) iodide (THF solution, 0.10 mmol, 1.0 equiv, 0.10 M) was added followed by H$_2$O (0.18 mL, 200 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$_2$). A preformed solution of two substrates (each 0.10 mmol, 1.0 equiv, stock solution in THF, 1.0 mL) was added and the reaction mixture was stirred until decolorization to white had occurred. The reaction mixture was diluted with CH$_2$Cl$_2$ (30 mL) and HCl (1 N, 30 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (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$_3$) and GC-MS to obtain conversion and yield using internal standard.

**Table SI-6.** Selectivity Study in the Reduction of Cyclic 1,3-Diimides using SmI$_2$–H$_2$O.$^a$

| entry | Substrate I | Substrate II | conv.$^b$ (I-red, %) | conv.$^b$ (II-red, %) | $k_I/k_R$-FG |
|-------|-------------|-------------|----------------------|----------------------|-------------|
| 1     | ![Substrate I](image1) | ![Substrate II](image2) | <2                   | 13                   | <1:20       |
| 2     | ![Substrate I](image3) | ![Substrate II](image4) | 24                   | 2                    | >20:1       |
| 3     | ![Substrate I](image5) | ![Substrate II](image6) | 18                   | <2                   | >20:1       |
| 4     | ![Substrate I](image7) | ![Substrate II](image8) | 30                   | 6.5                  | 82:18       |
| 5     | ![Substrate I](image9) | ![Substrate II](image10) | 53                   | <2                   | >20:1       |

$^a$Conditions: SmI$_2$ (1 equiv), H$_2$O (200 equiv), THF, room temperature, 10 s to 1 min. All reactions carried out using standard Schlenk techniques. $^b$Determined by $^1$H NMR (500 MHz) and/or GC-MS. Conversion = (100-SM). In all cases, rapid injection of substrate (THF solution) to the preformed SmI$_2$–H$_2$O complex was applied.
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Table SI-7. Selectivity Study in the Coupling of Cyclic 1,3-Diimides using SmI$_2$–H$_2$O.$^a$

| entry | Substrate I | Substrate II | conv.$^{b,c}$ (I-cycl, %) | conv.$^{b,c}$ (II-red/cycl, %) | $k_I/k_{II}$ |
|-------|-------------|--------------|---------------------------|-------------------------------|--------------|
| 1     | ![Substrate I](image1) | ![Substrate II](image2) | <2 | 33 | <1:20 |
| 2     | ![Substrate I](image3) | ![Substrate II](image4) | 2.7 | 14 | 16:84 |
| 3     | ![Substrate I](image5) | ![Substrate II](image6) | 3.5 | 12 | 23:77 |
| 4     | ![Substrate I](image7) | ![Substrate II](image8) | <2 | 23 | <1:20 |
| 5     | ![Substrate I](image9) | ![Substrate II](image10) | 25 | 3.0 | 89:11 |

$^a$Conditions: SmI$_2$ (1 equiv), H$_2$O (200 equiv), THF, room temperature, 10 s to 1 min. All reactions carried out using standard Schlenk techniques. $^b$Determined by $^1$H NMR (500 MHz) and/or GC-MS. Conversion = (100-SM). In all cases, rapid injection of substrate (THF solution) to the preformed SmI$_2$–H$_2$O complex was applied.

Selectivity studies have been carried out to determine electronic and steric factors that influence the rate of reduction of cyclic 1,3-diimides using the SmI$_2$–H$_2$O reagent. The data outlined in Tables SI-6 and SI-7 demonstrate three general trends and indicate that significant levels of selectivity are possible with this reagent system:

1) Chemoselectivity studies in the reduction of cyclic derivatives of carboxylic acids (Table SI-6, entries 1-3) illustrate that the SmI$_2$–H$_2$O system is selective for cyclic 1,3-diimides over lactones; however, cyclic 1,3-diesters are reduced preferentially. This outlines the following
reactivity scale for the SmI₂–H₂O system: Meldrum’s acids > cyclic 1,3-diimides > lactones, which is in agreement with the stabilization of ketyl-type radicals in these systems. It is worthwhile to note that the SmI₂–H₂O system is fully chemoselective over acyclic carboxylic acid derivatives (esters, carboxylic acids, amides) in that no reduction of these functional groups is observed even if excess of the reagent is used.

2) The reduction of cyclic 1,3-diimides using SmI₂–H₂O is facilitated by electron withdrawing groups and slowed down by steric substitution at the alpha carbon (Table SI-6, entries 4-5). This is consistent with stabilization of the ketyl radical intermediate by electron withdrawing groups and reflects the importance of coordination of Sm(III) to the ketyl-type radical in the transition state of the reaction. Note that this trend allows high levels of chemoselectivity to be achieved in the reduction by careful fine-tuning of both the Sm(II) reagent system and steric/electronic substitution of the substrate.

3) The selectivity studies on reductive cyclizations of cyclic 1,3-diimides using SmI₂–H₂O show that the cyclization rate is governed by electronic and steric properties of the \( \pi \)-acceptor (Table SI-7, entries 1-5). This is in agreement with the proposed mechanism and consistent with the previous findings on related stereoselective radical cyclizations.\textsuperscript{26-28} Overall, these general trends further indicate that chemoselectivity levels unattainable via ionic reaction pathways are accessible with Sm(II) reductants.
D) Deuterium Incorporation and Kinetic Isotope Effect Studies\textsuperscript{20-24}

Scheme SI-1. Determination of Deuterium Incorporation and Kinetic Isotope Effect.

A) Deuterium Incorporation Studies

\textit{**reduction**}

\[ \text{Me} \quad \text{N} \quad \text{O} \quad \text{N} \quad \text{C}_{10} \text{H}_{21} \quad \text{Me} \quad \text{Sml}_2 - \text{D}_2 \text{O} \quad \text{THF, RT} \]

\[ \text{Me} \quad \text{N} \quad \text{O} \quad \text{N} \quad \text{C}_{10} \text{H}_{21} \quad \text{Me} \quad 2i, >98\% \text{D}^\dagger \]

\textit{**cyclization**}

\[ \text{Me} \quad \text{N} \quad \text{O} \quad \text{N} \quad \text{C}_{10} \text{H}_{21} \quad \text{Me} \quad \text{Sml}_2 - \text{D}_2 \text{O} \quad \text{THF, RT} \]

\[ \text{Me} \quad \text{N} \quad \text{O} \quad \text{N} \quad \text{C}_{10} \text{H}_{21} \quad \text{Me} \quad 4d, f-h, >98\% \text{D}^\dagger \]

B) Kinetic Isotope Effect Studies

\textit{**reduction**}

\[ \text{Me} \quad \text{N} \quad \text{O} \quad \text{N} \quad \text{C}_{10} \text{H}_{21} \quad \text{Me} \quad \text{Sml}_2 - \text{D}_2 \text{O}/\text{H}_2 \text{O}^* \quad \text{THF, RT} \]

\[ \text{Me} \quad \text{N} \quad \text{O} \quad \text{N} \quad \text{C}_{10} \text{H}_{21} \quad \text{Me} \quad 2i, k_D/k_H = 1.49\pm0.1 \]

\textit{**cyclization**}

\[ \text{Me} \quad \text{N} \quad \text{O} \quad \text{N} \quad \text{C}_{10} \text{H}_{21} \quad \text{Me} \quad \text{Sml}_2 - \text{D}_2 \text{O}/\text{H}_2 \text{O}^* \quad \text{THF, RT} \]

\[ \text{Me} \quad \text{N} \quad \text{O} \quad \text{N} \quad \text{C}_{10} \text{H}_{21} \quad \text{Me} \quad 4d, f-h, k_D/k_H = 1.05-1.75\pm0.1 \]

\*\text{D}_2 \text{O} : \text{H}_2 \text{O} = 1:1

**General Procedure.** According to the general procedure for monoreduction or reductive cyclization, a cyclic 1,3-diimide (0.05-0.10 mmol) was reacted with SmI\textsubscript{2} (3-6 equiv), and D\textsubscript{2}O (200-1000 equiv, deuterium incorporation) or D\textsubscript{2}O/H\textsubscript{2}O (200-1000 equiv, 1:1, stock solution, KIE) for the indicated time at rt. After the standard work-up, the reaction mixture was diluted with CH\textsubscript{2}Cl\textsubscript{2} (30 mL) and HCl (1 N, 30 mL). The aqueous layer was extracted with CH\textsubscript{2}Cl\textsubscript{2} (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}) and/or GC-MS to obtain deuterium incorporation. Characterization data for all new compounds is given in the Experimental Part of the Supporting Information.
E) Evidence for Isomerization of Vinyl Radicals$^{25-27}$

Table SI-8. Evidence for Isomerization of Vinyl Radicals under Sm$_2$I$_2$–H$_2$O Conditions.$^a$

| entry | Sm$_2$I$_2$ (equiv) | R | H$_2$O (equiv) | time (min) | conv.$^c$ | yield$^c$ | dr$^c$ (E:Z) |
|-------|---------------------|---|---------------|------------|-----------|-----------|-------------|
| 1     | 6                   | Ph | 50            | 15 min     | >95       | 99        | 58:42       |
| 2     | 6                   | Ph | 200           | 15 min     | >95       | 99        | 37:63       |
| 3     | 6                   | Ph | 2400          | 15 min     | >95       | 99        | 24:76       |
| 4     | 6                   | TMS | 200          | 15 min     | >95       | 89        | >95:5       |
| 5     | 6                   | H$^{d}$ | 200         | 15 min     | >95       | 85        | >95:5       |
| 6     | 6                   | Ph$^{d}$ | 50          | 15 min     | >95       | 90        | 60:40       |
| 7     | 6                   | TMS$^{d}$ | 200        | 15 min     | >95       | 87        | >95:5       |

$^a$All reactions carried out using standard Schlenk techniques. $^b$Quenched with air after the indicated time. $^c$Determined by $^1$H NMR. $^d$Reaction carried out using D$_2$O instead of H$_2$O. Sm$_2$I$_2$ prepared from Sm metal and ICH$_2$CH$_2$I was used.

Reductive cyclizations of cyclic 1,3-diimides have been carried out at different concentrations of H$_2$O and with the Sm$_2$I$_2$–D$_2$O system to probe the stability of radical intermediates formed after initial reductive cyclization (Table SI-8). Alkyne tethers have been chosen as mechanistic probes because of the well-established propensity of related radicals to undergo anti radical cyclizations as well as the stability of the resulting vinyl radicals towards isomerization (inversion barrier of ca. 2 kcal/mol.$^{25-28}$ In the cyclizations of the phenyl-containing substrate (Table SI-8, entries 1-3), a gradual change in diastereoselectivity is observed at varied concentrations of H$_2$O. This suggests that the carbon-centered radicals formed in the reductive cyclizations mediated by Sm$_2$I$_2$–H$_2$O do not undergo instantaneous reduction/protonation despite the presence of a thermodynamically powerful reductant (Sm$_2$I$_2$–H$_2$O: -1.9 V vs Ag/AgNO$_3$)$^{29}$ and a large excess of the proton source. In the cyclizations of the TMS- and H-containing substrates (Table SI-8, entries 4-5) full and partial inversion of the vinyl radical is observed under the reduction conditions, respectively. The inversion in the first two substrates is also observed in the reactions mediated by Sm$_2$I$_2$–D$_2$O.
Table SI-8, entries 6-7). Overall, the results in Table SI-8 indicate that the extent of isomerization is governed by steric and electronic properties of the $\pi$-acceptor (Ph, TMS, H) and the concentration of $H_2O$ co-solvent (a thermodynamically more powerful reductant is formed at higher concentrations of $H_2O$)\(^{29}\) (entries 1-3). Application of the above findings to the cascade processes employing C-centered radicals is currently underway in our laboratory and these results will be reported shortly.

F) Additional Selectivity Studies

**Scheme SI-2. Additional Selectivity Studies in the Reduction of Cyclic 1,3-Diimides.**

**A) Reduction of cyclic urea**

$$
\text{Me:N=O:Me} \xrightarrow{\text{Sml}_2-H_2O, \text{THF, RT}} \text{Me:HN=HN:Me} \quad (\text{eq 1})
$$

Eq. 1. According to the general procedure for reduction of cyclic 1,3-diimides with Sml$_2$-H$_2$O, 1,3-dimethyltetrahydropyrimidin-2(1H)-one (0.10 mmol) was reacted with Sml$_2$ (0.40 mmol, 4 equiv) and H$_2$O (200 equiv) for 2 h at room temperature, which resulted in the formation of a characteristic burgundy-red color of the Sml$_2$(H$_2$O)$_n$ complex ($n > 5$ with respect to Sml$_2$). After the standard work-up as described above, the sample was analyzed by $^1$H NMR to obtain conversion and yield using internal standard: conversion <5%; yield of recovered starting material: >80%.

**B) Reduction of cyclic 1,3-malonamide**

$$
\text{Me:N=O:H:Me} \xrightarrow{\text{Sml}_2-H_2O, \text{THF, RT}} \text{Me:HN=HN:H:Me} \quad (\text{eq 2})
$$

Eq. 2. According to the general procedure for reduction of cyclic 1,3-diimides with Sml$_2$-H$_2$O, 5-isobutyl-1,3-dimethylidihydropyrimidine-4,6(1H,5H)-dione (0.10 mmol) was reacted with Sml$_2$ (0.60 mmol, 6 equiv) and H$_2$O (1000 equiv) for 1 h at room temperature, which resulted in the formation of a characteristic burgundy-red color of the Sml$_2$(H$_2$O)$_n$ complex ($n > 5$ with respect to Sml$_2$). After the standard work-up as described above, the sample was analyzed by $^1$H NMR to obtain conversion and yield using internal standard: conversion <5%; yield of recovered starting material: >95%. In another optimization run, a reaction
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Using SmI$_2$ (6 equiv) and H$_2$O (200 equiv) for 1 h at room temperature resulted in <5% conversion.

5-Isobutyl-1,3-dimethylidihydropyrimidine-4,6(1H,5H)-dione (SI-5). To a 50 mL round-bottomed flask charged with 1,3-dimethyl-5-(2-methylpropylidene)pyrimidine-2,4,6(1H,3H,5H)-trione prepared as described above (0.80 g, 3.8 mmol, 1.0 equiv) and THF (20 mL), DIBAL-H (1.0 M in hexanes, 20 mL, 4.0 equiv) was added dropwise at -78 °C. The reaction mixture was allowed to slowly warm up to room temperature over 15 h, quenched with an aqueous saturated solution of sodium potassium tartrate, extracted with ethyl acetate, concentrated and dried. Purification by chromatography using EtOAc/hexanes (70/30) afforded the title compound as a white solid (mp = 32-34 °C). Yield 68% (0.51 g). R$_f$ (70% EtOAc/hexanes) = 0.11. $^1$H NMR (400 MHz, CDCl$_3$) δ 0.87 (d, $J$ = 6.4 Hz, 6 H), 1.68 (t, $J$ = 6.8 Hz, 2 H), 1.70-1.81 (m, 1 H), 2.97 (s, 6 H), 3.05 (t, $J$ = 6.8 Hz, 1 H), 4.49 (d, $J$ = 8.7 Hz, 1 H), 4.53 (d, $J$ = 8.4 Hz, 1 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 22.4, 26.0, 32.7, 35.8, 48.4, 63.2, 168.7. IR (neat) 2955, 2923, 2866, 1657, 1485, 1439, 1401, 1369, 1264, 1224, 1102, 1064, 787 cm$^{-1}$. HRMS calcd for C$_{10}$H$_{19}$N$_3$O$_2$ (M$^+$ + H) 199.1442, found 199.1446.
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Structural Characterization and Additional Discussion

**Figure A.** ORTEP Structure of 4a (CCDC 948382).

**Figure B.** ORTEP Structure of 2f (CCDC 948381).
Additional discussion. The alpha-amino alcohol moiety is stabilized by a nonplanar arrangement of atoms. The X-ray crystal structure of 4a reveals that the C1–O1 bond (1.407 Å) is shorter than the average Csp3–O bond (1.432 Å), while the N1–C1 bond is 1.466 Å, which corresponds to a typical Csp3–N bond (1.469 Å). The C1–C4 bond length of 1.552 Å is slightly longer than the average Csp3–Csp3 bond (1.530 Å). The torsion angle between Nlp and C1–O1 of 57.3° is consistent with the absence of Nlp→σ* C–O interactions in this system. However, there exists a good overlap between O1lp1 and the N1–C1 bond (~172°) and between O1lp2 and the C1–C4 bonds (~191°). The shortened C1–O1 bond and the elongated C1–C4 bond are consistent with an anomeric effect resulting from Olp→σ* C1–N1 and Olp→σ* C1–C4 interactions, while the geometry of N1 atom (Nlp, N1–C1 bond length) indicates the beginning of the decomposition of the tetrahedral intermediate by the elimination of N(CO) group to give the open N-acyl urea derivative. Nevertheless, it should be noted that the α-amino alcohol function in this system is stabilized by the reduced Nlp→σ* C–O conjugation by the interaction with the adjacent carbonyl group. This is further indicated by the co-planarity of all six atoms comprising the uracil ring, with the C1 atom deviated from the plane of the ring by 6.9° and C2 by −14.6°.

The X-ray structure of a mono-cyclic analogue 2i reveals kinetic rather than thermodynamic stability (vide supra). The C1–O1 bond in 2i of 1.411 Å and the C1–N1 bond of 1.458 Å are in a similar range as for the bicyclic derivative 4a described above. However, the C1–C2 bond length of 1.519 Å is slightly shorter than the average Csp3–Csp3 bond (1.530 Å). The torsion angles between Nlp and C1–O1 of ~175° and Olp and C1–N1 of ~137° indicate a significant Nlp→σ* C1–O1 interaction in this system, and the absence of Olp→σ* C1–N1 conjugation. There exists a reasonably good arrangement between Olp→σ* C1–C2 (torsion angle of ~163°) and there is no evidence for anomeric effect involving Olp→σ* C1–H (torsion angle of ~137°). Finally, the O1–C1–C2–H2 torsion angle of ~180° reveals a perfect antiperiplanar arrangement between the alpha hydrogen atom and the hydroxyl group. These parameters are consistent with the beginning of the decomposition of the alpha amino alcohol moiety by the elimination of hydroxyl group to give the acyliminium. The structural differences between 4a and 2i are further emphasized by the bond lengths of the alpha hydroxyl N-acyl urea moiety (4a, distal N–C(O) bond length of 1.421 Å, C=O of 1.218 Å; 2i, distal N-C(O) bond length of 1.396 Å, C=O of 1.237 Å).
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Selective Reduction of Barbituric Acids using SmI$_2$–H$_2$O

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Selective Reduction of Barbituric Acids using SmI$_2$–H$_2$O

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Selective Reduction of Barbituric Acids using SmI$_2$ – H$_2$O

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