Supporting information

Cobaloxime-catalyzed hydration of terminal alkynes without acidic promoters

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Table of content

1. General remarks.................................................................................S2
2. Synthesis of cobaloximes........................................................................S2
3. Optimization Studies............................................................................S3
4. Mechanistic Studies..............................................................................S5
5. Experimental Procedure and Analytical Data of Products............S7
6. References..........................................................................................S14
7. $^1$H NMR and $^{13}$C NMR Spectra....................................................S16
1. General remarks

The reactions were carried out under air in a closed J. Young tube. The catalysts were prepared according to the reported procedure. $^1$H NMR and $^{13}$C NMR spectra were recorded in CDCl$_3$ solution on a Bruker AM 400 MHz instrument, Varian 300 MHz instrument. High-resolution mass spectral analysis (HRMS) data were measured on a Bruker ApexII mass spectrometer by means of the ESI technique. The IR spectra were recorded on Nicolet Nexus 670 FT-IR spectrometer. Column chromatography was performed on silica gel. $^1$H and $^{13}$C NMR spectra were recorded at 400 MHz and 100 MHz (or 300 MHz and 75 MHz) respectively using CDCl$_3$ as a solvent. Yields refer to isolated compounds, estimated to be > 95% pure as determined by $^1$H-NMR, and GC-analysis. Chemical shifts are reported as δ values relative to internal chloroform ($^1$H and $^{13}$C NMR relative to CHCl$_3$, δ 7.26 ppm for $^1$H NMR and δ 77.0 ppm for $^{13}$C NMR), multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). Coupling constants (J) are reported in Hertz (Hz). The product formation was monitored by $^1$H NMR using aliquots containing the solvent mixture. All commercial reagents and solvents were obtained from the commercial provider and used without further purification.

2 Synthesis of cobaloximes

2.1 $[\text{Co(dmgH)}(\text{dmgH}_2)\text{Cl}]$\textsuperscript{1}

To a solution of CoCl$_2$·6H$_2$O (5 g, 21.0 mmol, 1 eq.) in acetone (100 mL) was added a warmed solution of dimethylglyoxime (5 g, 43.1 mmol, 2.1 eq.) in acetone (150 mL). Air was bubbled through the resultant blue mixture and stirred for 20 minutes and then left to stand for 2 hours, yielding green crystals of $[\text{Co(dmgH)}(\text{dmgH}_2)\text{Cl}]$, which were filtered off and dried in a desiccator (7.51 g, 99%). $^1$H NMR (300 MHz, Chloroform-d) 2.11 (s, 12H).

2.2 $[\text{Co(dmgH)}(\text{dmgH}_2)\text{Br}_2]$\textsuperscript{1}

Procedure analogous to the preparation of 2.1

2.3 $[\text{Co(dmgH)}_2\text{ClPy}]$\textsuperscript{1}

To a stirred suspension of $[\text{Co(dmgH)}(\text{dmgH}_2)\text{Cl}]$ (1 g, 2.8 mmol, 1 eq.) and pyridine (0.25 mL, 2.8 mmol, 1 eq.) in dichloromethane (10 mL) was added NaHCO$_3$ (10 mL), and allowed to stir at room
temperature for 1 hour, at which point, the solution was diluted further with dichloromethane (20 mL) and washed with water (2 x 20 mL). The organic fractions were combined, dried over Na$_2$SO$_4$, filtered and evaporated to dryness, yielding [Co(dmgH)$_2$ClPy] as a brown crystalline solid (0.99 g, 89%). $^1$H NMR (400 MHz, Chloroform-d) δ 8.28 (dd, $J$ = 5.8 Hz, 2H), 7.69 (tt, $J$ = 7.6 Hz, 1H), 7.23 (dt, $J$ = 7.6 Hz, 1.4 Hz, 2H), 2.40 (s, 12H).

2.4 [Co(dmgH)$_2$BrPy]

![Diagram of Co(dmgH)$_2$BrPy]

Procedure analogous to the preparation of 2.3

2.5 [Co(dmgBF$_2$)$_2$•2H$_2$O]

Diethyl ether (150 mL, O$_2$-free) was added to a flask containing [Co(OAc)$_2$•4H$_2$O] (2.0 g, 8 mmol, 1 eq.) and dmgH$_2$ (1.9 g, 16 mmol, 2 eq.), followed by freshly distilled BF$_3$•Et$_2$O (10 mL, an excess). The mixture was stirred for 6 h under argon. The resulting solid was filtered under argon, washed with ice–cold water (3 x 10 mL, O$_2$-free) and air-dried. A brownish-red solid product was obtained (2.0 g, 4.8 mmol, 60% yield). IR (KBr) 3600, 3533, 3021, 2972, 2931, 1620, 1553, 1444, 1386, 1341, 1208, 1165, 1093, 1010, 954, 829, 627, 605 cm$^{-1}$.

3. Condition optimization of alkyne hydration

![Diagram of condition optimization of alkyne hydration]

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*Reaction conditions: 0.25 mmol of alkyne \(^1\)a, cobaloxime 2 mol%, 4 mol% additives in MeOH (1 mL), heated at the indicating temperature. *yield based on \(^19\)F NMR. *5 mol% Cobaloxime was used. *the reaction was carried out under an argon atmosphere. *the reaction was carried out under blue light. *the reaction was carried out in the dark.
4. Mechanistic Studies
4.1 XPS data of Cat 5 recovered after reaction.

Figure S1. XPS survey spectra of the recovered Cat 5.

Core level photoemission associated with elemental components of the catalyst is observed. Co 2p core level spectra of the recovered catalyst (Figure S2) show peaks centered at 781.21 eV (2p3/2) and 796.18 eV (2p1/2) with the expected 2:1 branching ratio. The 14.9 eV peak separation and the binding energy value are characteristic of the Co(III) oxidation state.\(^3\)
4.2 GC–MS and $^1$H NMR spectra of Co(dmgBF$_2$)$_2$•2H$_2$O catalyzed hydration of 1f in CD$_3$OD.

Figure S3. GC–MS spectra after 1.5 hours of reaction.

Figure S4. Enlarged GC-MS of P2 and M2.

Figure S5. Enlarged GC-MS of P3 and M3

Figure S6. H NMR spectra of 2f$^+$ and 3f
Reaction conditions: 0.25 mmol of alkyne 1f, cobaloxime (Cat 5.) 5 mol% in CD$_2$OD (1 mL), heated to the indicating temperature (65 °C) under aerobic conditions. The mixture was stirred for 1.5 h and monitored by GC–MS.

Reaction conditions: 0.25 mmol of alkyne 2f, cobaloxime (Cat 5.) 5 mol% in CD$_2$OD (1 mL), heated to the indicating temperature (65 °C) under aerobic conditions. The mixture was stirred for 4 d. The reaction mixture was carefully quenched by addition of 0.05 mL H$_2$O, before the tube was cooled to 25 °C. The volatiles were removed under reduced pressure and the pure product 2f* (95%) was obtained by flash chromatography of silica gel.

5. Experimental Procedure and Analytical Data of Products

5.1 Typical procedures for hydration of alkynes

1a:

To a solution of NaH (308 mg, 16 mmol, 1.2 eq.) in dry DMF (20 mL) at 0 °C was slowly added pent-4-yn-1-ol (1 mL, 13 mmol, 1 eq.). 1-(bromomethyl)-4-fluorobenzene (2 mL 16 mmol, 1.2 eq.) was added to the solution. The mixture was allowed to warm up to room temperature and to stir overnight. The reaction was quenched by water, and extracted by ethyl acetate. The organic phase was washed by brine and dried with Na$_2$SO$_4$. After concentration the crude was purified by silica gel chromatography to provide 1a* (1.01 g, 40% yield) as a colorless oil. $^1$H NMR (300 MHz, Chloroform-d) $\delta$ 7.37 – 7.22 (m, 2H), 7.06 – 6.96 (m, 2H), 4.45 (s, 2H), 3.55 (t, $J$ = 6.2 Hz, 2H), 2.30 (td, $J$ = 6.9 Hz, 2.7 Hz, 2H), 1.94 (t, $J$ = 2.7 Hz, 1H), 1.81 (p, $J$ = 6.6 Hz, 2H); $^{13}$C NMR (75 MHz, Chloroform-d) $\delta$ 162.2 (d, $J$ = 243.8 Hz), 134.1 (d, $J$ = 3 Hz), 129.2 (d, $J$ = 8 Hz), 115.1 (d, $J$ = 21 Hz), 83.8, 72.1, 68.5, 68.5, 28.5, 15.2; HRMS [ESI] calcd for C$_{12}$H$_{14}$FO [M+H]$^+$ 193.1023, found 193.1026.

1q:

To a solution of 5-hexyn-1-ol (630 mg, 6.4 mmol, 1 eq.) in dry DCM (18 mL) at 0 °C was added DMAP (800 mg, 6.4 mmol, 1 eq.), DCC (1.67 g, 8.2 mmol, 1.3 eq.) and benzoic acid (1 g, 8.2 mmol, 1.3 eq.). After addition, the solution was warmed up to room temperature and stirred for 5 hours. The reaction was quenched by H$_2$O, and extracted by DCM. The organic phase was washed with brine and dried by Na$_2$SO$_4$. After concentration the crude was purified by silica gel chromatography to provide 1q* (0.90 g 70% yield) as a yellow oil. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 8.10 – 7.95 (m, 2H), 7.54 (t, $J$ = 7.4 Hz, 1H), 7.42 (t, $J$ = 7.6 Hz, 2H), 4.34 (t, $J$ = 6.4 Hz, 2H), 2.27 (td, $J$ = 7.0, 2.6 Hz, 2H), 1.96 (t, $J$ = 2.6 Hz, 1H), 1.94 – 1.82 (m, 2H), 1.76 – 1.62 (m, 2H).
To a solution of NaH (57 mg, 2.4 mmol, 1.2 eq.) in dry DMF (5 mL) at 0 °C was slowly added 5-hexyn-1-ol (196 mg, 2 mmol, 1 eq.). The slurry followed by dropwise addition of 3-bromoprop-1-ene (0.46 g, 3.8 mmol, 1.9 eq.) under constant agitation. The mixture was allowed to warm up to room temperature and stir overnight. The reaction was quenched by water, and extracted by ethyl acetate. The organic phase was washed by brine and dried with Na₂SO₄. After concentration the crude was purified by silica gel chromatography to provide 1s⁵ (110 mg, 40% yield) as a colorless oil.¹H NMR (400 MHz, Chloroform-d) δ 6.11 – 5.75 (m, 1H), 5.26 (dd, J = 17.2 Hz, 1.6 Hz, 1H), 5.19 – 5.13 (m, 1H), 3.96 (dd, J = 5.6, 1.2 Hz, 2H), 3.45 (t, J = 6.3 Hz, 2H), 2.22 (td, J = 6.9, 2.6 Hz, 2H), 1.94 (t, J = 2.6 Hz, 1H), 1.81 – 1.48 (m, 4H).

1u

To a solution of 5-hexyn-1-ol (500 mg, 5.1 mmol, 1 eq.) in dry DCM (20 mL) at 0 °C was added DMAP (61 mg, 0.5 mmol, 0.1 eq.) and Boc₂O (1.17g, 5.35 mmol, 1.05 eq.). After addition, the solution warmed up to room temperature and stirred for 6 hours. The reaction was quenched by H₂O, and extracted by DCM. The organic phase was washed with brine and dried with Na₂SO₄. After concentration the crude was purified by silica gel chromatography to provide 1u (320 mg 31% yield) as a colorless oil.¹H NMR (300 MHz, Chloroform-d) δ 4.08 (t, J = 6.3 Hz, 2H), 2.22 (td, J = 7.0, 2.7 Hz, 2H), 1.94 (t, J = 2.6 Hz, 1H), 1.85 – 1.70 (m, 2H), 1.68 – 1.55 (m, 2H), 1.48 (s, 9H);¹³C NMR (100 MHz, Chloroform-d) δ 153.6, 83.8, 81.9, 68.7, 66.4, 27.8, 27.7, 24.7, 18.0; HRMS [ESI] calcd for C₁₁H₁₉O₃Na [M+Na]⁺ 221.1148, found 221.1145.

1v

To a stirring solution of 5-hexyn-1-ol (500 mg, 5.1 mmol, 1 eq.), 2,5-Dioxopyrrolidine (555 mg, 5.6 mmol, 1.1 eq.), and Ph₃P (1.47 g, 5.6 mmol, 1.1 eq.) in THF (22 mL) was added diisopropyl azodicarboxylate (957 mg, 5.6 mmol, 1.1 eq.) at 0 °C. The mixture was stirred for 30 min and allowed to come to room temperature. The reaction was allowed to stir for 7 h. The reaction was quenched by NaHCO₃, and extracted by ethyl acetate. The organic phase was washed with brine and dried by Na₂SO₄. After concentration the crude was purified by silica gel to provide 1v⁶ (350 mg, 38% yield) as a colorless oil.¹H NMR (300 MHz, Chloroform-d) δ 3.53 (t, J = 6.3 Hz, 2H), 2.22 (dt, J = 6.9, 1.5 Hz, 2H), 1.94 (t, J = 2.6 Hz, 1H), 1.76 – 1.63 (m, 2H), 1.58 – 1.45 (m, 2H).

1w:

A round-bottom flask was charged with 6-chlorohex-1-yne (1.05 g 4.5 mmol, 1 eq.) and 20 mL of dry DMF. Potassium phthalimide (2 g, 5.4 mmol, 1.2 eq.) was added to the yellowish solution. The yellowish suspension was heated at 70 °C for 24 h. The resulting solution was cooled to room temperature, and 70 mL of H₂O was added into the solution. The mixture was extracted under air with
Et₂O (4 × 70 mL), and the combined organic layers were dried over anhydrous MgSO₄, filtered, and concentrated on a rotary evaporator. The crude residue was purified by silica gel chromatography to provide 1w (1.7 g, 85% yield) as a white solid. ¹H NMR (300 MHz, Chloroform-d) δ 7.86-7.83 (m, 2H), 7.73-7.70 (m, 2H), 3.71 (t, J = 6.0 Hz, 2H), 2.25 (td, J = 7.0, 2.7 Hz, 2H), 1.96 (t, J = 2.7 Hz, 1 Hz), 1.86-1.77 (m, 2H), 1.63-1.53 (m, 2H).

1x:

To a clean, dry 25 mL two-neck round-bottom flask were added sodium hydride (364 mg, 15.2 mmol, 12 eq.) and anhydrous DMF (8 mL). The slurry was cooled to 0 °C followed by addition of Pregnenolone (0.4 g, 1.26 mmol, 1 eq.). The slurry followed by dropwise addition of 6-Chloro-1-hexyne (221 mg, 1.90 mmol, 1.5 eq.) under constant agitation. The mixture was stirred for 30 min and allowed to come to room temperature. The reaction was allowed to stir for 20 h. The reaction was quenched by water, and extracted by ethyl acetate. The combined organic layers were dried over anhydrous MgSO₄ and filtered. After concentration the crude was purified by silica gel to provide 1x (75 mg, 15% yield) as a colorless oil. ¹H NMR (400 MHz, Chloroform-d) δ 5.34 (d, J = 5.2 Hz, 1H), 3.48 (t, J = 5.8 Hz, 2H), 3.18-3.07 (m, 1H), 2.52 (t, J = 8.8 Hz, 1H), 2.40-2.30 (m, 1H), 2.21 (td, J = 7.2, 2.4 Hz, 3H), 2.12 (s, 3H), 2.07 – 1.95 (m, 2H), 1.94 (t, J = 2.6 Hz, 1H), 1.92 – 1.83 (m, 2H), 1.74-1.38 (m, 13H), 1.31-1.17 (m, 3H), 1.10-1.02 (m, 1H), 0.99 (s, 3H), 0.62 (s, 3H); ¹³C NMR (100 MHz, Chloroform-d) δ 209.5, 141.0, 121.1, 84.4, 78.9, 68.3, 67.3, 63.7, 56.9, 50.0, 44.0, 39.1, 38.8, 37.2, 36.9, 31.82, 31.79, 31.5, 29.2, 28.4, 25.3, 24.5, 22.8, 21.0, 19.4, 18.2, 13.2; HRMS [ESI] calcd for C₂₇H₄₆O₇Na [M+Na]+ 419.2922, found 419.2922.

1y:

To a clean, dry 20 mL round-bottom flask were added sodium hydride (399 mg, 16.6 mmol, 3 eq.) and anhydrous DMF (10 mL). The slurry was cooled to 0 °C followed by addition of Theophylline (1.0 g, 5.55 mmol, 1 eq.). The slurry followed by dropwise addition of 6-Chloro-1-hexyne (776 mg, 6.67 mmol, 1.2 eq.) under constant agitation. The mixture was stirred for 30 min and allowed to come to room temperature and the mixture was allowed to stir for 12 h at room temperature. The reaction was ended by addition of a large excess of water (10 mL) and the product extracted with ethyl acetate (5 × 25 mL). The combined organic layers were dried over anhydrous MgSO₄ and filtered. After concentration the crude was purified by silica gel to provide 1y (72 mg, 5% yield) as a white solid. m.p. 58.4-60.4 °C. ¹H NMR (400 MHz, Chloroform-d) δ 7.55 (s, 1H), 4.33 (t, J = 7.0 Hz, 2H), 3.60 (s, 3H), 3.41 (s, 3H), 2.25 (td, J = 6.8, 2.7 Hz, 2H), 2.07 – 1.98 (m, 2H), 1.97 (t, J = 2.6 Hz, 1H), 1.61 – 1.46 (m, 2H); ¹³C NMR (100 MHz, Chloroform-d) δ 155.0, 151.6, 148.9, 140.7, 106.9, 83.3, 69.1, 46.7, 29.9, 29.7, 27.9, 25.0, 17.9; HRMS [ESI] calcd for C₁₃H₁₇N₂O₂ [M+H]+ 261.1346, found 261.1349.

1z
To a clean, dry 20 mL round-bottom flask were added sodium hydride (115 mg, 4.79 mmol, 3 eq.) and anhydrous DMF (12 mL). The slurry was cooled to 0 °C followed by addition of Ethyl N-benzoyl-L-tyrosinate (500 mg, 1.6 mmol, 1 eq.). The slurry followed by dropwise addition of 6-Chloro-1-hexyne (186 mg, 1.6 mmol, 1 eq.) under constant agitation. The mixture was stirred for 30 min and allowed to come to room temperature and the mixture was allowed to stir for 7 h at room temperature. The reaction was ended by addition of a large excess of water (10 mL) and the product extracted with ethyl acetate. (5 × 10 mL). The combined organic layers were dried over anhydrous MgSO₄ and filtered. After concentration the crude was purified by silica gel to provide 1z (43.9 mg, 7% yield) as a white solid. m.p. 69.6-71.6 °C. ¹H NMR (400 MHz, Chloroform-d) δ 7.73 (d, J = 7.2 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.4 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 6.80 (d, J = 8.4 Hz, 2H), 6.61 (d, J = 7.6 Hz, 1H), 5.06 – 4.97 (m, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.95 (t, J = 6.2 Hz, 2H), 3.26 – 3.12 (m, 2H), 2.27 (td, J = 7.2, 2.5 Hz, 2H), 1.96 (t, J = 2.6 Hz, 1H), 1.93 – 1.85 (m, 2H), 1.76-1.66 (m, 2H), 1.29 (t, J = 7.2 Hz, 3H). ¹³C NMR (100 MHz, Chloroform-d) δ 171.6, 166.7, 158.1, 134.0, 131.7, 130.4, 128.6, 127.7, 127.0, 114.5, 84.0, 68.6, 67.2, 61.6, 53.6, 37.0, 28.2, 25.0, 18.1, 14.2; HRMS [ESI] calcd for C₂₅H₂₅NO₄ [M+H]+ 394.2013, found 394.2013.

1aa

In a 25 mL flask equipped with a stirring bar and a condenser, tetrabenzyld-g-glucose (400 mg, 1 mmol, 1 eq.), hex-5-yn-1-ol (363 mg, 5 mmol, 5 eq.), and BF₃·OEt₂ (420 mg, 4 mmol, 4 eq.) were dissolved in toluene (8 mL). The mixture was refluxed, and cooled to room temperature. The mixture was evaporated, and the residue was purified by silica gel column chromatography to afford 1aa (320 mg, 70%, a mixture of α/β isomers) as a colorless oil. ¹H NMR (400 MHz, Chloroform-d) δ 7.42-7.25 (m, 18H), 7.22-7.13 (m, 2H), 5.07-4.40 (m, 9H), 4.05-3.96 (m, 1H), 3.85-3.42 (m, 7H), 2.30-2.20 (m, 2H), 1.98 (t, J = 2.6 Hz, 1H), 1.88-1.58 (m, 4H).

5.2 Hydration of Terminal Alkynes 2 to Methyl Ketones.

A Representative Procedure for Hydration of Terminal Alkynes

(A) General Procedures.

A mixture of alkyne 1a (50 mg), cat.5 (5 mol%) in CH₂OH (0.25 mol/L) was heated at 65 °C under air for 3.5 h in a closed J. Young tube. The progress of the reaction was checked using TLC. The reaction mixture was carefully quenched by addition of H₂O (12 eq.), before the tube was cooled to 25 °C. The volatiles were removed under reduced pressure and the pure product 2aa as a colorless oil (52.5 mg, 96% yield) was obtained by flash chromatography of silica gel.

5-(4-fluorobenzyl)oxy)pentan-2-one (2a)

¹H NMR (300 MHz, Chloroform-d) δ 7.34-7.23 (m, 2H), 7.02 (t, J = 8.6 Hz, 2H), 4.43 (s, 2H), 3.47 (t, J = 6.2 Hz, 2H), 2.54 (t, J = 7.2 Hz, 2H), 2.13 (s, 3H), 1.95 – 1.83 (m, 2H); ¹³C NMR (75 MHz, Chloroform-d) δ 208.3, 162.1 (d, J = 243.8 Hz),
134.0 (d, J = 3 Hz), 129.1 (d, J = 8.2 Hz), 115.0 (d, J = 21 Hz), 71.9, 69.1, 40.1, 29.8, 23.7. Colorless oil. HRMS [ESI] calcd for C_{13}H_{13}FO_{3}Na [M+Na]^+ 233.0948, found 233.0950.

**Acetophenone (2b)**
Prepared according to general procedure A from 1b (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 5 h. Compound 2b was isolated as a colorless oil (52.9 mg, 96% yield). ^1H NMR (400 MHz, Chloroform-d) δ 7.99 – 7.93 (m, 2H), 7.56 (t, J = 8.0 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 2.61 (s, 3H). The spectral data were in agreement with literature values.

**1-(p-tolyl)ethan-1-one (2c)**
Prepared according to general procedure A from 1c (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 2.5 h. Compound 2c was isolated as a colorless oil (54.8 mg, 95% yield). ^1H NMR (300 MHz, Chloroform-d) δ 7.85 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 2.57 (s, 3H), 2.40 (s, 3H). The spectral data were in agreement with literature values.

**1-(4-methoxyphenyl)ethan-1-one (2d)**
Prepared according to general procedure A from 1d (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 4 h. Compound 2d was isolated as a colorless oil (51.1 mg, 90% yield). ^1H NMR (300 MHz, Chloroform-d) δ 7.92 (d, J = 9.0 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 3.85 (s, 3H), 2.54 (s, 3H). The spectral data were in agreement with literature values.

**1-(4-chlorophenyl)ethan-1-one (2e)**
Prepared according to general procedure A from 1e (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 3.5 h. Compound 2e was isolated as a colorless oil (53.2 mg, 94% yield). ^1H NMR (400 MHz, Chloroform-d) δ 7.88 (d, J = 8.8 Hz, 2H), 7.41 (d, J = 8.8 Hz, 2H), 2.57 (s, 3H). The spectral data were in agreement with literature values.

**1-(4-bromophenyl)ethan-1-one (2f)**
Prepared according to general procedure A from 1f (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 4.5 h. Compound 2f was isolated as a white solid (50.6 mg, 92% yield). ^1H NMR (300 MHz, Chloroform-d) δ 7.82 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.4 Hz, 2H), 2.59 (s, 3H). The spectral data were in agreement with literature values.

**1-bromo-4-(1,1-dimethoxyethyl)benzene (2f-Intermediate)**
^1H NMR (300 MHz, Chloroform-d) δ 7.47 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 3.17 (s, 6H), 1.51 (s, 3H). Colorless oil. The spectral data were in agreement with literature values.

**1-(4-fluorophenyl)ethan-1-one (2g)**
Prepared according to general procedure A from 1g (50 mg) and \textit{cat.5} (5 mol\%) in MeOH (0.25 mol/mL) at 65 °C for 3.5 h. Compound 2g was isolated as a colorless oil (54.0 mg, 94\% yield). $^1$H NMR (300 MHz, Chloroform-\textit{d}) $\delta$ 8.02-7.93 (m, 2H), 7.12 (t, $J$ =8.7 Hz, 2H), 2.58 (s, 3H). The spectral data were in agreement with literature values.$^5$

1-(4-nitrophenyl)ethan-1-one (2h)

Prepared according to general procedure A from 1h (50 mg) and \textit{cat.5} (5 mol\%) in MeOH (0.25 mol/mL) at 65 °C for 60 h. Compound 2h was isolated as a yellow solid (46.0 mg, 82\% yield). $^1$H NMR (300 MHz, Chloroform-\textit{d}) $\delta$ 8.29 (d, $J$ = 8.7 Hz, 2H), 8.10 (d, $J$ = 8.7 Hz, 2H), 2.67 (s, 3H). The spectral data were in agreement with literature values.$^{13}$

1-(3-methoxyphenyl)ethan-1-one (2i)

Prepared according to general procedure A from 1i (50 mg) and \textit{cat.5} (5 mol\%) in MeOH (0.25 mol/mL) at 65 °C for 2.5 h. Compound 2i was isolated as a colorless oil (54.5 mg, 96\% yield). $^1$H NMR (300 MHz, Chloroform-\textit{d}) $\delta$ 7.52 (d, $J$ = 7.5 Hz, 1H), 7.48 (s, 1H), 7.36 (t, $J$ = 8.0 Hz, 1H), 7.10 (dd, $J$ = 8.4, 2.7 Hz, 1H), 3.84 (s, 3H), 2.58 (s, 3H). The spectral data were in agreement with literature values.$^{14}$

1-(3-nitrophenyl)ethan-1-one (2j)

Prepared according to general procedure A from 1j (50 mg) and \textit{cat.5} (5 mol\%) in MeOH (0.25 mol/mL) at 65 °C for 49 h. Compound 2j was isolated as a yellow solid (51.1 mg, 91\% yield). $^1$H NMR (300 MHz, Chloroform-\textit{d}) $\delta$ 8.75 (t, $J$ = 1.8 Hz, 1H), 8.44-8.37 (m, 1H), 8.28 (dt, $J$ = 7.8 Hz, 1.4 Hz, 1H), 7.68 (t, $J$ = 8.0 Hz, 1H), 2.68 (s, 3H). The spectral data were in agreement with literature values.$^{11}$

1-(2-methoxyphenyl)ethan-1-one (2k)

Prepared according to general procedure A from 1k (50 mg) and \textit{cat.5} (5 mol\%) in MeOH (0.25 mol/mL) at 65 °C for 2.5 h. Compound 2k was isolated as a colorless oil (52.8 mg, 93\% yield). $^1$H NMR (400 MHz, Chloroform-\textit{d}) $\delta$ 7.72 (dd, $J$ = 7.6, 1.6 Hz, 1H), 7.47 – 7.42 (m, 1H), 7.01 – 6.91 (m, 2H), 3.89 (s, 3H), 2.60 (s, 3H). The spectral data were in agreement with literature values.$^{15}$

1-(2-nitrophenyl)ethan-1-one (2l)

Prepared according to general procedure A from 1l (50 mg) and \textit{cat.5} (5 mol\%) in MeOH (0.25 mol/mL) at 65 °C for 60 h. Compound 2l was isolated as a white solid (33.7 mg, 60\% yield). $^1$H NMR (300 MHz, Chloroform-\textit{d}) $\delta$ 8.09 (d, $J$ = 8.1 Hz, 1H), 7.72 (t, $J$ = 7.2 Hz, 1H), 7.60 (t, $J$ = 7.4 Hz, 1H), 7.43 (d, $J$ = 7.2 Hz, 1H), 2.56 (s, 3H). The spectral data were in agreement with literature values.$^{14}$

1-(3,4-dimethoxyphenyl)ethan-1-one (2m)

Prepared according to general procedure A from 1m (50 mg) and \textit{cat.5} (5 mol\%) in MeOH (0.25 mol/mL) at 65 °C for 2.5 h. Compound 2m was isolated as a white
solid (52.8 mg, 95% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.56 (d, $J = 8.4$ Hz, 1H), 7.51 (s, 1H), 6.87 (d, $J = 8.4$ Hz, 1H), 3.93 (s, 3H), 3.92 (s, 3H), 2.55 (s, 3H). The spectral data were in agreement with literature values.\textsuperscript{10} 

\begin{center} 
\textbf{1-(naphthalen-2-yl)ethan-1-one (2n)} 
\end{center}

Prepared according to general procedure A from 1n (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 3.5 h. Compound 2n was isolated as a white solid (53.1 mg, 95% yield). $^1$H NMR (300 MHz, Chloroform-$d$) $\delta$ 8.46 (s, 1H), 8.04 (dd, $J = 8.4$, 1.5 Hz, 1H), 7.97 (d, $J = 7.8$ Hz, 1H), 7.92-7.84 (m, 2H), 7.65-7.50 (m, 2H), 2.73 (s, 3H). The spectral data were in agreement with literature values.\textsuperscript{16} 

\begin{center} 
\textbf{1-(naphthalen-1-yl)ethan-1-one (2o)} 
\end{center}

Prepared according to general procedure A from 1o (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 2.5 h. Compound 2o was isolated as a yellow oil (52.0 mg, 93% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.80 (m, 2H), 2.12 (s, 3H), 1.72 (m, 4H). The spectral data were in agreement with literature values.\textsuperscript{10} 

\begin{center} 
\textbf{6-chlorohexan-2-one (2p)} 
\end{center}

Prepared according to general procedure A from 1p (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 2.5 h. Compound 2p was isolated as a colorless oil (56.6 mg, 98% yield). $^1$H NMR (300 MHz, Chloroform-$d$) $\delta$ 3.43 (t, $J = 6.3$ Hz, 2H), 2.38 (t, $J = 6.8$ Hz, 2H), 2.04 (s, 3H), 1.75-1.47 (m, 4H). The spectral data were in agreement with literature values.\textsuperscript{15} 

\begin{center} 
\textbf{5-oxohexyl benzoate (2q)} 
\end{center}

Prepared according to general procedure A from 1q (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 12 h. Compound 2q was isolated as a colorless oil (52.8 mg, 97% yield). $^1$H NMR (300 MHz, Chloroform-$d$) $\delta$ 8.04 (d, $J = 7.2$ Hz, 2H), 7.56 (t, $J = 7.4$ Hz, 1H), 7.43 (t, $J = 7.5$ Hz, 2H), 4.32 (t, $J = 6.0$ Hz, 2H), 2.52 (t, $J = 6.8$ Hz, 2H), 2.15 (s, 3H), 1.82 – 1.72 (m, 4H). The spectral data were in agreement with literature values.\textsuperscript{5} 

\begin{center} 
\textbf{6-tert-Butyldiphenylsilyloxy-2-hexanone (2r)} 
\end{center}

Prepared according to general procedure A from 1r (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 3 h. Compound 2r was isolated as a light yellow oil (31.6 mg, 60% yield). $^1$H NMR (300 MHz, Chloroform-$d$) $\delta$ 7.70 – 7.61 (m, 4H), 7.46 – 7.34 (m, 6H), 3.66 (t, $J = 6.2$ Hz, 2H), 2.41 (t, $J = 7.2$ Hz, 2H), 2.12 (s, 3H), 1.72 – 1.61 (m, 2H), 1.58 – 1.49 (m, 2H), 1.05 (s, 9H). The spectral data were in agreement with literature values.\textsuperscript{5} 

\begin{center} 
\textbf{6-(allyloxy)hexan-2-one (2s)} 
\end{center}

Prepared according to general procedure A from 1s (50 mg) and cat.5 (5
mol%) in MeOH (0.25 mol/mL) at 65 °C for 4.5 h. Compound 2s was isolated as a colorless oil (53.7 mg, 96% yield). 1H NMR (400 MHz, Chloroform-d) δ 6.02 – 5.73 (m, 1H), 5.25 (d, J = 17.2 Hz, 1H), 5.16 (d, J = 10.4 Hz, 1H), 3.95 (d, J = 6.0 Hz, 2H), 3.43 (t, J = 6.2 Hz, 2H), 2.45 (t, J = 7.2 Hz, 2H), 2.13 (s, 3H), 1.70 – 1.50 (m, 4H). The spectral data were in agreement with literature values.5

6-(methoxymethoxy)hexan-2-one (2t)
Prepared according to general procedure A from 1t (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 13 h. Compound 2t was isolated as a colorless oil (51.3 mg, 91% yield). 1H NMR (400 MHz, Chloroform-d) δ 4.56 (s, 2H), 3.48 (t, J = 6.2 Hz, 2H), 3.31 (s, 3H), 2.43 (t, J = 7.2 Hz, 2H), 2.10 (s, 3H), 1.66 – 1.51 (m, 4H); 13C NMR (100 MHz, Chloroform-d) δ 208.7, 96.3, 67.3, 55.0, 43.2, 29.8, 29.0, 20.4. HRMS [ESI] calcd for C8H10O3Na [M+Na]+ 183.0992, found 183.0989.

tert-butyl (5-oxohexyl) carbonate (2u)
Prepared according to general procedure A from 1u (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 20 h. Compound 2u was isolated as a colorless oil (46.9 mg, 86% yield). 1H NMR (300 MHz, Chloroform-d) δ 4.04 (t, J = 5.8 Hz, 2H), 2.45 (t, J = 6.6 Hz, 2H), 2.12 (s, 3H), 1.68-1.60 (m, 4H), 1.46 (s, 9H); 13C NMR (101 MHz, Chloroform-d) δ 208.3, 153.5, 81.9, 66.5, 43.0, 29.9, 28.0, 27.7, 20.0. HRMS [ESI] calcd for C19H30O3Na [M+Na]+ 239.1254, found 239.1251.

1-(5-oxohexyl)pyrrolidine-2,5-dione (2v)
Prepared according to general procedure A from 1v (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 6 h. Compound 2v was isolated as a colorless oil (44.0 mg, 80% yield). 1H NMR (300 MHz, Chloroform-d) δ 3.45 (t, J = 6.3 Hz, 2H), 2.66 (s, 4H), 2.42 (t, J = 6.4 Hz, 2H), 2.08 (s, 3H), 1.53 – 1.48 (m, 4H); 13C NMR (100 MHz, Chloroform-d) δ 208.2, 177.2, 42.6, 38.2, 29.9, 28.0, 26.9, 20.5. HRMS [ESI] calcd for C10H16NO3 [M+H]+ 198.1125, found 198.1122.

2-(5-oxohexyl)isoindoline-1,3-dione (2w)
Prepared according to general procedure A from 1w (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 3.5 h. Compound 2w was isolated as a white solid (53.4 mg, 99% yield). 1H NMR (300 MHz, Chloroform-d) δ 7.84 – 7.76 (m, 2H), 7.72-7.65 (m, 2H), 3.66 (t, J = 6.8 Hz, 2H), 2.46 (t, J = 6.9 Hz, 2H), 2.11 (s, 3H), 1.75 – 1.51 (m, 4H). The spectral data were in agreement with literature values.17

6-(((3S,8S,9S,10R,13S,14S,17S)-17-acetyl-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[alp]he nanthren-3-yloxy)hexan-2-one (2x)
Prepared according to general procedure A from 1x (50 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 5 h. Compound 2x was isolated as a white solid (51.2 mg, 98% yield). m.p. 94.8 – 96.8 °C. 1H NMR (400 MHz, Chloroform-d) δ 5.33 (d, J = 5.6 Hz, 1H), 3.45 (td, J = 6.4, 1.6 Hz, 2H), 3.16-3.06 (m, 1H), 2.52 (t, J = 8.8 Hz, 1H), 2.45 (t, J = 7.4 Hz, 2H), 2.38-2.31 (m, 1H), 2.22-2.14 (m, 2H), 2.13 (s, 3H), 2.11 (s, 3H), 2.06 – 1.81 (m, 4H), 1.71 – 1.37 (m, 13H), 1.25 – 1.02 (m, 3H), 0.98 (s, 3H), 0.62 (s, 3H); 13C NMR (100 MHz, Chloroform-d) δ 209.5, 209.0, 214.0, 121.1, 78.9, 67.6, 63.7, 56.9, 50.0, 44.0, 43.5, 39.1, 38.8, 37.2, 36.9, 31.8, 31.77, 31.5,
1,3-dimethyl-7-(5-oxohexyl)-3,7-dihydro-1H-purine-2,6-dione (2y)

Prepared according to general procedure A from 1y (40 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 20 h. Compound 2y was isolated as a white solid (40.2 mg, 94% yield). m.p. 38.0 – 40.0 °C. 

\[
{^1}H \text{ NMR} \ (400 \text{ MHz}, \ \text{Chloroform-}\text{d}) \ \delta \ 7.54 \ (s, 1H), \ 4.24 \ (t, \ J = 6.8 \text{ Hz}, 2H), \ 3.54 \ (s, 3H), \ 3.36 \ (s, 3H), \ 2.46 \ (t, \ J = 6.4 \text{ Hz}, 2H), \ 2.09 \ (s, 3H), \ 1.92-1.75 \ (m, 2H), \ 1.64 – 1.46 \ (m, 2H); \ \text{^13C NMR} \ (100 \text{ MHz}, \ \text{Chloroform-}\text{d}) \ \delta \ 207.9, \ 155.0, \ 151.5, \ 148.8, \ 140.8, \ 106.8, \ 46.9, \ 42.5, \ 30.2, \ 29.9, \ 29.7, \ 27.9, \ 20.1; \ \text{HRMS} \ [\text{ESI}] \ \text{calcd for} \ C_{24}H_{24}N_{4}O_{2}Na \ [\text{M+Na}^+] \ 437.3026, \ \text{found} \ 437.3026.
\]

(S)-ethyl 2-benzamido-3-((5-oxohexyl)oxy)phenyl)propanoate (2z)

Prepared according to general procedure A from 1z (20 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 18.5 h. Compound 2z was isolated as a colorless oil (19.4 mg, 90% yield). 

\[
{^1}H \text{ NMR} \ (400 \text{ MHz}, \ \text{Chloroform-}\text{d}) \ \delta \ 7.73 \ (d, J = 6.8 \text{ Hz}, 2H), \ 7.54 – 7.48 \ (m, 1H), \ 7.42 \ (t, \ J = 7.4 \text{ Hz}, 2H), \ 7.04 \ (d, \ J = 8.4 \text{ Hz}, 2H), \ 6.79 \ (d, \ J = 8.8 \text{ Hz}, 2H), \ 6.59 \ (d, \ J = 7.2 \text{ Hz}, 1H), \ 5.06-4.97 \ (m, 1H), \ 4.22 \ (q, \ J = 7.2 \text{ Hz}, 2H), \ 3.92 \ (t, \ J = 5.8 \text{ Hz}, 2H), \ 3.28 – 3.10 \ (m, 2H), \ 2.51 \ (t, \ J = 6.6 \text{ Hz}, 2H), \ 2.15 \ (s, 3H), \ 1.81-1.69 \ (m, 4H), \ 1.29 \ (t, \ J = 7.2 \text{ Hz}, 3H); \ \text{^13C NMR} \ (100 \text{ MHz}, \ \text{Chloroform-}\text{d}) \ \delta \ 208.6, \ 171.6, \ 166.7, \ 158.1, \ 134.0, \ 131.7, \ 130.4, \ 128.6, \ 127.7, \ 127.0, \ 114.5, \ 67.4, \ 61.6, \ 53.6, \ 43.2, \ 37.0, \ 29.9, \ 28.6, \ 20.4, \ 14.2; \ \text{HRMS} \ [\text{ESI}] \ \text{calcd for} \ C_{32}H_{32}NO_{5}Na \ [\text{M+Na}^+] \ 434.1938, \ \text{found} \ 434.1938.
\]

6-((3R,4S,5R,6R)-3,4,5-tris(benzylxylo)-6-((benzylxylo)methyl)dihydro-2H-pyran-2-yl)oxy)hexan-2-one (2aa)

Prepared according to general procedure A from 1aa (47.7 mg) and cat.5 (5 mol%) in MeOH (0.25 mol/mL) at 65 °C for 34 h. Compound 2aa was isolated as a colorless oil (45.1mg, 92% yield). 

\[
{^1}H \text{ NMR} \ (400 \text{ MHz}, \ \text{Chloroform-}\text{d}) \ \delta \ 7.38 – 7.30 \ (m, 12H), \ 7.28 – 7.24 \ (m, 6H), \ 7.17 – 7.11 \ (m, 2H), \ 5.00 – 4.70 \ (m, 5H), \ 4.66-4.36 \ (m, 4H), \ 3.97 \ (t, \ J = 9.3 \text{ Hz}, 1H), \ 3.80 – 3.49 \ (m, 6H), \ 3.48 – 3.38 \ (m, 1H), \ 2.48 – 2.39 \ (m, 2H), \ 2.10 \ (s, 3H), \ 1.72 – 1.55 \ (m, 4H). \ \text{The spectral data were in agreement with literature values.}
\]

6. References

7. \(^1\)H NMR, \(^{13}\)C NMR spectra

\(^1\)H NMR was recorded on Bruker 300 MHz; Solvent: CDCl\(_3\)

\(^{13}\)C NMR was recorded on Bruker 75 MHz; Solvent: CDCl\(_3\)
$^1$H NMR was recorded on Bruker 300 MHz; Solvent: CDCl$_3$

$^{13}$C NMR was recorded on Bruker 75 MHz; Solvent: CDCl$_3$
$^1$H NMR was recorded on Bruker 400 MHz; Solvent: CDCl$_3$
$^1$H NMR was recorded on Bruker 300 MHz; Solvent: CDCl$_3$

$^1$H NMR was recorded on Bruker 400 MHz; Solvent: CDCl$_3$
\[ \text{H NMR was recorded on Bruker 300 MHz; Solvent: CDCl}_3 \]

\[ \text{2f - intermediate} \]

\[ \text{H NMR was recorded on Bruker 300 MHz; Solvent: CDCl}_3 \]
$^1$H NMR was recorded on Bruker 300 MHz; Solvent: CDCl$_3$
$^1$H NMR was recorded on Bruker 300 MHz; Solvent: CDCl$_3$
$^1$H NMR was recorded on Bruker 400 MHz; Solvent: CDCl$_3$

$^1$H NMR was recorded on Bruker 300 MHz; Solvent: CDCl$_3$
**1H NMR was recorded on Bruker 400 MHz; Solvent: CDCl₃**

![Chemical structure 1](image1)

**1H NMR was recorded on Bruker 300 MHz; Solvent: CDCl₃**

![Chemical structure 2](image2)
$^1$H NMR was recorded on Bruker 400 MHz; Solvent: CDCl$_3$

$^1$H NMR was recorded on Bruker 300 MHz; Solvent: CDCl$_3$
$^1$H NMR was recorded on Bruker 300 MHz; Solvent: CDCl$_3$
$^1$H NMR was recorded on Bruker 400 MHz; Solvent: CDCl$_3$
$^1$H NMR was recorded on Bruker 300 MHz; Solvent: CDCl$_3$
$^{13}$C NMR was recorded on Bruker 100 MHz; Solvent: CDCl$_3$

$^1$H NMR was recorded on Bruker 300 MHz; Solvent: CDCl$_3$
$^{13}$C NMR was recorded on Bruker 100 MHz; Solvent: CDCl$_3$

$^1$H NMR was recorded on Bruker 300 MHz; Solvent: CDCl$_3$
$^{13}$C NMR was recorded on Bruker 100 MHz; Solvent: CDCl$_3$

$^1$H NMR was recorded on Bruker 300 MHz; Solvent: CDCl$_3$
$^1$H NMR was recorded on Bruker 400 MHz; Solvent: CDCl$_3$

$^{13}$C NMR was recorded on Bruker 100 MHz; Solvent: CDCl$_3$
1H NMR was recorded on Bruker 400 MHz; Solvent: CDCl₃

13C NMR was recorded on Bruker 100 MHz; Solvent: CDCl₃
$^1$H NMR was recorded on Bruker 400 MHz; Solvent: CDCl$_3$

$^{13}$C NMR was recorded on Bruker 100 MHz; Solvent: CDCl$_3$
$^{1}H$ NMR was recorded on Bruker 400 MHz; Solvent: CDCl$_3$

$^{13}$C NMR was recorded on Bruker 100 MHz; Solvent: CDCl$_3$
$^1$H NMR was recorded on Bruker 400 MHz; Solvent: CDCl$_3$

$^{13}$C NMR was recorded on Bruker 100 MHz; Solvent: CDCl$_3$
$^{1}H$ NMR was recorded on Bruker 400 MHz; Solvent: CDCl$_3$

$^{13}C$ NMR was recorded on Bruker 100 MHz; Solvent: CDCl$_3$
$^1$H NMR was recorded on Bruker 400 MHz; Solvent: CDCl$_3$