Supporting Information

Transesterification of Non-Activated Esters Promoted by Small Molecules Mimicking the Active Site of Hydrolases

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Experimental Procedures

1. General information

1.1. Materials and instrumentation

Reagents

Reagents were purchased and used without further purification unless otherwise noted. The solvents used were purified and dried following the standard methods.[1]

Purification of reaction crudes

Reactions were monitored by analytical thin layer chromatography using pre-coated aluminium-backed plates (0.2 mm silica gel 60 F254, Merck®) and visualized by UV light. Purification of compounds was performed using silica gel column chromatography (Chromagel 60A SdS. C.C. 70-200 μm) with solvent mixtures of increasing polarity as eluents and crystallization using different solvent mixtures.

Melting Points (m.p.)

Melting points were measured in a Leica Galen III microscope and were reported in °C.

IR spectroscopy

IR spectra were recorded using a Nicolet IR100 with NaCl crystals as films or with Nujol as solvent.

NMR spectroscopy

$^1$H and $^{13}$C NMR spectra were recorded at room temperature using Bruker models WP-200-SY, Varian Mercury 200 MHz and Bruker Advance NEO 400 MHz with a Prodigy CPPBBO BB-H&F z-gradient cryo-probe spectrometers. Chemical shifts were reported in ppm with the solvent signal ($^1$H/$^{13}$C: deuterated chloroform CDCl$_3$ 7.26/77.2 ppm, dimethylsulfoxide DMSO-d$_6$ 2.49/39.5 ppm or methanol CD$_3$OD-d$_4$ 3.3/49.0 ppm and tetramethylsilane TMS 0.00 ppm) as an internal standard using reported shifts.[2] Coupling constants ($^J$) were reported in Hertz. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; sext, sextet; m, multiplet; br, broad.

Mass spectrometry

Mass spectra were recorded on a quadrupole-TOF Applied Biosystems QSTAR XL and Waters ZQ 4000 spectrometers using electrospray ionization (ESI) or electronic impact (EI).

X-ray diffraction studies

X-ray diffraction studies were made in a Bruker Kappa Apex II with a CCD detector diffractometer.

1.2. General Procedures

General Procedure 1: Catalyst activation with NH$_3$.

Catalysts 3-12 appeared partially protonated after silica gel column chromatography purification, which could negatively bias their catalytic activity. In order to free-base the amine group, the catalyst was dissolved in CHCl$_3$ and washed with a small amount of 5% v/v aqueous solution of NH$_3$. The organic phase was dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure to yield the activated catalyst. Apparently NaHCO$_3$ and Na$_2$CO$_3$ were not successful bases to generate the activated catalyst as they seemed complexed by the oxyanion-hole.

General Procedure 2: Catalyst acetylation using vinyl acetate.

The required catalyst (ca. 10 mg) was dissolved in the minimum amount of vinyl acetate (ca. 500 μL) and the reaction mixture was stirred for 5 minutes. Then, the excess of vinyl acetate was removed in vacuo to afford the desired compound quantitatively.
2. Synthesis and Characterization

5-Bromo-2-naphthoic acid (13)

To a 2-naphthoic acid solution (11.0 g, 63.9 mmol) in 98% H$_2$SO$_4$ (80 mL) at 0ºC, NaBr (4.0 g, 38.9 mmol) was added portionwise for 15 minutes. The resulting reaction mixture was stirred under these conditions for one hour and the solid was collected by filtration under reduced pressure and recrystallized in 100 mL of 20% MeOH in DCM. Compound 13 (3.14 g, 32 %) was obtained as a white solid.

m.p.: >230ºC

IR (nujol, $\nu$ in cm$^{-1}$): 1677, 1625, 1554, 1492, 1339, 1301, 1197, 970, 924, 775.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.66 (s, 1H), 8.20 (d, $J = 8.5$ Hz, 1H), 8.18 (d, $J = 7.5$ Hz, 2H), 8.13 (dd, $J = 8.5$, 1.5 Hz, 1H), 8.00 (d, $J = 7.5$ Hz, 1H), 7.52 (t, $J = 7.5$ Hz, 1H).

$^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 167.0 (C), 133.6 (C), 133.0 (C), 132.3 (CH), 131.1 (CH), 129.7 (CH), 129.1 (C), 127.6 (CH), 127.0 (CH), 126.8 (CH), 121.6 (C).

HRMS (ESI-): Calculated for C$_{11}$H$_7$BrO$_2$ [M-H] 248.9556, found 248.9555.

5-Bromo-8-(chlorosulfonyl)-2-naphthoic acid (14)

Compound 13 (2.0 g, 8.0 mmol) was added to HSO$_3$Cl (10 mL, 150.2 mmol) at 0ºC and the reaction mixture was stirred under these conditions for one hour. Then, the reaction was warmed to 70ºC for 20 minutes, cooled down to room temperature and added over ice (100 g). Compound 14 (2.50 g, 90 %) was obtained as a white solid by filtration under reduced pressure.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.62 (s, 1H), 8.24 (d, $J = 8.8$ Hz, 1H), 8.12 (dd, $J = 8.8$, 1.6 Hz, 1H), 7.97 (d, $J = 7.8$ Hz, 1H), 7.92 (d, $J = 7.8$ Hz, 1H).

5-Bromo-8-(N-butylsulfamoyl)-2-naphthoic acid (15)

Compound 14 (200 mg, 0.6 mmol) was added to butylamine (5 mL, 50.6 mmol). After 5 minutes, the reaction was added to an aqueous 2M HCl solution (40 mL) and extracted with EtOAc (2x30 mL). The organic phase was dried over anhydrous Na$_2$SO$_4$, filtered and the solvent was removed under reduced pressure. Compound 15 (156 mg, 71 %) was obtained as a white solid.
**SUPPORTING INFORMATION**

m.p.: 174 – 176°C

IR (nujol, v in cm\(^{-1}\)): 2942, 1697, 1625, 1560, 1515, 1294, 1262, 1200, 1158, 1087, 1041, 950, 898, 840, 762, 639.

\(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) 9.42 (d, \(J = 1.5\) Hz, 1H), 8.40 (d, \(J = 8.9\) Hz, 1H), 8.25 (dd, \(J = 8.9, 1.5\) Hz, 1H), 8.18 (d, \(J = 7.9\) Hz, 1H), 8.17 (br t, \(J = 6.0\) Hz, NH), 8.05 (d, \(J = 7.9\) Hz, 1H), 2.85 (q, \(J = 6.9\) Hz, 2H), 1.32 (quin, \(J = 7.3\) Hz, 2H), 1.15 (hex, \(J = 7.3\) Hz, 2H), 0.70 (t, \(J = 7.3\) Hz, 3H).

\(^13\)C NMR (100 MHz, DMSO-d\(_6\)) \(\delta\) 166.8 (C), 137.6 (C), 133.7 (C), 131.1 (CH), 130.7 (C), 129.0 (CH), 128.2 (C), 128.1 (CH), 127.9 (CH), 127.9 (CH), 127.4 (C), 42.3 (CH\(_2\)), 31.2 (CH\(_2\)), 19.1 (CH\(_2\)), 13.3 (CH\(_3\)).

HRMS (ESI-): Calculated for \(\text{C}_{15}\text{H}_{15}\text{BrNO}_4\text{S} [\text{M-H}]^+\) 383.9910, found 383.9912.

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5-Bromo-8-(N-butylsulfamoyl)-N-(3-hydroxy-4-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydro-naphthalen-2-yl)-2-naphthamide (catalyst 3)

Compound 15 (150 mg, 0.39 mmol) was refluxed in SOCl\(_2\) (5 mL) for 30 minutes and stirred at room temperature for 2 hours. Then, it was concentrated under reduced pressure to yield the compound 15 acid chloride (quant.), which was used in the next step without further purification.

The acid chloride of 15 (157 mg, 0.39 mmol) was dissolved in EtOAc (10 mL) and was added over a stirred solution of amine 16.[3] (110 mg, 0.45 mmol) in a mixture of 10 mL EtOAc and 10 mL of an aqueous 4% Na\(_2\)CO\(_3\) saturated solution. The acid chloride reaction flask was washed with more of EtOAc (4 mL) and added over the reaction mixture. Then, the reaction mixture was transferred to a separatory funnel. The aqueous phase was extracted with EtOAc, the organic phase was washed with brine, dried over anhydrous Na\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography using mixtures of MeOH in EtOAc (1-20%) as eluent, yielding compound 3. The compound was then activated following the General Procedure 1 for catalyst activation with NH\(_3\), affording catalyst 3 (120 mg, 50%).

m.p.: glassy compound

IR (film, v in cm\(^{-1}\)): 3260, 3072, 2962, 2923, 2858, 1658, 1547, 1495, 1450, 1327, 1203, 1152, 905, 736.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.06 (d, \(J = 1.1\) Hz, 1H), 8.14 (d, \(J = 7.9\) Hz, 1H), 8.09 – 8.00 (m, 2H), 7.93 (d, \(J = 7.9\) Hz, 1H), 7.45 (br d, \(J = 8.0\) Hz, NH), 7.34 – 7.28 (m, 1H), 7.23 – 7.13 (m, 2H), 7.12 – 7.06 (m, 1H), 4.46 – 4.33 (m, 1H), 4.21 (t, \(J = 9.6\) Hz, 1H), 3.33 (dd, \(J = 16.1, 4.8\) Hz, 1H), 3.27 – 3.17 (m, 2H), 3.10 – 2.84 (m, 6H), 2.69 – 2.55 (m, 2H), 1.95 – 1.81 (m, 4H), 1.48 (quin, \(J = 7.4\) Hz, 3H), 1.28 (hex, \(J = 7.4\) Hz, 2H), 0.77 (t, \(J = 7.4\) Hz, 3H).

\(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 166.8 (C), 136.2 (C), 134.8 (C), 134.6 (C), 134.0 (C), 133.6 (C), 130.3 (CH), 129.9 (CH), 129.5 (CH), 128.9 (C), 128.6 (CH), 128.5 (C), 127.0 (CH), 126.8 (CH), 126.7 (2 CH), 123.3 (CH), 77.4 (CH), 62.8 (CH\(_2\)), 54.9 (2 CH\(_2\)), 51.7 (CH), 43.5 (CH), 43.0 (CH\(_2\)), 35.9 (CH\(_3\)), 32.3 (CH\(_2\)), 23.6 (2 CH\(_2\)), 19.9 (CH\(_2\)), 13.3 (CH\(_3\)).

HRMS (ESI+): Calculated for \(\text{C}_{30}\text{H}_{37}\text{BrN}_{3}\text{O}_{4}\text{S} [\text{M+H}]^+\) 614.1683, found 614.1677.
Following the General Procedure 2 for catalyst acetylation using vinyl acetate, the reaction of catalyst 3 (20 mg, 0.03 mmol) with 500 μL of vinyl acetate gave compound 3a (16 mg, 76%) as a yellowish oil.

\[ \text{3a} \]

\( ^1 \text{H NMR (400 MHz, CDCl}_3 \) δ 8.77 (s, 1H), 8.45 (d, \( J = 8.8 \text{ Hz}, 1 \text{H} \)), 8.18 (d, \( J = 7.9 \text{ Hz}, 1 \text{H} \)), 8.17 (dd, \( J = 8.8, 1.6 \text{ Hz}, 1 \text{H} \)), 7.94 (d, \( J = 7.9 \text{ Hz}, 1 \text{H} \)), 7.57 (br s, NH), 7.38 (d, \( J = 7.3 \text{ Hz}, 1 \text{H} \)), 7.25–7.11 (m, 3H), 6.84 (br s, NH), 5.43 (dd, \( J = 10.2, 6.9 \text{ Hz}, 1 \text{H} \)), 4.46–4.35 (m, 1H), 3.44 (dd, \( J = 15.7, 4.6 \text{ Hz}, 1 \text{H} \)), 3.37 (dd, \( J = 12.6, 6.7 \text{ Hz}, 1 \text{H} \)), 3.03–2.92 (m, 4H), 2.60–2.49 (m, 2H), 2.50–2.39 (m, 2H), 2.24 (s, 3H), 1.76–1.66 (m, 4H), 1.43 (m, 2H), 1.25 (quin, \( J = 7.6 \text{ Hz}, 2 \text{H} \)), 0.78 (t, \( J = 7.3 \text{ Hz}, 3 \text{H} \)).

\( ^{13} \text{C NMR (100 MHz, CDCl}_3 \) δ 175.6 (C), 167.0 (C), 136.4 (2 C), 134.9 (C), 134.1 (C), 133.8 (C), 130.8 (CH), 130.2 (CH), 129.3 (CH), 129.2 (C), 129.0 (CH), 128.6 (C), 128.2 (CH), 127.2 (CH), 126.9 (CH), 126.8 (CH), 122.9 (CH), 77.0 (CH), 62.1 (CH), 54.8 (2 CH), 51.9 (CH), 43.8 (CH), 42.7 (CH), 34.7 (CH), 31.9 (CH), 23.9 (2 CH), 21.6 (CH), 19.8 (CH), 13.6 (CH).

5-Bromo-8-(N-(4-dimethylamino)phenyl)sulfamoyl)-2-naphthoic acid (17)

\( \text{17} \)

Compound 14 (122 mg, 0.35 mmol) and N,N-dimethyl-p-phenylenediamine (78 mg, 0.57 mmol) were mixed in EtOAc (630 μL). The reaction mixture was stirred until a precipitate showed up. Then, the solvent was evaporated under reduced pressure, the crude product was suspended in MeOH–H₂O and the precipitate was collected by filtration yielding compound 17 (50 mg, 32%) which was used without further purification in the next reaction.

m.p.: 214–216°C
IR (nujol, \( \nu \) in cm⁻¹): 2929, 1690, 1612, 1554, 1521, 1346, 1292, 1246, 1200, 1152, 1048, 989, 905, 847, 756, 697, 639.

\( ^1 \text{H NMR (400 MHz, DMSO-d}_6 \) δ 10.23 (s, 1H), 9.38 (s, 1H), 8.37 (d, \( J = 8.9 \text{ Hz}, 1 \text{H} \)), 8.23 (dd, \( J = 8.9, 1.4 \text{ Hz}, 1 \text{H} \)), 8.12 (d, \( J = 8.0 \text{ Hz}, 1 \text{H} \)), 7.97 (d, \( J = 8.0 \text{ Hz}, 1 \text{H} \)), 6.75 (d, \( J = 7.9 \text{ Hz}, 2 \text{H} \)), 6.54 (d, \( J = 7.9 \text{ Hz}, 2 \text{H} \)), 2.78 (s, 6H).

\( ^{13} \text{C NMR (100 MHz, DMSO-d}_6 \) δ 166.8 (C), 148.0 (C, broad), 145.7 (C), 136.6 (C), 133.5 (C), 130.9 (CH), 130.8 (C), 130.2 (CH), 128.4 (C), 128.0 (CH), 127.9 (CH), 127.9 (C), 127.8 (CH), 124.3 (2 CH, broad), 113.1 (2 CH, broad), 40.4 (2 CH₃).

HRMS (ESI⁺): Calculated for C₁₉H₁₈BrN₂O₂S [M+H]⁺ 449.0166, found 449.0157.
The acid 17 (200 mg, 0.45 mmol), amine 16 (110 mg, 0.44 mmol) and DCC (92 mg, 0.45 mmol) were dissolved in DCM (2.5 mL) and left overnight. 1H NMR spectrum of an aliquot of the reaction mixture showed that the reaction was not finished, therefore more amine 16 (70 mg, 0.28 mmol) was added and the reaction was left overnight again. Next day, 1H NMR analysis showed that the reaction was finished and after silica gel column chromatography using mixtures of MeOH in DCM (0-1.2%) as eluent, compound 4 (30 mg, 10%) was obtained. The compound was activated following the General Procedure 1 for catalyst activation with NH3, affording catalyst 4 (15 mg) as a yellowish oil.

m.p.: glassy compound
IR (film, \(\nu\) in cm\(^{-1}\)): 3306, 3085, 2968, 2929, 2845, 1651, 1547, 1521, 1320, 1145, 944, 749.

1H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.25 (s, 1H), 8.13 (d, \(J = 8.8\) Hz, 1H), 7.98 (br d, \(J = 5.8\) Hz, NH), 7.86 (d, \(J = 8.8\) Hz, 1H), 7.86 (d, \(J = 7.9\) Hz, 1H), 7.72 (d, \(J = 7.9\) Hz, 1H), 7.31 – 7.23 (m, 1H), 7.20 – 7.09 (m, 2H), 7.06 (d, \(J = 6.1\) Hz, 1H), 6.77 (d, \(J = 9.0\) Hz, 2H), 6.38 (d, \(J = 9.0\) Hz, 2H), 4.42 – 4.29 (m, 1H), 4.21 (t, \(J = 9.4\) Hz, 1H), 3.41 (dd, \(J = 16.1, 4.8\) Hz, 1H), 3.26 – 3.09 (m, 2H), 3.09 – 2.98 (m, 1H), 2.90 (dd, \(J = 16.0, 11.4\) Hz, 1H), 2.85 – 2.75 (m, 2H), 2.79 (s, 6H), 2.60 – 2.52 (m, 2H), 1.84 – 1.73 (m, 4H).

13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 167.6 (C), 149.1 (C), 135.5 (C), 135.1 (C), 134.9 (C), 134.6 (C), 133.5 (C), 131.1 (CH), 129.9 (CH), 129.9 (CH), 129.3 (CH), 129.1 (C), 128.5 (C), 128.5 (CH), 126.3 (CH), 126.8 (2 CH), 126.5 (CH), 126.0 (CH), 124.6 (C), 124.0 (CH), 112.7 (2 CH), 76.5 (CH), 62.4 (CH\(_2\)), 54.9 (2 CH\(_2\)), 52.2 (CH), 43.8 (CH), 40.6 (2 CH\(_3\)), 35.9 (CH\(_2\)), 23.6 (2 CH\(_2\)).

HRMS (ESI+): Calculated for C\(_{34}\)H\(_{38}\)BrN\(_4\)O\(_4\)S [M+H]\(^+\) 677.1792, found 677.1789.

3-(5-Bromo-8-(N-(4-(dimethylamino)phenyl)sulfamoyl)-2-naphthamido)-1-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl acetate (catalyst 4a)

Following the General Procedure 2 for Catalyst acetylation using vinyl acetate, the reaction of catalyst 4 (15 mg, 0.02 mmol) with 500 \(\mu\)L of vinyl acetate yielded compound 4a (16 mg, quant.) as a yellowish oil.

1H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.96 (s, 1H), 8.45 (d, \(J = 8.9\) Hz, 1H), 8.22 (dd, \(J = 8.9, 1.5\) Hz, 1H), 7.99 (d, \(J = 7.9\) Hz, 1H), 7.80 (d, \(J = 7.9\) Hz, 1H), 7.74 (br d, \(J = 7.6\) Hz, NH), 7.38 (d, \(J = 7.2\) Hz, 1H), 7.25 – 7.11 (m, 3H), 6.80 (d, \(J = 9.0\) Hz, 2H), 6.45 (d, \(J = 9.0\) Hz, 2H), 5.47 (dd, \(J = 10.3, 6.9\) Hz, 1H), 4.50 – 4.37 (m, 1H), 3.42 (dd, \(J = 15.7, 4.5\) Hz, 1H), 3.38 (dd, \(J = 15.7, 4.5\) Hz, 1H), 3.38 (dd, \(J = 15.7, 4.5\) Hz, 1H), 2.90 (dd, \(J = 15.9, 12.5\) Hz, 1H), 2.83 (s, 6H), 2.85 – 2.76 (m, 2H), 2.60 – 2.49 (m, 2H), 2.49 – 2.40 (m, 2H), 2.18 (s, 3H), 1.77 – 1.66 (m, 4H).

13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 175.8 (C), 166.7 (C), 149.2 (C), 136.3 (C), 135.8 (C), 134.8 (C), 133.9 (C), 133.9 (C), 131.6 (CH), 130.2 (CH), 129.3 (CH), 129.3 (C), 129.0 (CH), 128.7 (C), 128.3 (CH), 127.2 (CH), 126.9 (CH), 126.8 (CH), 126.0 (2 CH), 124.4 (C), 122.8 (CH), 112.8 (2 CH), 77.4 (CH), 62.2 (CH\(_3\)), 54.9 (2 CH\(_3\)), 52.0 (CH), 43.8 (CH), 40.6 (2 CH\(_3\)), 34.8 (CH\(_2\)), 23.8 (2 CH\(_3\)), 21.7 (CH\(_3\)).
Compound 4b was prepared following the procedure described in the literature.[3]

5-Bromo-8-(N-p-tolyl)sulfamoyl)-2-naphthoic acid (18)

Compound 18 was prepared following the same procedure described for the synthesis of compound 17.

m.p.: 200 – 205°C
IR (nujol, v in cm⁻¹): 2916, 1690, 1619, 1560, 1333, 1301, 1262, 1200, 1145, 937, 900, 847, 756, 692, 631.
¹H NMR (400 MHz, DMSO-d₆) δ 10.71 (s, 1H), 9.39 (s, 1H), 8.36 (d, J = 8.9 Hz, 1H), 8.23 (dd, J = 8.9, 1.4 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.04 (d, J = 8.0 Hz, 1H), 6.96 (d, J = 8.2 Hz, 2H), 6.88 (d, J = 8.2 Hz, 2H), 2.13 (s, 3H).
¹³C NMR (100 MHz, DMSO-d₆) δ 166.8 (C), 136.3 (C), 134.5 (C), 133.6 (C), 133.5 (C), 130.9 (CH), 130.9 (C), 130.1 (CH), 129.6 (2 CH), 128.2 (C), 128.2 (C), 128.2 (CH), 128.0 (CH), 127.5 (CH), 120.8 (2 CH), 20.3 (CH₃).
HRMS (ESI-): Calculated for C₁₈H₁₃BrNO₄S [M-H] - 417.9754, found 417.9754.

5-Bromo-N-(3-hydroxy-4-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl)-8-(N-p-tolyl)sulfamoyl)-2-naphthamide (catalyst 5)

Compound 18 (278 mg, 0.66 mmol) was refluxed in SOCl₂ (6 mL) for 30 minutes and stirred at room temperature for 2 hours. Then, it was concentrated under reduced pressure to yield the compound 18 acid chloride, which was used in the next step without further purification.
The acid chloride of 18 (311 mg, 0.87 mmol) was dissolved in EtOAc (4 mL) and was added over a stirred solution of amine 16 (270 mg, 1.1 mmol) in a mixture of 4 mL EtOAc and 8 mL of an aqueous NaHCO₃ saturated solution. The acid chloride reaction flask was washed with more EtOAc (4 mL) and added over the reaction mixture. After 90 minutes a solid appeared in the reaction mixture and DCM (5 mL) was added. The reaction mixture was stirred 30 minutes more and then transferred to a separatory funnel. The aqueous phase was extracted with EtOAc, the organic phase was washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography using mixtures of MeOH in EtOAc (1-20%) as eluent, yielding compound 5 (90 mg, 16%). The compound was then activated following the General Procedure 1 for catalyst activation with NH₃, affording 62 mg of catalyst 5.

m.p.: glassy compound
IR (film, ν in cm⁻¹): 3351, 3286, 3092, 2958, 2923, 2858, 1645, 1547, 1508, 1456, 1333, 1158, 1054, 924, 749.

¹H NMR (400 MHz, CDCl₃) δ 9.20 (s, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 8.9 Hz, 1H), 7.93 (br d, J = 6.0 Hz, NH), 7.85 (d, J = 8.9 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 6.9 Hz, 1H), 7.22 – 7.11 (m, 2H), 7.08 (d, J = 6.7 Hz, 1H), 6.87 (d, J = 8.9 Hz, 2H), 6.84 (d, J = 8.9 Hz, 2H), 4.43 – 4.32 (m, 1H), 4.26 (dd, J = 10.2, 8.2 Hz, 1H), 3.43 (dd, J = 16.0, 4.7 Hz, 1H), 3.24 – 3.12 (m, 2H), 3.03 (dd, J = 12.7, 11.0 Hz, 1H), 2.91 (dd, J = 16.0, 11.0 Hz, 1H), 2.66 – 2.53 (m, 2H), 2.14 (s, 3H), 1.81 – 1.70 (m, 4H).

¹³C NMR (100 MHz, CDCl₃) δ 167.7 (C), 135.7 (C), 135.1 (C), 134.9 (C), 134.7 (C), 133.7 (C), 133.4 (C), 131.4 (CH), 130.0 (CH), 129.8 (2 CH), 129.4 (C), 129.3 (CH), 128.3 (C), 128.3 (CH), 127.1 (CH), 126.8 (CH), 126.6 (CH), 126.6 (CH), 123.9 (CH), 121.8 (2 CH), 75.7 (CH), 62.0 (CH₂), 54.9 (2 CH₂), 52.7 (CH), 44.6 (CH), 36.0 (CH₂), 23.6 (2 CH₂), 20.9 (CH₃).

HRMS (ESI+): Calculated for C₃₃H₃₇BrN₃O₄S [M+H]⁺ 648.1526, found 648.1520.

3-(5-Bromo-8-(N-(p-tolyl)sulfamoyl)-2-naphthamido)-1-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl acetate (catalyst 5a)

Following the General Procedure 2 for catalyst acetylation using vinyl acetate, the reaction of catalyst 5 (20 mg, 0.03 mmol) with 500 μL of vinyl acetate gave compound 5a (21 mg, quant.) as a yellowish oil.

¹H NMR (400 MHz, CDCl₃) δ 8.89 (s, 1H), 8.41 (d, J = 8.8 Hz, 1H), 8.17 (dd, J = 8.8, 1.5 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.68 (br d, J = 5.7 Hz, NH), 7.38 (d, J = 7.4 Hz, 1H), 7.25 – 7.09 (m, 3H), 6.94 (d, J = 8.7 Hz, 2H), 6.91 (d, J = 8.7 Hz, 2H), 5.50 (dd, J = 10.5, 6.9 Hz, 1H), 4.48 – 4.37 (m, 1H), 3.45 (dd, J = 15.7, 4.5 Hz, 1H), 3.39 (dd, J = 12.6, 6.7 Hz, 1H), 2.94 – 2.83 (m, 2H), 2.79 (dd, J = 12.4, 7.7 Hz, 1H), 2.62 – 2.51 (m, 2H), 2.50 – 2.40 (m, 2H), 2.27 (s, 3H), 2.20 (s, 3H), 1.78 – 1.67 (m, 4H).

¹³C NMR (100 MHz, CDCl₃) δ 176.2 (C), 166.8 (C), 136.3 (C), 135.5 (C), 135.0 (2 C), 134.0 (C), 133.9 (C), 133.8 (C), 131.7 (CH), 130.1 (CH), 129.9 (2 CH), 129.8 (C), 129.4 (CH), 129.0 (CH), 128.6 (C), 128.2 (CH), 127.3 (CH), 126.9 (CH), 126.8 (CH), 122.6 (CH), 121.4 (2 CH), 77.3 (CH), 62.3 (CH₂), 54.9 (2 CH₂), 52.1 (CH), 43.8 (CH), 34.7 (CH₂), 23.9 (2 CH₂), 21.8 (CH₃), 20.9 (CH₃).
5-Bromo-8-(N-(4-chlorophenyl)sulfamoyl)-2-naphthoic acid (19)

Compound 14 (200 mg, 0.63 mmol) and p-chloroaniline (97 mg, 0.76 mmol) were mixed with N,N'-dimethylaniline (1 mL). The reaction mixture was stirred for 3 hours. Then, it was added over a 30 mL of aqueous 4% HCl, extracted with EtOAC, washed with aqueous 4% HCl, dried over anhydrous Na$_2$SO$_4$, filtered and evaporated under reduced pressure. Then, the crude was triturated in DCM, collected by filtration and washed with DCM, yielding compound 19 (134 mg, 48%) which was used without further purification in the next reaction.

m.p.: >230ºC

IR (nujol, ν in cm$^{-1}$): 1690, 1632, 1567, 1495, 1340, 1301, 1262, 1203, 1145, 1093, 931, 847, 749, 730, 692, 646.

$^1$H NMR (400 MHz, DMSO-d$_6$) δ 11.06 (s, 1H), 9.37 (s, 1H), 8.38 (d, $J = 8.8$ Hz, 1H), 8.24 (dd, $J = 8.8$, 1.3 Hz, 1H), 8.15 (d, $J = 8.0$ Hz, 1H), 8.08 (d, $J = 8.0$ Hz, 1H), 7.24 (d, $J = 8.8$ Hz, 2H), 7.03 (d, $J = 8.8$ Hz, 2H).

$^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 166.7 (C), 136.2 (C), 135.9 (C), 133.6 (C), 131.1 (C), 131.0 (CH), 130.3 (CH), 129.2 (2 CH), 128.5 (C), 128.4 (C), 128.3 (CH), 128.0 (C), 127.2 (CH), 121.8 (2 CH).

HRMS (ESI-): Calculated for C$_{17}$H$_{10}$Br$_3$ClNO$_4$S [M-H] - 437.9207, found 437.9209.

5-Bromo-8-(N-(4-chlorophenyl)sulfamoyl)-N-(3-hydroxy-4-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydro-naphthalen-2-yl)-2-naphthamide (catalyst 6)

Compound 19 (96 mg, 0.22 mmol) was refluxed in SOCl$_2$ (5 mL) for 45 minutes. Then, it was cooled down to room temperature and evaporated under reduced pressure to yield the acid chloride of 19 quantitatively, which was used in the next step without further purification.

The compound 19 acid chloride (100 mg, 0.22 mmol) was dissolved in EtOAc (2.2 mL) and added over a stirred solution of amine 16 (78 mg, 0.32 mmol) in a mixture of 5.5 mL EtOAc and 5.5 mL of an aqueous saturated solution of Na$_2$CO$_3$. The acid chloride reaction flask was washed with more EtOAc (2.25 mL) and added over the reaction mixture. After 50 minutes the aqueous phase was extracted with EtOAc, dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography using mixtures of MeOH in EtOAc (0-25%) as eluent, yielding compound 6 (120 mg, 82%). The compound was activated following the General Procedure 1 for catalyst activation with NH$_3$, affording catalyst 6 (50 mg).

m.p.: glassy compound

IR (film, ν in cm$^{-1}$): 3416, 3098, 2981, 2929, 2852, 1651, 1560, 1482, 1333, 1288, 1171, 1106, 918, 834, 736.

$^1$H NMR (400 MHz, CDCl$_3$) δ 9.19 (s, 1H), 8.09 (br s, NH), 8.02 (d, $J = 8.0$ Hz, 1H), 7.89 (d, $J = 7.2$ Hz, 1H), 7.81 – 7.74 (m, 1H), 7.78 (d, $J = 8.0$ Hz, 1H), 7.34 (d, $J = 7.0$ Hz, 1H), 7.18 (t, $J = 7.0$ Hz, 1H), 7.14 (t, $J = 7.0$ Hz, 1H), 7.05 (d, $J = 7.0$ Hz, 1H), 6.97 (d, $J = 8.6$ Hz, 2H), 6.93 (d, $J = 8.6$ Hz, 2H), 4.47 – 4.33 (m, 1H), 4.32 (dd, $J = 10.0$, 8.3 Hz, 1H), 3.36 (dd, $J = 15.7$, 4.2 Hz, 1H), 3.26
Following the General Procedure 2 for catalyst acetylation using vinyl acetate, the reaction of catalyst 6 (30 mg, 0.05 mmol) with 500 μL of vinyl acetate gave compound 6a (32 mg, quant.) as a yellowish oil.

1H NMR (400 MHz, CDCl₃) δ 8.84 (s, 1H), 8.42 (d, J = 8.8 Hz, 1H), 8.16 (d, J = 8.8 Hz, 1H), 8.16 (d, J = 8.0 Hz, 2H), 7.89 (d, J = 8.0 Hz, 1H), 7.67 (br s, NH), 7.37 (d, J = 7.3 Hz, 1H), 7.24 – 7.08 (m, 4H), 7.00 (d, J = 7.8 Hz, 2H), 5.51 (t, J = 8.0 Hz, 1H), 4.49 – 4.34 (m, 1H), 3.55 – 3.34 (m, 2H), 2.96 – 2.76 (m, 3H), 2.64 – 2.53 (m, 2H), 2.53 – 2.42 (m, 2H), 2.31 (s, 3H), 1.80 – 1.69 (m, 4H).

13C NMR (100 MHz, CDCl₃) δ 176.6 (C), 166.9 (C), 136.1 (C), 135.3 (C), 135.2 (C), 135.0 (C), 134.0 (C), 133.7 (C), 131.8 (CH), 130.2 (C), 130.2 (C), 130.1 (C), 129.5 (2 CH), 129.0 (CH), 128.5 (C), 128.2 (CH), 127.4 (CH), 127.0 (CH), 126.9 (CH), 126.8 (CH), 122.4 (CH), 121.7 (2 CH), 77.4 (CH), 62.3 (CH₂), 54.9 (2 CH₂), 52.1 (CH), 43.8 (CH), 34.7 (CH₂), 23.8 (2 CH₂), 21.9 (CH₃).

5-bromo-N-butyl-8-(N-(4-chlorophenyl)sulfamoyl)-2-naphthamide (6b)

Compound 19 (220 mg, 0.50 mmol) was refluxed in SOCl₂ (5 mL) for 45 minutes. Then, it was cooled down to room temperature and evaporated under reduced pressure to yield the acid chloride of 19 quantitatively, which was used in the next step without further purification.

The compound 19 acid chloride (230 mg, 0.50 mmol) was dissolved in ethyl acetate and added over excess of butylamine. After 5 minutes the solution was transferred to a separatory funnel, washed with aqueous 2 M HCl, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude reaction mixture was purified by silica gel column, yielding compound 6b (90 mg, 36%).

m.p.: glassy compound
IR (film, ν in cm⁻¹): 3267, 3098, 2955, 2923, 2865, 1645, 1547, 1489, 1333, 1158.

1H NMR (400 MHz, CDCl₃) δ 9.40 (d, J = 1.2 Hz, 1H), 8.37 (d, J = 8.9 Hz, 1H), 8.05 (d, J = 7.9 Hz, 1H), 8.04 (dd, J = 8.9, 1.6 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.17 (t, J = 5.7 Hz, NH), 7.06 (d, J = 8.9 Hz, 2H), 6.97 (d, J = 8.9 Hz, 2H), 3.24 (dd, J = 13.4, 7.2 Hz, 2H), 1.46 – 1.34 (m, 2H), 1.18 (dq, J = 14.7, 7.3 Hz, 2H), 0.74 (t, J = 7.3 Hz, 3H).
4,7-Dibromo-3-hydroxy-2-naphthoic acid (20)

3-Hydroxy-2-naphthoic acid (20.4 g, 108.6 mmol) was dissolved in acetic acid and heated to reflux under stirring. When the solid was completely dissolved, bromine (14.5 mL, 282.9 mmol) was added dropwise and the reaction was stirred under reflux for 2 hours. Then, the reaction mixture was added over water, the solid was collected by filtration, washed with water and purified by recrystallization in acetic acid, yielding compound 20 (21 g, 56%).

m.p.: >230ºC
IR (nujol, v in cm⁻¹): 3246, 1671, 1615, 1327, 1281, 1197, 1152, 1067, 931, 808, 749, 632.

HRMS (ESI⁻): Calculated for C_{21}H_{19}Br_{35}Cl_{2}N_{2}O_{3}S [M-H] - 492.9994, found 492.9991.

4,7-Dibromo-8-(chlorosulfonyl)-3-hydroxy-2-naphthoic acid (21)

Compound 20 (340 mg, 0.98 mmol) was dissolved in chlorosulfonic acid (8 mL) and PCl₅ (300 mg, 1.44 mmol) was added. The reaction mixture was heated at 79ºC form 30 minutes and then cooled down to room temperature and added over ice. The precipitate was collected by filtration yielding compound 21 (300 mg, 69%) as a yellow solid. This compound was used in the next step without further purification.

1H NMR (400 MHz, DMSO-d₆) δ 10.17 (s, 1H), 7.92 (d, J = 9.1 Hz, 1H), 7.83 (d, J = 9.1 Hz, 1H).

HRMS (ESI⁻): Calculated for C_{11}H_{7}Br_{81}BrO_{3} [M-H] 344.8590, found 344.8589.

4,7-Dibromo-8-(N-butylsulfamoyl)-3-hydroxy-2-naphthoic acid (22)

Butylamine (5 mL, 50.6 mmol) was added over a stirred solution of compound 21 (300 mg, 0.67 mmol) in EtOAc (50 mL). After 30 minutes the reaction mixture was transferred to a separatory funnel and washed with an 5% HCl aqueous solution, dried over
anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure yielding compound 22 (302 mg, 94%) as a yellow solid, which was used in the next step without further purification.

m.p.: 218 – 222ºC
IR (neat, v in cm$^{-1}$): 3448, 3280, 2910, 2845, 1677, 1346, 1288, 1158, 1106, 970.
$^1$H NMR (400 MHz, DMSO-d$_6$) δ 9.89 (s, 1H), 8.20 (d, J = 9.2 Hz, 1H), 8.18 (br t, J = 5.7 Hz, NH), 8.02 (d, J = 9.2 Hz, 1H), 2.87 (q, J = 7.3 Hz, 2H), 1.30 (quin, J = 7.3 Hz, 2H), 1.14 (hex, J = 7.3 Hz, 2H), 0.69 (t, J = 7.3 Hz, 3H).

13C NMR (100 MHz, DMSO-d$_6$) δ 171.2 (C), 154.2 (C), 137.2 (C), 136.6 (CH), 135.1 (C), 130.7 (CH), 129.8 (CH), 125.0 (C), 120.0 (C), 116.9 (C), 106.5 (C), 42.0 (CH$_2$), 31.0 (CH$_2$), 19.1 (CH$_2$), 13.3 (CH$_3$).

HRMS (ESI-): Calculated for C$_{15}$H$_{14}$Br$_8$BrNO$_5$S [M-H] - 479.8944, found 479.8944.

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4-Bromo-8-(N-butylsulfamoyl)-3-hydroxy-2-naphthoic acid (23)

Zn (70 g, 1.1 mol) was added over a compound 22 solution (280 mg, 0.58 mmol) in acetic acid (25 mL). The reaction mixture was heated at 60ºC for 30 minutes. Then, it was cooled down to room temperature and the precipitate was filtered. The filtrate was concentrated under reduced pressure yielding compound 23 (270 mg, quant.) as a yellow solid which was used in the next step without further purification.

m.p.: 178 – 180ºC
IR (neat, v in cm$^{-1}$): 3552, 3299, 3182, 2949, 2923, 2865, 1671, 1489, 1417, 1313, 1126, 1108, 985, 862, 800.
$^1$H NMR (400 MHz, DMSO-d$_6$) δ 9.41 (s, 1H), 8.36 (dd, J = 8.6, 0.9 Hz, 1H), 8.06 (br t, J = 5.7 Hz, NH), 8.02 (dd, J = 7.3, 0.9 Hz, 1H), 7.83 (dd, J = 8.6, 7.3 Hz, 1H), 2.85 (q, J = 7.2 Hz, 2H), 1.32 (quin, J = 7.2 Hz, 2H), 1.17 (hex, J = 7.2 Hz, 2H), 0.72 (t, J = 7.2 Hz, 3H).

13C NMR (100 MHz, DMSO-d$_6$) δ 171.2 (C), 154.3 (C), 138.2 (C), 136.0 (C), 130.3 (CH), 129.1 (CH), 128.9 (CH), 126.3 (CH), 121.7 (C), 116.9 (C), 106.6 (C), 42.3 (CH$_2$), 31.3 (CH$_2$), 19.1 (CH$_2$), 13.4 (CH$_3$).

HRMS (ESI+): Calculated for C$_{15}$H$_{16}$Br$_8$BrNO$_5$SNa [M+Na]$^+$ 423.9825, found 423.9819.

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4-Bromo-8-(N-butylsulfamoyl)-3-hydroxy-N-(3-hydroxy-4-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydro-2-naphthyl)-2-naphthamide (catalyst 7)

Compound 23 (250 mg, 0.62 mmol) was refluxed in SOCl$_2$ (7 mL) for 25 minutes and then concentrated under reduced pressure to yield compound 23 acid chloride, which was used in the next step without further purification.

A solution of amine 16 (175 mg, 0.71 mmol) in EtOAc (20 mL) was added over compound 23 acid chloride (220 mg, 0.52 mmol) in EtOAc (15 mL) with a saturated NaHCO$_3$ aqueous solution (10 mL). The reaction mixture was stirred for 1 hour and then transferred to a separatory funnel. The organic phase was added over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography using 2.5% MeOH in DCM as eluent, yielding catalyst 7 (100 mg, 30 %) as a yellow solid. Compound 7 (30 mg) was then activated following the General Procedure 2 for catalyst activation with NH$_3$, affording 9 mg of catalyst 7.

m.p.: glassy compound
IR (film, $\nu$ in cm$^{-1}$): 3228, 3072, 2962, 2923, 2865, 1625, 1580, 1469.

$^1$H NMR (400 MHz, CD$_3$OD) $\delta$ 9.19 (s, 1H), 8.27 (d, $J = 8.7$ Hz, 1H), 7.83 (dd, $J = 7.2$, 1.0 Hz, 1H), 7.47 (dd, $J = 8.7$, 7.2 Hz, 1H), 7.36 (d, $J = 7.0$ Hz, 1H), 7.24 – 7.13 (m, 3H), 4.37 (dt, $J = 10.0$, 5.0 Hz, 1H), 4.01 (t, $J = 10.0$ Hz, 1H), 3.73 – 3.63 (m, 1H), 3.51 – 3.41 (m, 1H), 3.41 – 3.33 (m, 4H), 3.22 (dd, $J = 16.2$, 4.8 Hz, 1H), 2.95 (dd, $J = 15.8$, 11.4 Hz, 1H), 2.78 (dt, $J = 6.9$, 1.8 Hz, 2H), 2.10 – 1.99 (m, 4H), 1.36 – 1.11 (m, 4H), 0.71 (t, $J = 7.3$ Hz, 3H).

$^{13}$C NMR (100 MHz, CD$_3$OD) $\delta$ 170.8 (C), 163.8 (C), 138.1 (C), 137.9 (C), 136.2 (C), 134.8 (C), 131.6 (CH), 130.3 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 127.4 (CH), 127.1 (CH), 125.6 (CH), 125.1 (C), 120.1 (C), 112.9 (C), 77.3 (CH), 62.4 (CH$_2$), 56.3 (2 CH$_2$), 52.8 (CH), 44.7 (CH), 43.6 (CH$_2$), 32.7 (CH$_2$), 24.2 (2 CH$_3$), 20.6 (CH$_3$), 13.8 (CH$_3$).

HRMS (ESI+): Calculated for C$_{30}$H$_{37}$N$_3$O$_5$S [M+H]$^+$ 630.1632, found 630.1627.

3-(4-Bromo-8-(N-butylsulfamoyl)-3-hydroxy-2-naphthamido)-1-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl acetate (catalyst 7a)

Following the General Procedure 2 for catalyst acetylation using vinyl acetate, the catalyst 7 reaction (9 mg, 0.01 mmol) with 500 $\mu$L of vinyl acetate gave compound 7a (10.1 mg, quant.) as a yellowish oil.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.77 (s, 1H), 8.46 (d, $J = 8.6$ Hz, 1H), 8.20 (d, $J = 7.1$ Hz, 1H), 7.65 (dd, $J = 8.6$, 7.1 Hz, 1H), 7.35 (d, $J = 7.2$ Hz, 1H), 7.25 – 7.13 (m, 3H), 6.89 (br d, $J = 7.4$ Hz, NH), 5.53 (dd, $J = 9.3$, 7.3 Hz, 1H), 4.38 (dt, $J = 11.3$, 4.4 Hz, 1H), 3.49 – 3.24 (m, 3H), 3.01 – 2.78 (m, 4H), 2.68 – 2.58 (m, 2H), 2.58 – 2.43 (m, 2H), 2.19 (s, 3H), 1.84 – 1.70 (m, 4H), 1.45 – 1.34 (m, 2H), 1.29 – 1.16 (m, 2H), 0.77 (t, $J = 7.3$ Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 175.5 (C), 169.4 (C), 154.7 (C), 136.8 (C), 136.4 (C), 135.9 (C), 133.6 (C), 131.6 (CH), 129.1 (CH), 128.7 (CH), 128.2 (CH), 128.0 (CH), 127.2 (CH), 127.1 (CH), 123.3 (CH), 122.0 (C), 118.3 (C), 109.1 (C), 77.4 (CH), 61.9 (CH$_2$), 54.9 (2 CH$_2$), 52.4 (CH), 44.8 (CH), 42.7 (CH$_2$), 34.3 (CH$_2$), 31.9 (CH$_2$), 23.8 (2 CH$_3$), 21.6 (CH$_3$), 19.8 (CH$_3$), 13.6 (CH$_3$).

8-(Chlorosulfonyl)-3-hydroxy-7-methoxy-2-naphthoic acid (24)

Naphthoic acid (24) was synthesized as follows:

Sodium 3-hydroxy-7-methoxy-2-naphthoate (5.0 g, 20.8 mmol) was suspended in DCM (30 mL) at 0ºC and chlorosulfonic acid (15 mL, 225.3 mmol) was added dropwise with stirring. After 1 hour the reaction was poured slowly (very exothermic) over ice. EtOAc was added and the organic phase was separated, dried over anhydrous Na$_2$SO$_4$, filtered and evaporated under reduced pressure yielding compound 24 (5.6 g, 85%) as a green solid which was used without further purification in the next reaction.

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 9.93 (s, 1H), 7.75 (d, $J = 9.1$ Hz, 1H), 7.42 (d, $J = 9.1$ Hz, 1H), 7.22 (s, 1H), 3.82 (s, 3H).
Compound 24 (390 mg, 1.29 mmol) was added portion wise over BuNH₂ (4.5 mL) at 0°C. The reaction mixture was stirred for 30 minutes. Then, it was added over 50 mL of an aqueous 4% HCl solution with ice. The precipitate was collected by filtration yielding compound 25 (255 mg, 58%) as a brown solid which was used without further purification in the next reaction.

m.p.: >230°C
IR (nujol, \( \nu \) in cm\(^{-1} \)): 3306, 2929, 1677, 1606, 1521, 1333, 1262, 1165, 1126, 989, 911, 860, 795, 754, 671.
\(^1\)H NMR (400 MHz, DMSO-\( d_6 \)) \( \delta \) 9.71 (s, 1H), 8.06 (d, \( J = 9.3 \) Hz, 1H), 7.66 (d, \( J = 9.3 \) Hz, 1H), 7.39 (s, 1H), 7.36 (br t, \( J = 6.0 \) Hz, NH), 4.03 (s, 3H), 2.78 (q, \( J = 7.3 \) Hz, 2H), 1.35 (quin, \( J = 7.3 \) Hz, 2H), 1.21 (hex, \( J = 7.3 \) Hz, 2H), 0.75 (t, \( J = 7.3 \) Hz, 3H).
\(^{13}\)C NMR (100 MHz, DMSO-\( d_6 \)) \( \delta \) 171.6 (C), 154.4 (C), 154.4 (C), 133.2 (C), 133.2 (CH), 128.8 (CH), 123.6 (C), 121.5 (C), 117.6 (CH), 116.9 (C), 112.0 (CH), 57.2 (CH\(_3\)), 42.4 (CH\(_2\)), 31.0 (CH\(_2\)), 19.3 (CH\(_2\)), 13.5 (CH\(_3\)).
HRMS (ESI-): Calculated for C\(_{16}\)H\(_{18}\)NO\(_6\)S \([\text{M-H}]^-\) 352.0860, found 352.0858.

8-(N-Butylsulfamoyl)-3,7-dihydroxy-2-naphthoic acid (26)

Compound 26 was prepared following the same procedure as compound 28.

m.p.: 200 – 203°C
IR (nujol, \( \nu \) in cm\(^{-1} \)): 3280, 2942, 1690, 1619, 1567, 1534, 1405, 1197, 1145, 1100, 1077, 931, 866, 801, 723, 684.
\(^1\)H NMR (400 MHz, DMSO-\( d_6 \)) \( \delta \) 10.84 (br s, Ar-OH), 9.32 (s, 1H), 7.93 (d, \( J = 9.0 \) Hz, 1H), 7.77 (br t, \( J = 6.0 \) Hz, NH), 7.36 (s, 1H), 7.28 (d, \( J = 9.0 \) Hz, 1H), 2.80 (q, \( J = 7.2 \) Hz, 2H), 1.31 (quin, \( J = 7.2 \) Hz, 2H), 1.15 (hex, \( J = 7.2 \) Hz, 2H), 0.69 (t, \( J = 7.2 \) Hz, 3H).
\(^{13}\)C NMR (101 MHz, DMSO-\( d_6 \)) \( \delta \) 171.6 (C), 154.2 (C), 133.0 (C), 122.5 (CH), 119.2 (CH), 112.0 (CH), 57.2 (CH\(_3\)), 42.0 (CH\(_2\)), 31.0 (CH\(_2\)), 19.3 (CH\(_2\)), 13.5 (CH\(_3\)).
HRMS (ESI+): Calculated for C\(_{15}\)H\(_{17}\)NO\(_6\)S\(_2\)Na \([\text{M+Na}]^+\) 362.0669, found 362.0665.

8-(N-Butylsulfamoyl)-3,7-dihydroxy-N(3-hydroxy-4-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl)-2-naphthamide (catalyst 8)

Compound 26 (235 mg, 0.69 mmol) was refluxed in SOCl\(_2\) (5 mL) for 20 minutes and then concentrated under reduced pressure to yield compound 26 acid chloride, which was used in the next step without further purification.
The compound 26 acid chloride (302 mg, 0.69 mmol) was dissolved in 4 mL of EtOAc and added over a stirred solution of amine 16 (180 mg, 0.73 mmol) in a mixture of 3 mL EtOAc and 6 mL of an aqueous saturated solution of NaHCO₃. The acid chloride reaction flask was washed with 1 mL more of EtOAc and added over the reaction mixture. After 45 minutes the aqueous phase was extracted with EtOAc, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography using mixtures of MeOH in EtOAc (0-20%) as eluent, yielding compound 8 (120 mg, 31%). This compound was then activated following the General Procedure 1 for catalyst activation with NH₃, affording catalyst 8 (93 mg).

m.p.: glassy compound
IR (film, ν in cm⁻¹): 3072, 2988, 2916, 2858, 1651, 1573, 1463, 1392, 1346, 1249, 1119, 937, 873, 743.
¹H NMR (400 MHz, CD₃OD) δ 8.98 (s, 1H), 7.73 (d, J = 9.1 Hz, 1H), 7.34 (d, J = 7.0 Hz, 1H), 7.19 (s, 1H), 7.25-7.08 (m, 3H), 7.08 (d, J = 9.1 Hz, 1H), 4.33 (dt, J = 10.4, 5.0 Hz, 1H), 4.00 (dd, J = 9.8, 7.7 Hz, 1H), 3.42 (d, J = 9.1 Hz, 1H), 3.28-3.14 (m, 3H), 3.11-3.01 (m, 2H), 3.00-2.94 (m, 2H), 2.89 (dd, J = 16.0, 11.0 Hz, 1H), 2.78 (dt, J = 6.9, 1.5 Hz, 2H), 1.96-1.86 (m, 4H), 1.37-1.26 (m, 2H), 1.24-1.12 (m, 2H), 0.72 (t, J = 7.3 Hz, 3H).
¹³C NMR (100 MHz, CD₃OD) δ 170.3 (C), 157.2 (2 C), 135.9 (C), 135.6 (C), 134.9 (CH), 133.9 (C), 130.1 (CH), 128.2 (CH), 128.0 (CH), 127.8 (CH), 126.6 (CH), 123.3 (CH), 123.0 (C), 122.9 (C), 115.2 (CH), 113.8 (C), 77.0 (CH), 62.6 (CH₂), 55.9 (2 CH₂), 52.9 (CH), 45.0 (CH), 43.3 (CH₂), 36.1 (CH), 32.3 (CH₂), 24.3 (2 CH₃), 20.7 (CH₂), 13.8 (CH₃).
HRMS (ESI⁺): Calculated for C₃₀H₃₈N₃O₅S [M+H]⁺ 568.2476, found 568.2467.

3-(6-(N-Butylsulfamoyl)-3,7-dihydroxy-2-naphthamido)-1-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl acetate (catalyst 8a)

Following the General Procedure 2 for catalyst acetylation using vinyl acetate, the reaction of catalyst 8 (16 mg, 0.03 mmol) with 500 μL of vinyl acetate gave compound 8a (17.2 mg, quant.) as a yellowish oil.

¹H NMR (400 MHz, CDCl₃) δ 8.39 (s, 1H), 7.72 (d, J = 9.1 Hz, 1H), 7.34 (d, J = 7.2 Hz, 1H), 7.24 (s, 1H), 7.23-7.09 (m, 3H), 7.13 (d, J = 9.1 Hz, 1H), 5.45 (dd, J = 9.2, 7.8 Hz, 1H), 4.32 (dt, J = 11.3, 4.3 Hz, 1H), 3.42 (dd, J = 15.6, 4.3 Hz, 1H), 3.35 (dd, J = 12.8, 6.9 Hz, 1H), 2.89-2.88 (m, 2H), 2.89-2.72 (m, 3H), 2.62-2.52 (m, 2H), 2.52-2.41 (m, 2H), 2.19 (s, 3H), 1.79-1.66 (m, 4H), 1.48-1.36 (m, 2H), 1.31-1.15 (m, 2H), 0.76 (t, J = 7.3 Hz, 3H).
¹³C NMR (100 MHz, CDCl₃) δ 175.9 (C), 169.9 (C), 156.5 (C), 155.9 (C), 136.2 (C), 134.4 (CH), 133.6 (C), 133.1 (C), 129.0 (CH), 128.2 (CH), 127.1 (CH), 126.9 (CH), 123.1 (CH), 122.0 (C), 121.9 (CH), 118.2 (C), 114.5 (CH), 111.9 (C), 77.4 (CH), 62.1 (CH₂), 54.8 (2 CH₂), 52.3 (CH), 43.3 (CH₂), 42.4 (CH₂), 34.6 (CH₂), 31.6 (CH₂), 23.9 (2 CH₂), 21.7 (CH₃), 19.8 (CH₂), 13.6 (CH₃).

8-(N-(4-(Dimethylamino)phenyl)sulfamoyl)-3-hydroxy-7-methoxy-2-naphthoic acid (27)

Compound 24 (625 mg, 1.97 mmol) was added over a solution of N,N-dimethyl-p-phenylenediamine (875 mg, 6.42 mmol) in 20 mL EtOAc. The reaction mixture was stirred for 1 hour, then the solvent was evaporated under reduced pressure and the crude product
was suspended in MeOH and added over 44 mL of an aqueous 10% AcOH solution. The precipitate was collected by filtration and dried in an oven for 3 hours at 70 °C, yielding compound 27 (531 mg, 65%) which was used without further purification in the next reaction.

m.p.: >230 ºC
IR (nujol, \( \nu \) in cm\(^{-1} \)): 3273, 2929, 1677, 1607, 1554, 1515, 1327, 1262, 1152, 1093, 976, 866, 814, 730, 684.

\(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \( \delta \) 9.70 (br s, NH), 9.49 (s, 1H), 8.02 (d, \( J = 9.2 \) Hz, 1H), 7.63 (d, \( J = 9.2 \) Hz, 1H), 7.33 (s, 1H), 6.92 (d, \( J = 7.9 \) Hz, 2H), 6.51 (d, \( J = 7.9 \) Hz, 2H), 4.08 (s, 3H), 2.73 (s, 6H).

\(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)) \( \delta \) 171.5 (C), 154.9 (C), 154.4 (C), 147.7 (C), 133.7 (CH), 133.0 (C), 128.4 (CH), 126.5 (C), 124.1 (C), 123.1 (2 CH), 120.0 (C), 117.2 (C), 117.1 (CH), 112.7 (2 CH), 112.0 (CH), 57.1 (CH\(_3\)), 40.2 (2 CH\(_3\)).

HRMS (ESI-): Calculated for C\(_{20}\)H\(_{19}\)N\(_2\)O\(_6\)S [M - H] - 415.0969, found 415.0969.

8-(N-(4-(Dimethylamino)phenyl)sulfamoyl)-3,7-dihydroxy-2-naphthoic acid (28)

Compound 27 (531 mg, 1.28 mmol) was dissolved in 5 mL of DMF and Na\(_2\)S·9H\(_2\)O (1.54 g, 6.41 mmol) was added portionwise. The reaction mixture was heated at 120 ºC under stirring for 20 hours in a closed reaction vessel. Then, the reaction mixture was cooled down to room temperature and added over 100 mL of a 5% AcOH aqueous solution. The solid which appeared was filtered under vacuum and dried overnight yielding compound 28 (475 mg, 92%) as a light brown solid.

m.p.: 150 – 153 ºC
IR (nujol, \( \nu \) in cm\(^{-1} \)): 3228, 2923, 1664, 1606, 1573, 1515, 1223, 1113, 1022, 944, 877, 840, 730, 677.

\(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \( \delta \) 10.93 (br s, Ar-OH), 9.74 (br s, NH), 9.37 (s, 1H), 7.87 (d, \( J = 9.0 \) Hz, 1H), 7.31 (s, 1H), 7.22 (d, \( J = 9.0 \) Hz, 1H), 6.82 (d, \( J = 8.9 \) Hz, 2H), 6.49 (d, \( J = 8.9 \) Hz, 2H), 2.75 (s, 6H).

\(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)) \( \delta \) 171.5 (C), 154.6 (C), 154.5 (C), 148.2 (C), 133.8 (CH), 132.7 (C), 127.6 (CH), 125.6 (C), 124.2 (2 CH), 123.1 (C), 122.2 (CH), 116.7 (C), 114.8 (C), 112.6 (3 CH), 40.2 (2 CH\(_3\)).

HRMS (ESI-): Calculated for C\(_{19}\)H\(_{17}\)N\(_2\)O\(_6\)S [M - H] - 401.0812, found 401.0812.

3,7-Diacetoxy-8-(N-acetyl-N-(4-(dimethylamino)phenyl)sulfamoyl)-2-naphthoic acid (29)

Compound 28 (95 mg, 0.24 mmol) was suspended in a mixture of 2 mL of Ac\(_2\)O and 0.5 mL of DMF with 3 drops of 95% H\(_2\)SO\(_4\). The reaction mixture was stirred at 60 ºC until the solution became homogenous. Then, it was added over water and extracted with EtOAc twice. The organic phase was dried over anhydrous Na\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. \(^1\)H NMR showed the presence of some amount of the mixed anhydride of carboxylic acid. Then, MeOH (10 mL) was added and the reaction
mixture was heated at 65°C for 3 hours. Afterwards, it was evaporated under reduced pressure to yield compound 29 (70 mg, 55%), which was used in the next step without further purification.

8-(N-(4-(Dimethylamino)phenyl)sulfamoyl)-3,7-dihydroxy-N-(3-hydroxy-4-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl)-2-naphthamide (catalyst 9)

Compound 29 (110 mg, 0.21 mmol) was dissolved in DCM (5 mL) and PCl₅ (76 mg, 0.37 mmol) was added. The reaction mixture was stirred at room temperature for 5 minutes and then evaporated to dryness to yield compound 29 acid chloride quantitatively, which was used in the next step without further purification.

The acid chloride of 28 (63 mg, 0.12 mmol) was dissolved in 2 mL of DCM and added over a stirred solution of amine 16 (56 mg, 0.23 mmol) in a solution of N,N-dimethylaniline (30 μL, 0.24 mmol) in 3 mL of DCM. The reaction flask with the acid chloride was washed with 1 mL of DCM and added over the reaction mixture solution. After 10 minutes a ¹H NMR spectrum of an aliquot of the reaction mixture showed that the reaction was finished and the solvent was evaporated.

In order to hydrolyse the acetyl groups, 5 mL of MeOH were added to the reaction flask followed by NaOH (130 mg, 3.25 mmol). The reaction mixture was stirred for 2.5 hours, then quenched with 0.4 mL of AcOH and evaporated to dryness. The crude reaction mixture was purified by silica gel column chromatography using mixtures of MeOH in DCM (0-7%) as eluent yielding compound 9 (10 mg, 13%). The compound was activated following General Procedure 1 for catalyst activation with NH₃, affording 10 mg of catalyst 9.

m.p.: glassy compound

IR (film, ν in cm⁻¹): 3221, 3053, 2923, 2852, 1651, 1456, 1405, 1113, 957, 743.

¹H NMR (400 MHz, 5% CD₃OD in CDCl₃) δ 8.81 (s, 1H), 7.59 (d, J = 9.0 Hz, 1H), 7.23 – 7.04 (m, 5H), 6.91 (d, J = 9.0 Hz, 1H), 6.71 (d, J = 8.5 Hz, 2H), 6.40 (d, J = 8.5 Hz, 2H), 4.42 (dt, J = 11.1, 5.0 Hz, 1H), 4.16 – 4.02 (m, 1H), 3.33 – 2.81 (m, 9H), 2.78 (s, 6H), 1.97 – 1.74 (m, 4H).

¹³C NMR (100 MHz, 5% CD₃OD in CDCl₃) δ 170.5 (C), 156.5 (C), 149.3 (C), 134.8 (C), 134.7 (C), 134.3 (CH), 133.7 (C), 133.7 (C), 132.7 (C), 129.5 (CH), 127.1 (CH), 126.6 (CH), 126.4 (CH), 125.8 (2 CH), 124.3 (C), 122.7 (CH), 122.4 (CH), 121.6 (C), 114.5 (CH), 112.8 (2 CH), 111.3 (C), 77.4 (CH), 62.2 (2 CH₂), 54.8 (2 CH₂), 51.3 (CH), 42.9 (CH), 40.6 (2 CH₂), 35.3 (CH₂), 23.5 (2 CH₂).

HRMS (ESI+): Calculated for C₃₄H₃₉N₄O₆S [M+H]⁺ 631.2585, found 631.2584.

Following the General Procedure 2 for catalyst acetylation using vinyl acetate, the reaction of catalyst 9 (10 mg, 0.02 mmol) with 500 μL of vinyl acetate gave compound 9a (10.7 mg, quant.) as a yellowish oil.

³-(N-(4-(Dimethylamino)phenyl)sulfamoyl)-3,7-dihydroxy-2-naphthamido)-1-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl acetate (catalyst 9a)

Following the General Procedure 2 for catalyst acetylation using vinyl acetate, the reaction of catalyst 9 (10 mg, 0.02 mmol) with 500 μL of vinyl acetate gave compound 9a (10.7 mg, quant.) as a yellowish oil.

¹H NMR (400 MHz, CDCl₃) δ 8.64 (s, 1H), 7.68 (d, J = 9.1 Hz, 1H), 7.34 (d, J = 7.3 Hz, 1H), 7.28 (s, 1H), 7.24 – 7.13 (m, 3H), 7.00 (d, J = 9.1 Hz, 1H), 6.77 (d, J = 8.8 Hz, 2H), 6.45 (d, J = 8.8 Hz, 2H), 5.66 – 5.52 (m, 1H), 4.49 – 4.36 (m, 1H), 3.47 – 3.33 (m, 3H), 3.05 – 2.88 (m, 2H), 2.85 (s, 6H), 2.72 – 2.40 (m, 4H), 2.07 (s, 3H), 1.84 – 1.70 (m, 4H).
SUPPORTING INFORMATION

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 169.9 (C), 156.9 (C), 156.1 (C), 149.6 (C), 134.4 (CH), 134.0 (C), 133.0 (C), 129.1 (CH), 128.1 (CH), 127.1 (CH), 126.7 (CH), 125.1 (C), 123.5 (C), 123.0 (CH), 122.0 (2 CH), 118.0 (C), 114.6 (CH), 112.7 (2 CH), 111.6 (C), 77.4 (CH), 55.0 (CH$_2$), 52.0 (CH), 43.9 (CH), 34.5 (CH$_2$), 29.8 (CH$_2$), 23.7 (2 CH$_2$), 14.3 (CH$_3$).

3-Hydroxy-7-methoxy-8-((N-p-toly)sulfamoyl)-2-naphthoic acid (30)

Compound 24 (300 mg, 0.95 mmol) was mixed with p-toluidine (200 mg, 1.87 mmol) in 2 mL of N,N'-dimethylaniline. The reaction mixture was stirred for 1 hour, then 2 mL of EtOAc were added to solubilize the precipitate. The organic solvent was evaporated under reduced pressure, the crude was dissolved in MeOH and added over an aqueous solution of 4% HCl. The precipitate was collected by filtration. The solid was suspended in DCM and filtered again, yielding compound 30 (360 mg, 98%) which was used without further purification in the next reaction.

m.p.: >230ºC
IR (nujol, $\nu$ in cm$^{-1}$): 3267, 2929, 1664, 1619, 1521, 1327, 1249, 1152, 976, 911, 808, 723, 697, 615.
$^1$H NMR (400 MHz, DMSO-d$_6$) δ 9.96 (br s, NH), 9.74 (s, 1H), 8.02 (d, $J = 9.3$ Hz, 1H), 7.58 (d, $J = 9.3$ Hz, 1H), 7.36 (s, 1H), 6.97 (d, $J = 8.5$ Hz, 2H), 6.92 (d, $J = 8.5$ Hz, 2H), 4.01 (s, 3H), 2.09 (s, 3H).
$^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 171.5 (C), 155.1 (C), 154.4 (C), 135.3 (C), 134.0 (CH), 134.0 (C), 133.0 (C), 132.8 (C), 129.4 (2 CH), 128.2 (CH), 124.1 (C), 119.6 (2 CH), 117.2 (CH), 117.2 (C), 112.2 (CH), 57.2 (CH$_3$), 20.2 (CH$_3$).
HRMS (ESI-): Calculated for C$_{19}$H$_{16}$NO$_6$S [M-H] 386.0703, found 386.0703.

3,7-Dihydroxy-8-(N(p-toly)sulfamoyl)-2-naphthoic acid (31)

Compound 30 (154 mg, 0.40 mmol) was dissolved in DMF (1.5 mL) and Na$_2$S·9H$_2$O (354 mg, 1.47 mmol) was added portionwise. The reaction was stirred at 120 ºC for 14.5 hours in a closed reaction vessel. Then, it was cooled down to room temperature and added over an aqueous solution of HCl 2M. The aqueous phase was extracted with EtOAc (x2), washed with water (x2), dried over anhydrous Na$_2$SO$_4$, filtered and evaporated under reduced pressure. The crude was suspended in DCM and the precipitate was collected by filtration under vacuum, yielding compound 31 (70 mg, 47%) which was used without further purification in the next reaction.

m.p.: 224 – 226ºC
IR (nujol, $\nu$ in cm$^{-1}$): 3293, 2910, 1684, 1619, 1521, 1275, 1216, 1132, 1035, 937, 866, 801, 723, 665.
$^1$H NMR (400 MHz, DMSO-d$_6$) δ 11.08 (br s, Ar-OH), 10.12 (br s, NH), 9.46 (s, 1H), 7.87 (d, $J = 9.2$ Hz, 1H), 7.31 (s, 1H), 7.22 (d, $J = 9.2$ Hz, 1H), 6.94 (s, 4H), 2.11 (s, 3H).
$^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 171.5 (C), 154.7 (C), 154.4 (C), 135.3 (C), 134.0 (CH), 133.0 (C), 132.8 (C), 129.4 (2 CH), 128.2 (CH), 124.1 (C), 119.6 (2 CH), 117.2 (CH), 117.2 (C), 112.2 (CH), 57.2 (CH$_3$), 20.2 (CH$_3$).
HRMS (ESI-): Calculated for C$_{19}$H$_{14}$NO$_6$S [M-H] 372.0547, found 372.0546.
SUPPORTING INFORMATION

3,7-Diacetoxy-8-(N-acetyl-N-(p-tolyl)sulfamoyl)-2-naphthoic acid (32)

![Chemical Structure of 32](image)

Compound 31 (470 mg, 1.26 mmol) was suspended in Ac₂O (7 mL) and 2 drops of 95% H₂SO₄ were added. The reaction mixture was stirred until the solution became homogeneous. Then it was added over water (50 mL) and filtered under vacuum, yielding compound 32 (548 mg, 87%) which was used without further purification in the next step.

3,7-Dihydroxy-N-(3-hydroxy-4-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl)-8-(N-(p-tolyl)sulfamoyl)-2-naphthamide (catalyst 10)

![Chemical Structure of 10](image)

Compound 32 (112 mg, 0.22 mmol) was dissolved in SOCl₂ (2 mL) and refluxed until the solution became homogenous. Then it was evaporated under reduced pressure to yield compound 32 acid chloride quantitatively, which was used in the next step without further purification.

The compound 31 acid chloride (116 mg, 0.22 mmol) was dissolved in DCM (3 mL) and added over a stirred solution of amine 16 (117 mg, 0.48 mmol) and N,N'-dimethylaniline (56 μL, 0.44 mmol) in DCM. (4 mL) The reaction flask with the acid chloride was washed with 2 mL of DCM and added over the reaction mixture solution.

The acetyl groups were hydrolysed with NaOH in MeOH and then the reaction mixture was quenched with AcOH. After filtration and purification by column chromatography, catalyst 10 was obtained (110 mg, 83%). 12 mg of compound 10 were activated following the General Procedure 1 for catalyst activation with NH₃, affording the acid free catalyst 10 (12 mg, 9%).

m.p.: glassy compound
IR (film, ν in cm⁻¹): 3234, 3014, 2916, 2832, 1651, 1580, 1405, 1210, 1113, 756.

¹H NMR (400 MHz, 5% CD₂OD in CDCl₃) δ 8.92 (s, 1H), 7.71 (d, J = 9.0 Hz, 1H), 7.36 (s, 1H), 7.31 – 7.16 (m, 4H and NH), 7.06 (d, J = 9.0 Hz, 1H), 6.98 (d, J = 8.1 Hz, 2H), 6.91 (d, J = 8.1 Hz, 2H), 4.53 (dt, J = 11.0, 4.7 Hz, 1H), 4.38 – 4.26 (m, 1H), 3.53 – 2.98 (m, 9H), 2.24 (s, 3H), 2.15 – 2.00 (m, 4H).

¹³C NMR (100 MHz, 5% CD₂OD in CDCl₃) δ 170.3 (C), 156.6 (C), 135.2 (C), 135.1 (C), 134.6 (CH), 133.5 (C), 133.0 (C), 132.7 (C), 129.8 (2 CH), 129.7 (CH), 127.4 (CH), 126.8 (CH), 126.5 (CH), 122.7 (CH), 122.4 (CH), 122.0 (2 CH), 121.7 (C), 114.5 (CH), 111.3 (C), 77.4 (CH), 61.9 (CH₂), 55.1 (2 CH₂), 51.4 (CH), 43.0 (CH), 35.2 (CH₂), 23.3 (2 CH₂), 20.8 (CH₃).

HRMS (ESI+): Calculated for C₃₃H₃₆N₃O₆S [M+H]⁺ 602.7255, found 602.2312.
3-(3,7-Dihydroxy-8-(N-(p-tolyl)sulfamoyl)-2-naphthamido)-1-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl acetate (catalyst 10a)

Following the General Procedure 2 for catalyst acetylation using vinyl acetate, the reaction of catalyst 10 (12 mg, 0.02 mmol) with 500 μL of vinyl acetate gave compound 10a (12.8 mg, quant.) as a yellowish oil.

\[ \text{1H NMR (400 MHz, CDCl}_3 \text{) } \delta 10.37 \text{ (br s, OH), 8.73 (s, 1H), 7.67 (d, } J = 9.1 \text{ Hz, 1H), 7.25 (s, 1H), 7.28 – 7.17 \text{ (m, 4H), 7.03 (d, } J = 9.1 \text{ Hz, 1H), 6.94 (d, } J = 8.0 \text{ Hz, 2H), 6.89 (d, } J = 8.0 \text{ Hz, 2H), 6.04 – 5.76 \text{ (m, 1H), 4.57 – 4.42 \text{ (m, 1H), 3.67 – 2.52 \text{ (m, 9H), 2.20 \text{ (s, 3H), 2.12 \text{ (s, 3H), 2.02 – 1.81 \text{ (m, 4H).}}}} \]

\[ \text{13C NMR (100 MHz, CDCl}_3 \text{) } \delta 170.2 \text{ (C), 156.9 \text{ (C), 156.2 \text{ (C), 135.5 \text{ (C), 135.5 \text{ (C), 134.7 \text{ (CH), 133.5 \text{ (C), 133.0 \text{ (C), 129.9 \text{ (2 CH), 129.8 \text{ (CH), 129.4 \text{ (CH), 128.1 (CH), 127.5 (CH), 122.8 (CH), 122.3 (2 CH), 121.9 (C), 121.8 (C), 121.1 (C), 118.3 (C), 114.6 (2 CH), 111.6 (C), 77.4 (CH), 61.8 (CH2), 55.2 (2 CH2), 51.7 (CH), 44.3 (CH), 34.0 (CH2), 23.5 (2 CH2), 21.5 (CH3), 21.0 (CH3).}}}} \]

8-(N-(4-Chlorophenyl)sulfamoyl)-3-hydroxy-7-methoxy-2-naphthoic acid (33)

Compound 24 (680 mg, 2.15 mmol) was added over a solution of p-chloroaniline (450 mg, 3.53 mmol) in 2 mL of N,N'-dimethylaniline. The reaction mixture was stirred for 1 hour, then added over 40 mL of a 4% HCl aqueous solution. The flask was washed with MeOH and the precipitate was collected by filtration, yielding compound 33 (625 mg, 71%), which was used without further purification in the next step.

m.p.: >230°C

IR (nujol, v in cm^{-1}): 3260, 1671, 1612, 1515, 1340, 1262, 1158, 1093, 970, 918, 877, 814, 723, 678.

\[ \text{1H NMR (400 MHz, DMSO-d}_6 \text{) } \delta 10.34 \text{ (br s, NH), 9.72 (s, 1H), 8.05 (d, } J = 9.3 \text{ Hz, 1H), 7.58 (d, } J = 9.3 \text{ Hz, 1H), 7.38 (s, 1H), 7.20 \text{ (d, } J = 8.8 \text{ Hz, 2H), 7.08 (d, } J = 8.8 \text{ Hz, 2H), 3.97 (s, 3H).}} \]

\[ \text{13C NMR (100 MHz, DMSO-d}_6 \text{) } \delta 171.4 \text{ (C), 155.1 (C), 154.52 (C), 137.1 (C), 134.3 (CH), 133.0 (C), 129.0 (2 CH), 128.1 (CH), 127.5 (C), 123.9 (C), 120.4 (2 CH), 119.2 (C), 117.4 (C), 117.2 (CH), 112.4 (CH), 57.2 (CH3).}} \]

HRMS (ESI-): Calculated for C_{18}H_{13}ClNO_6S \text{ [M-H]}^+ \text{ 406.0157, found 406.0156.}
**SUPPORTING INFORMATION**

8-(N-(4-Chlorophenyl)sulfamoyl)-3-hydroxy-N-(3-hydroxy-4-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl)-7-methoxy-2-naphthamide (11)

Compound 33 (195 mg, 0.48 mmol) was refluxed in SOCl₂ (2.5 mL) for 30 minutes. Then, it was cooled down to room temperature and evaporated under reduced pressure to yield compound 33 acid chloride quantitatively, which was used in the next step without further purification.

The acid chloride of 33 (204 mg, 0.48 mmol) was dissolved in 3 mL of EtOAc and 1 mL of DCM and added over a stirred mixture of amine 16 (117 mg, 0.47 mmol) in 4 mL of EtOAc and 4 mL of a saturated aqueous solution of NaHCO₃. The flask with the acid chloride was washed with 3 mL EtOAc and 2 mL of DCM and added over the reaction mixture. A precipitate was formed. THF and DCM were added to dissolve it fruitlessly. The reaction mixture was stirred for 21.5 hours, then transferred to a separatory funnel. The aqueous phase was extracted first with EtOAc and then with DCM. The organic phases were combined, dried over anhydrous Na₂SO₄, filtered, and evaporated under reduced pressure. The crude product was purified by silica gel chromatography column with mixtures of MeOH in EtOAc (0-25%) yielding compound 11 (134 mg, 45%). The compound was activated following the General Procedure 1 for catalyst activation with NH₃, affording 129 mg of catalyst 11.

m.p.: glassy compound
IR (film, υ in cm⁻¹): 3323, 2962, 2929, 1651, 918, 834, 730.

1H NMR (400 MHz, CDCl₃) δ 9.29 (br s, OH), 8.26 (s, 1H), 7.37 (d, J = 7.0 Hz, 1H), 7.25 – 7.10 (m, 3H), 6.98 (d, J = 8.8 Hz, 2H), 6.97 (s, 1H), 6.96 (d, J = 7.0 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 4.50 (m, 1H), 4.30 (dd, J = 10.1, 8.7 Hz, 1H), 3.85 (s, 3H), 3.40 (dd, J = 16.4, 5.0 Hz, 1H), 3.37 – 3.27 (m, 2H), 3.21 (t, J = 12.6 Hz, 1H), 3.08 – 2.94 (m, 3H), 2.87 – 2.71 (m, 2H), 1.86 – 1.68 (m, 4H).

13C NMR (100 MHz, CDCl₃) δ 171.0 (C), 154.9 (C), 154.0 (C), 136.5 (C), 134.9 (C), 133.9 (C), 133.4 (CH), 132.2 (C), 129.6 (CH), 129.1 (2 CH), 129.1 (C), 127.2 (CH), 126.7 (CH), 126.4 (CH), 125.7 (CH), 124.0 (2 CH), 120.2 (2 CH), 119.5 (C), 118.6 (C), 114.5 (CH), 112.1 (CH), 77.4 (CH), 62.3 (CH₂), 56.7 (CH₃), 54.9 (2 CH₂), 51.7 (CH), 43.2 (CH), 36.2 (CH₂), 23.5 (2 CH₃).

HRMS (ESI+): Calculated for C₃₃H₃₅ClN₄O₆ [M+H]⁺ 636.1930, found 636.1923.

3-(8-(N-(4-Chlorophenyl)sulfamoyl)-3-hydroxy-7-methoxy-2-naphthamido)-1-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl acetate (11a)

Following the General Procedure 2 for catalyst acetylation using vinyl acetate, the reaction of catalyst 11 (30 mg, 0.05 mmol) with 500 μL of vinyl acetate gave 32 mg (quant.) of compound 11a as a yellowish oil.

1H NMR (400 MHz, CDCl₃) δ 9.20 (s, 1H), 7.78 (d, J = 9.2 Hz, 1H), 7.39 (d, J = 7.0 Hz, 1H), 7.21 (m, 5H), 7.10 (d, J = 9.5 Hz, 2H), 7.07 (d, J = 9.5 Hz, 2H), 5.55 (dd, J = 8.2, 6.5 Hz, 1H), 4.46 (dt, J = 9.6, 4.9 Hz, 1H), 4.07 (s, 3H), 3.35 (dd, J = 14.1, 6.2 Hz, 2H), 3.04 (dd, J = 15.9, 10.1 Hz, 1H), 2.97 (dd, J = 12.5, 4.4 Hz, 1H), 2.89 – 2.79 (m, 1H), 2.65 – 2.49 (m, 2H), 2.49 – 2.37 (m, 2H), 2.14 (s, 3H), 1.69 – 1.58 (m, 4H).

13C NMR (100 MHz, CDCl₃) δ 173.1 (C), 170.2 (C), 155.8 (C), 155.6 (C), 135.9 (C), 134.5 (CH), 133.7 (C), 133.1 (C), 130.3 (C), 129.3 (2 CH), 129.3 (C), 129.1 (CH), 128.4 (CH), 126.9 (CH), 126.9 (CH), 124.1 (C), 123.9 (CH), 122.1 (2 CH), 120.5 (C), 119.9 (C), 116.6 (CH), 113.2 (CH), 77.4 (CH), 61.6 (CH₂), 58.1 (CH₃), 55.0 (2 CH₂), 50.8 (CH), 43.8 (CH), 34.0 (CH₂), 23.7 (2 CH₂), 21.4 (CH₃).
Compound 33 (145 mg, 0.36 mmol) was dissolved in 1.5 mL of DMF and Na₂S·9H₂O (708 mg, 2.95 mmol) was added portionwise. The reaction mixture was heated at 120°C under stirring for 24 hours in a closed reaction vessel. Analysis of an aliquot by 1H NMR showed that the reaction was not finished (probably due to old-wet Na₂S). More Na₂S·9H₂O was added (714 mg, 2.97 mmol) and the reaction mixture was heated at 120°C under stirring for 3 days. Then, it was cooled down to room temperature and added over 100 mL of an aqueous solution of 4% HCl. The aqueous phase was extracted with EtOAc twice, washed with water twice, dissolved in MeOH and added over water. The solid was filtered under vacuum yielding compound 34 (70 mg, 50%).

m.p.: 190 – 193°C
IR (nujol, ν in cm⁻¹): 3312, 1664, 1619, 1521, 1314, 1262, 1203, 1132, 1031, 937, 877, 821, 723, 678.
1H NMR (400 MHz, DMSO-d₆) δ 11.22 (br s, Ar-OH), 10.41 (br s, NH), 9.50 (s, 1H), 7.87 (d, J = 9.2 Hz, 1H), 7.32 (s, 1H), 7.24 – 7.18 (m, 3H), 7.06 (d, J = 8.8 Hz, 2H).
13C NMR (100 MHz, DMSO-d₆) δ 171.5 (C), 154.6 (C), 154.5 (C), 137.0 (C), 134.1 (CH), 132.6 (C), 128.9 (2 CH), 127.6 (C), 127.4 (CH), 123.5 (C), 122.0 (CH), 120.8 (2 CH), 116.8 (C), 115.3 (C), 112.7 (CH).
HRMS (ESI-): Calculated for C₁₇H₁₁ClN₂O₆ [M-H]⁻ 392.0001, found 392.0001.

3,7-Diacetoxy-8-(N-acetyl-N-(4-chlorophenyl)sulfamoyl)-2-naphthoic acid (35)

Compound 34 (190 mg, 0.48 mmol) was dissolved in Ac₂O (5 mL) and 3 drops of 95% H₂SO₄ were added. The reaction mixture was stirred for 2 hours at room temperature and then added over ice and water and extracted with EtOAc twice. The organic phase was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to yield compound 35 (190 mg, 76 %), which was used in the next step without further purification.
3-(8-(N-(4-Chlorophenyl)sulfamoyl)-3,7-dihydroxy-N-(3-hydroxy-4-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl)-2-naphthamido)propan-2-yl acetate (catalyst 12a)

Following the General Procedure 2 for catalyst acetylation using vinyl acetate, the reaction of catalyst 12 (20 mg, 0.03 mmol) with 500 μL of vinyl acetate gave compound 12a (21.4 mg, quant.) as a yellowish oil.

1H NMR (400 MHz, CDCl3) δ 10.48 (br s, OH), 8.78 (s, 1H), 7.69 (d, J = 9.1 Hz, 1H), 7.34 – 7.20 (m, 5H), 7.10 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 9.1 Hz, 1H), 6.99 (d, J = 8.6 Hz, 2H), 6.36 – 6.26 (m, 1H), 4.75 – 4.55 (m, 1H), 3.84 – 3.72 (m, 1H), 3.65 – 3.33 (m, 4H), 3.31 – 3.18 (m, 1H), 3.09 – 2.93 (m, 1H), 2.96 – 2.75 (m, 2H), 2.12 (s, 3H), 2.10 – 1.96 (m, 4H).

13C NMR (100 MHz, CDCl3) δ 170.4 (C), 157.1 (C), 156.4 (C), 135.9 (C), 135.8 (C), 135.6 (C), 134.8 (CH), 133.5 (C), 132.9 (C), 129.9 (CH), 129.3 (2 CH), 128.4 (C), 128.0 (CH), 127.5 (CH), 127.3 (CH), 122.7 (CH), 122.3 (CH), 122.1 (2 CH), 121.8 (C), 118.3 (C), 114.5 (CH), 111.3 (C), 77.4 (CH), 60.7 (CH2), 56.3 (2 CH2), 50.1 (CH), 44.4 (CH), 34.0 (CH2), 23.2 (2 CH2), 21.3 (CH3).

Supporting Information

8-(N-(4-Chlorophenyl)sulfamoyl)-3,7-dihydroxy-N-(3-hydroxy-4-(pyrrolidin-1-ylmethyl)-1,2,3,4-tetrahydronaphthalen-2-yl)-2-naphthamide (catalyst 12)

Compound 34 (190 mg, 0.37 mmol) was dissolved in DCM (13 mL) and PCl5 (172 mg, 0.83 mmol) was added portionwise. The reaction mixture was stirred for 15 minutes at room temperature and then concentrated under reduced pressure to yield the acid chloride of compound 34 quantitatively, which was used in the next step without further purification.

The compound 34 acid chloride (199 mg, 0.37 mmol) was dissolved in DCM (3 mL) and added over a stirred solution of amine 16 (115 mg, 0.47 mmol) and N,N'-dimethylaniline (100 μL, 0.79 mmol) in DCM (10 mL). The acid chloride reaction flask was washed with 2 mL more of DCM and added over the reaction mixture. After 30 minutes, a 1H NMR spectrum of an aliquot of the reaction showed some starting material and more amine 16 (17 mg, 0.069 mmol) was added. The reaction mixture was stirred 75 minutes more and then the solvent was evaporated.

To hydrolyse the acetyl groups, 10 mL of MeOH were added to the reaction flask followed by NaOH (110 mg, 2.75 mmol). The reaction mixture was stirred for 15 minutes, neutralized with AcOH and evaporated under reduced pressure. Azeotropic distillation with toluene in the rotary evaporator was performed to eliminate the excess of AcOH. The crude reaction product was purified by silica gel column chromatography using mixtures of MeOH in EtOAc (0-40%) as eluent, yielding compound 12 (70 mg, 30%). This compound was then activated following the General Procedure 1 for catalyst activation with NH3, affording 59 mg of catalyst 12.

m.p.: glassy compound

IR (film, ν in cm⁻¹): 3221, 3053, 3000, 2988, 2923, 1664, 1482, 1418, 1199, 617.

1H NMR (400 MHz, 5% CD3OD in CDCl3) δ 8.79 (s, 1H), 7.60 (d, J = 9.2 Hz, 1H), 7.20 – 7.06 (m, 5H), 7.03 (d, J = 8.6 Hz, 2H), 6.98 (d, J = 9.2 Hz, 1H), 6.86 (d, J = 8.6 Hz, 2H), 4.38 (dt, J = 11.2, 4.8 Hz, 1H), 4.15 – 4.07 (m, 1H), 3.39 – 2.80 (m, 9H), 2.05 – 1.90 (m, 4H).

13C NMR (100 MHz, 5% CD3OD in CDCl3) δ 170.3 (C), 156.8 (C), 156.5 (C), 156.3 (C), 154.4 (C), 154.4 (C), 153.5 (C), 134.8 (CH), 133.1 (C), 132.8 (C), 130.2 (C), 129.7 (CH), 129.3 (2 CH), 127.3 (CH), 126.8 (CH), 126.6 (CH), 122.4 (2 CH), 122.2 (2 CH), 121.2 (C), 114.8 (CH), 110.9 (C), 74.6 (CH), 62.0 (CH2), 55.0 (2 CH2), 51.5 (CH), 43.0 (CH), 35.2 (CH2), 23.3 (2 CH2).

HRMS (ESI+): Calculated for C62H30Cl2N2O5S [M+H]+ 622.1773, found 622.1768.
### 3. Crystallographic Data for compound 4b

CCDC 2144211 contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

| Property                              | Value                                      |
|---------------------------------------|--------------------------------------------|
| Empirical formula                     | C_{40}H_{40}BrN_{5}O_{8}S                       |
| Molecular weight                      | 861.71                                      |
| Temperature                           | 298(2) K                                    |
| Wavelength                            | 1.54178 Å                                   |
| Crystal system, space group           | monoclinic, P2/n                            |
| Unit cell dimensions                  | a = 21.6694(11)Å, α = 90deg.               |
|                                       | b = 9.9720(6)Å, β = 99.534(4)deg.          |
|                                       | c = 21.8858(11)Å, γ = 90deg.               |
| Volume                                | 4663.9(4)Å³                                 |
| Z, Calculated density                 | 4, 1.227Mg/m³                                |
| Absorption coefficient                | 2.364 mm⁻¹                                  |
| F(000)                                | 1780                                        |
| Crystal size                          | 0.15 x 0.12 x 0.10 mm                       |
| Theta range for data collection       | 4.10 to 67.73 deg.                          |
| Limiting indexes                      | -25≤h≤25, -9≤k≤11, -25≤l≤25                 |
| Reflections collected / unique       | 35063 / 7876 [R(int) = 0.0989]              |
| Refinement method                     | Full-matrix least-squares on F2             |
| Data / restraints / parameters        | 7876 / 0 / 507                              |
| Goodness-of-fit on F2                 | 1.068                                       |
| Final R indices [I>2σ(I)]            | R1 = 0.0945, wR2 = 0.2893                   |
| R indices (all data)                  | R1 = 0.1648, wR2 = 0.3390                   |
| Largest diff. peak and hole           | 0.968 and -0.423 e. Å³                     |

![Chemical Structure of 4b](image_url)
Results and Discussion

4. Kinetic Studies

4.1. Methanolysis Studies
To test the hydrolytic activity of the catalysts, reaction rates were measured for the methanolysis of acetylated catalysts 3a – 12a. Due to the high reactivity of these catalysts in neat methanol, in order to being able to measure the half-life of the catalyst deacetylation, a solution of CD$_3$OD 5% in CDCl$_3$ was used. The reaction progress was followed by integration of the $^1$H NMR signals of the product and the starting material and compared with acetylated catalyst 3a which was used as reference. 10 mg ca. of acetylated catalyst 3a – 12a and 10 mg ca. of acetylated catalyst 3a as reference were dissolved into 600 µL of a 5% solution of CD$_3$OD in CDCl$_3$ and $^1$H NMR spectra were recorded periodically at 20ºC. In these conditions, CD$_3$OD concentration can be considered constant, and pseudo-first order conditions can be applied.

![Figure S1](image1.png)

**Figure S1.** General overview for the methanolysis reaction of 3a – 12a.

The following equation was employed:

$$v = -\frac{\partial [3a - 12a]}{\partial t} = k[3a - 12a]^m[CD_3OD]^n = k'[3a - 12a]$$

$$m = n = 1 ; [CD_3OD] = constant \text{ (pseudo-first order conditions)}$$

$$\int_{[3a-12a]_0}^{[3a-12a]} \frac{\partial [3a - 12a]}{[3a - 12a]} = -k' \int_{t_0}^{t} \frac{\partial t}{t}$$

$$\ln[3a - 12a] - \ln[3a - 12a]_0 = -k't$$

$$\ln[3a - 12a] = \ln[3a - 12a]_0 - k't \rightarrow t_{1/2} = \frac{\ln[2]}{k}$$

![Figure S2](image2.png)

**Figure S2.** General formula for methanolysis studies.

From equation S1, plotting $\ln[3a - 12a]$ versus time a straight line is obtained. From the slope of this line $k'$ can be measured, and consequently the $t_{1/2}$ for methanolysis of 3a – 12a. The concentration of starting material and product was calculated as molar fraction (X). $t_{1/2}$ of each acetylated catalyst 3a – 12a was normalized with the $t_{1/2}$ of acetylated 3a.
Methanolysis results

Table S1. Half-lives for the methanolysis reaction of catalysts 3a – 12a in 5% CD₃OD in CDCl₃.

| Entry | Catalyst | \( t_{1/2} \) 3a/min | \( t_{1/2} \) 3a – 12a/min | \( \frac{t_{1/2} \text{3a}}{t_{1/2} \text{3a} - 12a} \) |
|-------|----------|----------------------|-----------------------------|----------------------------------|
| 1     | 3a       | 2.49[H]             | 2.49[H]                     | 1                                |
| 2     | 4a       | 36.64               | 23.98                       | 1.53                             |
| 3     | 5a       | 41.51               | 19.09                       | 2.17                             |
| 4     | 6a       | 38.72               | 10.98                       | 3.53                             |
| 5     | 7a       | 43.32               | 9.61                        | 4.51                             |
| 6     | 8a       | 34.31               | 3.86                        | 8.89                             |
| 7     | 9a       | 40.77               | 5.76                        | 7.08                             |
| 8     | 10a      | 38.51               | 3.69                        | 10.44                            |
| 9     | 11a      | 37.47               | 15.83                       | 2.37                             |
| 10    | 12a      | 39.38               | 2.63                        | 14.97                            |

[a] Half-life in min measured in neat CD₃OD

Figure S3. Plotting of \( \frac{t_{1/2} \text{3a}}{t_{1/2} \text{3a} - 12a} \) vs time.
SUPPORTING INFORMATION

Catalyst 3
Methanolysis study was performed in neat CD$_3$OD. 1$_3$s and 1$_{3a}$ signals from the $^1$H NMR spectra (Figure S5 as example) were integrated to calculate the molar fraction (X). All data are collected in Table S2 and plotting Ln[X$_{3a}$] versus time gave the equation shown in Figure S4, from which the half-life was calculated:

Table S2. Variation of molar fraction with time for methanolysis of $3a$.

| Entry | Time/min | X$_{3a}$ | X$_3$ | Ln(X$_{3a}$) |
|-------|----------|----------|------|-------------|
| 1     | 1.83     | 0.54     | 0.48 | -0.615185639|
| 2     | 3.03     | 0.39     | 0.61 | -0.935164081|
| 3     | 4.07     | 0.32     | 0.68 | -1.147402453|
| 4     | 5.07     | 0.22     | 0.78 | -1.497386409|
| 5     | 6.07     | 0.16     | 0.84 | -1.837369988|
| 6     | 8.68     | 0.08     | 0.92 | -2.482403528|

[a] Time relative to the first NMR measured.

Figure S4. Plotting of Ln[X$_{3a}$] vs time.

Figure S5. $^1$H NMR spectrum (9.8 – 7.6 ppm) for methanolysis of $3a$ at 4 min in neat CD$_3$OD.
Catalyst 3 with compound 6b

Methanolysis study was performed in neat CD$_3$OD using 3a and 1 equivalent of 6b. All data are collected in Table S3 and plotting Ln[X$_{3a}$] versus time gave the equation shown in Figure S6, from which the half-life was calculated:

Table S3. Variation of molar fraction with time for methanolysis of 3a.

| Entry | Time[a]/min | X$_{3a}$ | X$_3$ | Ln(X$_{3a}$) |
|-------|-------------|---------|------|-------------|
| 1     | 1.15        | 0.68    | 0.32 | -0.391145054|
| 2     | 1.98        | 0.58    | 0.42 | -0.542544701|
| 3     | 2.63        | 0.50    | 0.50 | -0.6931747181|
| 4     | 3.3         | 0.43    | 0.57 | -0.854717793|
| 5     | 3.97        | 0.33    | 0.67 | -1.101766865|
| 6     | 4.77        | 0.26    | 0.74 | -1.328996545|
| 7     | 6.77        | 0.14    | 0.86 | -1.973919369|
| 8     | 8.2         | 0.10    | 0.90 | -2.320898763|

[a] Time relative to the first NMR measured.

Figure S6. Plotting of Ln[X$_{3a}$] vs time.

\[ y = -0.2861x + 0.0212 \]

\[ r^2 = 0.99 \]

\[ t_{1/2} = 2.42 \text{ min} \]
### Table S4. Variation of molar fraction with time for methanolysis of 3a.

| Entry | Time/min | 3a | 3b | Ln(X3a) |
|-------|----------|----|----|---------|
| 1     | 2.00     | 0.83| 0.17| -0.18061776 |
| 2     | 3.00     | 0.80| 0.20| -0.25418301 |
| 3     | 4.00     | 0.82| 0.18| -0.20052513 |
| 4     | 5.00     | 0.78| 0.22| -0.24717259 |
| 5     | 6.00     | 0.71| 0.29| -0.34797722 |
| 6     | 7.00     | 0.73| 0.27| -0.32019764 |
| 7     | 8.00     | 0.77| 0.23| -0.25847208 |
| 8     | 9.00     | 0.74| 0.26| -0.29524093 |
| 9     | 10.00    | 0.73| 0.27| -0.31313049 |
| 10    | 11.00    | 0.68| 0.32| -0.39153503 |
| 11    | 12.00    | 0.66| 0.34| -0.41742617 |
| 12    | 13.00    | 0.67| 0.33| -0.39480852 |
| 13    | 14.00    | 0.69| 0.31| -0.37166699 |
| 14    | 15.00    | 0.64| 0.36| -0.45196642 |
| 15    | 16.00    | 0.58| 0.42| -0.54615416 |
| 16    | 17.00    | 0.64| 0.36| -0.44577497 |
| 17    | 18.00    | 0.56| 0.44| -0.57172078 |
| 18    | 19.00    | 0.70| 0.30| -0.36158288 |
| 19    | 20.00    | 0.62| 0.38| -0.47021608 |
| 20    | 21.00    | 0.61| 0.39| -0.50016904 |
| 21    | 22.00    | 0.53| 0.47| -0.64248526 |
| 22    | 23.00    | 0.52| 0.48| -0.65203763 |
| 23    | 24.00    | 0.55| 0.45| -0.60611762 |
| 24    | 25.00    | 0.52| 0.48| -0.64757433 |
| 25    | 26.00    | 0.54| 0.46| -0.61402280 |
| 26    | 27.00    | 0.53| 0.47| -0.65480277 |
| 27    | 28.00    | 0.49| 0.51| -0.71627287 |
| 28    | 29.00    | 0.50| 0.50| -0.68493858 |
| 29    | 30.00    | 0.45| 0.55| -0.68276831 |
| 30    | 31.00    | 0.51| 0.49| -0.68003661 |
| 31    | 32.00    | 0.46| 0.54| -0.78711551 |
| 32    | 33.00    | 0.48| 0.52| -0.74196115 |
| 33    | 34.00    | 0.43| 0.57| -0.83243047 |
| 34    | 35.00    | 0.44| 0.56| -0.81969172 |
| 35    | 36.00    | 0.42| 0.58| -0.86358591 |

[a] Time relative to the first NMR measured.
Table S5. Variation of molar fraction with time for methanolysis of 4a.

| Entry | Time (min) | X₃a | X₄a | Ln[X₄a] |
|-------|-----------|-----|-----|---------|
| 1     | 2.00      | 0.60| 0.29| -0.218819358 |
| 2     | 3.00      | 0.78| 0.22| -0.246231089 |
| 3     | 4.00      | 0.78| 0.22| -0.252900786 |
| 4     | 5.00      | 0.75| 0.25| -0.287780149 |
| 5     | 6.00      | 0.71| 0.29| -0.346147835 |
| 6     | 7.00      | 0.71| 0.29| -0.34813578 |
| 7     | 8.00      | 0.71| 0.29| -0.343756621 |
| 8     | 9.00      | 0.69| 0.31| -0.368800212 |
| 9     | 10.00     | 0.60| 0.40| -0.509770384 |
| 10    | 11.00     | 0.61| 0.39| -0.502057344 |
| 11    | 12.00     | 0.58| 0.42| -0.54792074 |
| 12    | 13.00     | 0.56| 0.44| -0.575977739 |
| 13    | 14.00     | 0.56| 0.44| -0.565963933 |
| 14    | 15.00     | 0.53| 0.47| -0.641401499 |
| 15    | 16.00     | 0.49| 0.51| -0.718893037 |
| 16    | 17.00     | 0.54| 0.46| -0.624238736 |
| 17    | 18.00     | 0.46| 0.54| -0.770688254 |
| 18    | 19.00     | 0.53| 0.47| -0.639259511 |
| 19    | 20.00     | 0.51| 0.49| -0.681738544 |
| 20    | 21.00     | 0.47| 0.53| -0.757419223 |
| 21    | 22.00     | 0.43| 0.57| -0.843145805 |
| 22    | 23.00     | 0.46| 0.54| -0.785871709 |
| 23    | 24.00     | 0.41| 0.59| -0.880939058 |
| 24    | 25.00     | 0.44| 0.56| -0.813963361 |
| 25    | 26.00     | 0.39| 0.61| -0.945662703 |
| 26    | 27.00     | 0.41| 0.59| -0.889194675 |
| 27    | 28.00     | 0.35| 0.65| -1.046350899 |
| 28    | 29.00     | 0.37| 0.63| -0.985309885 |
| 29    | 30.00     | 0.34| 0.66| -1.068111289 |
| 30    | 31.00     | 0.39| 0.61| -0.943334273 |
| 31    | 32.00     | 0.32| 0.68| -1.144260992 |
| 32    | 33.00     | 0.34| 0.66| -1.089727905 |
| 33    | 34.00     | 0.30| 0.70| -1.192068467 |
| 34    | 35.00     | 0.31| 0.69| -1.180544591 |
| 35    | 36.00     | 0.30| 0.70| -1.213484821 |
| 36    | 37.00     | 0.33| 0.67| -1.116586939 |
| 37    | 38.00     | 0.26| 0.74| -1.339718516 |
| 38    | 39.00     | 0.27| 0.73| -1.295731897 |
| 39    | 40.00     | 0.26| 0.74| -1.354316218 |
| 40    | 41.00     | 0.26| 0.74| -1.336668008 |
| 41    | 42.00     | 0.25| 0.75| -1.402174254 |
| 42    | 43.00     | 0.25| 0.75| -1.395688833 |
| 43    | 44.00     | 0.22| 0.76| -1.522079855 |
| 44    | 45.00     | 0.25| 0.75| -1.37828002 |
| 45    | 46.00     | 0.22| 0.78| -1.517328627 |
| 46    | 47.00     | 0.23| 0.77| -1.475927876 |

[a] Time relative to the first NMR measured

Figure S7. Plotting of Ln[X₄a] vs time (left) and Ln[X₃a] vs time (right).
Figure S8. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 4a at 21 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

$3 \quad R = OH$

$3a \quad R = Ac$

$4 \quad R = OH$

$4a \quad R = Ac$
SUPPORTING INFORMATION

Catalyst 5

1s, 1sa, 1s and 1sa signals from the 1H NMR spectra (Figure 10 as example) were integrated to calculate the molar fraction (X). All data are collected in Table S6 and Table S7; plotting Ln[Xsa-sa] versus time gave the equation shown in Figure S9 from which the half-life was calculated:

Table S6. Variation of molar fraction with time for methanolysis of 3a.

| Entry | Time[&s/min] | Xsa | Xs | Ln(Xsa) |
|-------|--------------|-----|----|---------|
| 1     | 3.25         | 0.85| 0.15| -0.157003749 |
| 2     | 4.25         | 0.84| 0.16| -0.173953307 |
| 3     | 5.25         | 0.82| 0.18| -0.199850859 |
| 4     | 6.25         | 0.78| 0.22| -0.254642218 |
| 5     | 7.25         | 0.78| 0.22| -0.254642218 |
| 6     | 8.25         | 0.77| 0.23| -0.262364264 |
| 7     | 9.25         | 0.78| 0.22| -0.254642218 |
| 8     | 10.25        | 0.75| 0.25| -0.292869614 |
| 9     | 11.25        | 0.80| 0.20| -0.233143551 |
| 10    | 12.25        | 0.71| 0.29| -0.336472237 |
| 11    | 13.25        | 0.74| 0.26| -0.3074847 |
| 12    | 14.25        | 0.70| 0.30| -0.35065872 |
| 13    | 15.25        | 0.74| 0.26| -0.3074847 |
| 14    | 16.25        | 0.69| 0.31| -0.371563556 |
| 15    | 17.25        | 0.73| 0.27| -0.31481074 |
| 16    | 18.25        | 0.74| 0.26| -0.300104992 |
| 17    | 19.25        | 0.68| 0.32| -0.378436436 |
| 18    | 20.25        | 0.66| 0.34| -0.412109651 |
| 19    | 21.25        | 0.65| 0.35| -0.425267735 |
| 20    | 22.25        | 0.60| 0.40| -0.506817602 |
| 21    | 23.25        | 0.63| 0.37| -0.46374016 |
| 22    | 24.25        | 0.58| 0.42| -0.542324291 |
| 23    | 25.25        | 0.67| 0.33| -0.405465108 |
| 24    | 26.25        | 0.62| 0.38| -0.478234179 |
| 25    | 27.25        | 0.58| 0.42| -0.536493371 |
| 26    | 28.25        | 0.60| 0.40| -0.518793793 |
| 27    | 29.25        | 0.56| 0.44| -0.570979547 |

28 30.25 0.59 0.41 -0.524726529
29 31.25 0.56 0.42 -0.548121409
30 32.25 0.60 0.43 -0.512832626
31 33.25 0.52 0.48 -0.657520003
32 36.25 0.46 0.54 -0.770108222
33 37.25 0.47 0.53 -0.746679474
34 38.25 0.46 0.52 -0.737164066
35 39.25 0.52 0.48 -0.657520003
36 40.25 0.49 0.51 -0.708035793
37 41.25 0.45 0.55 -0.806475866
38 42.25 0.41 0.59 -0.887891257
39 43.25 0.49 0.51 -0.722705983
40 44.25 0.32 0.48 -0.662987973
41 45.25 0.44 0.56 -0.819779831
42 46.25 0.45 0.55 -0.806475866
43 47.25 0.39 0.61 -0.943905898
44 48.25 0.40 0.60 -0.912228271
45 49.25 0.40 0.60 -0.920282753
46 50.25 0.36 0.62 -0.955114448
47 51.25 0.34 0.66 -1.068153081
48 52.25 0.38 0.62 -0.993502221
49 53.25 0.36 0.64 -1.026041596
50 54.25 0.36 0.62 -0.893502221
51 55.25 0.34 0.66 -1.07183616

[a] Time relative to the first NMR measured
Table S7. Variation of molar fraction with time for methanolysis of 5a.

| Entry | Time[min] | X3a | X5a | $\text{Ln}(X_3a)$ |
|-------|-----------|-----|-----|------------------|
| 1     | 3.25      | 0.84| 0.16| -0.180261824    |
| 2     | 4.25      | 0.77| 0.23| -0.265281136     |
| 3     | 5.25      | 0.77| 0.23| -0.259511195     |
| 4     | 6.25      | 0.77| 0.23| -0.260283098     |
| 5     | 7.25      | 0.70| 0.30| -0.3661614542    |
| 6     | 8.25      | 0.70| 0.30| -0.354171814     |
| 7     | 9.25      | 0.66| 0.34| -0.42199441      |
| 8     | 10.25     | 0.64| 0.36| -0.451985124     |
| 9     | 11.25     | 0.59| 0.41| -0.523855124     |
| 10    | 12.25     | 0.55| 0.45| -0.595166772     |
| 11    | 13.25     | 0.54| 0.46| -0.617639625     |
| 12    | 14.25     | 0.55| 0.45| -0.589350387     |
| 13    | 15.25     | 0.52| 0.48| -0.658242624     |
| 14    | 16.25     | 0.52| 0.48| -0.649850375     |
| 15    | 17.25     | 0.53| 0.47| -0.633427940     |
| 16    | 18.25     | 0.46| 0.54| -0.786673239     |
| 17    | 19.25     | 0.51| 0.49| -0.660075099     |
| 18    | 20.25     | 0.43| 0.57| -0.844890797     |
| 19    | 21.25     | 0.45| 0.55| -0.8031193       |
| 20    | 22.25     | 0.41| 0.59| -0.890972624     |
| 21    | 23.25     | 0.43| 0.57| -0.842445842     |
| 22    | 24.25     | 0.36| 0.65| -1.063272262     |
| 23    | 25.25     | 0.34| 0.66| -1.072636802     |
| 24    | 26.25     | 0.38| 0.62| -0.962036754     |
| 25    | 27.25     | 0.35| 0.65| -1.043804052     |
| 26    | 28.25     | 0.36| 0.64| -1.011600912     |
| 27    | 29.25     | 0.32| 0.68| -1.145132304     |
| 28    | 30.25     | 0.33| 0.67| -1.098612289     |
| 29    | 31.25     | 0.35| 0.65| -1.044124103     |
| 30    | 32.25     | 0.28| 0.72| -1.289533845     |
| 31    | 33.25     | 0.26| 0.72| -1.267846211     |
| 32    | 34.25     | 0.28| 0.72| -1.261477296     |
| 33    | 35.25     | 0.22| 0.78| -1.521469139     |
| 34    | 36.25     | 0.25| 0.75| -1.392091479     |
| 35    | 37.25     | 0.22| 0.78| -1.535826095     |
| 36    | 40.25     | 0.20| 0.80| -1.596450717     |
| 37    | 41.25     | 0.17| 0.83| -1.747586251     |

[a] Time relative to the first NMR measured.

Figure S9. Plotting of \(\text{Ln}(X_{3a})\) vs time (left) and \(\text{Ln}(X_{5a})\) vs time (right).

\[ t_{1/2} = 41.51 \text{ min} \]

\[ t_{1/2} = 19.09 \text{ min} \]
Figure S10. $^1$H NMR spectrum (9.6 – 7.4 ppm) for methanolysis of 3a and 5a at 12 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

3 R = OH
3a R = Ac
5 R = OH
5a R = Ac
Catalyst 6

16, 16a, 13 and 13a signals from the 1H NMR spectra (Figure S12 as example) were integrated to calculate the molar fraction (X). All data are collected in Table S8 and Table S9; plotting Ln[X_{16+16a}] versus time gave the equation shown in Figura S11 from which the half-life was calculated:

Table S8. Variation of molar fraction with time for methanolysis of 3a.

| Entry | Time (min) | Xe | Xa | Ln(Xe) |
|-------|------------|----|----|--------|
| 1     | 2.25       | 0.96| 0.04| -0.039220713 |
| 2     | 3.25       | 0.92| 0.08| -0.086177696 |
| 3     | 4.25       | 0.92| 0.08| -0.086177696 |
| 4     | 5.25       | 0.88| 0.12| -0.122171633 |
| 5     | 6.25       | 0.91| 0.09| -0.09531018  |
| 6     | 7.25       | 0.88| 0.12| -0.131028262 |
| 7     | 8.25       | 0.81| 0.19| -0.207014169 |
| 8     | 9.25       | 0.83| 0.17| -0.182321557 |
| 9     | 10.25      | 0.83| 0.17| -0.182321557 |
| 10    | 11.25      | 0.82| 0.18| -0.198850859 |
| 11    | 12.25      | 0.83| 0.17| -0.1962036 |
| 12    | 13.25      | 0.80| 0.20| -0.223143551 |
| 13    | 14.25      | 0.78| 0.21| -0.23111721 |
| 14    | 15.25      | 0.76| 0.24| -0.277631737 |
| 15    | 16.25      | 0.74| 0.26| -0.300104592 |
| 16    | 17.25      | 0.72| 0.28| -0.322083499 |
| 17    | 18.25      | 0.72| 0.28| -0.322083499 |
| 18    | 19.25      | 0.65| 0.35| -0.425267375 |
| 19    | 20.25      | 0.65| 0.35| -0.431782416 |
| 20    | 21.25      | 0.71| 0.29| -0.336472237 |
| 21    | 22.25      | 0.68| 0.32| -0.378436436 |
| 22    | 23.25      | 0.63| 0.37| -0.463734016 |
| 23    | 24.25      | 0.63| 0.38| -0.470003629 |
| 24    | 25.25      | 0.65| 0.35| -0.438254931 |
| 25    | 26.25      | 0.60| 0.40| -0.512826269 |
| 26    | 27.25      | 0.57| 0.43| -0.553885113 |
| 27    | 28.25      | 0.57| 0.43| -0.565313809 |
| 28    | 29.25      | 0.59| 0.41| -0.562782529 |
| 29    | 30.25      | 0.62| 0.38| -0.476234179 |
| 30    | 31.25      | 0.58| 0.44| -0.570997547 |
| 31    | 32.25      | 0.57| 0.43| -0.559615786 |
| 32    | 33.25      | 0.53| 0.47| -0.625938431 |
| 33    | 34.25      | 0.51| 0.49| -0.667829373 |
| 34    | 35.25      | 0.56| 0.44| -0.576613664 |
| 35    | 36.25      | 0.51| 0.49| -0.672444743 |
| 36    | 37.25      | 0.48| 0.52| -0.727548607 |
| 37    | 38.25      | 0.46| 0.54| -0.793753418 |
| 38    | 39.25      | 0.46| 0.54| -0.799324877 |
| 39    | 40.25      | 0.42| 0.58| -0.858661169 |
| 40    | 41.25      | 0.48| 0.52| -0.737164066 |
| 41    | 42.25      | 0.46| 0.54| -0.779108223 |
| 42    | 43.25      | 0.40| 0.60| -0.904218151 |
| 43    | 44.25      | 0.47| 0.53| -0.746687947 |
| 44    | 45.25      | 0.46| 0.54| -0.774727168 |
| 45    | 46.25      | 0.44| 0.56| -0.819775831 |

[a] Time relative to the first NMR measured.
Table S9. Variation of molar fraction with time for methanolysis of 6a.

| Entry | Time[\(^\text{a}\)] min | \(X_{6a}\) | \(X_6\) | \(\ln(X_{6a})\) |
|-------|-------------------------|----------|-------|-----------------|
| 1     | 2.25                    | 0.91     | 0.09  | -0.098849335    |
| 2     | 3.25                    | 0.83     | 0.17  | -0.184374102    |
| 3     | 4.25                    | 0.77     | 0.23  | -0.262364284    |
| 4     | 5.25                    | 0.70     | 0.30  | -0.356674944    |
| 5     | 6.25                    | 0.65     | 0.35  | -0.437138606    |
| 6     | 7.25                    | 0.62     | 0.38  | -0.476399448    |
| 7     | 8.25                    | 0.59     | 0.41  | -0.526825965    |
| 8     | 9.25                    | 0.56     | 0.44  | -0.575364145    |
| 9     | 10.25                   | 0.52     | 0.48  | -0.651474484    |
| 10    | 11.25                   | 0.50     | 0.50  | -0.692147181    |
| 11    | 12.25                   | 0.43     | 0.57  | -0.836246024    |
| 12    | 13.25                   | 0.44     | 0.56  | -0.816207273    |
| 13    | 14.25                   | 0.41     | 0.59  | -0.897941593    |
| 14    | 15.25                   | 0.39     | 0.61  | -0.938269639    |
| 15    | 16.25                   | 0.36     | 0.64  | -1.029619417    |
| 16    | 17.25                   | 0.33     | 0.67  | -1.107506959    |
| 17    | 18.25                   | 0.31     | 0.69  | -1.161413191    |
| 18    | 19.25                   | 0.31     | 0.69  | -1.162311308    |
| 19    | 20.25                   | 0.31     | 0.69  | -1.16760516     |
| 20    | 21.25                   | 0.25     | 0.75  | -1.403993938    |
| 21    | 22.25                   | 0.24     | 0.76  | -1.432103897    |
| 22    | 23.25                   | 0.27     | 0.73  | -1.313172096    |
| 23    | 24.25                   | 0.25     | 0.75  | -1.405342556    |
| 24    | 25.25                   | 0.18     | 0.82  | -1.741927095    |
| 25    | 26.25                   | 0.17     | 0.83  | -1.779336949    |
| 26    | 27.25                   | 0.18     | 0.83  | -1.742969305    |
| 27    | 28.25                   | 0.19     | 0.81  | -1.686398954    |
| 28    | 29.25                   | 0.16     | 0.84  | -1.857717437    |
| 29    | 30.25                   | 0.15     | 0.85  | -1.885691289    |
| 30    | 31.25                   | 0.13     | 0.87  | -2.008214832    |

\(\text{[a]}\) Time relative to the first NMR measured.

Figure S11. Plotting of Ln\([X_{3a}]\) vs time (left) and Ln\([X_{6a}]\) vs time (right).
Figure S12. $^1$H NMR spectrum (9.6 – 7.4 ppm) for methanolysis of 3a and 6a at 9 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

$R = OH$

$R = Ac$

$3a$

$6a$
**SUPPORTING INFORMATION**

Catalyst 7

The 17, 17a, 13 and 13a signals from the 1H NMR spectra (Figure S14 as example) were integrated to calculate the molar fraction (X). All data are collected in Table S10 and Table S11; plotting Ln[Xₐₙₐ/ₐ] versus time gave the equation shown in Figure S13 from which the half-life was calculated:

Table S10. Variation of molar fraction with time for methanolysis of 3a.

| Entry | Time (min) | Xₐₙₐ | Xₐ | Ln[Xₐₙₐ] |
|-------|------------|------|----|---------|
| 1     | 12         | 0.91 | 0.09 | -0.093945613 |
| 2     | 13         | 0.93 | 0.07 | -0.069992372 |
| 3     | 14         | 0.97 | 0.03 | -0.026641931 |
| 4     | 15         | 0.86 | 0.12 | -0.123102197 |
| 5     | 16         | 0.85 | 0.14 | -0.168053585 |
| 6     | 17         | 0.67 | 0.13 | -0.14019663 |
| 7     | 18         | 0.85 | 0.05 | -0.051643333 |
| 8     | 19         | 0.85 | 0.15 | -0.168053585 |
| 9     | 20         | 0.85 | 0.15 | -0.162433929 |
| 10    | 21         | 0.78 | 0.22 | -0.242161557 |
| 11    | 22         | 0.82 | 0.18 | -0.200488661 |
| 12    | 23         | 0.88 | 0.12 | -0.128832872 |
| 13    | 24         | 0.81 | 0.19 | -0.21710797 |
| 14    | 25         | 0.73 | 0.27 | -0.311554429 |
| 15    | 26         | 0.82 | 0.18 | -0.200488661 |
| 16    | 27         | 0.78 | 0.22 | -0.242161557 |
| 17    | 28         | 0.79 | 0.19 | -0.247250627 |
| 18    | 29         | 0.61 | 0.19 | -0.216320326 |
| 19    | 30         | 0.77 | 0.23 | -0.262364284 |
| 20    | 31         | 0.73 | 0.22 | -0.267351806 |
| 21    | 32         | 0.67 | 0.33 | -0.406464468 |
| 22    | 33         | 0.68 | 0.32 | -0.384851897 |
| 23    | 34         | 0.68 | 0.32 | -0.384851897 |
| 24    | 35         | 0.66 | 0.34 | -0.419368013 |
| 25    | 36         | 0.64 | 0.36 | -0.44843831 |

Table S11. Variation of molar fraction with time for methanolysis of 7a.

| Entry | Time (min) | Xₐₙₐ | Xₐ | Ln[Xₐₙₐ] |
|-------|------------|------|----|---------|
| 1     | 2          | 0.74 | 0.26 | -0.294923234 |
| 2     | 3          | 0.59 | 0.41 | -0.52788769 |
| 3     | 4          | 0.71 | 0.29 | -0.33672237 |
| 4     | 5          | 0.61 | 0.35 | -0.46535629 |
| 5     | 6          | 0.52 | 0.48 | -0.651786248 |
| 6     | 7          | 0.49 | 0.51 | -0.717389793 |
| 7     | 8          | 0.45 | 0.55 | -0.798028871 |
| 8     | 9          | 0.46 | 0.54 | -0.78581538 |
| 9     | 10         | 0.36 | 0.64 | -1.017643226 |
| 10    | 11         | 0.36 | 0.64 | -1.028319417 |
| 11    | 12         | 0.36 | 0.68 | -1.135637611 |
| 12    | 13         | 0.29 | 0.71 | -1.223910005 |

Methanolysis 3a vs 7a

![Methanolysis 3a vs 7a](image)

Figure S13. Plotting of Ln[Xₐₙₐ] vs time (left) and Ln[Xₐₙₐ] vs time (right).

[a] Time relative to the first NMR measured.

Methanolysis 3a vs 7a

![Methanolysis 3a vs 7a](image)

Figure S13. Plotting of Ln[Xₐₙₐ] vs time (left) and Ln[Xₐₙₐ] vs time (right).
Figure S14. $^1$H NMR spectrum (9.6 – 7.4 ppm) for methanolysis of 3a and 7a at 10 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 
Table S12. Variation of molar fraction with time for methanolysis of 3a.

| Entry | Time/min | X8a | X7a | Ln[X7a] |
|-------|----------|-----|-----|---------|
| 1     | 2.06     | 0.93| 0.17| 1.182321557 |
| 2     | 2.93666667 | 0.92 | 0.16 | -0.198050859 |
| 3     | 3.81333333 | 0.61 | 0.19 | -0.207014169 |
| 4     | 4.69     | 0.78 | 0.22 | -0.246600703 |
| 5     | 5.56666667 | 0.78 | 0.22 | -0.246600703 |
| 6     | 6.44333333 | 0.74 | 0.26 | -0.3074847 |
| 7     | 7.32     | 0.74 | 0.26 | -0.3074847 |
| 8     | 8.19666667 | 0.70 | 0.30 | -0.35065872 |
| 9     | 9.07333333 | 0.70 | 0.30 | -0.35065872 |
| 10    | 9.95     | 0.69 | 0.31 | -0.365431141 |
| 11    | 10.82666667 | 0.70 | 0.30 | -0.35065872 |
| 12    | 11.70333333 | 0.67 | 0.33 | -0.405465108 |
| 13    | 12.56    | 0.67 | 0.33 | -0.405465108 |
| 14    | 13.45666667 | 0.67 | 0.33 | -0.405465108 |
| 15    | 14.33333333 | 0.64 | 0.36 | -0.444685821 |
| 16    | 15.21    | 0.63 | 0.37 | -0.457424847 |
| 17    | 16.08666667 | 0.61 | 0.39 | -0.494698242 |
| 18    | 16.96333333 | 0.63 | 0.38 | -0.470003629 |
| 19    | 17.84    | 0.60 | 0.40 | -0.512823626 |
| 20    | 18.71666667 | 0.58 | 0.42 | -0.536493371 |
| 21    | 19.59333333 | 0.56 | 0.44 | -0.562261562 |
| 22    | 20.47    | 0.57 | 0.43 | -0.585313809 |
| 23    | 21.34666667 | 0.57 | 0.43 | -0.596157888 |
| 24    | 22.22333333 | 0.53 | 0.47 | -0.625938431 |
| 25    | 23.1     | 0.54 | 0.46 | -0.615856399 |
| 26    | 23.97666667 | 0.52 | 0.48 | -0.647103242 |
| 27    | 24.85333333 | 0.52 | 0.48 | -0.662887973 |
| 28    | 25.73    | 0.51 | 0.49 | -0.676293737 |
| 29    | 26.60666667 | 0.49 | 0.51 | -0.717839793 |
| 30    | 27.48333333 | 0.51 | 0.49 | -0.672944473 |
| 31    | 28.36    | 0.47 | 0.53 | -0.765467842 |
| 32    | 29.23666667 | 0.50 | 0.50 | -0.688134639 |
| 33    | 30.11333333 | 0.47 | 0.53 | -0.760856299 |
| 34    | 30.99    | 0.46 | 0.54 | -0.793961544 |
| 35    | 31.86666667 | 0.44 | 0.56 | -0.824175443 |
| 36    | 32.74333333 | 0.44 | 0.57 | -0.841567186 |
| 37    | 33.62    | 0.44 | 0.56 | -0.824175443 |
| 38    | 34.49666667 | 0.44 | 0.57 | -0.845868268 |
| 39    | 35.37333333 | 0.44 | 0.56 | -0.819798831 |
| 40    | 36.25    | 0.43 | 0.57 | -0.845868268 |
| 41    | 37.12666667 | 0.42 | 0.58 | -0.875468737 |
| 42    | 38.00333333 | 0.41 | 0.59 | -0.891998039 |
| 43    | 38.88    | 0.39 | 0.61 | -0.932164081 |
| 44    | 39.75666667 | 0.37 | 0.63 | -0.989541194 |
| 45    | 40.63333333 | 0.36 | 0.64 | -1.022450928 |

Table S13. Variation of molar fraction with time for methanolysis of 8a.

| Entry | Time/min | X8a | X7a | Ln[X7a] |
|-------|----------|-----|-----|---------|
| 1     | 2.06     | 1.00| 0.00| -0.55764797 |
| 2     | 2.93666667 | 0.21 | 0.79 | -1.314368243 |
| 3     | 3.81333333 | 0.27 | 0.75 | -1.599595427 |
| 4     | 4.69     | 0.21 | 0.79 | -1.857958080 |
| 5     | 5.56666667 | 0.16 | 0.84 | -1.658357507 |
| 6     | 6.44333333 | 0.19 | 0.81 | -2.073164122 |
| 7     | 7.32     | 0.13 | 0.87 | -1.851608489 |
| 8     | 8.19666667 | 0.16 | 0.84 | -1.799912733 |
| 9     | 9.07333333 | 0.17 | 0.83 | -2.387894704 |
| 10    | 9.95     | 0.09 | 0.91 | -2.830578792 |

Methanolysis 3a vs 8a

Methanolysis 8a vs 3a

Figure S15. Plotting of Ln[Xa] vs time (left) and Ln[Xa] vs time (right).
Figure S16. $^1$H NMR spectrum (9.6 – 7.4 ppm) for methanolysis of 3a and 8a at 7.01 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 
SUPPORTING INFORMATION

Catalyst 9

1a, 1aa, 1b and 1ab signals from the 1H NMR spectra (Figure S18 as example) were integrated to calculate the molar fraction (X). All data are collected in Table S14 and Table S15; plotting \(\ln(X_{9a}/X_{a})\) versus time gave the equation shown in Figure S17 from which the half-life was calculated:

Table S14. Variation of molar fraction with time for methanolysis of 3a.

| Entry | Time(min) | \(X_{3a}\) | \(X_{a}\) | \(\ln(X_{9a}/X_{a})\) |
|-------|-----------|-------------|-------------|---------------------|
| 1     | 2         | 0.84        | 0.16        | -0.173952307       |
| 2     | 3         | 0.85        | 0.13        | -0.10514438        |
| 3     | 4         | 0.81        | 0.19        | -0.21511138        |
| 4     | 5         | 0.80        | 0.20        | -0.22314355        |
| 5     | 6         | 0.79        | 0.21        | -0.23111721        |
| 6     | 7         | 0.76        | 0.24        | -0.27763173        |
| 7     | 8         | 0.76        | 0.24        | -0.27763173        |
| 8     | 9         | 0.74        | 0.26        | -0.30010458        |
| 9     | 10        | 0.75        | 0.25        | -0.30669614        |
| 10    | 11        | 0.75        | 0.25        | -0.32669614        |
| 11    | 12        | 0.71        | 0.29        | -0.33472237        |
| 12    | 13        | 0.70        | 0.30        | -0.350666872       |
| 13    | 14        | 0.68        | 0.32        | -0.385262401       |
| 14    | 15        | 0.69        | 0.31        | -0.371563562       |
| 15    | 16        | 0.66        | 0.34        | -0.418710335       |
| 16    | 17        | 0.66        | 0.34        | -0.421209651       |
| 17    | 18        | 0.66        | 0.34        | -0.421209651       |
| 18    | 19        | 0.64        | 0.36        | -0.51075619        |
| 19    | 20        | 0.62        | 0.38        | -0.476234179       |
| 20    | 21        | 0.63        | 0.37        | -0.463734016       |
| 21    | 22        | 0.61        | 0.39        | -0.500772588       |
| 22    | 23        | 0.61        | 0.39        | -0.500772588       |
| 23    | 24        | 0.58        | 0.42        | -0.542324291       |
| 24    | 25        | 0.60        | 0.40        | -0.51283626        |
| 25    | 26        | 0.58        | 0.42        | -0.54821409        |
| 26    | 27        | 0.57        | 0.43        | -0.56531385        |

Table S15. Variation of molar fraction with time for methanolysis of 9a.

| Entry | Time(min) | \(X_{9a}\) | \(X_{a}\) | \(\ln(X_{9a}/X_{a})\) |
|-------|-----------|-------------|-------------|---------------------|
| 1     | 2         | 0.64        | 0.36        | -0.44391389         |
| 2     | 3         | 0.53        | 0.47        | -0.635989767       |
| 3     | 4         | 0.47        | 0.53        | -0.751416089       |
| 4     | 5         | 0.41        | 0.59        | -0.867303195       |
| 5     | 6         | 0.43        | 0.57        | -0.84729786        |
| 6     | 7         | 0.37        | 0.63        | -0.986494991       |
| 7     | 8         | 0.28        | 0.72        | -1.262241714       |
| 8     | 9         | 0.26        | 0.72        | -1.270462564       |
| 9     | 10        | 0.27        | 0.73        | -1.32175584        |
| 10    | 11        | 0.20        | 0.80        | -1.609437912       |
| 11    | 12        | 0.17        | 0.83        | -1.757857918       |
| 12    | 13        | 0.18        | 0.82        | -1.712978591       |
| 13    | 14        | 0.14        | 0.86        | -1.961658506       |

(a) Time relative to the first NMR measured.

Methanolysis 3a vs 9a

Methanolysis 3a vs 9a

time (min)

Figure S17. Plotting of \(\ln(X_{9a}/X_{a})\) vs time (left) and \(\ln(X_{9a}/X_{a})\) vs time (right).
Figure S18. $^1$H NMR spectrum (9.6 – 7.4 ppm) for methanolysis of 3a and 9a at 6 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 
**SUPPORTING INFORMATION**

Catalyst 10

10a, 10b, 1a and 1a signals from the 1H NMR spectra (Figure S20 as example) were integrated to calculate the molar fraction (X). All data are collected in Table S16 and Table S17; plotting Ln[Xa+10a] versus time gave the equation shown in Figure S19 from which the half-life was calculated:

Table S16. Variation of molar fraction with time for methanolysis of 3a.

| Entry | Time (min) | \(X_a\) | \(X_{10a}\) | \(\text{Ln}(X_{10a})\) |
|-------|------------|---------|-------------|------------------------|
| 1     | 2          | 0.73    | 0.27        | -0.31481074            |
| 2     | 3.0357     | 0.71    | 0.29        | -0.33439704            |
| 3     | 4.0714     | 0.71    | 0.29        | -0.336472237           |
| 4     | 5.1071     | 0.70    | 0.30        | -0.357674444           |
| 5     | 6.1429     | 0.68    | 0.32        | -0.385282401           |
| 6     | 7.1765     | 0.66    | 0.34        | -0.412106961           |
| 7     | 8.2142     | 0.65    | 0.35        | -0.438254931           |
| 8     | 9.2499     | 0.61    | 0.39        | -0.46580015            |
| 9     | 10.2866    | 0.61    | 0.39        | -0.49466242            |
| 10    | 11.3213    | 0.61    | 0.39        | -0.52850005            |
| 11    | 12.357     | 0.58    | 0.42        | -0.542324291           |
| 12    | 13.3927    | 0.56    | 0.44        | -0.55221562            |
| 13    | 14.4284    | 0.56    | 0.44        | -0.56221562            |
| 14    | 15.4641    | 0.56    | 0.44        | -0.57786665            |
| 15    | 16.4998    | 0.53    | 0.47        | -0.625938431           |
| 16    | 17.5355    | 0.53    | 0.47        | -0.636576829           |
| 17    | 18.5712    | 0.55    | 0.45        | -0.64315667            |
| 18    | 19.6089    | 0.52    | 0.48        | -0.66267973            |
| 19    | 20.6426    | 0.47    | 0.53        | -0.751416089           |
| 20    | 21.6783    | 0.50    | 0.50        | -0.70309751            |
| 21    | 22.714     | 0.51    | 0.49        | -0.672944473           |
| 22    | 23.7497    | 0.47    | 0.53        | -0.751416089           |
| 23    | 24.7854    | 0.48    | 0.52        | -0.741977345           |
| 24    | 25.8211    | 0.47    | 0.53        | -0.746678947           |
| 25    | 26.8568    | 0.43    | 0.57        | -0.837247525           |
| 26    | 27.8925    | 0.43    | 0.57        | -0.83586268            |
| 27    | 28.9282    | 0.45    | 0.55        | -0.804475866           |
| 28    | 29.9639    | 0.43    | 0.57        | -0.837247525           |
| 29    | 30.9996    | 0.41    | 0.59        | -0.89198903            |
| 30    | 32.0353    | 0.40    | 0.60        | -0.926219303           |
| 31    | 33.071     | 0.38    | 0.62        | -0.959350221           |

Table S17. Variation of molar fraction with time for methanolysis of 10a.

| Entry | Time (min) | \(X_{10a}\) | \(X_a\) | \(\text{Ln}(X_{10a})\) |
|-------|------------|-------------|---------|------------------------|
| 1     | 2          | 0.36        | 0.64    | -1.01637419            |
| 2     | 3.0357     | 0.25        | 0.75    | -1.396244992           |
| 3     | 4.0714     | 0.21        | 0.79    | -1.570598079           |
| 4     | 5.1071     | 0.20        | 0.80    | -1.591893603           |
| 5     | 6.1428     | 0.17        | 0.83    | -1.791759469           |
| 6     | 7.1765     | 0.13        | 0.87    | -2.01044467            |
| 7     | 8.2142     | 0.13        | 0.87    | -2.094223344           |
| 8     | 9.2499     | 0.08        | 0.92    | -2.525726444           |
| 9     | 11.3213    | 0.05        | 0.95    | -2.913902255           |

[a] Time relative to the first NMR measured.
**Figure S19.** Plotting of Ln[X₃a] vs time (left) and Ln[X₁₀a] vs time (right).

**Figure S20.** ¹H NMR spectrum (9.6 – 7.4 ppm) for methanolysis of 3a and 10a at 2.07 min relative to the first NMR measured in 5% CD₃OD in CDCl₃.
Table S18. Variation of molar fraction with time for methanolysis of 3a.

| Entry | Time (min) | X1a | X3 | Ln(X1a) |
|-------|------------|-----|----|---------|
| 1     | 2          | 0.78| 0.22| -2.46580078|
| 2     | 3.0125     | 0.80| 0.20| -2.23143551|
| 3     | 4.025      | 0.78| 0.22| -2.54642218|
| 4     | 5.0375     | 0.76| 0.24| -2.70027137|
| 5     | 6.05       | 0.77| 0.23| -2.82384624|
| 6     | 7.0625     | 0.74| 0.28| -3.0774847|
| 7     | 8.075      | 0.71| 0.29| -3.36472237|
| 8     | 9.0875     | 0.72| 0.28| -3.29303747|
| 9     | 10         | 0.71| 0.29| -3.36472237|
| 10    | 11.1125    | 0.72| 0.28| -3.29303747|
| 11    | 12.125     | 0.68| 0.32| -0.392042088|
| 12    | 13.1375    | 0.71| 0.29| -3.43589704|
| 13    | 14.15      | 0.68| 0.32| -0.392042088|
| 14    | 15.1625    | 0.65| 0.35| -0.25267735|
| 15    | 16.17      | 0.60| 0.40| -0.508617602|
| 16    | 17.18      | 0.63| 0.38| -0.470003629|
| 17    | 18.2       | 0.63| 0.38| -0.470003629|
| 18    | 19.2125    | 0.63| 0.37| -0.57428487|
| 19    | 20.225     | 0.56| 0.44| -0.58221562|
| 20    | 21.2375    | 0.56| 0.44| -0.576613364|
| 21    | 22.25      | 0.55| 0.45| -0.604315967|
| 22    | 23.2625    | 0.58| 0.44| -0.58221562|
| 23    | 24.275     | 0.56| 0.44| -0.58221562|
| 24    | 25.2875    | 0.54| 0.46| -0.620576486|
| 25    | 26.3       | 0.51| 0.49| -0.697629373|
| 26    | 27.3125    | 0.51| 0.49| -0.672944473|
| 27    | 28.325     | 0.51| 0.49| -0.672944473|

Table S19. Variation of molar fraction with time for methanolysis of 11a.

| Entry | Time (min) | X1a | X3 | Ln(X1a) |
|-------|------------|-----|----|---------|
| 1     | 2          | 0.79| 0.21| -0.24162057|
| 2     | 3.0125     | 0.75| 0.25| -0.28357529|
| 3     | 4.025      | 0.72| 0.28| -0.33240155|
| 4     | 5.0375     | 0.68| 0.32| -0.380463806|
| 5     | 6.05       | 0.68| 0.32| -0.386416913|
| 6     | 7.0625     | 0.65| 0.35| -0.436427334|
| 7     | 8.075      | 0.60| 0.40| -0.518797393|
| 8     | 9.0875     | 0.61| 0.39| -0.498246842|
| 9     | 10         | 0.59| 0.41| -0.522521664|
| 10    | 11.1125    | 0.53| 0.47| -0.34650974|
| 11    | 12.125     | 0.52| 0.48| -0.466627165|
| 12    | 13.1375    | 0.49| 0.51| -0.704981638|
| 13    | 14.15      | 0.48| 0.52| -0.735076795|
| 14    | 15.1625    | 0.45| 0.55| -0.78645736|
| 15    | 16.17      | 0.42| 0.58| -0.879249466|

Catalyst 11

11a, 11a, 1a and 1a signals from the 1H NMR spectra (Figure S22 as example) were integrated to calculate the molar fraction (X). All data are collected in Table S18 and Table S19; plotting Ln(X3a/11a) versus time gave the equation shown in Figure S21 from which the half-life was calculated:

\[ y = -0.0438x - 0.1310 \]

\[ r^2 = 0.98 \]
Figure S22. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure 2.

$^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure S22. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure 2. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure S22. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure 2. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure S22. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure 2. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure S22. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure 2. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure S22. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure 2. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure S22. $^1$H NMR spectrum (9.8 – 7.4 ppm) for methanolysis of 3a and 11a at 16.20 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 

Figure 2.
Variation of molar fraction with time for methanolysis of 3a.

| Entry | Time (min) | Xa, Xb | Lt(Xa) |
|-------|------------|--------|--------|
| 1     | 1.5        | 0.70   | -0.39056872 |
| 2     | 2.5        | 0.69   | 0.37193556  |
| 3     | 3.5        | 0.68   | -0.38592401 |
| 4     | 4.5        | 0.66   | -0.41210961 |
| 5     | 5.5        | 0.66   | -0.41871033 |
| 6     | 6.5        | 0.64   | -0.45107561 |
| 7     | 7.5        | 0.62   | -0.47623417 |
| 8     | 8.5        | 0.61   | -0.48850015 |
| 9     | 9.5        | 0.60   | -0.51282362 |
| 10    | 10.5       | 0.61   | -0.49850015 |
| 11    | 11.5       | 0.60   | -0.51879373 |
| 12    | 12.5       | 0.57   | -0.56531389 |
| 13    | 13.5       | 0.56   | -0.56221562 |
| 14    | 14.5       | 0.56   | -0.57681336 |
| 15    | 15.5       | 0.53   | -0.62593843 |
| 16    | 16.5       | 0.53   | -0.63127177 |
| 17    | 17.5       | 0.52   | -0.65235186 |
| 18    | 18.5       | 0.50   | -0.69813472 |
| 19    | 19.5       | 0.50   | -0.69813472 |
| 20    | 20.5       | 0.51   | -0.67294447 |
| 21    | 21.5       | 0.49   | -0.71783973 |
| 22    | 22.5       | 0.49   | -0.71783973 |
| 23    | 23.5       | 0.47   | -0.76546784 |
| 24    | 24.5       | 0.45   | -0.78845736 |
| 25    | 25.5       | 0.45   | -0.79750719 |
| 26    | 26.5       | 0.44   | -0.81090216 |
| 27    | 27.5       | 0.43   | -0.85415328 |

[a] Time relative to the first NMR measured.

Methanolysis 3a vs 12a

![Figure S23](image-url)
Figure S24. $^1$H NMR spectrum (9.6 – 7.4 ppm) for methanolysis of 3a and 12a at 1 min relative to the first NMR measured in 5% CD$_3$OD in CDCl$_3$. 
4.2. Hydrolysis studies

Hydrolysis of acetylated catalyst 3a

Acetylated catalyst 3a (1.72 mg, 0.0028 mmol) was dissolved in 0.625 mL of a 4/1 v/v solution of DMSO-\textsubscript{d6}/D\textsubscript{2}O. \textsuperscript{1}H NMR spectra were recorded periodically and were integrated to calculate the molar fractions (X). All data are collected in Table S22; plotting Ln[X\textsubscript{3a}] versus time gave the equation shown in Figure S25 from which the half-life was calculated.

Table S22. Variation of molar fraction with time for hydrolysis of 3a.

| Entry | Time\(\text{min}\) | \(X\textsubscript{3a}\) | \(X\textsubscript{3}\) | Ln(X\textsubscript{3a}) |
|-------|-------------------|-----------------|-----------------|------------------|
| 1     | 0                 | 1               | 0               | -0.96698385      |
| 2     | 235.2             | 0.62            | 0.38            | -1.3012913       |
| 3     | 445.2             | 0.75            | 0.25            | -1.58310844      |
| 4     | 570               | 0.79            | 0.21            | -0.96698385      |

[a] Time relative to the first NMR measured.

Figure S25. Plotting of Ln[X\textsubscript{3a}] vs time.

Hydrolysis of 2-ethylhexyl acetate under biphasic conditions

Catalyst 3 (ca. 10 mg, 0.0162 mmol, 0.5 mol%) was dissolved in 2-ethylhexyl acetate (ca. 500 mg, 3.84 mmol), mixed with 1 mL of a saturated aqueous solution of Na\textsubscript{2}CO\textsubscript{3}, K\textsubscript{2}HPO\textsubscript{4} or N,N-diisopropylethylamine and stirred in a closed reaction vessel for 13 hours at 100 °C. Traces of product were detected by \textsuperscript{1}H NMR.

Hydrolysis of 2-ethylhexyl acetate under biphasic conditions with THF

Catalyst 3 (12.88 mg, 0.021 mmol, 0.5 mol%) was dissolved in 2-ethylhexyl acetate (500 mg, 3.84 mmol), THF (0.5 mL), mixed with 0.5 mL of a saturated aqueous solution of Na\textsubscript{2}CO\textsubscript{3} and stirred in a closed reaction vessel for 79.7 hours at 100 °C. 2.5 % yield was determined by \textsuperscript{1}H NMR integration after removing THF under vacuum. A control reaction was set up in the absence of catalyst, showing a 0.8% yield.

Hydrolysis of ethyl acetate under homogenous conditions

Catalyst 3 (12.88 mg, 2.1 mmol, 2.2 mol%) was dissolved in 0.3 mL of a homogenous mixture of EtOAc/Et\textsubscript{3}N/CD\textsubscript{3}CN/D\textsubscript{2}O 5.6/7.8/2.8/1 v/v and heated at 50 °C for 48.5 hours in a sealed NMR tube. The reaction progress was determined by \textsuperscript{1}H NMR analysis.

4.3. Transesterification studies

Transesterification of ethyl acetate

Catalysts 3, 3+6b, 6b and 10 were used to promote the transesterification of ethyl acetate with methanol. 1 mol% of catalyst was dissolved in a 1:1.4 v/v mixture of EtOAc:MeOH and the subsequent solution was placed into a sealed NMR tube with a sealed capillar tube inside containing D\textsubscript{2}O to lock the NMR spectrometer. The sample was heated at 50°C and \textsuperscript{1}H NMR spectra were recorded periodically. The reaction progress was followed by integration of the \textsuperscript{1}H NMR signals of the product and the starting material.
Ethyl acetate transesterification with methanol

Figure S26: Plotting of methyl acetate yield vs time (left) and \(^1\)H NMR spectra for transesterification of ethyl acetate with methanol catalysed with 3, 3+6b, 6b and 10.
Table S23. Transesterification of ethyl acetate with methanol using 10.

| Entry | Time/h | CH\textsubscript{3}COOCH\textsubscript{2}CH\textsubscript{3}[a] | CH\textsubscript{3}COOCH\textsubscript{3} \textsubscript{+} CH\textsubscript{3}CH\textsubscript{2}OH[a] | Yield/% |
|-------|--------|-------------------|---------------------------------|--------|
| 1     | 0      | 2                 | ---                             | 0      |
| 2     | 22.5   | 29.4              | 5                               | 6.4    |
| 3     | 56.3   | 10.9              | 5                               | 15.5   |
| 4     | 118.3  | 5.4               | 5                               | 27.0   |
| 5     | 175.3  | 3.1               | 5                               | 39.2   |
| 6     | 285.6  | 2.4               | 5                               | 45.5   |
| 7     | 622.1  | 1.5               | 5                               | 57.1   |

[a] Integral value for protons in bold

Table S24. Transesterification of ethyl acetate with methanol using 3.

| Entry | Time/h | CH\textsubscript{3}COOCH\textsubscript{2}CH\textsubscript{3}[a] | CH\textsubscript{3}COOCH\textsubscript{3} \textsubscript{+} CH\textsubscript{3}CH\textsubscript{2}OH[a] | Yield/% |
|-------|--------|-------------------|---------------------------------|--------|
| 1     | 0      | 2                 | ---                             | 0      |
| 2     | 135    | 10.14             | 5                               | 16.5   |
| 3     | 276.5  | 4.59              | 5                               | 30.3   |
| 4     | 381.3  | 3.18              | 5                               | 38.6   |
| 5     | 443.1  | 2.60              | 5                               | 43.5   |

[a] Integral value for protons in bold

Table S25. Transesterification of ethyl acetate with methanol using 3-6b.

| Entry | Time/h | CH\textsubscript{3}COOCH\textsubscript{2}CH\textsubscript{3}[a] | CH\textsubscript{3}COOCH\textsubscript{3} \textsubscript{+} CH\textsubscript{3}CH\textsubscript{2}OH[a] | Yield/% |
|-------|--------|-------------------|---------------------------------|--------|
| 1     | 0      | 2                 | ---                             | 0      |
| 2     | 135    | 11.64             | 5                               | 14.7   |
| 3     | 276.5  | 5.43              | 5                               | 26.9   |
| 4     | 381.3  | 3.95              | 5                               | 33.6   |
| 5     | 443.1  | 3.21              | 5                               | 38.4   |

[a] Integral value for protons in bold

Table S26. Transesterification of ethyl acetate with methanol using 6b.

| Entry | Time/h | CH\textsubscript{3}COOCH\textsubscript{2}CH\textsubscript{3}[a] | CH\textsubscript{3}COOCH\textsubscript{3} \textsubscript{+} CH\textsubscript{3}CH\textsubscript{2}OH[a] | Yield/% |
|-------|--------|-------------------|---------------------------------|--------|
| 1     | 0      | 2                 | ---                             | 0      |
| 2     | 135    | 2                 | ---                             | 0      |
| 3     | 276.5  | 2                 | ---                             | 0      |
| 4     | 381.3  | 2                 | ---                             | 0      |
| 5     | 443.1  | 2                 | ---                             | 0      |

[a] Integral value for protons in bold
Transesterification of acetylcholine

7.5 mg of catalyst 3 (2 mol%) were dissolved in a mixture of acetylcholine chloride (111 mg, 0.61 mmol), ethyl acetate (0.124 mL, 1.27 mmol) and methanol (0.176 mL, 3.03 mmol). The solution was placed into a sealed NMR tube with a sealed capilar tube inside containing D$_2$O to lock the NMR spectrometer. The sample was heated at 50°C for 62 hours. The reaction progress was followed by integration of the $^1$H NMR signals of the product and the starting material.

![Chemical structure](image)

Figure S27. Competitive transesterification of acetylcholine and ethyl acetate with methanol (1:2:4.8 mol ratio) using catalyst 3 (2 mol%) at 50°C. Yield was determined by $^1$H NMR integration.
Figure S28. $^1$H and $^{13}$C NMR spectra of compound 13 in DMSO-d$_6$. 
Figure S29. $^1$H and $^{13}$C NMR spectra of compound 15 in DMSO-d$_6$.
Figure S3. $^{1}H$ and $^{13}C$ NMR spectra of catalyst 3 in CDCl$_3$. 
Figure S31. $^1$H and $^{13}$C NMR spectra of catalyst 3a in CDCl$_3$. 
Figure S32. $^1$H and $^{13}$C NMR spectra of compound 17 in DMSO-d$_6$. 
Figure S33. $^1$H and $^{13}$C NMR spectra of catalyst 4 in CDCl$_3$
Figure S3. $\text{H}$ and $\text{C}$ NMR spectra of catalyst 4a in CDCl$_3$. 

- 175.81
- 166.69
- 149.24
- 133.91
- 131.63
- 130.20
- 129.33
- 128.96
- 128.25
- 127.32
- 126.91
- 126.01
- 122.81
- 77.36
- 62.24
- 54.88
- 51.97
- 43.82
- 40.61
- 34.78
- 23.81
- 21.73
Figure S3. $^\text{1}H$ and $^{13}C$ NMR spectra of compound 18 in DMSO-d$_6$. 

SUPPORTING INFORMATION
Figure S36. $^1$H and $^{13}$C NMR spectra of catalyst 5 in CDCl$_3$. 
Figure S3. $^1$H and $^{13}$C NMR spectra of catalyst 5a in CDCl$_3$. 
Figure S38. $^1$H and $^{13}$C NMR spectra of compound 19 in DMSO-$d_6$. 
Figure S39. $^1$H and $^{13}$C NMR spectra of catalyst 6 in CDCl$_3$. 
Figure S40. $^1$H and $^{13}$C NMR spectra of catalyst 6a in CDCl$_3$. 
Figure S41. ${^1}H$ and ${^{13}C}$ NMR spectra of catalyst 6a in CDCl$_3$. 
Figure S42. $^1$H and $^{13}$C NMR spectra of compound 20 in DMSO-d$_6$. 
Figure S43. \(^1\)H and \(^{13}\)C NMR spectra of compound 22 in DMSO-\(d_6\).
Figure S44. $^1$H and $^{13}$C NMR spectra of compound 23 in DMSO-d6.
Figure S45. $^1$H and $^{13}$C NMR spectra of catalyst 7 in CD$_3$OD.
Figure S46. $^1$H and $^{13}$C NMR spectra of catalyst 7a in CDCl$_3$.
Figure S47. $^1$H and $^{13}$C NMR spectra of compound 25 in DMSO-$d_6$. 
Figure S48. $^1$H and $^{13}$C NMR spectra of compound 26 in DMSO-d$_6$. 
Figure S49. $^1$H and $^{13}$C NMR spectra of catalyst 8 in CDCl$_3$. 
Figure S5. ¹H and ¹³C NMR spectra of catalyst 8a in CDCl₃.
Figure S51. $^1$H and $^{13}$C NMR spectra of compound 27 in DMSO-d$_6$. 
Figure S52. $^1$H and $^{13}$C NMR spectra of compound 28 in DMSO-d$_6$. 
Figure S5. $^1$H and $^{13}$C NMR spectra of catalyst 9 in 5% CD$_3$OD in CDCl$_3$. 

[Spectral details and peaks highlighted]
Figure S54. $^1$H and $^{13}$C NMR spectra of catalyst 9a in CDCl$_3$. 
Figure S5. $^1$H and $^{13}$C NMR spectra of compound 30 in DMSO-$d_6$. 
Figure S56. $^1$H and $^{13}$C NMR spectra of compound 31 in DMSO-$d_6$. 
Figure S57. $^1$H and $^{13}$C NMR spectra of catalyst 10 in CDCl$_3$. 
Figure S58. $^1$H and $^{13}$C NMR spectra of catalyst 10a in CDCl$_3$. 
Figure S59. $^1$H and $^{13}$C NMR spectra of compound 33 in DMSO-$d_6$. 
Figure S60. $^1$H and $^{13}$C NMR spectra of catalyst 11 in CDCl$_3$. 
Figure S61. $^1$H and $^{13}$C NMR spectra of catalyst 11a in CDCl₃.
Figure S62. $^1$H and $^{13}$C NMR spectra of compound 34 in DMSO-$d_6$. 
Figure S63. $^1$H and $^{13}$C NMR spectra of catalyst 12 in 5% CD$_3$OD in CDCl$_3$. 
Figure S64. $^1$H and $^{13}$C NMR spectra of catalyst 12a in CDCl$_3$. 
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