Supporting information

A simple, safe and robust system for hydrogenation "without high-pressure gases" under batch and flow conditions using a liquid organic hydrogen carrier.

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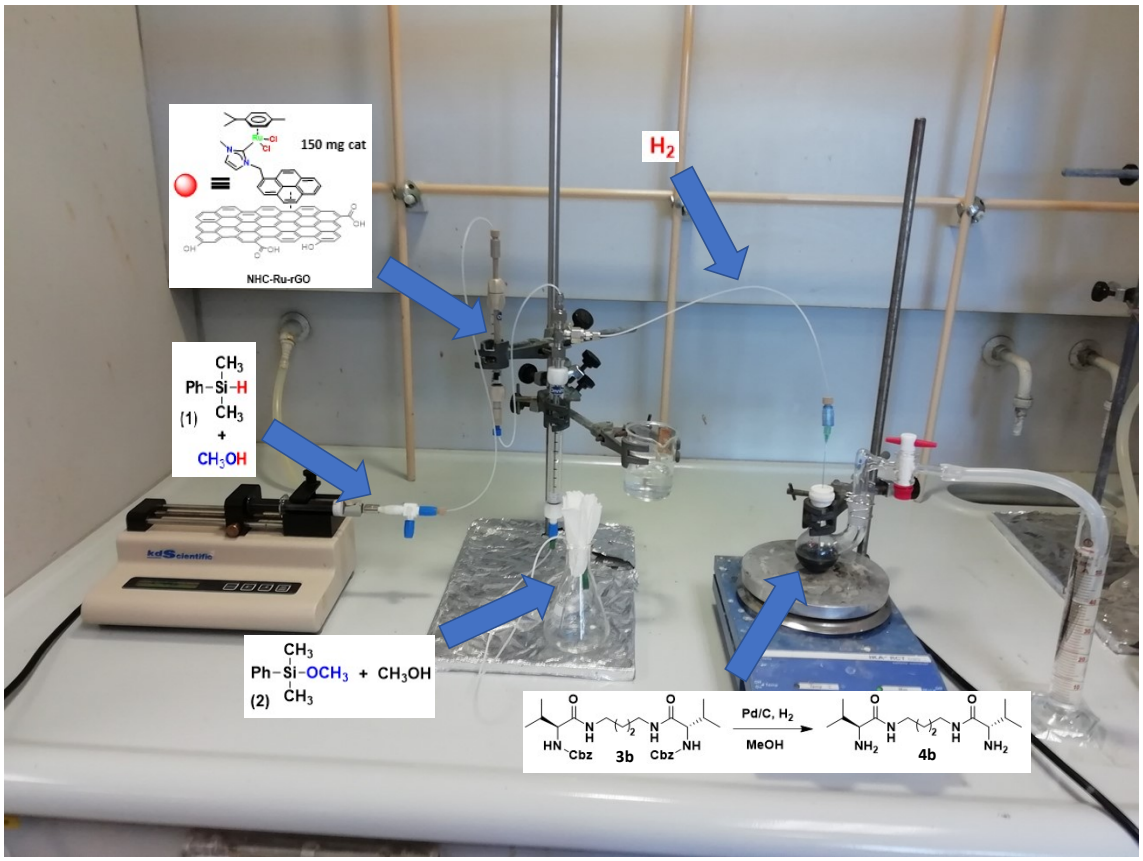
Separate ESI file attached.

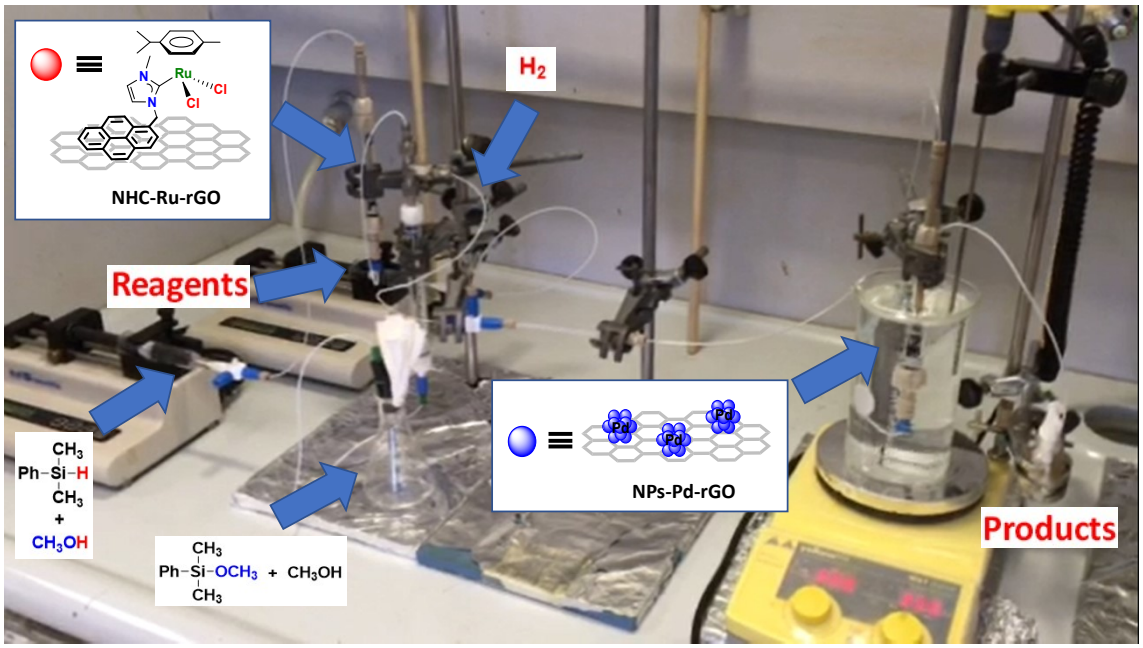
SI2. Video of set-up optimized to continuous production of hydrogen.

Separate ESI file attached.

SI3. Set-up for the hydrogenation of different reagents under batch conditions.

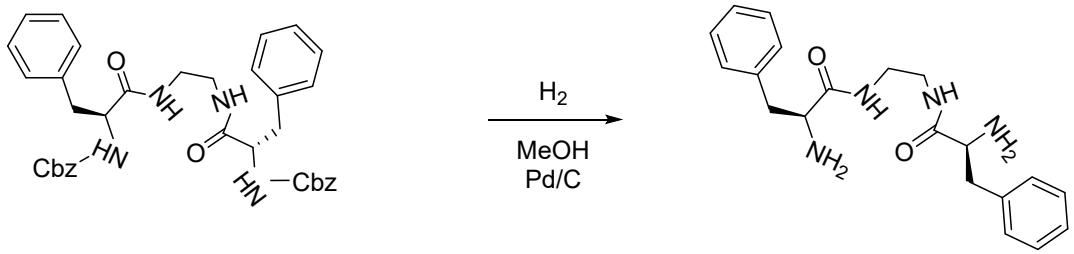


SI4. Set-up for the hydrogenation of different reagents under flow conditions.



SI5. Video of the hydrogenation of different reagents under flow conditions.

Separate ESI file attached.



Experimental: 0.352g (0.565 mmol) of N-Cbz-PheA2 (**3a**) were added to 15mL of MeOH in a 50mL twin-neck round bottom flask. After two minutes of sonication, a white suspension was observed. The suspension was purged with three N_2 balloons and stirred at room temperature. 0.120g (10mol%) of Pd/C (5% metal basis) were added to the flask while another N_2 balloon was purging the system to maintain the inert atmosphere. The exit of the reactor was bubbled into the suspension through a syringe needle, serving as the hydrogen source. To avoid over-pressures, another syringe needle connected to a flow tube was introduced on the suspension and bubbled into a water solution, where some bubbles could be observed. After 4 hours of reaction, the black suspension was filtered off with the aid of Celite and the final clear methanolic solution was dried under reduced vacuum at 35 ºC, affording pure **4a** as a white solid. Yield: 94% (0.188 g, 0.531 mmol).

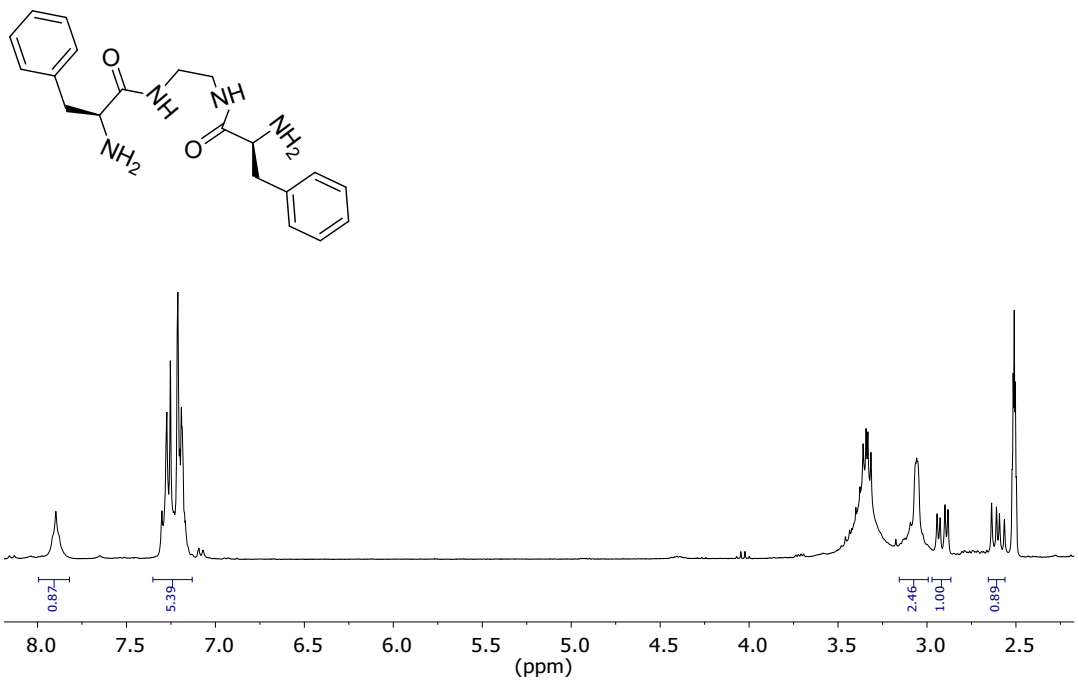
Characterization:

mp= 118-119 °C;

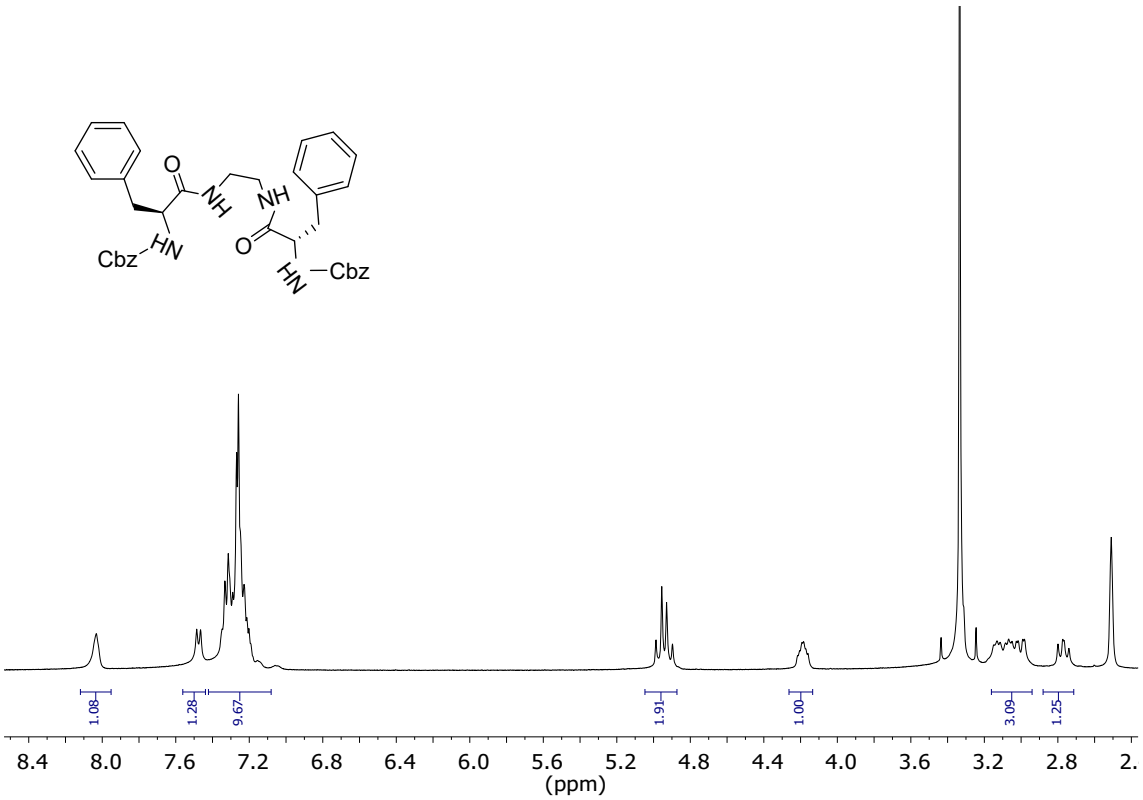
$[\alpha]^{25}_{D}$= -86.9º (c = 0.1, $CHCl_3$); IR(KBr): 3358, 3299, 1655, 1529 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6)(δ, ppm): δ= 7.89 (d, *J* = 5.8 Hz, 1H), 7.35 – 7.13 (m, 5H), 3.16 – 2.99 (m, 2H), 2.91 (dd, *J* = 13.3, 5.1 Hz, 1H), 2.60 (dd, *J* = 13.3, 8.2 Hz, 1H); ^{13}C-NMR (125 MHz, CDCl3) (δ, ppm): δ= 39.1, 40.9, 56.2, 126.3, 128.2, 128.8, 137.4, 174.7;

ESI-MS (*m*/*z*) 355.1 ($M + H^+$), 377.1 ($M + Na^+$);

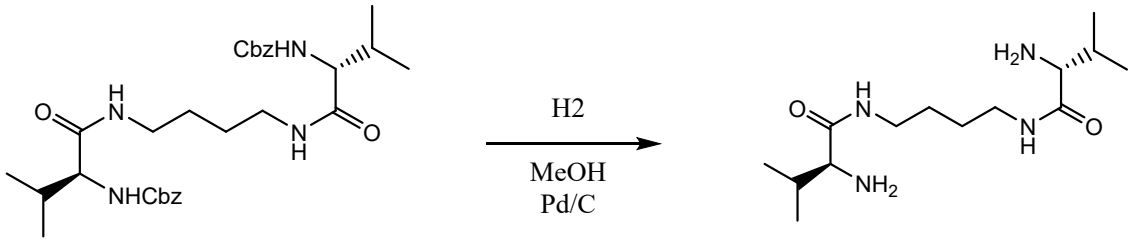
Anal. Calcd. For $C_{20}H_{26}N_4O_2$: C, 67.8; H, 7.4; N, 15.8. Found: C, 67.9; H, 7.8; N, 16.0.



SI6. ^{1}H-NMR spectrum of 3a in DMSO-d_6.



SI7. ^{1}H-NMR spectrum of 3b in DMSO-d_6.



Experimental: 0.643g (1.159 mmol) of N-Cbz-ValA4 (**3b**) were added to 20mL of MeOH in a 50mL twin-neck round bottom flask. After two minutes of sonication, a white suspension was observed. The suspension was purged with three N_2 balloons and stirred at room temperature. 0.246g (10mol%) of Pd/C (5% metal basis) were added to the flask while another N_2 balloon was purging the system to maintain the inert atmosphere. The exit of the reactor was bubbled into the suspension through a syringe needle, serving as the hydrogen source. To avoid over-pressures, another syringe needle connected to a flow tube was introduced on the suspension and bubbled into a water solution, where some bubbles could be observed. After 4 hours of reaction, the black suspension was filtered off with the aid of Celite and the final clear methanolic solution was dried under reduced vacuum at 35 ºC, affording pure **4b** as a white solid. Yield: 96% (0.318 g, 1.113 mmol). Characterization:

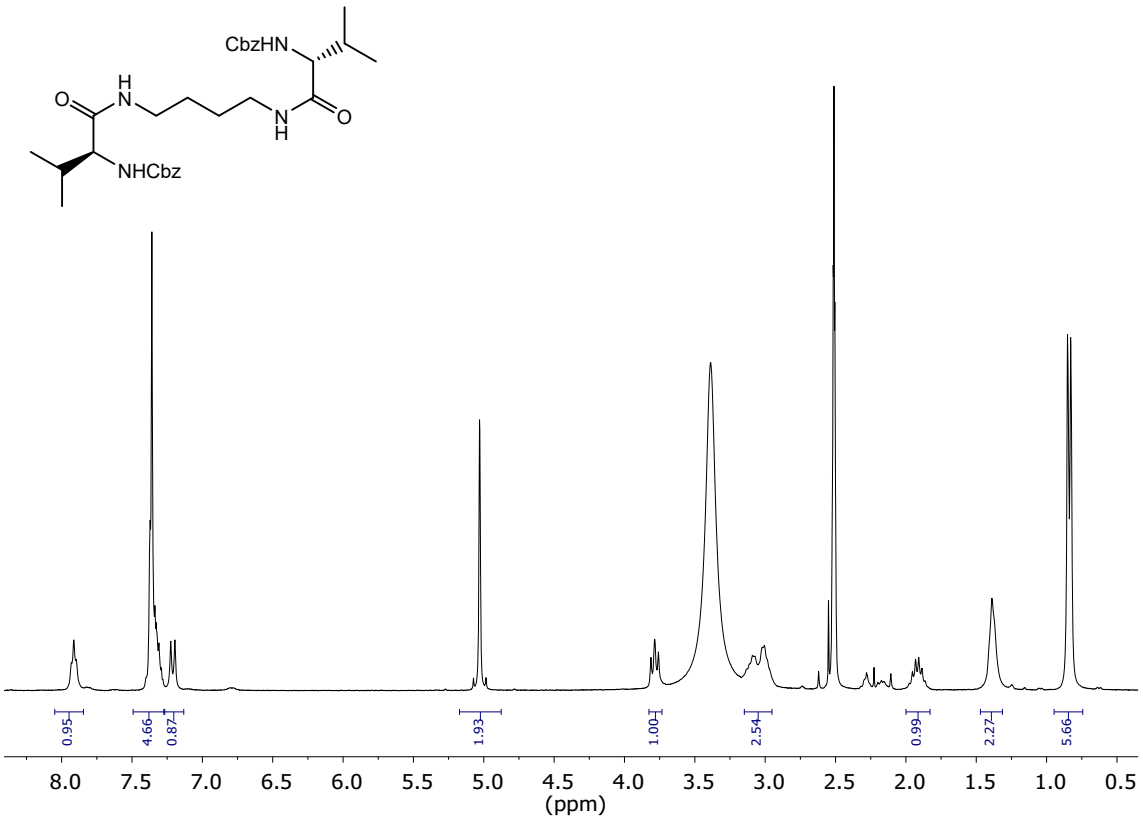
mp 109-110 °C;

$[\alpha]^{25}_D$ = -48.4° (c 0.1, $CHCl_3$); IR (KBr) 3294, 1641, 1547 cm^{-1} ;

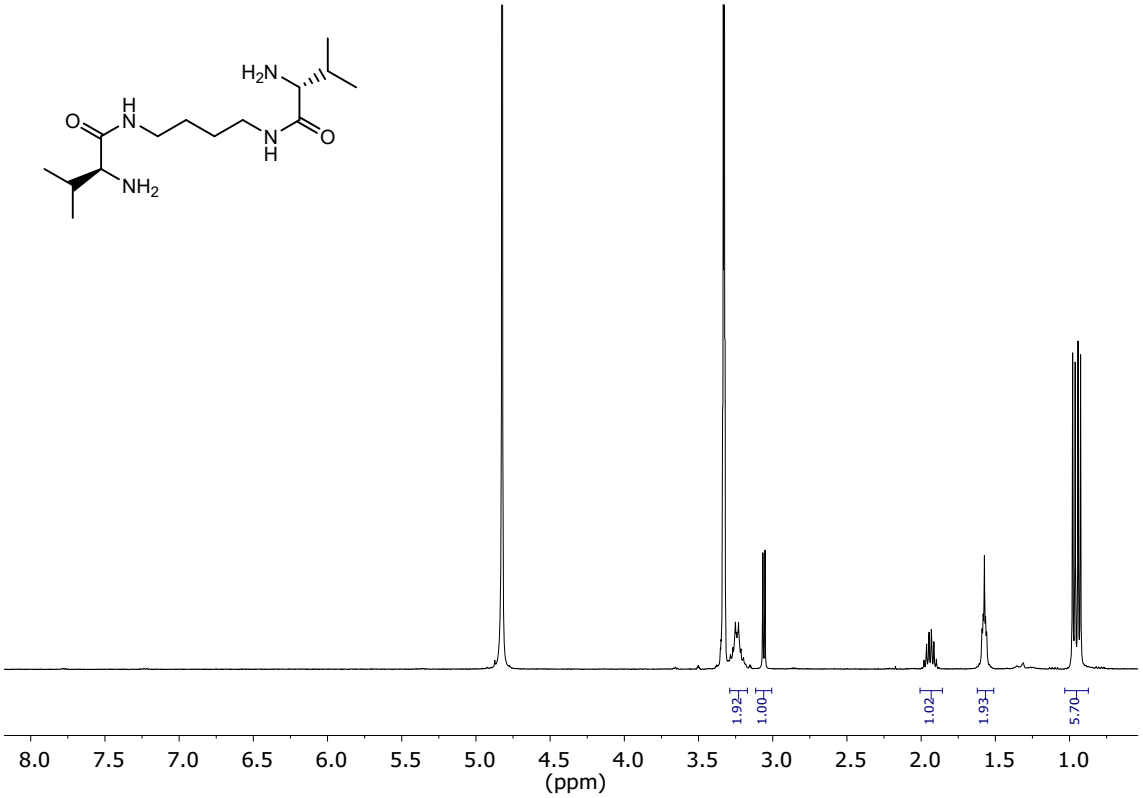
^{1}H-NMR (300 MHz, CDCl3) δ= 0.71 (d, 6H, J = 6.8 Hz), 0.85 (d, 6H, J= 7.1 Hz), 1.39-1.43 (m, 8H), 2.08 (m, 2H), 3.05 (d, 2H, J = 4.2 Hz), 3.14 (m, 4H), 7.27 (br s, 2H); ^{13}C-NMR (75 MHz,$CDCl_3$) δ= 16.2, 19.5, 27.0, 30.9, 38.4, 60.2, 174.1;

ESI-MS m/z = 143.2 (M + 2H+);

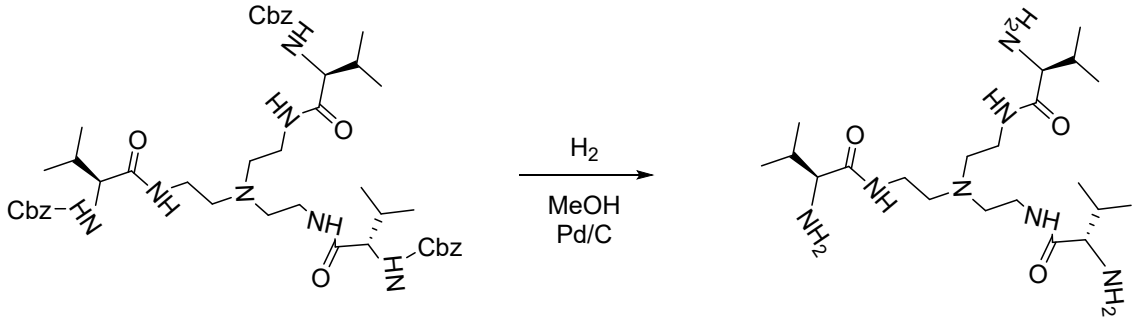
Anal. Calcd. for C14H30N4O2: C, 58.7; H, 10.6; N, 19.6. Found: C, 58.9; H, 10.8; N 19.7.



SI8. ^{1}H-NMR spectrum of 3b in DMSO-d_6.



SI9. ^{1}H-NMR spectrum of 4b in CD_3OD.



Experimental: 0.482g (0.570 mmol) of N-Cbz-Val-TREN (**3c**) were added to 15mL of MeOH in a 50mL twin-neck round bottom flask. After two minutes of sonication, a clear solution was observed. The solution was purged with three N_2 balloons and stirred at room temperature. 0.121g (10mol%) of Pd/C (5% metal basis) were added to the flask while another N_2 balloon was purging the system to maintain the inert atmosphere. The exit of the reactor was bubbled into the suspension through a syringe needle, serving as the hydrogen source. To avoid over-pressures, another syringe needle connected to a flow tube was introduced on the suspension and bubbled into a water solution, where some bubbles could be observed. After 3 hours of reaction, the black suspension was filtered off with the aid of Celite and the final clear methanolic solution was dried under reduced vacuum at 35 ºC, affording pure **4c** as a colourless oil. Yield: 98% (0.248 g, 0.558 mmol). Characterization:

mp= 118-123 °C;

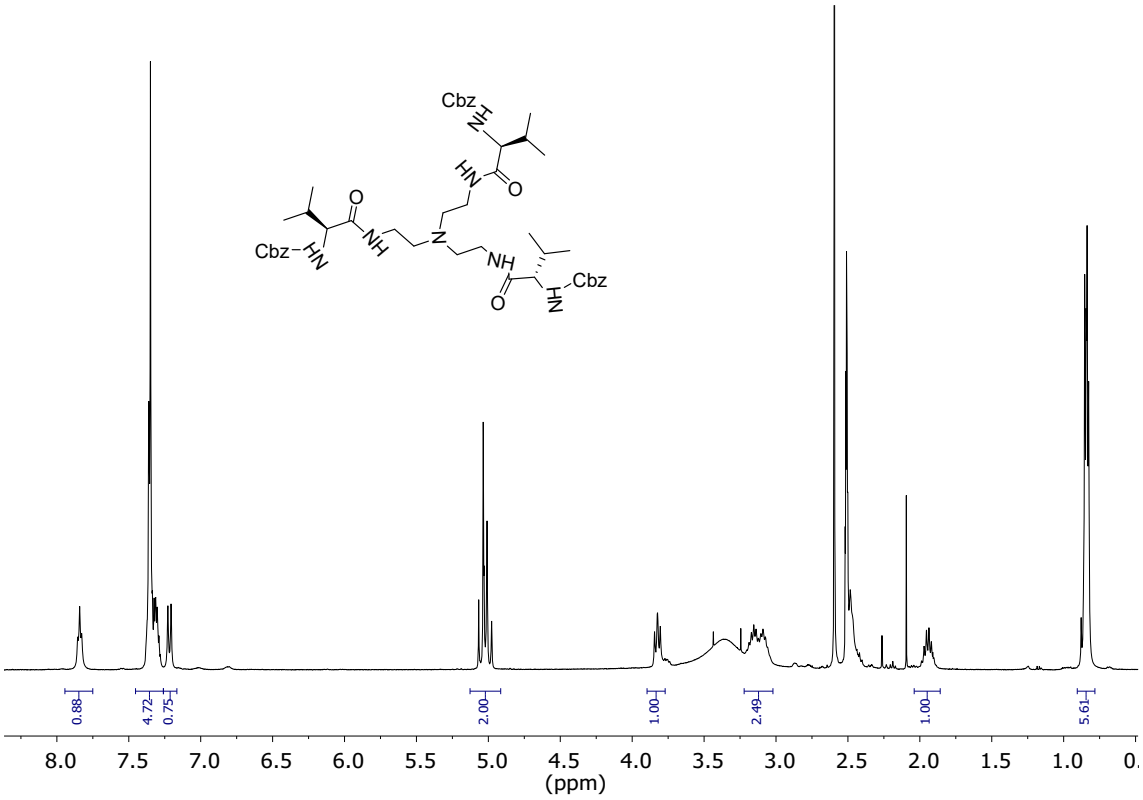
$[\alpha]^{25}_{D}$= -10.4º (c = 0.01, $CHCl_3$);

ATR-FTIR: 3290, 2956, 1629, 1555, 1464, 1229, 1103, 1088 cm^{-1}; ^{1}H-NMR (300 MHz, CD_3OD)(δ, ppm): δ= 3.21 – 3.16 (m, 2H), 3.01 (d, *J* = 5.6 Hz, 1H), 2.55 (t, *J* = 6.4 Hz, 2H), 1.87 (pd, *J* = 6.9, 5.6 Hz, 1H), 0.85 (dd, *J* = 15.4, 6.9 Hz, 6H); ^{13}C-NMR (125 MHz, CDCl3) (δ, ppm): δ= 16.4, 19.7, 31.1, 37.3, 54.4, 60.4, 174.6;

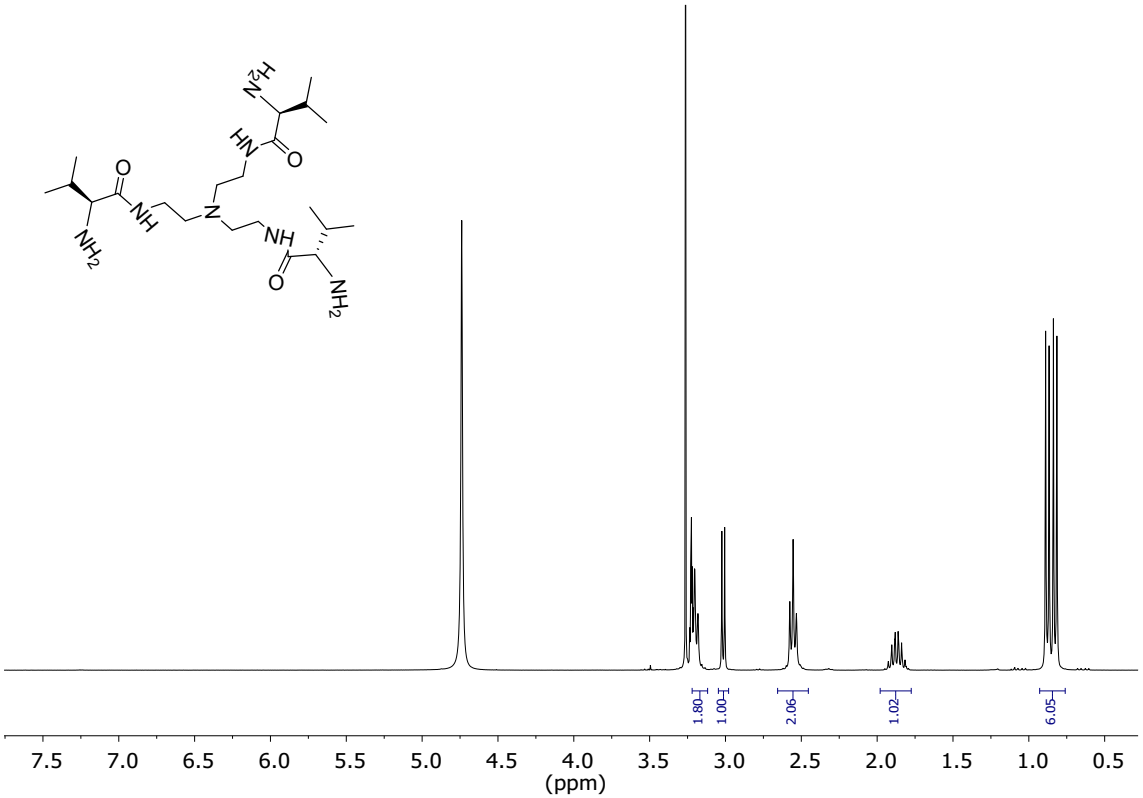
ATR-FTIR: 3282, 2958, 1639, 1534 cm-1;

HRMS (ESI-TOF)+ Calc for C21H45N7O3 [**9**+H]+ 444.3662 m/z, found 444.3662 m/z;

Anal. calcd. for C21H45N7O3: C, 56.86, H, 10.22, N, 22.10, found: C, 56.6, H, 10.0, N, 22.0.



SI10. ^{1}H-NMR spectrum of 3c in DMSO-d_6.



SI11. ^{1}H-NMR spectrum of 4c in CD_3OD.