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Molecular Flavin Catalysts for C-H Functionalisation and Dehydroamino Acid Derivatisation

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1. Materials and Methods

1.1. Synthetic Techniques, Solvents, and Chemicals

Room temperature is defined as 21–23°C. All reactions with air-sensitive reactants were carried out under an argon atmosphere (Ar 4.8) applying standard *Schlenk* technique. Unless otherwise noted, all chemicals were obtained from Sigma-Aldrich, Acros, TCI, abcr, Fisher Scientific, or Alfa Aesar and used without further purification. Dichloromethane (2×MB-KOL-A type 2, aluminium oxide), diethyl ether (1×MB-KOL-A type 2, aluminium oxide), and tetrahydrofuran (2×MB-KOL-M type 2, 3 Å molecular sieves) were obtained from an MBSPS 800 MBraun solvent purification system. All other solvents were purchased from commercial suppliers and used without further purification unless otherwise noted.

1.2. NMR Spectroscopy

NMR spectra were recorded on Bruker AVHD-300, AVHD-400, AVHD-500, or AV-III-500 spectrometers at ambient temperature unless otherwise noted. Deuterated NMR solvents were purchased from Deutero GmbH or Sigma-Aldrich and were used without further purification. Spectra were processed with MestReNova 10.0.1 using the manual phasing and polynomial baseline correction capabilities. Splitting was determined using the multiplet analysis function with manual intervention as necessary. Spectral data is reported as follows: Chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), multiplet (m)], coupling constant, integration, assignment). Broad signals are labeled as such (br). Chemical shifts are reported in ppm (δ) and coupling constants are reported in Hz. Resonances are referenced to solvent residual signals.[1] Assignment of all signals was performed by two-dimensional experiments (^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC-ME, and ^{1}H-^{13}C HMBC). In cases where an unambiguous assignment was not possible, this is indicated by "/" between atom positions in question, while "," is used in cases where resonances of two or more atoms overlap. Apparent multiplets which occur as a result of accidental equality of coupling constants to those of

[1] G. R. Fulmer, A. J. M. Miller, N. H. Sherden, H. E. Gottlieb, A. Nudelman, B. M. Stoltz, J. E. Bercaw, K. I. Goldberg, *Organometallics* **2010**, *29*, 2176–2179.

magnetically non-equivalent protons are marked as virtual (*virt.*). Note: Small deviations in chemical shifts may be observed depending on the concentration of NMR samples.

1.3. Mass Spectrometry

High-resolution mass spectrometry was performed on Thermo Scientific LTQ-FT Ultra (HR-ESI) or DFS GC-MS (HR-EI) instruments.

1.4. Infrared Spectroscopy

Infrared spectra were recorded on a Perkin Elmer Frontier ATR/FT-IR spectrometer, and $\tilde{\nu}_{max}$ are reported in cm^{-1}. The signal intensity is assigned using the following abbreviations: s (strong), m (medium), and w (weak).

1.5. Liquid Chromatography

Analytical HPLC measurements were performed on Thermo Fisher Ultimate 3000 series instruments equipped with a Diode Array Detector and/or MS Detector.

Analytical thin-layer chromatography was performed using 60 Å Silica Gel F254 (Merck) pre-coated glass plates. TLC plates were visualized by irradiation with a UV lamp or staining. Preparative flash column chromatography was performed on silica 60 (Merck, 230-400 mesh).

1.6. Photochemistry

UV/Vis spectroscopy was performed with a Perkin Elmer Lambda 35 UV/Vis spectrometer. Spectra were recorded using a Hellma precision cell made of quartz SUPRASIL®.

Luminescence experiments were performed on Horiba Scientific FluoroMax-4P instrument (part number J810005 rev. C) equipped with a continuous Xe-source for steady state spectra. Spectra were recorded in quartz tubes (4 mm internal diameter) in a quartz dewar vessel which was filled with liquid nitrogen for recording spectra at cryogenic temperatures (77K). All solutions were handled under a dry nitrogen atmosphere to ensure that no oxygen was present during the measurements.

Initial screening of photochemical reactions were performed with a Kessil® A160WE Tuna Blue LED (**figure SI-01**). Optimized photochemical reactions were carried out in crimp-cap vials using a 1W 451 nm LED (Osram Oslon SSL 80 LDCQ7P-2U3U, 1W, 451 nm, 80°, 350 mA, 1000 mW / 28 lm, 1000 mA ca. 210%) (**figure SI-02**).

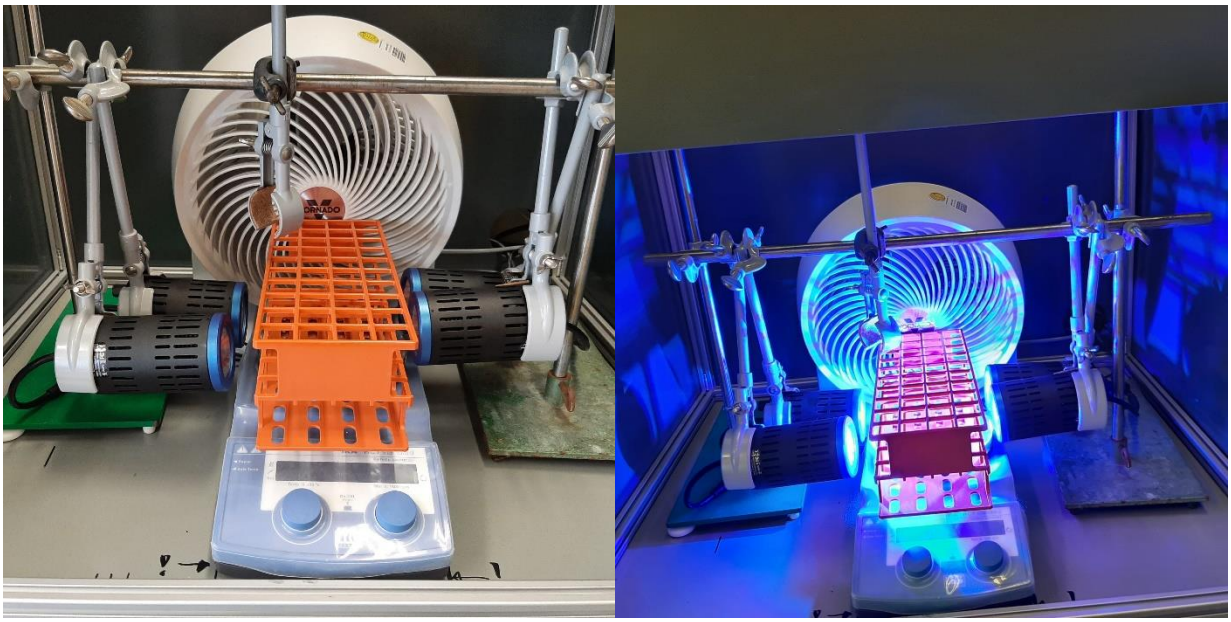


Figure SI-01: Kessil® A160WE Tuna Blue irradiation setup disabled (left) and enabled (right).

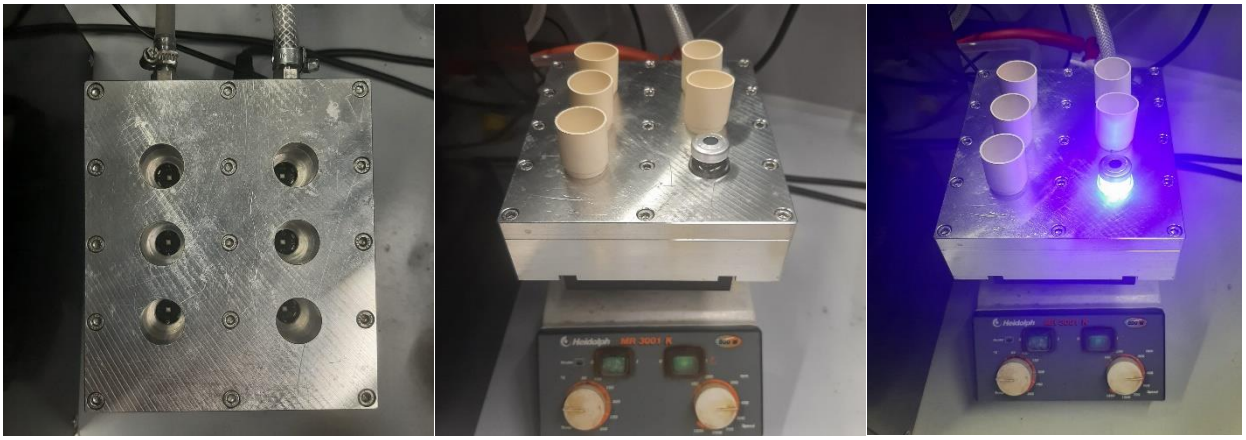
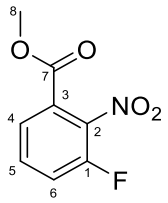


Figure SI-02: Irradiation setup (λ_{max} = 451 nm) with six slots from above (left), disabled (middle) and enabled (right).

2. Synthetic Procedures

2.1. Flavin Synthesis

2.1.1. Methyl 3-fluoro-2-nitrobenzoate (SI-01)



SI-01

This is a known compound and it has been synthesized according to a modified literature procedure.[2] 3-Fluoro-2-nitrobenzoic acid (3.00 g, 16.2 mmol, 1.00 equiv.) and oxalyl chloride (1.42 mL, 2.10 g, 16.5 mmol, 1.02 equiv.) were suspended in DCM (anhydrous, 48.0 mL, 0.34 M) in a 250 mL *Schlenk* flask. Then DMF (18 drops) was slowly added dropwise to the mixture followed by stirring for one hour at room temperature. MeOH (17.7 mL, 14.0 g, 438 mmol, 27.0 equiv.) was added after which the mixture was cooled down to 0 °C. NEt_3 (11.3 mL, 8.20 g, 81.0 mmol, 5.00 equiv.) was added carefully, which led to gas formation and the mixture was stirred for three additional hours which resulted in a yellow solution. Water (150 mL) was added, the reaction mixture extracted with DCM (3 x 150 mL) and the combined organic phases were washed with citric acid (10 % aqueous, 1 x 150 mL) and $NaHCO_3$ solution (sat., aqueous, 1 x 150 mL). The organic phase was dried over Na_2SO_4 and concentrated *in vacuo* to give methyl 3-fluoro-2-nitrobenzoate (**SI-01**).

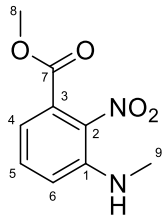
White solid (3.08 g, 15.5 mmol, 95 %); **TLC** (silica, DCM/MeOH 98:2): R_f = 0.91 [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 7.82 (dt, 1H, $^3J_{H\text{-}H}$ = 7.9, $^4J_{H\text{-}H}$ = 1.2 Hz, H-4), 7.58 (dd, 1H, $^3J_{H\text{-}H}$ = 8.8, 7.9 Hz, H-5), 7.46 (dd, 1H, $^3J_{H\text{-}H}$ = 8.8, $^4J_{H\text{-}H}$ = 1.2 Hz, H-6), 3.92 (s, 3H, H-8); **^{13}C{^{1}H} NMR** (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 163.0 (C-7), 153.7 (d, $^1J_{C\text{-}F}$ = 258.2 Hz, C-1), 139.5 (bs, C-2), 131.7 (C-5), 126.6 (C-4), 125.3 (C-3), 121.5 (d, $^2J_{C\text{-}F}$ = 19.4 Hz, C-6), 53.5 (C-8); **IR**: (ATR) $\tilde{\nu}$ [cm^{-1}]= 3084 (w, C-HAr), 2967 (w, C-H), 2853 (w, C-H), 1726 (s, C=O), 1591 (m,

[2] A. Shatskiy *et al.*, *ChemSusChem* **2019**, *12*, 2251.

C=C), 1541 (s, C=C), 1294 (s, C-N), 1007 (s), 902 (m), 761 (s, C-H_{Ar}), 721 (m, C-H_{Ar}). Analytical data is in accordance to literature. [2]

[2] A. Shatskiy *et al.*, *ChemSusChem* **2019**, *12*, 2251.

2.1.2. Methyl 3-(methylamino)-2-nitrobenzoate (SI-02)



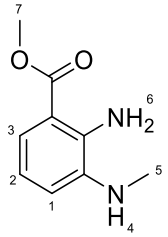
SI-02

This is a known compound and it has been synthesized according to a modified literature procedure.[2] In a 100 mL flask, methyl 3-fluoro-2-nitrobenzoate (**SI-01**) (3.08 g, 15.4 mmol, 1.00 equiv.) was mixed with K_2CO_3 (3.20 g, 23.2 mmol, 1.50 equiv.) and then $MeNH_2$ in THF (2 M, 38.6 mL, 77.2 mmol, 5.00 equiv.) was added. After stirring at room temperature overnight, the reaction mixture was concentrated, water (100 mL) was added and extracted with DCM (3 x 100 mL) from the reaction solution. The combined organic phases were washed with $NaHCO_3$ solution (sat., aqueous, 1 x 100 mL), dried over Na_2SO_4 and concentrated to give methyl 3-(methylamino)-2-nitrobenzoate (**SI-02**).

Red-orange oil (3.23 g, 15.4 mmol, 99%); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.73 [colored compound]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 7.54 (s, 1H, NH), 7.43 (ddt, 1H, $^3J_{H\text{-}H}$ = 9.0, 7.1, $^4J_{H\text{-}H}$ = 0.9 Hz, H-5), 6.92 (dd, 1H, $^3J_{H\text{-}H}$ = 9.0, $^4J_{H\text{-}H}$ = 1.4 Hz, H-6), 6.76 (dt, 1H, $^3J_{H\text{-}H}$ = 7.1, $^4J_{H\text{-}H}$ = 1.4 Hz, H-4), 3.88 (s, 3H, H-8), 3.01 (s, 3H, H-9); **^{13}C{^{1}H} NMR** (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 168.0 (C-7), 145.6 (C-1), 134.7 (C-5), 132.3 (C-3), 130.5 (C-2), 116.1 (C-4), 115.5 (C-6), 53.3 (C-8), 30.2 (C-9); **IR**: (ATR) $\tilde{\nu}$ [cm^{-1}] = 3397 (w, N-H), 2954 (w, C-H), 1732 (s, C=O), 1612 (s, C=C), 1550 (s, C=C), 1511 (s, C=C), 1289 (s, C-N), 1178 (m, C-O), 1121 (m), 1054 (m), 904 (m, N-H), 795 (m, C-H_{Ar}), 704 (m, C-H_{Ar}). Analytical data is in accordance to literature.[2]

[2] A. Shatskiy *et al.*, *ChemSusChem* **2019**, *12*, 2251.

2.1.3. Methyl 2-amino-3-(methylamino)benzoate (SI-03)



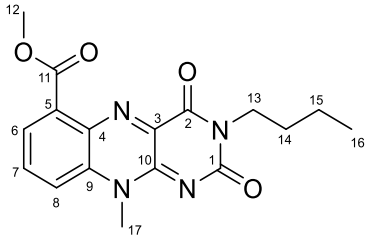
SI-03

The procedure for the reduction is literature-known.[3] Methyl 3-(methylamino)-2-nitrobenzoate (**SI-02**) (3.23g, 15.4 mmol, 1.00 equiv.) together with $Pd(OAc)_2$ (172 mg, 768 µmol, 0.05 equiv.) were dissolved in THF (87 mL) to give a dark-red solution. Subsequently KF (1.79 g, 30.7 mmol, 2.00 equiv.) was dissolved in water (35 mL) and added to the solution (0.13 M) while stirring. The reaction mixture was degassed by bubbling argon through the solution for 15 minutes followed by the slow addition of PMHS (3.70 mL, 61.5 mmol, 4.00 equiv.) under cooling (0 °C) to form a black solution. After stirring for an additional 40 minutes at room temperature, the reaction was extracted with DCM (3 x 150 mL) and washed with water (150 mL). The organic phase was filtered through a pad of neutral aluminium oxide (top layer) and Celite® (bottom layer) and rinsed with ethyl acetate (EA). Concentration *in vacuo* gave methyl 2-amino-3-(methylamino)benzoate (**SI-03**).

Light-brown solid (2.77 g, 15.4 mmol, 99 %); **TLC** (silica, DCM/MeOH 98:2): R_f = 0.71 [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 7.51 (d, 1H, $^3J_{H\text{-}H}$ = 8.1, H-3), 6.91 (d, 1H, $^3J_{H\text{-}H}$ = 7.6, H-1), 6.81 – 6.62 (m, 1H, H-2), 5.50 (bs, 2H, H-6), 3.88 (s, 3H, H-7), 2.90 (s, 3H, H-5). The signal for H-4 was not observed. The product is prone to oxidation by O_2 from air and was, therefore, used for the next step without further purification.

[3] R. Rahaim, R. Maleczka, *Org. Lett.* **2005**, *22*, 5087.

2.1.4. Methyl 3-butyl-10-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[*g*]pteridine-6-carboxylate (14)



14

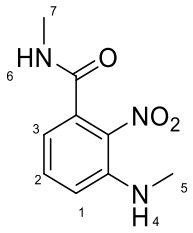
A *Schlenk* flask was filled with *N*-butylbarbituric acid (7.08 g, 38.4 mmol, 2.50 equiv.) and ruthenium(III) chloride trihydrate (101 mg, 384 µmol, 0.03 equiv.) under argon atmosphere. The solids were dissolved in DCM (anhydrous, 78 mL, 0.5 M (w. r. t. *N*-butylbarbituric acid)) and water (distilled, 3.9 mL, 10 M (w. r. t. *N*-butylbarbituric acid)). Under stirring at room temperature, *tert*-butylhydroperoxide (70% in water, 10.6 mL, 76.9 mmol, 5.00 equiv.) was added dropwise by syringe pump over the course of 22 hours. Then, the mixture was stirred until completion of the reaction was confirmed by TLC (DCM/MeOH 9:1, R_f = 0.41 (*N*-butylbarbituric acid), 0.05 (Product)).

In the second step of the reaction, methyl 2-amino-3-(methylamino)benzoate (**SI-03**) (2.77 g, 15.4 mmol, 1.00 equiv.) was dissolved in half of the total amount of glacial acetic acid (0.5 * 155 mL = 77.5 mL, 0.1 M), to which subsequently B_2O_3 (1.07 g, 15.4 mmol, 1.00 equiv.) was added. Under cooling (0 °C) the reaction mixture from the first part was slowly added to the solution of the amine while the remaining acetic acid (77.5 mL) was used to rinse the flask of the reaction mixture. After stirring the reaction over night at room temperature, completion was confirmed by TLC (DCM/Aceton 9:1, R_f = 0.22). The solvent was removed *in vacuo* until only a dark yellow oil remained. After partitioning of the crude mixture between DCM/H_2O, and removal of the solvent *in vacuo*, the product was purified by flash column chromatography (silica, DCM/Ac 9:1) and methyl 3-butyl-10-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[*g*]-pteridine-6-carboxylate (**14**) was isolated.

Yellow solid (3.10 g, 9.06 mmol, 59 %); **TLC** (silica, DCM/Ac 9:1): R_f = 0.22 [colored compound]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 7.92 (dd, 1H, $^3J_{H\text{-}H}$ = 8.4, 7.4 Hz, H-7), 7.87 (dd, 1H, $^3J_{H\text{-}H}$ = 7.4, $^4J_{H\text{-}H}$ = 1.4 Hz, H-6), 7.75 (dd, 1H, $^3J_{H\text{-}H}$ = 8.4, $^4J_{H\text{-}H}$ = 1.4 Hz, H-8),

4.13 (s, 3H, H-17), 4.11 – 4.08 (m, 2H, H-13), 4.08 (s, 3H, H-12), 1.71 (tt, 2H, $^{3}J_{H\text{-}H}$ = 7.8, 6.5 Hz, H-14), 1.42 (*virt.* h, 2H, $^{3}J_{H\text{-}H} \approx {}^{3}J_{H\text{-}H}$ = 7.8 Hz, H-15), 0.96 (t, 3H, $^{3}J_{H\text{-}H}$ = 7.8 Hz, H-16); **^{13}C{^{1}H} NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 166.3 (C-11), 158.8 (C-1/2), 155.5 (C-1/2), 149.1 (C-10), 137.9 (C-3), 135.5 (C-5), 135.0 (C-7), 133.5 (C-9), 133.1 (C-4), 127.0 (C-6), 117.9 (C-8), 53.5 (C-12), 42.3 (C-13), 32.4 (C-17), 29.9 (C-14), 20.4 (C-15), 14.0 (C-16). **HR-MS** (ESI^+): *m/z* = calc. for $[C_{17}H_{18}N_4O_4+H]^+$: 343.1401 ($[M+H]^+$); found: 343.1404; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 2958 (w, C-H), 2873 (w, C-H), 1733 (m, C=O), 1658 (s, C=O), 1565 (vs, C=N), 1433 (m, C=C), 1407 (m, C=C), 1360 (m, C=C), 1190 (s, C-N), 1031 (m), 929 (m), 766 (m, C-H_{Ar}).

2.1.5. *N*-Methyl-3-(methylamino)-2-nitrobenzamide (SI-04)



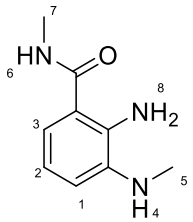
SI-04

We adopted a literature-known procedure for the nucleophilic aromatic substitution.[4] To a solution of 3-fluoro-2-nitrobenzoic acid (2.00 g, 10.8 mmol, 1.00 equiv.) in DCM (33 mL, 0.33 M) oxalyl chloride (1.85 mL, 21.6 mmol, 2.00 equiv.) and 14 drops of DMF were added dropwise, whereupon a yellow reaction mixture resulted. The solution was stirred for one hour at room temperature, followed by evaporation of DCM and excess oxalyl chloride. The dark yellow residue was cooled to 0 °C and treated with K_2CO_3 (5.97 g, 43.2 mmol, 4.00 equiv.) and methylamine (2 M in THF, 54.0 mL, 108 mmol, 10.0 equiv.). After 15 minutes, the ice bath was removed and the pale yellow solution was stirred for 18 hours at room temperature. All volatiles were removed under reduced pressure and the residue was partitioned between $NaHCO_3$ solution (sat., aqueous, 80 mL) and DCM (80 mL). The aqueous phase was extracted with DCM (3 x 80 mL) and the combined organic layers were washed with $NaHCO_3$ solution (sat., aqueous, 80 mL), dried over Na_2SO_4, filtered and concentrated to give *N*-methyl-3-(methylamino)-2-nitrobenzamide (**SI-04**), which was used without further purification.

Orange solid (1.75 g, 8.37 mmol, 78 %); **TLC** (silica, DCM/Ac 9:1): R_f = 0.57 [colored compound]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 7.61 (bs, 1H, H-6), 7.39 (dd, 1H, $^3J_{H\text{-}H}$ = 8.7 Hz, 7.1 Hz, H-2), 6.88 (dd, 1H, $^3J_{H\text{-}H}$ = 8.7 Hz, $^4J_{H\text{-}H}$ = 1.3 Hz, H-1), 6.65 (dd, 1H, $^3J_{H\text{-}H}$ = 7.1 Hz, $^4J_{H\text{-}H}$ = 1.3 Hz, H-3), 5.67 (bs, 1H, H-4), 3.00 (d, 3H, $^3J_{H\text{-}H}$ = 4.9 Hz, H-5), 3.00 (s, 3H, H-7).

[4] S. W. Goldstein *et al., J. Chem. Educ.* **2017**, *94*, 1388.

2.1.6. 2-Amino-*N*-methyl-3-(methylamino)benzamide (SI-05)



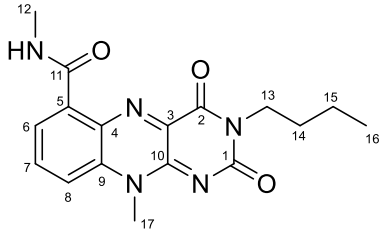
SI-05

We adapted a literature-known reduction method for nitroarenes.[3] $Pd(OAc)_2$ (93.9 mg, 418 µmol, 0.05 equiv.) was added to *N*-methyl-3-(methylamino)-2-nitrobenzamide (**SI-04**) (1.75 g, 8.37 mmol, 1.00 equiv.) and suspended in THF (45 mL, 0.19 M). After the addition of a solution of KF (972 mg, 16.7 mmol, 2.00 equiv.) in water (18 mL), the mixture was purged with argon for 15 minutes and cooled to 0 °C. PMHS (2.01 mL, 33.5 mmol, 4.00 equiv.) was added over a period of ten minutes, which lead to a blackening of the solution. After two hours, the reaction mixture was filtered over absorbent cotton, washed with water (80 mL) and extracted with DCM (3 x 80 mL). The combined organic layers were washed with water (80 mL) and filtered over a column (Al_2O_3/Celite® 1:1) which was rinsed with EtOAc (20 mL). The resulting filtrate was concentrated to give 2-amino-*N*-methyl-3-(methylamino)benzamide (**SI-05**), which was used without further purification.

Brown solid (1.50 g, 8.37 mmol, quant.); **TLC** (silica, DCM/MeOH 95:5): R_f = 0.32 [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 6.92 (dd, 1H, $^3J_{H\text{-}H}$ = 7.9 Hz, $^4J_{H\text{-}H}$ = 1.4 Hz, H-3), 6.85 (dd, 1H, $^3J_{H\text{-}H}$ = 7.9 Hz, $^4J_{H\text{-}H}$ = 1.4 Hz, H-1), 6.74 (t, 1H, $^3J_{H\text{-}H}$ = 7.9 Hz, 7.9 Hz, H-2), 6.09 (s, 1H, H-6), 5.47 (bs, 2H, H-8), 2.97 (d, 3H, $^3J_{H\text{-}H}$ = 4.9 Hz, H-7), 2.89 (s, 3H, H-5). The signal for H-4 was not observed. The product is prone to oxidation by O_2 from air and was, therefore, used for the next step without further purification.

[3] R. Rahaim, R. Maleczka, *Org. Lett.* **2005**, *22*, 5087.

2.1.7. 3-Butyl-*N*,10-dimethyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[*g*]pteridine-6-carboxamide (15)



15

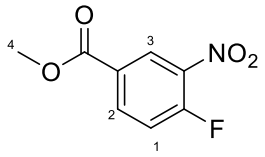
A *Schlenk* flask was filled with *N*-butylbarbituric acid (1.17 g, 6.37 mmol, 2.50 equiv.) and ruthenium(III) chloride trihydrate (16.7 mg, 63.7 µmol, 0.03 equiv.) under argon atmosphere. The solids were dissolved in DCM (anhydrous, 13 mL, 0.5 M (w. r. t. *N*-butylbarbituric acid)) and water (distilled, 0.64 mL, 10 M (w. r. t., *N*-butylbarbituric acid)). Under stirring at room temperature, *tert*-butylhydroperoxide (70% in water, 1.76 mL, 12.7 mmol, 5.00 equiv.) was added dropwise by syringe pump over the course of 22 hours. Then, the mixture was stirred until completion of the reaction was confirmed by TLC (DCM/MeOH 9:1, R_f = 0.41 (*N*-butylbarbituric acid), 0.05 (Product)).

In the second step of the reaction 2-amino-*N*-methyl-3-(methylamino)benzamide (**SI-05**) (457 mg, 2.55 mmol, 1.00 equiv.) was dissolved in half of the total amount of glacial acetic acid (0.5 * 13 mL = 6.5 mL, 0.1 M), to which subsequently B_2O_3 (178 mg, 2.55 mmol, 1.00 equiv.) was added. Under cooling (0 °C) the reaction mixture from the first part was slowly added to the solution of the amine while the remaining acetic acid (6.5 mL) was used to rinse the flask of the reaction mixture. After stirring the reaction over night at room temperature, completion was confirmed by TLC (DCM/Aceton 9:1, R_f = 0.22). The solvent was removed *in vacuo* until only a dark yellow oil remained. After partitioning of the crude mixture between DCM/H_2O and removal of the solvent *in vacuo*, the product was purified by flash column chromatography (1st column: silica, DCM/Ac 9:1; 2nd column: EtOAc/MeOH 18:1 → 14:1 → 10:1) and 3-butyl-*N*,10-dimethyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[*g*]pteridine-6-carboxamide (**15**) was isolated.

Red solid (366 mg, 1.07 mmol, 42%); **TLC** (silica, DCM/MeOH 9:1): R_f = 0.41 [colored compound]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 10.08 (s, 1H, NH), 8.70 (dd, 1H, $^3J_{H\text{-}H}$ = 7.7 Hz, $^4J_{H\text{-}H}$ = 1.3 Hz, H-6), 8.02 (dd, 1H, $^3J_{H\text{-}H}$ = 8.6 Hz, 7.7 Hz, H-7), 7.78 (dd, 1H,

$^{3}J_{H\text{-}H}$ = 8.6 Hz, $^{4}J_{H\text{-}H}$ = 1.3 Hz, H-8), 4.17 (s, 3H, H-17), 4.11 (t, 2H, $^{3}J_{H\text{-}H}$ = 7.6 Hz, H-13), 3.17 (d, 3H, $^{3}J_{H\text{-}H}$ = 4.8 Hz, H-12), 1.72 (*virt.* p, 2H, $^{3}J_{H\text{-}H} \approx {}^{3}J_{H\text{-}H}$ = 7.6 Hz, H-14), 1.44 (*virt.* sext, 2H, $^{3}J_{H\text{-}H} \approx {}^{3}J_{H\text{-}H}$ = 7.5 Hz, H-15), 0.98 (t, 3H, $^{3}J_{H\text{-}H}$ = 7.4 Hz, H-16); **^{13}C{^{1}H} NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 164.0 (C-11), 158.8 (C-1), 155.3 (C-2), 149.1 (C-10), 136.0 (C-7), 135.8 (C-3), 133.8 (C-9), 132.8 (C-5), 132.7 (C-4), 130.2 (C-6), 118.2 (C-8), 42.4 (C-15), 32.8 (C-17), 30.0 (C-14), 27.2 (C-12), 20.4 (C-15), 14.0 (C-16); **HR-MS** (ESI^+): *m/z* = calc. for $[C_{17}H_{19}N_5O_3+Na]^+$: 364.1380 ($[M+Na]^+$); found 364.1381; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3263 (m, N-H), 2955 (w, C-H), 2934 (w, C-H), 1707 (m, C=O), 1655 (s, C=O), 1644 (s, C=O), 1558 (s, C=N), 1527 (s, C=N), 1432 (m, C=C), 1405 (m, C=C), 1332 (m, C=C), 1187 (s, C-N), 986 (m), 767 (s, C-H_{Ar}), 697 (m, C-HAr).

2.1.8. Methyl 4-fluoro-3-nitrobenzoate (SI-06)



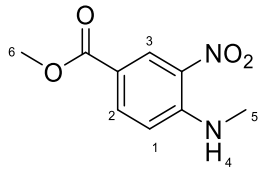
SI-06

This is a known compound and it has been synthesized according to a modified literature procedure.[5] H_2SO_4 (conc., 57.9 µL, 1.08 mmol, 0.20 equiv.) was added to a solution of 4-fluoro-3-nitrobenzoic acid (1.00 g, 5.40 mmol, 1.00 equiv.) in MeOH (27 mL, 0.20 M). The reaction mixture was stirred for 48 hours at 80 °C using a reflux condenser. After cooling to room temperature, the solution was partitioned between water (20 mL) and DCM (3 x 20 mL). The combined organic layers were washed with $NaHCO_3$ solution (sat., aqueous, 20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated. Methyl 4-fluoro-3-nitrobenzoate (**SI-06**) was used without further purification.

Yellow solid (1.02 g, 5.12 mmol, 95%); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.87 [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 8.74 (dd, 1H, $^4J_{H\text{-}F}$ = 7.2 Hz, $^4J_{H\text{-}H}$ = 2.2 Hz, H-3), 8.32 (ddd, 1H, $^3J_{H\text{-}H}$ = 8.7 Hz, $^4J_{H\text{-}F}$ = 4.2 Hz, $^4J_{H\text{-}H}$ = 2.2 Hz, H-2), 7.38 (dd, 1H, $^3J_{H\text{-}F}$ = 10.2 Hz, $^3J_{H\text{-}H}$ = 8.7 Hz, H-1), 3.98 (s, 3H, H-4). Analytical data is in accordance with literature.[5]

[5] S. A. Dietrich *et al.*, *Chem. Eur. J.* **2009**, *15*, 10144.

2.1.9. Methyl 4-(methylamino)-3-nitrobenzoate (SI-07)



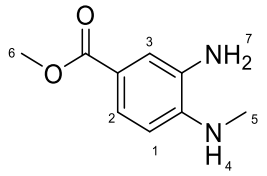
SI-07

We adapted a literature-known procedure for the nucleophilic aromatic substitution.[4] A flask was filled with methyl 4-fluoro-3-nitrobenzoate (**SI-06**) (1.02 g, 5.12 mmol, 1.00 equiv.) and was cooled to 0 °C. Then K_2CO_3 (1.42 g, 10.2 mmol, 2.00 equiv.) was added and subsequently methylamine (2 M in THF, 12.8 mL, 25.6 mmol, 5.00 equiv.). After 15 minutes the ice bath was removed, and the pale-yellow solution was stirred for 25 hours at room temperature. All volatiles were then removed under reduced pressure and the residue was partitioned between $NaHCO_3$ solution (sat., aqueous, 80 mL) and DCM (3 x 80 mL). The combined organic layers were washed with $NaHCO_3$ solution (sat., aqueous, 80 mL), dried over Na_2SO_4, filtered and concentrated. Methyl 4-(methylamino)-3-nitrobenzoate (**SI-07**) was used without further purification.

Yellow solid (1.06 g, 5.03 mmol, 98%); **TLC** (silica, DCM/EtOAc 1:1): R_f = 0.72 [colored compound]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 8.89 (dd, 1H, $^4J_{H\text{-}H}$ = 2.1 Hz, H-3), 8.35 (bs, 1H, H-4), 8.09 (dd, 1H, $^3J_{H\text{-}H}$ = 9.0 Hz, $^4J_{H\text{-}H}$ = 2.1 Hz, H-2), 6.87 (d, 1H, $^3J_{H\text{-}H}$ = 9.0 Hz, H-1), 3.90 (s, 3H, H-6), 3.09 (d, 3H, $^3J_{H\text{-}H}$ = 5.1 Hz, H-5).

[4] S. W. Goldstein *et al.*, *J. Chem. Educ.* **2017**, *94*, 1388.

2.1.10. Methyl 3-amino-4-(methylamino)benzoate (SI-08)



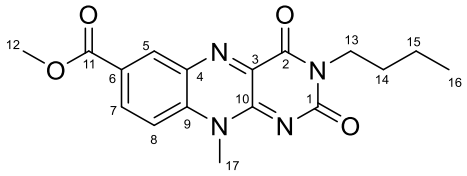
SI-08

We adapted a literature-known reduction method for nitroarenes.[3] $Pd(OAc)_2$ (56.5 mg, 251 µmol, 0.05 equiv.) was added to methyl 4-(methylamino)-3-nitrobenzoate (**SI-07**) (1.06 g, 5.03 mmol, 1.00 equiv.) and both solids were suspended in THF (23 mL, 0.22 M). After the addition of a solution of KF (584 mg, 10.1 mmol, 2.00 equiv.) in water (9 mL), the mixture was purged with argon for 15 minutes and cooled to 0 °C. PMHS (1.21 mL, 20.1 mmol, 4.00 equiv.) was added over a period of ten minutes, which resulted in a blackening of the solution. After two hours, the reaction mixture was filtered over absorbent cotton and was partitioned between water (80 mL) and DCM (3 x 80 mL). The combined organic layers were washed with water (80 mL) and filtered over a column (Al_2O_3/Celite® 1:1) which was rinsed with EtOAc (20 mL). The orange filtrate was concentrated to give methyl 3-amino-4-(methylamino)benzoate (**SI-08**) which was used without further purification.

Brown solid (906 mg, 5.03 mmol, quant.); **TLC** (silica, DCM/MeOH 95:5): R_f = 0.32 [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 7.62 (dd, 1H, $^3J_{H\text{-}H}$ = 8.3 Hz, $^4J_{H\text{-}H}$ = 1.9 Hz, H-2), 7.42 (d, 1H, $^4J_{H\text{-}H}$ = 1.9 Hz, H-3), 6.61 (d, 1H, $^3J_{H\text{-}H}$ = 8.3 Hz, H-1), 3.85 (s, 3H, H-6), 3.43 (bs, 2H, H-7), 2.92 (s, 3H, H-1). The signal for H-4 was not observed. The product is prone to oxidation by O_2 from air and was, therefore, used for the next step without purification.

[3] R. Rahaim, R. Maleczka, *Org. Lett.* **2005**, *22*, 5087.

2.1.11. Methyl 3-butyl-10-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[*g*]pteridine-7-carboxylate (16)



16

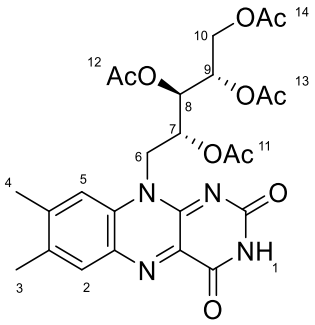
A *Schlenk* flask was filled with *N*-butylbarbituric acid (2.32 g, 12.6 mmol, 2.50 equiv.) and ruthenium(III) chloride trihydrate (32.9 mg, 126 µmol, 0.03 equiv.) under argon atmosphere. The solids were dissolved in DCM (anhydrous, 25 mL, 0.5 M (w. r. t. *N*-butylbarbituric acid)) and water (distilled, 1.27 mL, 10 M (w. r. t. *N*-butylbarbituric acid)). Under stirring at room temperature, *tert*-butylhydroperoxide (70% in water, 3.49 mL, 25.2 mmol, 5.00 equiv.) was added dropwise by syringe pump over the course of 22 hours. Then, the mixture was stirred until completion of the reaction was confirmed by TLC (DCM/MeOH 9:1, R_f = 0.41 (*N*-butylbarbituric acid), 0.05 (Product)).

In the second step of the reaction methyl 3-amino-4-(methylamino)benzoate (**SI-08**) (906 mg, 5.03 mmol, 1.00 equiv.) was dissolved in half of the total amount of glacial acetic acid (0.5 * 26 mL = 13 mL, 0.1 M), to which subsequently B_2O_3 (351 mg, 5.03 mmol, 1.00 equiv.) was added. Under cooling (0 °C) the reaction mixture from the first part was slowly added to the solution of the amine while the remaining acetic acid (13 mL) was used to rinse the flask of the reaction mixture. After stirring the reaction over night at room temperature, completion was confirmed by TLC (DCM/Aceton 9:1, R_f = 0.22). The solvent was removed *in vacuo* until only a dark yellow oil remained. After partitioning of the crude mixture between DCM/H_2O and removal of the solvent *in vacuo*, the product was purified by flash column chromatography (1st column: silica, PE/EtOAc 1:1 → EtOAc; 2nd column: DCM/Ac 25:1 → 20:1 → 15:1 → 7:1 → 1:1) and methyl 3-butyl-10-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[*g*]pteridine-7-carboxylate (**16**) was isolated.

Yellow solid (561 mg, 1.64 mmol, 33%); **TLC** (silica, DCM/MeOH 9:1): R_f = 0.51 [colored compound]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 8.97 (d, 1H, $^4J_{H\text{-}H}$ = 2.0 Hz, H-5), 8.50 (dd, 1H, $^3J_{H\text{-}H}$ = 9.0 Hz, $^4J_{H\text{-}H}$ = 2.0 Hz, H-7), 7.67 (d, 1H, $^3J_{H\text{-}H}$ = 9.0 Hz, H-8), 4.12 (s, 3H,

H-17), 4.11 (t, 2H, $^{3}J_{H\text{-}H}$ = 7.5 Hz, H-13), 4.01 (s, 3H, H-12), 1.71 (*virt.* p, 2H, $^{3}J_{H\text{-}H} \approx {}^{3}J_{H\text{-}H}$ = 7.5 Hz, H-14), 1.43 (*virt.* sext, 2H, $^{3}J_{H\text{-}H} \approx {}^{3}J_{H\text{-}H}$ = 7.4 Hz, H-15), 0.97 (t, 3H, $^{3}J_{H\text{-}H}$ = 7.4 Hz, H-16); **^{13}C{^{1}H} NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 165.2 (C-11), 159.1 (C-1), 155.4 (C-2), 149.7 (C-10), 138.3 (C-3), 136.2 (C-9), 135.8 (C-7), 135.1 (C-5), 135.0 (C-4), 128.4 (C-6), 115.4 (C-8), 53.0 (C-12), 42.2 (C-13), 32.3 (C-17), 29.9 (C-14), 20.3 (C-15), 14.0 (C-16). **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{17}H_{18}N_4O_4+H]^+$: 343.1401 ($[M+H]^+$); found 343.1403; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 2959 (w, C-H), 2874 (w, C-H), 1719 (s, C=O), 1648 (s, C=O), 1588 (s, C=O), 1550 (s, C=N), 1525 (s, C=N), 1403 (m, C=C), 1190 (s, C=N), 989 (m), 765 (m, C-H_{Ar}), 755 (m, C-H_{Ar}).

2.1.12. Riboflavin tetraacetate (SI-09)



SI-09

This is a known compound and it has been synthesized according to a modified literature procedure.[6] In a round-bottom flask, riboflavin (3.00 g, 7.97 mmol, 1.00 equiv.) was suspended in a mixture of acetic acid (125 mL, 2.19 mol, 274 equiv.) and acetic anhydride (125 mL, 1.32 mol, 165 equiv.). While stirring, perchloric acid (aqueous, 70 wt. %, 0.70 mL, 8.10 mmol, 1.01 equiv.) was added and the mixture was stirred at 40 °C for 18 hours overnight. After completion of the reaction, acetic anhydride was neutralized by carefully adding ice water (250 mL). After an hour, the mixture was transferred to a separatory funnel and extracted with DCM (3 x 100 mL). The combined organic phase was washed with brine (100 mL) and then transferred to an *Erlenmeyer*-flask. $NaHCO_3$ solution (sat., aqueous, 450 mL) was added and the mixture was mixed thoroughly. A solution of sodium hydroxide (1 M) was added dropwise until a pH of 7 was reached. The organic phase was separated and the aqueous phase was extracted with DCM (3 x 50 mL). The combined organic phase was dried over Na_2SO_4, filtered and the solvent was evaporated *in vacuo*. The crude product was then recrystallized in ethanol (113 mL) at 95 °C. After cooling, the yellow solid was filtered using a *Büchner*-funnel, washed with a small amount of cold ethanol and dried at reduced pressure to give riboflavin tetraacetate (**SI-09**).

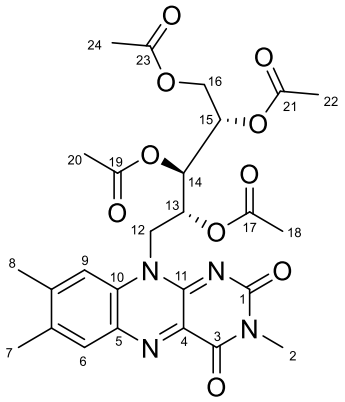
Yellow solid (3.60 g, 6.61 mmol, 83%); **TLC** (silica, DCM/MeOH 9:1): R_f = 0.53 [colored compound]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 8.36 (s, 1H), 8.04 (s, 1H), 7.56 (s, 1H), 5.67 (d, $J_{H\text{-}H}$ = 9.6 Hz, 1H), 5.51 – 5.38 (m, 2H), 4.90 (bs, 2H), 4.44 (dd, $J_{H\text{-}H}$ = 12.4, 2.8 Hz,

[6] J. B. Metternich *et al.*, *Chem. Eur. J.* **2018**, *24*, 4228.

1H), 4.24 (dd, $J_{H\text{-}H}$ = 12.4, 5.8 Hz, 1H), 2.57 (s, 3H), 2.45 (s, 3H), 2.28 (s, 3H), 2.21 (s, 3H), 2.08 (s, 3H), 1.76 (s, 3H). Analytical data is in accordance to literature.[6]

[6] J. B. Metternich *et al.*, *Chem. Eur. J.* **2018**, *24*, 4228.

2.1.13. N3-Methyl riboflavin tetraacetate (SI-10)



SI-10

This is a known compound and it has been synthesized according to a modified literature procedure.[7] In a round-bottom flask, riboflavin tetraacetate (**SI-09**) (1.85 g, 3.40 mmol, 1.00 equiv.) and K_2CO_3 (942 mg, 6.82 mmol, 2.00 equiv.) were dissolved in DMF (6.80 mL, 88.4 mmol, 26.0 equiv.). Iodomethane (1.20 mL, 19.3 mmol, 5.67 equiv.) was added carefully and the reaction mixture was stirred for four hours at room temperature. After diluting with DCM (15 mL), aqueous ammonia solution (25 wt. %, 14 mL, 20.4 mmol, 6.00 equiv.) was added to neutralize remaining iodomethane. Phases were separated and the organic phase was washed with $NaHCO_3$ solution (sat., aqueous, 70 mL). The aqueous layer was extracted with DCM (100 mL), the organic phases were combined and washed with citric acid solution (10 wt. %, 70 mL) and brine (70 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (silica, eluent: DCM/Ac 9:1) to give N3-methyl riboflavin tetraacetate (**SI-10**).

Orange solid (1.74 g, 3.12 mmol, 92%); **TLC** (silica, DCM/Ac 7:3): R_f = 0.75 [colored compound]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 8.05 (s, 1H), 7.54 (s, 1H), 5.68 (d, $^3J_{H\text{-}H}$ = 9.0 Hz, 1H), 5.47 (d, $^3J_{H\text{-}H}$ = 7.0 Hz, 1H), 5.41 (td, $^3J_{H\text{-}H}$ = 6.2, $^4J_{H\text{-}H}$ = 2.9 Hz, 1H), 4.91 (bs, 2H), 4.43 (dd, $^3J_{H\text{-}H}$ = 12.4, $^4J_{H\text{-}H}$ = 2.8 Hz, 1H), 4.25 (dd, $^3J_{H\text{-}H}$ = 12.4, 5.8 Hz, 1H), 3.50 (s, 3H), 2.55 (s, 3H), 2.44 (s, 3H), 2.30 (s, 3H), 2.22 (s, 3H), 2.08 (s, 3H), 1.74 (s, 3H); **HR-MS** (ESI$^+$): *m/z* = calc. for

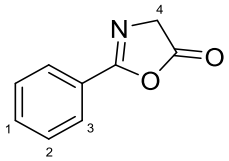
[7] M. März *et al.*, *Org. Biomol. Chem.* **2017**, *15*, 1970.

$[C_{26}H_{30}N_4O_{10}+H]^+$: 559.2035 ($[M+H]^+$); found: 559.2037. Analytical data is in accordance to literature.[7]

[7] M. März *et al.*, *Org. Biomol. Chem.* **2017**, *15*, 1970.

2.2. Substrate Synthesis

2.2.1. 2-phenyloxazol-5(4*H*)-one (SI-11)



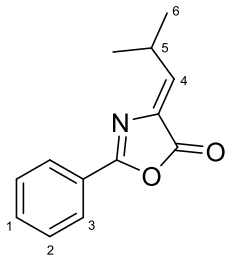
SI-11

This is a known compound and it has been synthesized according to a modified literature procedure.[8] Hippuric acid (**34**) (3.00 g, 16.7 mmol, 1.00 equiv.) and EDCI • HCl (4.17 g, 21.8 mmol, 1.30 equiv.) were dissolved in DCM (anhydrous, 34 mL, 0.50 M) and stirred at room temperature for 45 minutes under argon atmosphere. Subsequently the reaction was quenched with water and the organic layer was separated and washed with water (2 x 150 mL) and brine (1 x 150 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to give 2-phenyloxazol-5(4*H*)-one (**SI-11**).

Orange solid (2.37 g, 14.7 mmol, 88%); **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 8.02 - 7.96 (m, 2H, H-3), 7.61 – 7.56 (m, 1H, H-1), 7.52 – 7.47 (m, 2H, H-2), 4.43 (s, 2H, H-4). Analytical data is in accordance to literature.[8]

[8] H.-Q. Cao *et al.*, *Org. Lett.* **2020**, *22*, 6414.

2.2.2. (*Z*)-4-(2-methylpropylidene)-2-phenyloxazol-5(4*H*)-one (SI-12)



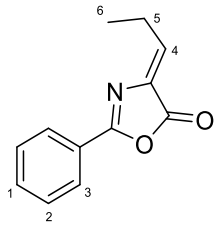
SI-12

This is a known compound and it has been synthesized according to a modified literature procedure.[8] To a solution of 2-phenyloxazol-5(4*H*)-one (**SI-11**) (700 mg, 4.34 mmol, 1.00 equiv.) in DCM (anhydrous, 11.0 mL, 0.39 M) under argon atmosphere, first activated molecular sieves 4 Å (3.00 g) and Al_2O_3 (3.00 g, 29.4 mmol, 6.80 equiv.) were added, then isobutyraldehyde (1.98 mL, 21.7 mmol, 5.00 equiv.) was added dropwise by syringe. The reaction mixture was stirred at room temperature for 22 hours, then filtered through a pad of Celite®. The resulting solution was concentrated *in vacuo*. Further purification was achieved by flash column chromatography (silica, PE/EtOAc 98:2), to afford (*Z*)-4-(2-methylpropylidene)-2-phenyloxazol-5(4*H*)-one (**SI-12**).

White solid (*Z*-Isomer, 137 mg, 0.64 mmol, 15%) **TLC** (silica, PE/EtOAc 98:2): R_f = 0.30 [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 8.11 – 8.07 (m, 2H, H-3), 7.61 – 7.56 (m, 1H, H-1), 7.53 – 7.48 (m, 2H, H-2), 6.54 (d, 1H, $^3J_{H\text{-}H}$ = 10.0 Hz, H-4), 3.32 (dp, 1H, $^3J_{H\text{-}H}$ = 10.0, 6.7 Hz, H–5), 1.19 (d, 6H, $^3J_{H\text{-}H}$ = 7.8 Hz, H-6). Analytical data is in accordance to literature.[8]

[8] H.-Q. Cao *et al.*, *Org. Lett.* **2020**, *22*, 6414.

2.2.3. (*Z*)-2-phenyl-4-propylideneoxazol-5(4*H*)-one (SI-13)



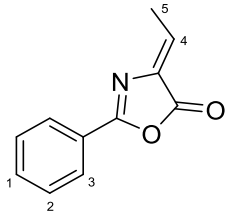
SI-13

This is a known compound and it has been synthesized according to a modified literature procedure.[8] To a solution of 2-phenyloxazol-5(4*H*)-one (**SI-11**) (700 mg, 4.34 mmol, 1.00 equiv.) in DCM (anhydrous, 11.0 mL, 0.39 M) under argon atmosphere, first activated molecular sieves 4 Å (3.00 g) and Al_2O_3 (2.20 g, 21.6 mmol, 5.00 equiv.) was added, then propionaldehyde (1.56 mL, 21.7 mmol, 5.00 equiv.) was added dropwise by syringe. The reaction mixture was stirred at room temperature for 22 hours, then filtered through a pad of Celite®. The resulting solution was concentrated *in vacuo*. Further purification was achieved by flash column chromatography (silica, PE/EtOAc 98:2), to afford (*Z*)-2-phenyl-4-propylideneoxazol-5(4*H*)-one (**SI-13**).

White solid (*Z*-Isomer, 82.0 mg, 0.41 mmol, 10%); **TLC** (silica, PE/EtOAc 98:2): *R*f = 0.30 [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 8.11 – 8.07 (m, 2H, H-3), 7.61 – 7.56 (m, 1H, H-1), 7.52 – 7.47 (m, 2H, H-2), 6.69 (t, 1H, $^3J_{H\text{-}H}$ = 7.9 Hz, H-4), 2.7 (p, 2H, $^3J_{H\text{-}H}$ = 7.9 Hz, H-5), 1.23 - 1.16 (m, 3H, H-6). Analytical data is in accordance to literature.[8]

[8] H.-Q. Cao *et al.*, *Org. Lett.* **2020**, *22*, 6414.

2.2.4. (*Z*)-4-ethylidene-2-phenyloxazol-5(4*H*)-one (SI-14)



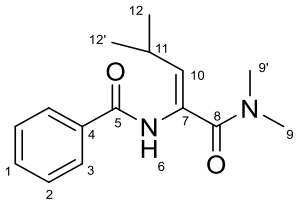
SI-14

This is a known compound and it has been synthesized according to a modified literature procedure.[9] To a solution of 2-phenyloxazol-5(4*H*)-one (**SI-11**) (700 mg, 4.34 mmol, 1.00 equiv.) in DCM (anhydrous, 11.0 mL, 0.39 M) under argon atmosphere, first activated molecular sieves 3 Å (4.00 g) and Al_2O_3 (2.21 g, 21.6 mmol, 5.00 equiv.) was added, then acetaldehyde (1.22 mL, 21.7 mmol, 5.00 equiv.) was added dropwise by syringe. The reaction mixture was stirred at room temperature for 22 hours, then filtered through a pad of Celite®. The resulting solution was concentrated *in vacuo*. Further purification was achieved by flash column chromatography (silica, PE/EtOAc 98:2), to afford (*Z*)-4-ethylidene-2-phenyloxazol-5(4*H*)-one (**SI-14**).

White solid (*Z*-Isomer, 114 mg, 0.61 mmol, 14%); **TLC** (silica, PE/EtOAc 98:2): R_f = 0.27 [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 8.12 – 8.07 (m, 2H, H-3), 7.61 – 7.57 (m, 1H, H-1), 7.53 – 7.48 (m, 2H, H-2), 6.76 (q, 1H, $^3J_{H\text{-}H}$ = 7.5 Hz, H-4), 2.26 (d, 3H, $^3J_{H\text{-}H}$ = 7.5 Hz, H-5). Analytical data is in accordance to literature.[9]

[9] E. Cerutti *et al.*, *J. Phys. Chem. A* **2015**, *119*, 11271.

2.2.5. (*Z*)-*N*-(1-(Dimethylamino)-4-methyl-1-oxopent-2-en-2-yl)benzamide (SI-15)



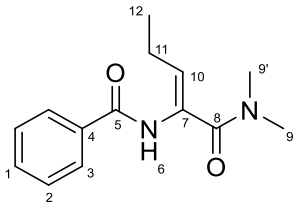
SI-15

The synthesis was performed analogously to a literature-known procedure.[8] (*Z*)-4-(2-methylpropylidene)-2-phenyloxazol-5(4*H*)-one (**SI-12**) (100 mg, 0.46 mmol, 1.00 equiv.) and dimethylamine (2.0 M THF, 6.97 mL, 13.9 mmol, 30.00 equiv.) were stirred at room temperature for 90 minutes. Volatiles were removed under reduced pressure to obtain (*Z*)-*N*-(1-(dimethylamino)- 4-methyl-1-oxopent-2-en-2-yl)benzamide (**SI-15**).

White solid (100 mg, 0.38 mmol, 83%); **TLC** (silica, PE/EtOAc 6:4): R_f = 0.08 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 9.79 (s, 1H, H-6), 7.93 - 7.91 (m, 2H, H-3), 7.59 - 7.55 (m, 1H, H-1), 7.51 - 7.47 (m, 2H, H-2), 5.22 (dd, $^3J_{H\text{-}H}$ = 9.9 Hz, $^4J_{H\text{-}H}$ = 1.2 Hz, 1H, H-10), 3.08 (s, 3H, H-9, 2.83 (s, 3H, H-9'), 2.77 (dt, $^3J_{H\text{-}H}$ = 9.8 Hz, $^3J_{H\text{-}H}$ = 6.6 Hz, 1H, H-11), 0.99 (d, 6H, $^3J_{H\text{-}H}$ = 6.7 Hz, H-12, H-12'); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 168.2 (C-5), 165.4 (C-8), 133.3 (C-4), 132.5 (C-10), 131.8 (C-1), 128.4 (2C, C-2), 127.8 (3C, C-3, C-7), 38.9 (C-9', overlap with deuterated solvent residual signal), 34.8 (C-9), 25.7 (C-11), 22.1 (2C, C-12, C-12'); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{15}H_{20}N_2O_2+Na]^+$: 283.1417 ($[M+Na]^+$); found: 283.1414; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3166 (m, N-H), 3073 (w, C-H), 2958 (m, C-H), 2927 (m, C-H), 1655 (m, C=O), 1610 (s, C=O), 1581 (m, C=C), 1481 (s, C=C), 1290 (m), 691 (s, C-H_{Ar}), 656 (s, C-H_{Ar}).

[8] H.-Q. Cao *et al.*, *Org. Lett.* **2020**, *22*, 6414.

2.2.6. (*Z*)-*N*-(1-(Dimethylamino)-1-oxopent-2-en-2-yl)benzamide (SI-16)



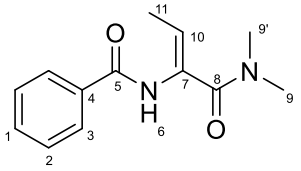
SI-16

The synthesis was performed analogously to a literature-known procedure.[8] (*Z*)-2-phenyl-4-propylideneoxazol-5(4*H*)-one (**SI-13**) (100 mg, 0.49 mmol, 1.00 equiv.) and dimethylamine (2.0 M in THF, 7.45 mL, 14.9 mmol, 30.00 equiv.) were stirred at room temperature for 60 minutes. Volatiles were removed under reduced pressure to obtain (*Z*)-*N*-(1-(dimethylamino)-1-oxopent-2-en-2-yl)benzamide (**SI-16**).

White solid (111 mg, 0.48 mmol, 97%); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.10 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 9.80 (s, 1H, H-6), 7.93 – 7.91 (m, 2H, H-3), 7.59 - 7.55 (m, 1H, H-1), 7.51 - 7.47 (m, 2H, H-2), 5.39 (td, 1H, $^3J_{H\text{-}H}$ = 7.4 Hz, $^4J_{H\text{-}H}$ = 1.15 Hz, H-10), 3.07 (s, 3H, H9), 2.87 (s, 3H, H-9'), 2.17 (p, 2H, $^3J_{H\text{-}H}$ = 7.4 Hz, H-11), 0.99 (t, 3H, $^3J_{H\text{-}H}$ = 7.4 Hz, H-12). **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 168.0 (C-5), 165.2 (C-8), 133.3 (C-4), 131.8 (C-1), 129.5 (C-7), 128.4 (2C, C-2), 127.8 (2C, C-3), 127.2 (C-10), 38.9 (C-9', overlap with deuterated solvent residual signal), 34.8 (C-9), 19.8 (C-11), 13.2 (C-12); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{14}H_{18}N_2O_2+Na]^+$: 269.1260 ($[M+Na]^+$); found: 269.1259; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3159 (m, N-H), 3070 (w, C-H), 2971 (m, C-H), 2933 (m, C-H), 1665 (m, C=O), 1607 (s, C=O), 1580 (m, C=C), 1484 (s, C=C), 1293 (m), 705 (s, C-H_{Ar}), 655 (s, C-H_{Ar}).

[8] H.-Q. Cao *et al.*, *Org. Lett.* **2020**, *22*, 6414.

2.2.7. (*Z*)-*N*-(1-(Dimethylamino)-1-oxobut-2-en-2-yl)benzamide ((*Z*)-40)



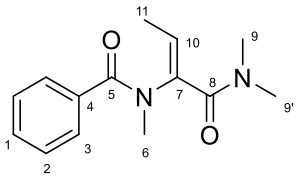
(*Z*)-40

The synthesis was performed analogously to a literature-known procedure.[8] (*Z*)-4-ethylidene-2-phenyloxazol-5(4*H*)-one (**SI-14**) (200 mg, 1.07 mmol, 1.00 equiv.) and dimethylamine (2.0 M in THF, 16.0 mL, 32.0 mmol, 30.00 equiv.) were stirred at room temperature for 60 minutes. Volatiles were removed under reduced pressure to obtain (*Z*)-*N*-(1-(dimethylamino)-1-oxobut-2-en-2-yl)benzamide (**(*Z*)-40**).

White solid (211 mg, 0.90 mmol, 85%); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.06 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 9.79 (s, 1H, H-6), 7.94 – 7.92 (m, 2H, H-3), 7.59 - 7.55 (m, 1H, H-1), 7.51 - 7.48 (m, 2H, H-2), 5.51 (qd, 1H, $^3J_{H\text{-}H}$ = 7.0 Hz, $^4J_{H\text{-}H}$ = 1.17 Hz, H-10), 3.05 (s, 3H, H9), 2.83 (s, 3H, H-9'), 1.72 (d, 3H, $^3J_{H\text{-}H}$ = 7.0 Hz, H-11); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 168.0 (C-5), 165.1 (C-8), 133.3 (C-4), 131.8 (C-1), 131.2 (C-7), 128.4 (2C, C-2), 127.8 (2C, C-3), 120.4 (C-10), 38.6 (C-9', overlap with deuterated solvent residual signal), 34.5 (C-9), 12.5 (C-11); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{13}H_{16}N_2O_2+Na]^+$: 255.1104 ($[M+Na]^+$); found: 255.1104; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3174 (m, N-H), 3066 (w, C-H), 2983 (m, C-H), 2920 (m, C-H), 1660 (m, C=O), 1605 (s, C=O), 1579 (m, C=C), 1484 (s, C=C), 1291 (m), 698 (s, C-H_{Ar}), 652 (s, C-H_{Ar}).

[8] H.-Q. Cao *et al.*, *Org. Lett.* **2020**, *22*, 6414.

2.2.8. (*Z*)-*N*-(1-(Dimethylamino)-1-oxobut-2-en-2-yl)-*N*-methylbenzamide ((*Z*)-41)



(*Z*)-41

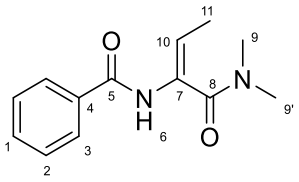
The synthesis was performed analogously to a literature-known procedure.[10] A round bottom flask was conditioned under argon atmosphere using the *Schlenk*-technique. NaH (60%, 19.4 mg, 0.48 mmol, 1.50 equiv.) was added, suspended in THF (2.5 ml) and cooled using an ice bath. (*Z*)-*N*-(1-(Dimethylamino)-1-oxobut-2-en-2-yl)benzamide (**(*Z*)-40**) (75 mg, 323 µmol, 1.00 equiv.) was added and the suspension was stirred for 15 minutes. After cessation of gas generation, the ice bath was removed and the methylation reaction was started by addition of iodomethane (0.20 ml, 3.21 mmol, 10.0 equiv.). The mixture was stirred at room temperature overnight. Residual iodomethane and THF were removed under reduced pressure using a cooling trap. Citric acid (10 %, aqueous, 1 x 25 ml) and DCM (50 ml) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with DCM (1 x 25 ml) and the combined organic layers were washed with $NaHCO_3$ solution (sat., aqueous, 1 x 25 ml), dried over Na_2SO_4 and the solvent was removed *in vacuo* to give (*Z*)-*N*-(1-(dimethylamino)-1-oxobut-2-en-2-yl)-*N*-methylbenzamide (**(*Z*)-41**).

Pale-yellow oil (78.8 mg, 320 µmol, 99 %); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.10 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 7.49 - 7.38 (m, 3H, H-3, H-1), 7.38 – 7.31 (m, 2H, H-2), 5.69 (q, $^3J_{H\text{-}H}$ = 7.0 Hz, 1H, H-10), 3.07 (s, 3H, H-6), 2.60 (bs, 6H, H-9, H-9'), 1.60 (d, $^3J_{H\text{-}H}$ = 7.0 Hz, 3H, H-11); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 170.7 (C-5), 167.0 (C-8), 136.6 (C-4), 135.4 (C-7), 129.9 (C-1), 128.5 (C-10), 128.0 (2C, C-2), 127.1 (2C, C-3), 39.9 (C-9, overlap with deuterated solvent residual signal), 39.8 (C-9', overlap with deuterated solvent residual signal), 35.8 (C-6), 13.4 (C-11); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{14}H_{18}N_2O_2+Na]^+$: 269.1260 ($[M+Na]^+$); found: 269.1261; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3065 (w, C-H),

[10] E. Becalli *et al.*, *Tetrahedron* **2005**, *61*, 61.

3028 (w, C-H), 2935 (m, C-H), 1626 (s, C=O), 1575 (m, C=C), 1490 (m, C=C), 1365 (s, C-H), 1072 (m), 710 (m, C-H_{Ar}), 699 (m, C-H_{Ar}).

2.2.9. (*E*)-*N*-(1-(Dimethylamino)-1-oxobut-2-en-2-yl)benzamide ((*E*)-40)



(*E*)-40

The synthesis was performed analogously to a literature-known procedure.[11] Triethylenediamine (108 mg, 963 µmol, 1.13 equiv.), *N*-iodosuccinimide (184 mg, 818 µmol, 0.96 equiv.) and (*Z*)-*N*-(1-(dimethylamino)-1-oxobut-2-en-2-yl)benzamide (**(*Z*)-40**) (198 mg, 852 µmol, 1.00 eq.) were combined in DCM (anhydrous, 20 ml) and the reaction was stirred vigorously at room temperature for six hours. After addition of ethyl acetate (170 ml), the mixture was washed with citric acid (10%, aqueous, 1 x 50 ml), $NaHCO_3$ solution (sat., aqueous, 1 x 50 ml), Na_2SO_3 solution (10% w/w, aqueous, 1 x 50 ml) and brine (1 x 50 ml). The organic layer was dried over Na_2SO_4 and the solvent was removed *in vacuo*. *N*-(1-(Dimethylamino)-3-iodo-1-oxobut-2-en-2-yl)benzamide (241 mg, 673 µmol, 82%) was obtained as a pale-yellow solid and was used directly as crude for the next step.

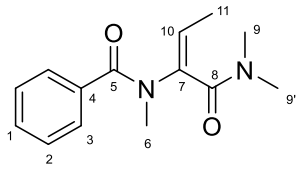
In a *Schlenk* flask containing palladium on charcoal (10 % w/w, 367 mg, 345 µmol, 0.51 equiv.), triethylamine (0.12 ml, 831 µmol, 1.20 equiv.) and methanol (53 ml) were conditioned under argon atmosphere by carefully reducing the pressure until methanol started to evaporate, and subsequently backfilling with hydrogen gas. The reaction was stirred for about 100 minutes at room temperature. Over a span of 15 minutes, a solution of *N*-(1-(dimethylamino)-3-iodo-1-oxobut-2-en-2-yl)benzamide (241 mg, 673 µmol, 1.00 equiv.) in methanol (34 ml) was added, the flask was washed with methanol (10 ml) and the mixture was stirred for 3.5 hours. The hydrogen balloon was then removed and hydrogen gas was cast out of the solution by bubbling argon through the mixture for 5 minutes. The reaction mixture was filtered through Celite® and solvent was removed *in vacuo*. Ethyl acetate (100 ml) was added and the solution was washed with Na_2SO_3 solution (10% w/w, aqueous, 1 x 40 ml). The aqueous layer was extracted with ethyl acetate (1 x 100 ml), the combined organic layers were washed with brine (1 x 80 ml), dried over Na_2SO_4

[11] H. A. Grab *et al.*, *Angew. Chem. Int. Ed.* **2020**, *59*, 12357.

and the solvent was removed *in vacuo* to give (*E*)-*N*-(1-(dimethylamino)-1-oxobut-2-en-2-yl)benzamide (**(*E*)-40**).

Pale yellow oil (146 mg, 630 µmol, *E/Z* 7:1, 95 %); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.08 [UV];.**^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 10.01 (s, 1H, H-6), 7.88 (dd, $^3J_{H-H}$ = 8.4, $^4J_{H-H}$ = 1.4 Hz, 2H, H-3), 7.59 - 7.53 (m, 1H, H-1), 7.52 - 7.44 (m, 2H, H-2), 5.58 (q, $^3J_{H-H}$ = 7.2 Hz, 1H, H-10), 3.00 (s, 3H, H-9/H-9'), 2.88 (s, 3H, H-9/H-9'), 1.60 (d, $^3J_{H-H}$ = 7.2 Hz, 3H, H-11); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 165.9 (C-8), 164.2 (C-5), 133.4 (C-4), 132.0 (C-7), 131.7 (C-1), 128.4 (2C, C-2), 127.6 (2C, C-3), 112.3 (C-10), 37.5 (C-9), 33.9 (C-9'), 12.2 (C-11); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{13}H_{16}N_2O_2+Na]^+$: 255.1104 ($[M+Na]^+$); found: 255.1105; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3179 (m, N-H), 3065 (w, C-H), 2983 (m, C-H), 2918 (m, C-H), 1660 (m, C=O), 1610 (s, C=O), 1580 (m, C=C), 1484 (s, C=C), 1291 (m), 705 (s, C-H_{Ar}), 660 (s, C-H_{Ar}).

2.2.10. (*E*)-*N*-(1-(Dimethylamino)-1-oxobut-2-en-2-yl)-*N*-methylbenzamide ((*E*)-41)



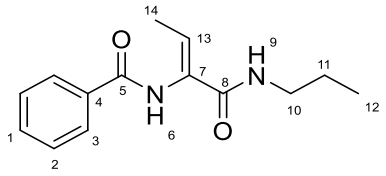
(*E*)-41

The synthesis was performed analogously to a literature-known procedure.[10] A round bottom flask was conditioned under argon atmosphere using the *Schlenk*-technique. NaH (60%, 19.4 mg, 0.48 mmol, 1.50 equiv.) was added, suspended in THF (2.5 ml) and cooled using an ice bath. (*E*)-*N*-(1-(Dimethylamino)-1-oxobut-2-en-2-yl)benzamide (**(*E*)-40**) (75 mg, 323 µmol, 1.00 equiv.) was added and the suspension was stirred for 15 minutes. After cessation of gas generation, the ice bath was removed and the methylation reaction was started by addition of iodomethane (0.20 ml, 3.21 mmol, 10.0 equiv.). The mixture was stirred at room temperature overnight. Residual iodomethane and THF was removed under reduced pressure using a cooling trap. Citric acid (10 %, aqueous, 1 x 25 ml) and DCM (50 ml) were added and the layers were separated. The aqueous layer was extracted with DCM (1 x 25 ml) and the combined organic layers were washed with $NaHCO_3$ solution (sat., aqueous, 1 x 25 ml), dried over Na_2SO_4 and the solvent was removed *in vacuo* to give (*E*)-*N*-(1-(dimethylamino)-1-oxobut-2-en-2-yl)-*N*-methylbenzamide (**(*E*)-41**).

Pale-yellow oil (69.1 mg, 280 µmol, 86 %); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.12 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 7.59 – 7.53 (m, 2H, H-3), 7.45 - 7.35 (m, 3H, H-1, H-2), 5.47 (bs, 1H, H-10), 3.06 (s, 3H, H-6), 2.83 (s, 6H, H-9, H-9'), 1.47 (s, 3H, H-11); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 169.9 (C-5), 165.6 (C-8), 136.1 (C-7), 129.8 (C-1), 128.3 (C-10), 128.0 (2C, C-2), 127.6 (2C, C-3), 127.1 (C-4), 37.1 (C-9', overlap with deuterated solvent residual signal), 35.8 (C-6), 34.1 (C-9), 13.1 (C-11); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{14}H_{18}N_2O_2+Na]^+$: 269.1260 ($[M+Na]^+$); found: 269.1262; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3058 (w, C-H), 3027 (w, C-H), 2925 (m, C-H), 1626 (s, C=O), 1578 (m, C=C), 1494 (m, C=C), 1365 (s, C-H), 1070 (m), 723 (m, C-H_{Ar}), 701 (m, C-H_{Ar}).

[10] E. Becalli *et al.*, *Tetrahedron* **2005**, *61*, 61.

2.2.11. (*Z*)-*N*-(1-oxo-1-(propylamino)but-2-en-2-yl)benzamide (SI-17)



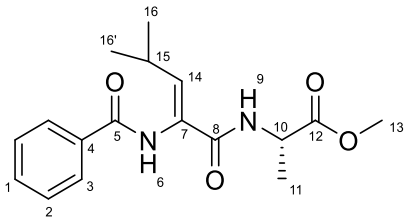
SI-17

The synthesis was performed analogously to a literature-known procedure.[8] (*Z*)-4-ethylidene-2-phenyloxazol-5(4*H*)-one (**SI-14**) (200 mg, 1.07 mmol, 1.00 equiv.) and propylamine (2.63 mL, 32.0 mmol, 30.00 equiv.) were stirred at room temperature for 60 minutes. Volatiles were removed under reduced pressure to obtain (*Z*)-*N*-(1-oxo-1-(propylamino)but-2-en-2-yl)benzamide (**SI-17**).

Colorless oil (238 mg, 0.97 mmol, 91%); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.21 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 9.43 (s, 1H, H-6), 7.97 (d, $^3J_{H\text{-}H}$ = 7.4 Hz, 2H, H-3), 7.87 (t, $^3J_{H\text{-}H}$ = 5.4 Hz, 1H, H-9), 7.61 - 7.53 (m, 1H, H-1), 7.49 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 2H, H-2), 6.41 (q, $^3J_{H\text{-}H}$ = 6.9 Hz, 1H, H-13), 3.05 (*virt.* q, $^3J_{H\text{-}H} \approx {}^3J_{H\text{-}H}$ = 6.6 Hz, 2H, H-10), 1.64 (d, $^3J_{H\text{-}H}$ = 6.9 Hz, 3H, H-14), 1.43 (*virt.* h, $^3J_{H\text{-}H} \approx {}^3J_{H\text{-}H}$ = 7.4 Hz, 2H, H-11), 0.82 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 3H, H-12); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 165.3 (C-5), 164.4 (C-8), 134.0 (C-4), 131.9 (C-7), 131.5 (C-1), 128.2 (2C, C-2), 127.9 (2C, C-3), 127.5 (C-13), 40.7 (C-10), 22.4 (C-11), 13.2 (C-14), 11.5 (C-12); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{14}H_{18}N_2O_2+Na]^+$: 269.1260 ($[M+Na]^+$); found: 269.1257; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3322 (m, N-H), 3238 (m, N-H), 3067 (w, C-H), 2964 (m, C-H), 2927 (m, C-H), 1633 (s, C=O), 1602 (m, C=O), 1580 (m, C=C), 1478 (s, C=C), 1278 (m), 730 (s, C-H_{Ar}), 689 (s, C-H_{Ar}), 674 (s, C-H_{Ar}).

[8] H.-Q. Cao *et al.*, *Org. Lett.* **2020**, *22*, 6414.

2.2.12. Methyl (*Z*)-(2-benzamido-4-methylpent-2-enoyl)-*L*-alaninate (SI-18)



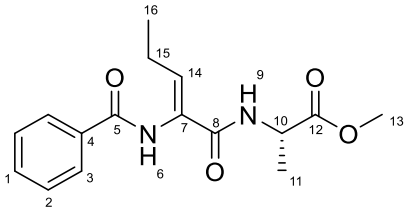
SI-18

The synthesis was performed analogously to a literature-known procedure.[12] *L*-Alanine methyl ester hydrochloride (237 mg, 1.70 mmol, 2.00 equiv.) was dissolved in EtOH (7 mL, 0.12 M) and NEt_3 (0.24 mL, 1.70 mmol, 2.00 equiv.) as well as (*Z*)-4-(2-methylpropylidene)-2-phenyloxazol-5(4*H*)-one (**SI-12**) (183 mg, 0.85 mmol, 1.00 equiv.) were added. The reaction mixture was stirred at room temperature over night. The crude product was applied on Celite® and purified by flash column chromatography (silica, PE/EtOAc 70:30) to obtain methyl (*Z*)-(2-benzamido-4-methylpent-2-enoyl)-*L*-alaninate (**SI-18**).

White solid (111 mg, 0.35 mmol, 41%); **TLC** (silica, PE/EtOAc 70:30): R_f = 0.42 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 9.43 (s, 1H, H-6), 8.20 (d, 1H, $^3J_{H\text{-}H}$ = 7.2 Hz, H-9), 7.97 – 7.95 (m, 2H, H-3), 7.59 – 7.55 (m, 1H, H-1), 7.51 – 7.47 (m, 2H, H-2), 6.30 – 6.28 (m, 1H, H-14), 4.35 (p, 1H, $^3J_{H\text{-}H}$ = 7.2 Hz, H-10), 3.61 (s, 3H, H-13), 2.61 – 2.54 (m, 1H, H-15), 1.30 (d, 3H, $^3J_{H\text{-}H}$ = 7.2 Hz, H-11), 0.99 (t, $^3J_{H\text{-}H}$ = 6.5 Hz, 6H, H-16, H-16'); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 173.1 (C-12), 165.8 (C-5), 164.5 (C-8), 140.8 (C-14), 134.0 (C-4), 131.6 (C-1), 128.3 (2C, C-2), 128.1 (C-7), 127.9 (2C, C-3), 51.9 (C-13), 48.0 (C-10), 26.7 (C-15), 21.8 (2C, C-16, C-16'), 16.9 (C-11); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{17}H_{22}N_2O_4+Na]^+$: 341.1472 ($[M+Na]^+$); found: 341.1469; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3235 (m, N-H), 3049 (w, C-H), 2960 (m, C-H), 1751 (s, C=O), 1634 (s, C=O), 1604 (m, C=O), 1580 (m, C=C), 1518 (s, C=C), 1484 (s, C=C), 1275 (m), 1155 (m, C-O), 743 (m, C-H_{Ar}), 691 (s, C-H_{Ar}).

[12] C. Y. Lee *et al.*, *Tetrahedron* **2012**, *68*, 5850.

2.2.13. Methyl (*Z*)-(2-benzamidopent-2-enoyl)-*L*-alaninate (SI-19)



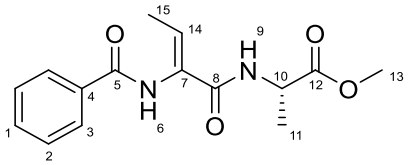
SI-19

The synthesis was performed analogously to a literature-known procedure.[12] *L*-Alanine methyl ester hydrochloride (227 mg, 1.63 mmol, 2.00 equiv.) was dissolved in EtOH (7 mL, 0.11 M) and NEt_3 (0.23 mL, 1.63 mmol, 2.00 equiv.) as well as (*Z*)-2-phenyl-4-propylideneoxazol-5(4H)-one (**SI-13**) (164 mg, 0.81 mmol, 1.00 equiv.) were added. The reaction mixture was stirred at room temperature over night. The crude product was applied on Celite® and purified by flash column chromatography (silica, PE/EtOAc 70:30) to obtain methyl (*Z*)-(2-benzamidopent-2-enoyl)-*L*-alaninate (**SI-19**).

White solid (51.7 mg, 0.17 mmol, 21%); **TLC** (silica, PE/EtOAc 70:30): R_f = 0.35 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 9.44 (s, 1H, H-6), 8.24 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 1H, H-9), 7.99 - 7.89 (m, 2H, H-3), 7.58 - 7.54 (m, 1H, H-1), 7.52 - 7.47 (m, 2H, H-2), 6.43 - 6.36 (m, 1H, H-14), 4.34 (p, $^3J_{H\text{-}H}$ = 7.2 Hz, 1H, H-10), 3.61 (s, 3H, H-13), 2.16 - 2.01 (m, 2H, H-15), 1.30 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 3H, H-11), 0.99 (t, $^3J_{H\text{-}H}$ = 7.5 Hz, 3H, H-16); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 173.1 (C-12), 165.5 (C-5), 164.5 (C-8), 135.3 (C-14), 134.0 (C-4), 131.6 (C-1), 129.5 (C-7), 128.3 (2C, C-2), 127.9 (2C, C-3), 51.9 (C-13), 48.0 (C-10), 20.8 (C-15), 16.9 (C-11), 12.9 (C-16); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{16}H_{20}N_2O_4+Na]^+$: 327.1315 ($[M+Na]^+$); found: 327.1315; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3216 (m, N-H), 3054 (w, C-H), 2981 (m, C-H), 1751 (s, C=O), 1634 (s, C=O), 1604 (m, C=O), 1580 (m, C=C), 1515 (s, C=C), 1484 (s, C=C), 1277 (m), 1157 (m, C-O), 742 (m, C-H_{Ar}), 693 (s, C-H_{Ar}).

[12] C. Y. Lee *et al.*, *Tetrahedron* **2012**, *68*, 5850.

2.2.14. Methyl (*Z*)-(2-benzamidobut-2-enoyl)-*L*-alaninate (SI-20)



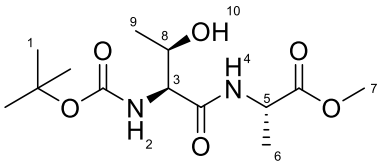
SI-20

The synthesis was performed analogously to a literature-known procedure.[12] *L*-Alanine methyl ester hydrochloride (447 mg, 3.21 mmol, 2.00 equiv.) was dissolved in EtOH (7 mL, 0.23 M) and NEt_3 (0.44 mL, 3.21 mmol, 2.00 equiv.) as well as (*Z*)-4-ethylidene-2-5(4H)-one (**SI-14**) (300 mg, 1.60 mmol, 1.00 equiv.) were added. The reaction mixture was stirred at room temperature over night. The crude product was applied on Celite® and purified by flash column chromatography (silica, PE/EtOAc 70:30) to obtain methyl (*Z*)-(2-benzamidobut-2-enoyl)-*L*-alaninate (**SI-20**).

White solid (62.5 mg, 0.23 mmol, 15%); **TLC** (silica, PE/EtOAc 70:30): R_f = 0.10 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 9.46 (s, 1H, H-6), 8.24 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 1H, H-9), 8.06 - 7.88 (m, 2H, H-3), 7.59 - 7.54 (m, 1H, H-1), 7.52 - 7.47 (m, 2H, H-2), 6.51 - 6.45 (m, 1H, H-14), 4.34 (p, $^3J_{H\text{-}H}$ = 7.2 Hz, 1H, H-10), 3.61 (s, 3H, H-13), 1.67 (d, $^3J_{H\text{-}H}$ = 7.0 Hz, 3H, H-15), 1.30 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 3H, H-11).**^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 173.1 (C-12), 165.3 (C-5), 164.4 (C-8), 134.0 (C-4), 131.6 (C-1), 131.1 (C-7), 128.7 (C-14), 128.3 (2C, C-2), 127.9 (2C, C-3), 51.9 (C-13), 48.0 (C-10), 16.9 (C-11), 13.4 (C-15); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{15}H_{18}N_2O_4+Na]^+$: 313.1159 ($[M+Na]^+$); found: 313.1156; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3227 (m, N-H), 3058 (w, C-H), 2983 (m, C-H), 1755 (s, C=O), 1633 (s, C=O), 1604 (m, C=O), 1580 (m, C=C), 1515 (s, C=C), 1485 (s, C=C), 1276 (m), 1154 (m, C-O), 746 (m, C-H_{Ar}), 693 (s, C-H_{Ar}).

[12] C. Y. Lee *et al.*, *Tetrahedron* **2012**, *68*, 5850.

2.2.15. Methyl (*tert*-butoxycarbonyl)-*L*-threonyl-*L*-alaninate (SI-21)



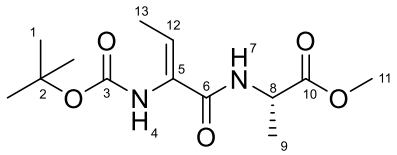
SI-21

The synthesis was performed analogously to a literature-known procedure.[13] (*tert*-Butoxycarbonyl)-*L*-threonine (864 mg, 3.94 mmol, 1.10 equiv.), 1*H*-1,2,3-benzotriazol-1-ol monohydrate (823 mg, 5.37 mmol, 1.50 equiv.) and methyl *L*-alaninate hydrochloride (500 mg, 3.58 mmol, 1.00 equiv.) were dissolved in DCM (18 mL, 0.20 M). First *N*,*N*-diisopropylethylamine (3.05 mL, 17.9 mmol, 5.00 equiv.) and then 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (755 mg, 3.94 mmol, 1.10 equiv.) were added and stirred at room temperature for 20 hours. Ethyl acetate (50 mL) and citric acid (aq., 10 %, 50 mL) were added and the layers were separated. The organic phase was washed with $NaHCO_3$ solution (sat., 50 mL) and brine (50 mL) and dried with Na_2SO_4. The crude product was concentrated *in vacuo* and purified by column chromatography (silica, PE/EtOAc 9:1 → 30:70) to give methyl (*tert*-butoxycarbonyl)-*L*-threonyl-*L*-alaninate (**SI-21**), which was directly subjected to the next step.

Pale-yellow oil (723 mg, 2.36 mmol, 66%); **TLC** (silica, PE/EtOAc 30:70): R_f = 0.43 [CAM]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 8.16 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 1H, H-4), 6.33 (d, $^3J_{H\text{-}H}$ = 7.9 Hz, 1H, H-2), 4.72 (d, $^3J_{H\text{-}H}$ = 5.3 Hz, 1H, H-8), 4.29 (p, $^3J_{H\text{-}H}$ = 7.2 Hz, 1H, H-5), 3.89 – 3.79 (m, 2H, H-3, H-10), 3.61 (s, 3H, H-7), 1.39 (s, 9H, H-1), 1.28 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 3H, H-6), 1.06 (d, $^3J_{H\text{-}H}$ = 5.3 Hz, 3H, H-9). Analytical data is in accordance to literature.[13]

[13] Q. Wang *et al.*, *Org. Lett.* **2021**, *14*, 3372.

2.2.16. (*Z*)-(2-((*tert*-Butoxycarbonyl)amino)but-2-enoyl)-*L*-alaninate (SI-22)



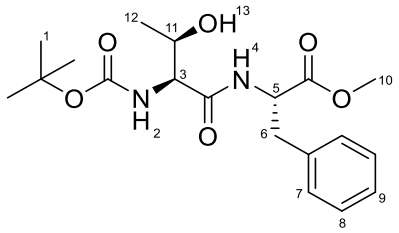
SI-22

The synthesis was performed analogously to a literature-known procedure.[14] Methyl (*tert*-butoxycarbonyl)-*L*-threonyl-*L*-alaninate (**SI-21**) (320 mg, 1.05 mmol, 1.00 equiv.) was dissolved in chloroform (19 mL, 0.05 M) and triethylamine (0.88 mL, 6.31 mmol, 6.00 equiv.) was added. At 0°C methanesulfonyl chloride (0.33 mL, 4.21 mmol, 4.00 equiv.) was added slowly to the solution and the reaction was stirred for three hours at room temperature. 1,8-Diazabicyclo[5.4.0]undec-7-ene (0.94 mL, 6.31 mmol, 6.00 equiv.) was added and the mixture was stirred for one hour at room temperature before it was stirred for 15 hours at 80°C. The reaction mixture was concentrated *in vacuo* and and dissolved in EtOAc (50 mL). The solution was washed with citric acid (aq., 10%, 3 x 50 mL), $NaHCO_3$ solution (sat., 50 mL), water (50 mL) and brine (50 mL). Drying with Na_2SO_4 and removal of the solvent *in vacuo* yielded methyl (*Z*)-(2-((*tert*-butoxycarbonyl)amino)but-2-enoyl)-*L*-alaninate (**SI-22**).

Pale-yellow oil (187 mg, 0.65 mmol, 62%); **TLC** (silica, PE/EtOAc 30:70): R_f = 0.53 [CAM]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 8.14 – 7.92 (m, 2H, H-4, H-7), 6.12 (bs, 1H, H-12), 4.32 (p, $^3J_{H\text{-}H}$ = 7.2 Hz, 1H, H-8), 3.61 (s, 3H, H-11), 1.63 (d, $^3J_{H\text{-}H}$ = 7.0, 3H, H-13), 1.39 (s, 9H, H-1), 1.30 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 3H, H-9); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 173.1 (C-10), 164.8 (C-6), 153.4 (C-3), 131.0 (C-5), 125.4 (C-12), 78.6 (C-2), 51.9 (C-11), 47.8 (C-8), 28.1 (3C, C-1), 17.0 (C-9), 12.9 (C-13); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{13}H_{22}N_2O_5+Na]^+$: 309.1421 ($[M+Na]^+$); found: 309.1423; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3327 (m, N-H), 2981 (m, C-H), 1720 (s, C=O), 1678 (s, C=O), 1454 (m, C-H), 1367 (m, C-H), 1215 (m), 1154 (s, C-O).

[14] W. Liu *et al.*, *J. Am. Chem. Soc.* **2011**, *133*, 14216.

2.2.17. Methyl (*tert*-butoxycarbonyl)-*L*-threonyl-*L*-phenylalaninate (SI-23)



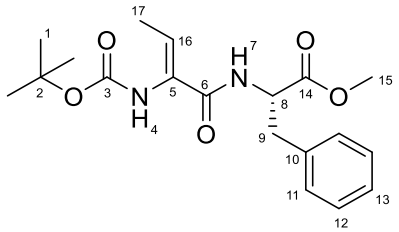
SI-23

The synthesis was performed analogously to a literature-known procedure.[13] (*tert*-Butoxycarbonyl)-*L*-threonine (1.73 g, 7.88 mmol, 1.10 equiv.), 1*H*-1,2,3-benzotriazol-1-ol monohydrate (1.64 g, 10.7 mmol, 1.50 equiv.) and methyl *L*-phenylalaninate hydrochloride (1.54 g, 7.16 mmol, 1.00 equiv.) were dissolved in DCM (36 mL, 0.20 M). First *N*,*N*-diisopropylethylamine (6.10 mL, 35.8 mmol, 5.00 equiv.) and then 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (1.51 g, 7.88 mmol, 1.10 equiv.) were added and stirred at room temperature for 20 hours. Ethyl acetate (100 mL) and citric acid (aq., 10 %, 100 mL) were added and the layers were separated. The organic phase was washed with $NaHCO_3$ solution (sat., 100 mL) and brine (100 mL) and dried with Na_2SO_4. The crude product was concentrated *in vacuo* and purified by column chromatography (silica, PE/EtOAc 9:1 → 30:70) to give methyl (*tert*-butoxycarbonyl)-*L*-threonyl-*L*-phenylalaninate (**SI-23**) which was directly subjected to the next step.

Pale-yellow oil (2.15 g, 5.65 mmol, 79%); **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 7.32 - 7.27 (m, 2H, H-8), 7.26 - 7.21 (m, 1H, H-9), 7.15 - 7.10 (m, 2H, H-7), 6.90 (d, $^3J_{H\text{-}H}$ = 8.2 Hz, 1H, H-2/3/4/5), 5.33 (d, $^3J_{H\text{-}H}$ = 8.2 Hz, 1H, H-2/3/4/5), 4.85 (q, $^3J_{H\text{-}H}$ = 6.6 Hz, 1H, H-11), 4.31 (d, $^3J_{H\text{-}H}$ = 7.3 Hz, 1H, H-2/3/4/5), 4.04 (dd, $^3J_{H\text{-}H}$ = 7.7, 1H, H-2/3/4/5), 3.73 (s, 3H, H-10), 3.18 (dd, $^2J_{H\text{-}H}$ = 14.0, $^3J_{H\text{-}H}$ = 5.6 Hz, 1H, H-6), 3.03 (dd, $^2J_{H\text{-}H}$ = 13.9, $^3J_{H\text{-}H}$ = 7.0 Hz, 1H, H-6), 2.73 (s, 1H, H-13), 1.44 (s, 9H, H-1), 1.15 (d, $^3J_{H\text{-}H}$ = 6.6 Hz, 3H, H-12). Analytical data is in accordance to literature.[15]

[13] Q. Wang *et al.*, *Org. Lett.* **2021**, *14*, 3372.
[15] M. Lei *et al.*, *Bioorg. Med. Chem.* **2019**, *27*, 4151.

2.2.18. Methyl (*Z*)-(2-((*tert*-butoxycarbonyl)amino)but-2-enoyl)-*L*-phenylalaninate (SI-24)



SI-24

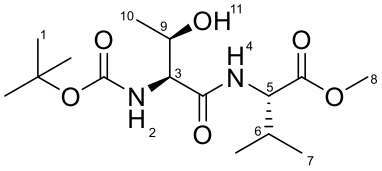
The synthesis was performed analogously to a literature-known procedure.[14] Methyl (*tert*-butoxycarbonyl)-*L*-threonyl-*L*-phenylalaninate (**SI-23**) (2.15 g, 5.65 mmol, 1.00 equiv.) was dissolved in chloroform (120 mL, 0.05 M) and triethylamine (2.40 mL, 17.1 mmol, 3.00 equiv.) was added. At 0°C methanesulfonyl chloride (0.90 mL, 11.4 mmol, 2.00 equiv.) was added slowly to the solution and the reaction was stirred for three hours at room temperature. 1,8-Diazabicyclo[5.4.0]undec-7-ene (2.56 mL, 17.1 mmol, 3.00 equiv.) was added and the mixture was stirred for one hour at room temperature before it was stirred for 15 hours at 80°C. The reaction mixture was concentrated *in vacuo* and dissolved in EtOAc (250 mL). The solution was washed with citric acid (aq., 10%, 3 x 250 mL), $NaHCO_3$ solution (sat., 250 mL), water (250 mL) and brine (250 mL). Drying with Na_2SO_4 and removal of the solvent *in vacuo* yielded methyl (*Z*)-(2-((*tert*-butoxycarbonyl)amino)but-2-enoyl)-*L*-phenylalaninate (**SI-24**).

Pale-yellow solid (1.80 g, 4.97 mmol, 88%); **TLC** (silica, PE/EtOAc 50:50): R_f = 0.55 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 8.01 (bs, 2H, H-4, H-7), 7.30 - 7.17 (m, 5H, H-11, H-12, H-13), 6.14 (s, 1H, H-16), 4.51 (td, $^3J_{H\text{-}H}$ = 8.0, 6.2 Hz, 1H, H-8), 3.59 (s, 3H, H-15), 3.09 - 2.97 (m, 2H, H-9), 1.61 (d, $^3J_{H\text{-}H}$ = 7.0 Hz, 3H, H-17), 1.36 (s, 9H, H-1); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 172.0 (C-14), 164.9 (C-6), 153.4 (C-3), 137.4 (C-10), 131.0 (C-5), 129.1 (2C, C-11), 128.3 (2C, C-12/C-13), 126.5 (2C, C-12/C-13, C-16), 78.6 (C-2), 54.0 (C-8), 51.9 (C-15), 36.6 (C-9), 28.0 (3C, C-1), 12.9 (C-17); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{19}H_{26}N_2O_5+Na]^+$: 385.1734 ($[M+Na]^+$); found: 385.1736; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3430 (m, N-H),

[14] W. Liu *et al.*, *J. Am. Chem. Soc.* **2011**, *133*, 14216.

3245 (m, N-H), 3033 (w, C-H), 2977 (m, C-H), 1736 (m, C=O), 1711 (s, C=O), 1626 (s, C=O), 1510 (s, C=C), 1326 (s, C-H), 1164 (s, C-O), 736 (s, C-H_{Ar}), 701 (s, C-H_{Ar}), 654 (m, C-H_{Ar}).

2.2.19. Methyl (*tert*-butoxycarbonyl)-*L*-threonyl-*L*-valinate (SI-25)



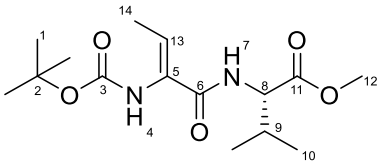
SI-25

The synthesis was performed analogously to a literature-known procedure.[13] (*tert*-Butoxycarbonyl)-*L*-threonine (1.73 g, 7.88 mmol, 1.10 equiv.), 1*H*-1,2,3-benzotriazol-1-ol monohydrate (1.64 g, 10.7 mmol, 1.50 equiv.) and methyl L-valinate hydrochloride (1.20 g, 7.16 mmol, 1.00 equiv.) were dissolved in DCM (36 mL, 0.20 M). First *N*,*N*-diisopropylethylamine (6.10 mL, 35.8 mmol, 5.00 equiv.) and then 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (1.51 g, 7.88 mmol, 1.10 equiv.) were added and stirred at room temperature for 20 hours. Ethyl acetate (100 mL) and citric acid (aq., 10 %, 100 mL) were added and the layers were separated. The organic phase was washed with $NaHCO_3$ solution (sat., 100 mL) and brine (100 mL) and dried with Na_2SO_4. The crude product was concentrated *in vacuo* and purified by column chromatography (silica, PE/EtOAc 9:1 → 30:70) to give methyl (*tert*-butoxycarbonyl)-*L*-threonyl-*L*-valinate (**SI-25**).

Pale-yellow oil (2.17 g, 6.52 mmol, 91%); **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 7.08 - 6.94 (m, 1H, H-4), 5.51 (d, $^3J_{H\text{-}H}$ = 8.2 Hz, 1H, H-2), 4.50 (dd, $^3J_{H\text{-}H}$ = 8.8, 4.9 Hz, 1H, H-5), 4.41 – 4.30 (m, 1H, H-3/9), 4.08 – 4.00 (m, 1H, H-3/9), 3.74 (s, 3H, H-8), 3.36 (s, 1H, H-11), 2.20 (pd, $^3J_{H\text{-}H}$ = 6.9, 4.9 Hz, 1H, H-6), 1.46 (s, 9H, H-1), 1.20 (d, $^3J_{H\text{-}H}$ = 6.5 Hz, 3H, H-10), 0.93 (d, $^3J_{H\text{-}H}$ = 6.8 Hz, 3H, H-7), 0.90 (d, $^3J_{H\text{-}H}$ = 6.9 Hz, 3H, H-7). Analytical data is in accordance to literature.[16]

[13] Q. Wang *et al.*, *Org. Lett.* **2021**, *14*, 3372.
[16] Y. M. Sorokina *et al.*, *Russ. J. Org. Chem.* **2012**, *48*, 1297.

2.2.20. Methyl (*Z*)-(2-((*tert*-butoxycarbonyl)amino)but-2-enoyl)-*L*-valinate (SI-26)



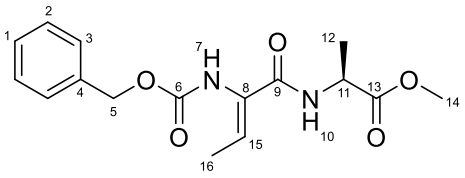
SI-26

The synthesis was performed analogously to a literature-known procedure.[14] Methyl (*tert*-butoxycarbonyl)-*L*-threonyl-*L*-valinate (**SI-25**) (2.17 g, 6.52 mmol, 1.00 equiv.) was dissolved in chloroform (130 mL, 0.05 M) and triethylamine (2.70 mL, 19.5 mmol, 3.00 equiv.) was added. At 0°C methanesulfonyl chloride (1.00 mL, 13.0 mmol, 2.00 equiv.) was added slowly to the solution and the reaction was stirred for three hours at room temperature. 1,8-Diazabicyclo[5.4.0]undec-7-ene (2.91 mL, 19.5 mmol, 3.00 equiv.) was added and the mixture was stirred for one hour at room temperature before it was stirred for 15 hours at 80°C. The reaction mixture was concentrated *in vacuo* and dissolved in EtOAc. The solution was washed with citric acid (aq., 10%, 3 x 250 mL), $NaHCO_3$ solution (sat., 250 mL), water (250 mL) and brine (250 mL). Drying with Na_2SO_4, removal of the solvent *in vacuo* and subsequent column chromatography (silica, PE/EtOAc 1:1) yielded methyl (*Z*)-(2-((*tert*-butoxycarbonyl)amino)but-2-enoyl)-*L*-valinate (**SI-26**).

Pale-yellow oil (1.38 g, 4.39 mmol, 67%); **TLC** (silica, PE/EtOAc 50:50): R_f = 0.58 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 8.25 – 8.11 (m, 1H, H-4/7), 7.63 (s, 1H, H-4/7), 6.19 (s, 1H, H-13), 4.27 – 4.14 (m, 1H, H-8), 3.63 (s, 3H, H-12), 2.19 - 2.02 (m, 1H, H-9), 1.64 (d, $^3J_{H\text{-}H}$ = 7.0, 3H, H-14), 1.39 (s, 9H, H-1), 0.91 – 0.84 (m, 6H, H-10); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 172.1 (C-11), 165.0 (C-6), 153.5 (C-3), 131.0 (C-5), 126.5 (C-13), 78.7 (C-2), 57.8 (C-8), 51.7 (C-12), 30.1 (C-9), 28.0 (3C, C-1), 19.0 (2C, C-10), 12.8 (C-14); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{15}H_{26}N_2O_5+Na]^+$: 337.1734 ($[M+Na]^+$); found: 313.1736; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3301 (m, N-H), 2970 (m, C-H), 1724 (s, C=O), 1678 (s, C=O), 1513 (m, C-H), 1367 (m, C-H), 1208 (m), 1158 (s, C-O).

[14] W. Liu *et al.*, *J. Am. Chem. Soc.* **2011**, *133*, 14216.

2.2.21. Methyl (*Z*)-(2-(((benzyloxy)carbonyl)amino)but-2-enoyl)-*L*-alaninate (SI-27)



SI-27

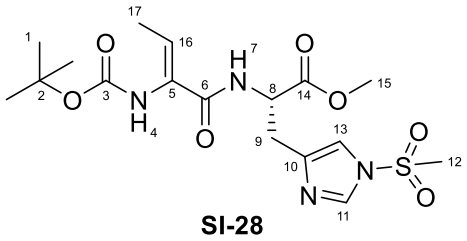
The synthesis was performed analogously to a literature-known procedure.[13] ((Benzyloxy)carbonyl)-*L*-threonine (947 mg,3.74 mmol, 1.10 equiv.), 1*H*-1,2,3-benzotriazol-1-ol monohydrate (781 mg, 5.19 mmol, 1.50 equiv.) and methyl *L*-alaninate hydrochloride (475 mg, 3.40 mmol, 1.00 equiv.) were dissolved in DCM (17 mL, 0.20 M). First *N*,*N*-diisopropylethylamine (2.96 mL, 17.0 mmol, 5.00 equiv.) and then 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (717 mg, 3.74 mmol, 1.10 equiv.) were added and stirred at room temperature for 20 hours. Ethyl acetate (100 mL) and citric acid (aq., 10 %, 100 mL) were added and the layers were separated. The organic phase was washed with $NaHCO_3$ solution (sat., 100 mL) and brine (100 mL) and dried with Na_2SO_4. The crude product was concentrated *in vacuo* and used for the next step without further purification.

The next step was performed analogously to a literature-known procedure.[14] The crude product of the first step (870 mg, 2.57 mmol, 1.00 equiv.) was dissolved in chloroform (48 mL, 0.05 M) and triethylamine (2.15 mL, 15.4 mmol, 6.00 equiv.) was added. At 0°C methanesulfonyl chloride (796 µL, 10.3 mmol, 4.00 equiv.) was added slowly to the solution and the reaction was stirred for three hours at room temperature. 1,8-Diazabicyclo[5.4.0]undec-7-ene (2.30 mL, 15.4 mmol, 6.00 equiv.) was added and the mixture was stirred for one hour at room temperature before it was stirred for 15 hours at 80°C. The reaction mixture was concentrated *in vacuo* and dissolved in EtOAc. The solution was washed with citric acid (aq., 10%, 3 x 250 mL), $NaHCO_3$ solution (sat., 250 mL), water (250 mL) and brine (250 mL). Drying with Na_2SO_4, removal of the solvent *in vacuo* and subsequent column chromatography (silica, PE/EtOAc 6:4) yielded methyl (*Z*)-(2-(((benzyloxy)carbonyl)amino)but-2-enoyl)-*L*-alaninate (**SI-27**).

[13] Q. Wang *et al.*, *Org. Lett.* **2021**, *14*, 3372.
[14] W. Liu *et al.*, *J. Am. Chem. Soc.* **2011**, *133*, 14216.

Yellow oil (382 mg, 1.19 mmol, 35 % over two steps); **TLC** (silica, PE/EtOAc 6:4): R_f = 0.11 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 8.57 (s, 1H, H-7), 8.19 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 1H, H-10), 7.43 – 7.27 (m, 5H, H-1, H-2, H-3), 6.22 (bs, 1H, H-15), 5.05 (s, 2H, H-5), 4.31 (*virt.* p, $^3J_{H\text{-}H} \approx {}^3J_{H\text{-}H}$ = 7.2 Hz, 1H, H-11), 3.60 (s, 3H, H-14), 1.64 (d, $^3J_{H\text{-}H}$ = 6.9, 3H, H-16), 1.28 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 3H, H-12); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 173.0 (C-13), 164.5 (C-9), 154.1 (C-6), 136.8 (C-4), 130.9 (C-8), 128.3 (C-1/C-2/C-3), 127.8 (C-1/C-2/C-3), 127.6 (C-1/C-2/C-3), 126.4 (C-15), 65.7 (C-5), 51.8 (C-14), 47.9 (C-11), 16.8 (C-12), 12.8 (C-16); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{16}H_{20}N_2O_5+H]^+$: 321.1445 ($[M+H]^+$); found: 321.1434; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3273 (m, N-H), 2985 (w, C-H), 2953 (w, C-H), 1719 (s, C=O), 1673 (m, C=O), 1632 (s, C=O), 1508 (s, C=C), 1454 (m, C-H), 1217 (s, C-N), 1154 (m, C-O), 739 (m, C-H_{Ar}), 698 (m, C-H_{Ar}).

2.2.22. Methyl (*Z*)-N$^{\alpha}$-(2-((*tert*-butoxycarbonyl)amino)but-2-enoyl)-N$^{\tau}$-(methylsulfonyl)-*L*-histidinate (SI-28)



SI-28

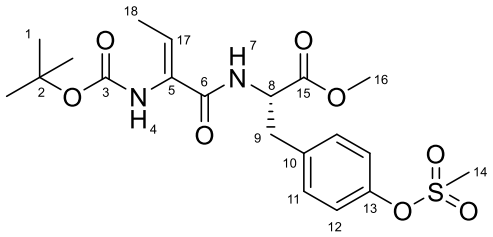
The synthesis was performed analogously to a literature-known procedure.[13] (*tert*-Butoxycarbonyl)-*L*-threonine (820 mg, 3.74 mmol, 1.10 equiv.), 1*H*-1,2,3-benzotriazol-1-ol monohydrate (781 mg, 5.10 mmol, 1.50 equiv.) and methyl *L*-histidinate dihydrochloride (823 mg, 3.40 mmol, 1.00 equiv.) were dissolved in DCM (17 mL, 0.20 M). First *N*,*N*-diisopropylethylamine (4.15 mL, 23.8 mmol, 7.00 equiv.) and then 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (717 mg, 3.74 mmol, 1.10 equiv.) were added and stirred at room temperature for 20 hours. Ethyl acetate (100 mL) and citric acid (aq., 10 %, 100 mL) were added and the layers were separated. The organic phase was washed with $NaHCO_3$ solution (sat., 100 mL) and brine (100 mL) and dried with Na_2SO_4. The crude product was concentrated *in vacuo* and used for the next step without further purification.

The next step was performed analogously to a literature-known procedure.[14] The crude product of the first step (800 mg, 2.16 mmol, 1.00 equiv.) was dissolved in chloroform (40 mL, 0.05 M) and triethylamine (1.81 mL, 13.0 mmol, 6.00 equiv.) was added. At 0°C methanesulfonyl chloride (669 µL, 8.64 mmol, 4.00 equiv.) was added slowly to the solution and the reaction was stirred for three hours at room temperature. 1,8-Diazabicyclo[5.4.0]undec-7-ene (1.93 mL, 13.0 mmol, 6.00 equiv.) was added and the mixture was stirred for one hour at room temperature before it was stirred for 15 hours at 80°C. The reaction mixture was concentrated *in vacuo* and dissolved in EtOAc. The solution was washed with citric acid (aq., 10%, 3 x 250 mL), $NaHCO_3$ solution (sat., 250 mL), water (250 mL) and brine (250 mL). Drying with Na_2SO_4, removal of the solvent *in vacuo* and subsequent column chromatography (silica, PE/EtOAc 2:8) yielded methyl (*Z*)-N$^{\alpha}$-(2-((*tert*-butoxycarbonyl)amino)but-2-enoyl)-N$^{\tau}$-(methylsulfonyl)histidinate (**SI-28**).

[13] Q. Wang *et al.*, *Org. Lett.* **2021**, *14*, 3372.
[14] W. Liu *et al.*, *J. Am. Chem. Soc.* **2011**, *133*, 14216.

Colorless oil (160 mg, 0.37 mmol, 11 % over two steps); **TLC** (silica, PE/EtOAc 2:8): R_f = 0.12 [CAM]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 8.16 (bs, 1H, H-4), 8.09 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 1H, H-7), 8.05 (d, $^4J_{H\text{-}H}$ = 1.4 Hz, 1H, H-11), 7.37 (d, $^4J_{H\text{-}H}$ = 1.4 Hz, 1H, H-13), 6.14 (bs, 1H, H-16), 4.65 – 4.54 (m, 1H, H-8), 3.60 (s, 3H, H-15), 3.59 (s, 3H, H-12), 3.02 – 2.93 (m, 2H, H-9), 1.62 (d, $^3J_{H\text{-}H}$ = 7.0 Hz, 3H, H-17), 1.37 (bs, 9H, H-1); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 171.8 (C-14), 164.9 (C-6), 153.5 (C-3), 139.5 (C-10, 136.5 (C-11), 131.1 (C-5), 126.5 (C-16), 115.1 (C-13), 78.7 (C-2), 52.0 (C-15), 51.8 (C-8), 42.6 (C-12), 29.4 (C-9), 28.0 (3C, C-1), 12.8 (C-17); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{17}H_{26}N_4O_7+Na]^+$: 453.1414 ($[M+Na]^+$); found: 453.1400; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3278 (w, N-H), 2979 (w, C-H), 2929 (w, C-H), 1710 (s, C=O), 1674 (m, C=O), 1637 (m, C=O), 1481 (m, C=C), 1367 (s, C-H), 1247 (m, C-N), 1219 (m, SO_2), 1174 (s, C-O), 1084 (s, C-N), 773 (s, C-H_{Ar}), 737 (m, C-H_{Ar}).

2.2.23. Methyl (*S*,*Z*)-2-(2-((*tert*-butoxycarbonyl)amino)but-2-enamido)-3-(4-((methylsulfonyl)oxy)phenyl)propanoate (SI-29)



SI-29

The synthesis was performed analogously to a literature-known procedure.[13] (*tert*-Butoxycarbonyl)-*L*-threonine (820 mg, 3.74 mmol, 1.10 equiv.), 1*H*-1,2,3-benzotriazol-1-ol monohydrate (781 mg, 5.10 mmol, 1.50 equiv.) and methyl *L*-tyrosinate (663 mg, 3.40 mmol, 1.00 equiv.) were dissolved in DCM (17 mL, 0.20 M). First *N*,*N*-diisopropylethylamine (1.78 mL, 10.2 mmol, 3.00 equiv.) and then 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (717 mg, 3.74 mmol, 1.10 equiv.) were added and stirred at room temperature for 20 hours. Ethyl acetate (100 mL) and citric acid (aq., 10 %, 100 mL) were added and the layers were separated. The organic phase was washed with $NaHCO_3$ solution (sat., 100 mL) and brine (100 mL) and dried with Na_2SO_4. The crude product was concentrated *in vacuo* and used for the next step without further purification.

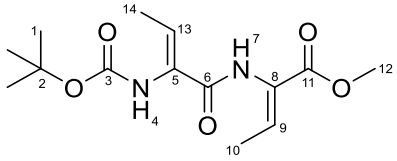
The next step was performed analogously to a literature-known procedure.[14] The crude product of the first step (1.35 g, 3.40 mmol, 1.00 equiv.) was dissolved in chloroform (63 mL, 0.05 M) and triethylamine (2.85 mL, 20.4 mmol, 6.00 equiv.) was added. At 0°C methanesulfonyl chloride (1.05 mL, 13.6 mmol, 4.00 equiv.) was added slowly to the solution and the reaction was stirred for three hours at room temperature. 1,8-Diazabicyclo[5.4.0]undec-7-ene (3.05 mL, 20.4 mmol, 6.00 equiv.) was added and the mixture was stirred for one hour at room temperature before it was stirred for 15 hours at 80°C. The reaction mixture was concentrated *in vacuo* and dissolved in EtOAc. The solution was washed with citric acid (aq., 10%, 3 x 250 mL), $NaHCO_3$ solution (sat., 250 mL), water (250 mL) and brine (250 mL). Drying with Na_2SO_4, removal of the solvent *in vacuo* and subsequent column chromatography (silica, PE/EtOAc 1:1) yielded methyl (*Z*)-2-(2-

[13] Q. Wang *et al.*, *Org. Lett.* **2021**, *14*, 3372.
[14] W. Liu *et al.*, *J. Am. Chem. Soc.* **2011**, *133*, 14216.

((*tert*-butoxycarbonyl)amino)but-2-enamido)-3-(4-((methylsulfonyl)oxy)phenyl)propanoate (**SI-29**).

Colorless oil (410 mg, 0.90 mmol, 26 % over two steps); **TLC** (silica, PE/EtOAc 2:8): R_f = 0.56 [CAM]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 8.17 – 7.87 (m, 2H, H-4, H-7), 7.41 – 7.29 (m, 2H, H-11), 7.26 – 7.19 (m, 2H, H-12), 6.11 (bs, 1H, H-17), 4.52 (td, $^3J_{H\text{-}H}$ = 8.5, 5.7 Hz, 1H, H-8), 3.60 (s, 3H, H-16), 3.33 (s, 3H, H-14), 3.14 – 2.99 (m, 2H, H-9), 1.61 (d, $^3J_{H\text{-}H}$ = 7.0 Hz, 3H, H-18), 1.37 (bs, 9H, H-1); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 171.9 (C-15), 165.0 (C-6), 153.4 (C-3), 147.8 (C-13), 136.9 (C-10), 130.8 (2C, C-5, C-11), 126.4 (C-17), 122.0 (C-12), 78.6 (C-2), 53.7 (C-8), 51.9 (C-16), 37.2 (C-14), 35.7 (C-9), 28.0 (3C, C-1), 12.9 (C-18); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{20}H_{28}N_2O_8S+H]^+$: 457.1639 ($[M+H]^+$); found: 457.1642; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3288 (w, N-H), 2980(w, C-H), 1719 (m, C=O), 1672 (m, C=O), 1639 (m, C=O), 1502 (s, C=C), 1364 (s, C-H), 1245 (m, C-N), 1199 (m, SO_2), 1149 (s, C-O), 868 (s, C-H_{Ar}), 734 (C-H_{Ar}).

2.2.24. Methyl (*Z*)-2-((*Z*)-2-((*tert*-butoxycarbonyl)amino)but-2-enamido)but-2-enoate (SI-30)



SI-30

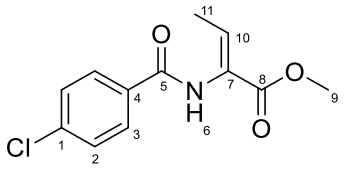
The synthesis was performed analogously to a literature-known procedure.[13] (*tert*-Butoxycarbonyl)-*L*-threonine (1.03 g, 4.72 mmol, 1.10 equiv.), 1*H*-1,2,3-benzotriazol-1-ol monohydrate (985 mg, 6.43 mmol, 1.50 equiv.) and methyl *L*-threoninate hydrochloride (727 mg, 4.29 mmol, 1.00 equiv.) were dissolved in DCM (21.5 mL, 0.20 M). First *N*,*N*-diisopropylethylamine (3.65 mL, 21.4 mmol, 5.00 equiv.) and then 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (904 mg, 4.72 mmol, 1.10 equiv.) were added and stirred at room temperature for 20 hours. Ethyl acetate (100 mL) and citric acid (aq., 10 %, 100 mL) were added and the layers were separated. The organic phase was washed with $NaHCO_3$ solution (sat., 100 mL) and brine (100 mL) and dried with Na_2SO_4. The crude product was concentrated *in vacuo* and used for the next step without further purification.

The next step was performed analogously to a literature-known procedure.[14] The crude product of the first step (673 mg, 2.01 mmol, 1.00 equiv.) was dissolved in chloroform (37 mL, 0.05 M) and triethylamine (1.68 mL, 12.1 mmol, 6.00 equiv.) was added. At 0°C methanesulfonyl chloride (623 µL, 8.05 mmol, 4.00 equiv.) was added slowly to the solution and the reaction was stirred for three hours at room temperature. 1,8-Diazabicyclo[5.4.0]undec-7-ene (1.80 mL, 12.1 mmol, 6.00 equiv.) was added and the mixture was stirred for one hour at room temperature before it was stirred for 15 hours at 80°C. The reaction mixture was concentrated *in vacuo* and dissolved in EtOAc. The solution was washed with citric acid (aq., 10%, 3 x 250 mL), $NaHCO_3$ solution (sat., 250 mL), water (250 mL) and brine (250 mL). Drying with Na_2SO_4, removal of the solvent *in vacuo* and subsequent column chromatography (silica, PE/EtOAc 8:2) yielded methyl (*Z*)-2-((*Z*)-2-((*tert*-butoxycarbonyl)amino)but-2-enamido)but-2-enoate (**SI-30**).

[13] Q. Wang *et al.*, *Org. Lett.* **2021**, *14*, 3372.
[14] W. Liu *et al.*, *J. Am. Chem. Soc.* **2011**, *133*, 14216.

Colorless oil (228 mg, 0.76 mmol, 18 % over two steps); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.37 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 9.02 (s, 1H, H-4/H-7), 8.28 (s, 1H, H-4/H-7), 6.61 – 6.39 (m, 1H, H-9), 6.27 – 6.00 (m, 1H, H-13), 3.62 (s, 3H, H-12), 1.68 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 3H, H-10), 1.66 (d, $^3J_{H\text{-}H}$ = 7.0 Hz, 3H, H-14), 1.39 (bs, 9H, H-1); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 164.9 (C-11), 163.9 (C-6), 153.5 (C-3), 132.6 (C-9), 131.5 (C-5/C-8), 128.3 (C-5/C-8), 125.7 (C-13), 78.7 (C-2), 51.8 (C-12), 28.1 (3C, C-1), 13.5 (C-10), 12.8 (C-14); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{14}H_{22}N_2O_5+Na]^+$: 321.1421 ($[M+Na]^+$); found: 321.1411; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3273 (m, N-H), 3116 (w), 2934 (w, C-H), 1697 (s, C=O), 1665 (m, C=O), 1638 (m, C=O), 1510 (m), 1365 (s, C-H), 1258 (m, C-N), 1164 (m, C-O), 1071 (m, C-N), 780 (m).

2.2.25. Methyl (*Z*)-2-(4-chlorobenzamido)but-2-enoate (23)



23

The synthesis was performed analogously to a literature-known procedure.[17] 4-Chlorobenzamide (1.49 g, 9.57 mmol, 1.00 equiv.), methyl 2-oxobutanoate (1.00 g, 8.61 mmol, 0.90 equiv.), *p*-TsOH (182 mg, 957 µmol, 0.10 equiv.) and 4-methoxyphenol (11.9 mg, 95.7 µmol, 0.01 equiv.) were dissolved in toluene (70 mL, 0.12 M) and stirred at 140 °C for 19 hours with a *Dean-Stark* apparatus. $NaHCO_3$ solution (sat., aqueous, 100 mL) was added and the layers were separated. The aqueous phase was extracted with DCM (2 x 100 mL) and the combined organic phases were washed with water (150 mL). After drying with Na_2SO_4 the organic layer was concentrated *in vacuo* and the crude product was purified by column chromatography (silica, PE/EtOAc 90:10 → 50:50) to give methyl (*Z*)-2-(4-chlorobenzamido)but-2-enoate (**23**).

Orange solid (1.11 g, 4.36 mmol, 51%); **TLC** (silica, PE/EtOAc 50:50): R_f = 0.56 [UV]; **^{1}H NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 9.76 (s, 1H, H-6), 7.96 - 7.94 (m, 2H, H-3), 7.60 - 7.58 (m, 2H, H-2), 6.68 (q, $^3J_{H\text{-}H}$ = 7.1 Hz, 1H, H-10), 3.66 (s, 3H, H-9), 1.75 (d, $^3J_{H\text{-}H}$ = 7.1 Hz, 3H, H-11); **^{13}C{^{1}H} NMR** (500 MHz, DMSO-d_6, 298 K) δ (ppm) = 164.7 (C-8), 164.5 (C-5), 136.7 (C-1), 133.7 (C-10), 132.2 (C-4), 129.6 (2C, C-3), 128.6 (2C, C-2), 128.2 (C-7), 52.0 (C-9), 13.6 (C-11); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{12}H_{12}ClNO_3+H]^+$: 254.0578 ($[M+H]^+$); found: 254.0582; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3282 (m, N-H), 2982 (w, C-H), 2954 (w, C-H), 1729 (s, C=O), 1645 (s, C=O), 1508 (s, C=C), 1481 (s, C=C), 1306 (s, C-H), 1258 (s, C-O), 1015 (s, C-Cl), 833 (m, C-Cl), 767 (s, C-H_{Ar}), 757 (s, C-H_{Ar}).

[17] G. Storch, O. Trapp, *Nat. Chem.* **2016**, *9*, 179.

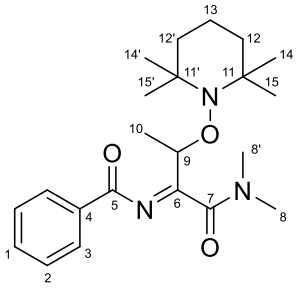
3. Catalytic Experiments

3.1. General Procedure

A crimp-cap vial equipped with a stir bar was filled with substrate (36.0 μmol, 1.00 equiv.), the flavin photocatalyst (**14)** (2.46 mg, 7.20 μmol, 0.20 equiv.) and TEMPO (16.9 mg, 108 μmol, 3.00 equiv.). Subsequently the vial was sealed with a septum and the atmosphere was changed by evacuating and backfilling the vial with Ar for three times. Then the solid components were dissolved in DCM (anhydrous, 2.00 mL, 18.0 mM). If the substrate was an oil/liquid it was dissolved in DCM and added to the vial as a solution. The reaction solution was irradiated with blue LED light (λ = 451 nm, 1 W) under rapid stirring. After 16 hours, the solution was dried *in vacuo* and dissolved in CD_2Cl_2 followed by the addition of trimethylbenze-1,3,5-tricarboxylate (3.00 mg, 12.0 μmol, 0.33 equiv.) as internal NMR standard (10 s relaxation time; the integral of the internal standard (8.83 ppm) was set to 1.00 → integral of the α-hydroxylamine proton gives NMR-yield (**figure SI-03**)). The NMR sample was purified by flash column chromatography (silica, PE/EtOAc 9:1).

3.2. Example Reaction

3.2.1. *N*-(1-(Dimethylamino)-1-oxo-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butan-2-ylidene)benzamide (25)



25

The reaction was performed according to the general procedure in section **3.1.**.

Colorless oil (10.1 mg, 26.1 µmol, 73 %); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.12 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.93 - 7.83 (m, 2H, H-3), 7.62 - 7.53 (m, 1H, H-1), 7.52 - 7.40 (m, 2H, H-2), 5.05 (q, 1H, $^3J_{H\text{-}H}$ = 6.6 Hz, H-9), 3.02 (s, 3H, H-8/8'), 2.88 (s, 3H, H-8/8'), 1.61 (d, 3H, $^3J_{H\text{-}H}$ = 6.6 Hz, H-10), 1.55 – 1.42 (m, 4H, H-12, 12'), 1.40 – 1.28 (m, 2H, H-13), 1.20 (s, 3H, H-14'/15'), 1.14 (s, 3H, H-14'/15'), 1.02 (s, 3H, H-14/H-15), 1.00 (s, 3H, H-15/H-14); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 178.9 (C-5), 170.2 (C-7), 165.7 (C-6), 133.9 (C-1), 132.5 (C-4), 129.8 (2C, C-3), 129.0 (2C, C-2), 80.4 (C-9), 61.7 (C-11/C-11'), 59.7 (C-11/C-11'), 41.0 (C-12/C-12'), 40.8 (C-14/C-15), 38.3 (C-8/C-8'), 34.6 (C-14'/C-15'), 34.2 (C-12/C-12'), 34.1 (C-8/C-8'), 20.9 (C-14/C-15), 20.6 (C-14/C-15), 18.3 (C-10), 17.6 (C-13); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{22}H_{33}N_3O_3+H]^+$: 388.2595 ($[M+H]^+$); found: 388.2596; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3057 (w, C-H), 2937 (m, C-H), 2873 (w, C-H), 1666 (m, C=O), 1616 (s, C=O), 1576 (m, C=N), 1478 (m, C=C), 1380 (s, C-H), 721 (s, C-H_{Ar}), 703 (s, C-H_{Ar}).

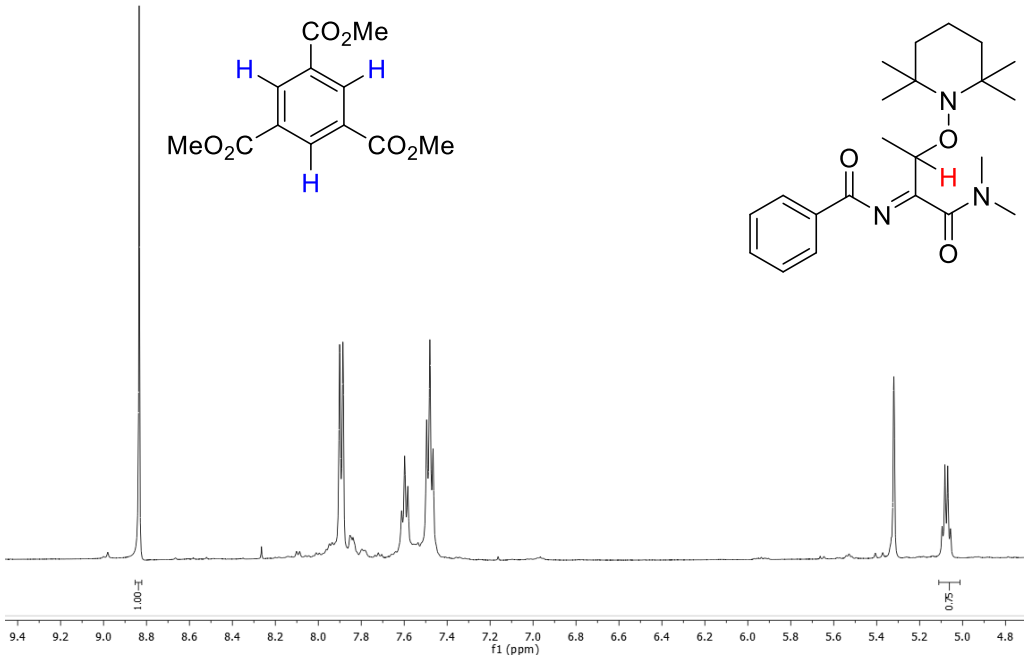
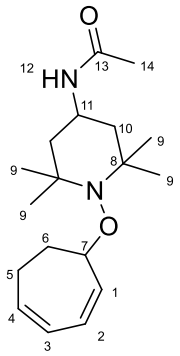


Figure SI-03: NMR spectrum of the crude catalysis reaction of product **25**. This reaction corresponds to 75% yield.

3.3. Oxidation of 1,3-Cycloheptadiene with Bobbitt's Salt

3.3.1. *N*-(1-(Cyclohepta-2,4-dien-1-yloxy)-2,2,6,6-tetramethylpiperidin-4-yl)acetamide (22)



22

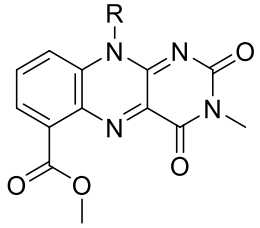
A *Schlenk* tube equipped with a stir bar was filled with flavin catalyst (**14**) (6.85 mg, 20.0 µmol, 0.20 equiv.), potassium phosphate (25.5 mg, 120 µmol, 1.20 equiv.) and 4-acetamido-2,2,6,6-tetramethyl-1-oxopiperidin-1-ium tetrafluoroborate (**21**) (30.0 mg, 100 µmol, 1.00 equiv.). Subsequently the tube was sealed with a septum and the atmosphere was changed by evacuating and backfilling the vial with Ar for three times. Then the solid components were dissolved in 1,4-dioxane (anhydrous, 1.00 mL, 0.1 M) and 1,3-cycloheptadiene (25.0 µL, 230 µmol, 2.30 equiv.) was added. The solution was irradiated with blue Kessil© light under rapid stirring. After four hours, the solution was dried *in vacuo* and dissolved in $CDCl_3$ followed by the addition of trimethylbenze-1,3,5-tricarboxylate (3.00 mg, 12.0 µmol, 0.12 equiv.) as internal NMR standard. The NMR sample was purified by flash column chromatography (silica, PE/EtOAc 7:3 → 6:4), which gave *N*-(1-(cyclohepta-2,4-dien-1-yloxy)-2,2,6,6-tetramethylpiperidin-4-yl)acetamide (**22**).

Pale yellow solid (11.3 mg, 36.9 µmol, 37%); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.18 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 6.16 - 6.03 (m, 1H, H-1), 5.95 (dt, $^3J_{H\text{-}H}$ = 11.7, 5.8 Hz, 1H, H-4), 5.87 - 5.75 (m, 2H, H-2, H-3), 5.11 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 1H, H-12), 4.43 (dt, $^3J_{H\text{-}H}$ = 6.7, 3.2 Hz, 1H, H-7), 4.13 (tdt, $^3J_{H\text{-}H}$ = 12.1, 8.0, 4.0 Hz, 1H, H-11), 2.45 - 2.20 (m, 2H, H-5), 2.16 - 2.07 (m, 1H, H-6), 1.94 (s, 3H, H-14), 1.89 – 1.75 (m, 3H, H-6, H-10), 1.37 - 1.28 (m, 2H, H-10), 1.22 (s, 3H, H-9), 1.21 (s, 3H, H-9), 1.20 (s, 3H, H-9), 1.17 (s, 3H, H-9); **^{13}C{^{1}H} NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 169.4 (C-13), 135.7 (C-4), 134.4 (C-1), 124.6 (C-2/C-3),

124.5 (C-2/C-3), 81.4 (C-7), 60.3 (C-8), 60.0 (C-8), 46.3 (2C, C-10), 41.2 (C-11), 34.4 (C-9), 34.3 (C-9), 30.7 (C-6), 26.0 (C-5), 23.7 (C-14), 21.1 (2C, C-9); **HR-MS** (ESI^+): *m/z* = calc. for $[C_{18}H_{30}N_2O_2+H]^+$: 307.2380 ($[M+H]^+$); found: 307.2383; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3277 (m, N-H), 3073 (w, C-H), 2974 (m, C-H), 2934 (m, C-H), 1637 (s, C=O), 1549 (s, C=C), 1440 (m, C-H), 1370 (s, C-H), 1036 (m, C-H), 975 (m, C-H), 734 (m).

3.3.2. Screening Regarding the Oxidation of 1,3-Cycloheptadiene with Bobbitt's Salt

Initial screening was performed in the photo-setup with four Kessil Tuna Blue© irradiating the sample using flavin **SI-31** (10 mol%). The NMR-yield (*vs.* internal standard) of product **22** is reported. Entry #17 turned out to work best for this catalytic system.



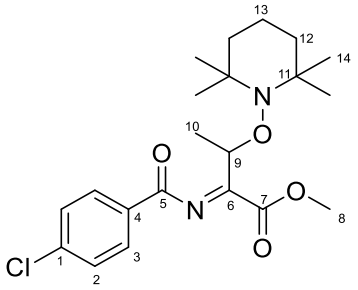
SI-31

#	Catalyst[a]	Solvent[b]	Base[c]	Time	NMR-yield
1	**SI-31**	CF_3Ph	Py	9h	14%
2	**SI-31**	DMF	Py	9h	16%
3	**SI-31**	MTBE	Py	9h	32%
4	**SI-31**	EtOH	Py	9h	8%
5	**SI-31**	DMC	Py	9h	10%
6	**SI-31**	MTBE	K_2CO_3	4h	8%
7	**SI-31**	MTBE	Cs_2CO_3	4h	24%
8	**SI-31**	MTBE	K_3PO_4	4h	45%
9	**SI-31**	MTBE	Li_3PO_4	4h	0%
10	**SI-31**	MTBE	Na_3PO_4	4h	14%
11	**SI-31**	MTBE	2,6-Lutidin	4h	12%
12	**SI-31**	MTBE	2,6-bis-^{t}Bu-Py	9h	8%
13	**SI-31**	MTBE	Py	2d	45%
14	**SI-31**	MTBE	K_3PO_4	9h	45%
15	**SI-31**	CF_3Ph	K_3PO_4	4h	32%
16	**SI-31**	DCM	K_3PO_4	4h	32%
17	**SI-31**	1,4-Dioxane	K_3PO_4	4h	48%
18	**14**[d]	1,4-Dioxane	K_3PO_4	4h	42%
19	**RFTA-Me**[d]	1,4-Dioxane	K_3PO_4	4h	24%

[a]: initial screening was done with flavins bearing various alkyl groups in N10 position. [b]: 50 mM; [c]: 1.20 equiv.; [d]: 20 mol% of catalyst were used.

3.4. Amino acid derivatization

3.4.1. Methyl 2-((4-chlorobenzoyl)imino)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butanoate (24)

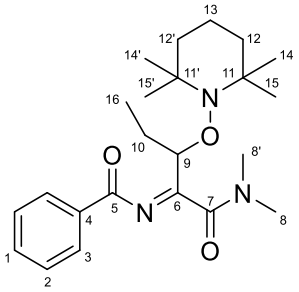


24

The reaction was performed according to the general procedure in section **3.1.**. Instead of 16 hours the sample was irradiated for 24 hours. The product was purified by flash column chromatography (silica, PE/EtOAc 95:5).

Colorless oil (2.00 mg, 4.89 µmol, 14 %); **TLC** (silica, PE/EtOAc 95:5): R_f = 0.20 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.86 - 7.80 (m, 2H, H-3), 7.47 - 7.42 (m, 2H, H-2), 4.94 (q, $^3J_{H\text{-}H}$ = 6.8 Hz, 1H, H-9), 3.79 (s, 3H, H-8), 1.58 (d, $^3J_{H\text{-}H}$ = 6.8 Hz, 4H, H-10, H-13), 1.47 - 1.37 (m, 4H, H-12), 1.33 – 1.24 (m, 1H, H-13), 1.18 (s, 3H, H-14), 1.08 (s, 3H, H-14), 1.04 (s, 3H, H-14), 0.97 (s, 3H, H-14); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 178.0 (C-5), 164.8 (C-7), 162.0 (C-6), 140.0 (C-1), 131.5 (C-4), 130.9 (2C, C-3), 129.4 (2C, C-2), 81.7 (C-9), 60.8 (C-11), 60.0 (C-11), 53.5 (C-8), 40.7 (2C, C-12, C-14), 34.6 (C-14), 34.2 (C-12), 20.7 (C-14), 20.4 (C-14), 19.5 (C-10), 17.6 (C-13); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{21}H_{29}ClN_2O_4+H]^+$: 409.1889 ($[M+H]^+$); found: 409.1896; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 2980 (w, C-H), 2928 (m, C-H), 2854 (m, C-H), 1738 (m, C=O), 1695 (s, C=O), 1593 (s, C=N), 1439 (m, C=C), 1380 (m, C-H), 1272 (s, C-O), 1092 (s, C-Cl), 847 (m, C-Cl), 763 (s, C-H), 732 (m, C-H).

3.4.2. N-(1-(dimethylamino)-1-oxo-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentan-2-ylidene)benzamide (26)

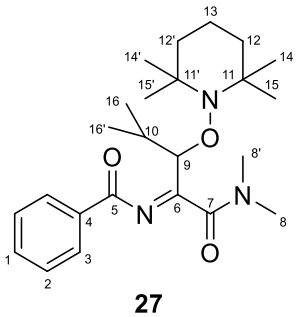


26

The reaction was performed according to the general procedure in section **3.1.**.

Colorless oil (11.1 mg, 27.7 µmol, 77 %); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.13 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.92 - 7.84 (m, 2H, H-3), 7.63 - 7.54 (m, 1H, H-1), 7.49 - 7.42 (m, 2H, H-2), 4.74 (dd, 1H, $^3J_{H\text{-}H}$ = 10.2 Hz, $^4J_{H\text{-}H}$ = 3.3 Hz, H-9), 3.02 (s, 3H, H-8/8'), 2.85 (s, 3H, H-8/8'), 2.44 (dq, 1H, $^3J_{H\text{-}H}$ = 7.5 Hz, $^3J_{H\text{-}H}$ = 3.3 Hz, H-10), 2.03 - 1.91 (m, 1H, H-10'), 1.73 – 1.42 (m, 6H, H-13, H-12, H-12'), 1.32 - 1.26 (m, 3H, H-14'/15'), 1.23 – 1.15 (m, 3H, H-14'/15'), 1.10 (s, 6H, H-14,15), 1.04 (t, 3H, $^3J_{H\text{-}H}$ = 7.5 Hz, H-16); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 178.9 (C-5), 168.5 (C-7), 165.6 (C-6), 133.9 (C-1), 132.7 (C-4), 129.9 (2C, C-3), 129.0 (2C, C-2), 86.4 (C-9), 61.6 (C-11/C-11'), 59.9 (C-11/C-11'), 41.0 (2C, C-12, C-12'), 38.4 (C-8/8'), 34.4 (C-14/C-15), 34.1 (C-8/8'), 30.2 (C-14'/C-15'), 24.2 (C-10), 21.0 (C-14'/15'), 20.8 (C-14/15), 17.7 (C-13), 10.7 (C-16); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{23}H_{35}N_3O_3+H]^+$: 402.2752 ($[M+H]^+$); found: 402.2758. **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3061 (w, C-H), 2933 (m, C-H), 2875 (w, C-H), 1725 (m, C=O), 1639 (m, C=O), 1576 (m, C=N), 1449 (m, C=C), 1379 (s, C-H), 1249 (m), 744 (s, C-H_{Ar}), 719 (s, C-H_{Ar}).

3.4.3. *N*-(1-(dimethylamino)-4-methyl-1-oxo-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentan-2-ylidene)benzamide (27)

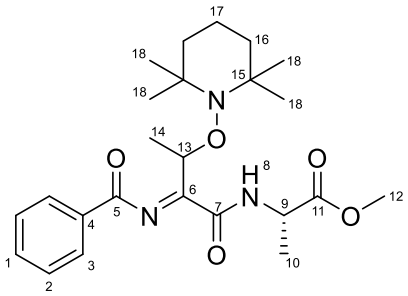


27

The reaction was performed according to the general procedure in section **3.1.**.

Colorless oil (11.0 mg, 26.5 µmol, 74 %); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.32 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.92 - 7.86 (m, 2H, H-3), 7.60 - 7.52 (m, 1H, H-1), 7.48 - 7.39 (m, 2H, H-2), 4.89 (d, 1H, $^4J_{H\text{-}H}$ = 4.2 Hz, H-9), 3.09 (s, 3H, H-8/8'), 2.86 (s, 3H, H-8/8'), 2.61 (*virt.* pd, 1H, $^3J_{H\text{-}H} \approx {}^3J_{H\text{-}H}$ = 7.0 Hz, $^3J_{H\text{-}H}$ = 4.2 Hz, H-10), 1.80-1.51 (m, 2H, H-13), 1.48 – 1.38 (m, 4H, H-12,12'), 1.27 (s, 3H, H-14/H-15), 1.22 (s, 3H, H-14/H-15), 1.18 (d, 3H, $^3J_{H\text{-}H}$ = 7.0 Hz, H-16/H-16'), 1.16 (d, $^3J_{H\text{-}H}$ = 7.0 Hz, 3H, H-16/H-16'), 1.15 – 0.95 (m, 6H, H-14'/15'); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 178.6 (C-5), 169.5 (C-7), 165.9 (C-6), 133.6 (C-1), 133.2 (C-4), 129.8 (2C, C-3), 128.9 (2C, C-2), 87.7 (C-9), 61.4 (C-11/C-11'), 60.8 (C-11/C-11'), 41.3 (2C, C-12, C-12'), 38.3 (C-8/8'), 34.5 (C-8/8'), 34.3 (C-14/C-15), 31.1 (C-10), 30.1 (C-14'/C-15'), 21.0 (C-14/C-15), 20.6 (C-14'/C-15'), 20.3 (C-16/C-16'), 18.4 (C-16/C-16'), 17.5 (C-13); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{24}H_{37}N_3O_3+H]^+$: 416.2908 ($[M+H]^+$); found: 416.2909. **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3061 (w, C-H), 2931 (m, C-H), 2873 (w, C-H), 1717 (m, C=O), 1641 (m, C=O), 1577 (m, C=N), 1449 (m, C=C), 1382 (s, C-H), 1260 (m), 716 (s, C-H_{Ar}).

3.4.4. Methyl (2-(benzoylimino)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butanoyl)-*L*-alaninate (29)

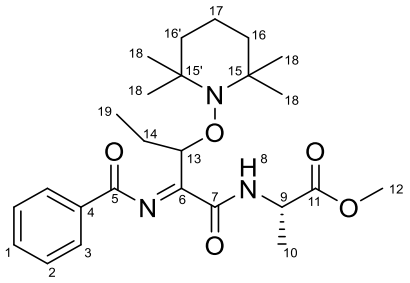


29

The reaction was performed according to the general procedure in section **3.1.**. The product was obtained as a mixture of diastereomers.

Colorless oil (7.50 mg, 16.8 µmol, 47 %, d.r.: 1:1); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.08 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 8.22 – 8.09 (m, 1H, H-8$^{a/b}$), 7.90 – 7.72 (m, 4H, H-3$^{a/b}$), 7.59 – 7.50 (m, 2H, H-1$^{a/b}$), 7.50 – 7.39 (m, 4H, H-2$^{a/b}$), 6.25 – 5.57 (m, 1H, H-8$^{a/b}$), 5.32 – 5.27 (m, 1H, H-13$^{a/b}$), 5.14 – 5.04 (m, 1H, H-13$^{a/b}$), 4.66 – 4.47 (m, 2H, H-9$^{a/b}$), 3.74 (d, 6H, H-12$^{a/b}$), 1.62 – 1.58 (m, 2H, H-17$^{a/b}$), 1.58 (d, $^3J_{H-H}$ = 6.9 Hz, 3H, H-10$^{a/b}$), 1.55 (d, $^3J_{H-H}$ = 6.9 Hz, 3H, H-10$^{a/b}$), 1.48 – 1.35 (m, 16H, 2 x H-14$^{a/b}$, 4 x H-16$^{a/b}$, 2 x H-18$^{a/b}$), 1.32 – 1.25 (m, 6H, 4 x H-16$^{a/b}$, 2 x H-17$^{a/b}$), 1.24 – 1.15 (m, 6H, H-18$^{a/b}$), 1.14 – 1.05 (m, 9H, H-18$^{a/b}$), 1.00 (s, 3H, H-18$^{a/b}$); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 179.0 (C-5$^{a/b}$), 178.9 (C-5$^{a/b}$), 173.0 (C-11$^{a/b}$), 172.9 (C-11$^{a/b}$), 164.8 (C-6$^{a/b}$), 164.2 (C-6$^{a/b}$), 160.6 (C-7$^{a/b}$), 160.2 (C-7$^{a/b}$), 133.5 (2C, C-4$^{a/b}$), 133.42 (C-1$^{a/b}$), 133.35 (C-1$^{a/b}$), 129.3 (C-3$^{a/b}$), 129.2 (C-3$^{a/b}$), 129.1 (C-3$^{a/b}$), 128.9 (4C, C-2$^{a/b}$), 127.8 (C-3$^{a/b}$), 81.6 (C3$^{a/b}$), 80.4 (C-13$^{a/b}$), 60.9 (C-15$^{a/b}$), 60.8 (C-15$^{a/b}$), 60.5 (C-15$^{a/b}$), 60.2 (C-15$^{a/b}$), 53.0 (2C, C-12$^{a/b}$), 49.0 (2C, C-9$^{a/b}$), 40.6 (2C, C-16$^{a/b}$), 34.4 (C-18$^{a/b}$), 34.3 (C-18$^{a/b}$), 34.2 (C-18$^{a/b}$), 34.0 (C-18$^{a/b}$), 30.2 (2C, C-16$^{a/b}$), 21.1 (C-18$^{a/b}$), 20.9 (C-18$^{a/b}$), 20.6 (C-18$^{a/b}$), 20.4 (C-18$^{a/b}$), 19.8 (2C, C-10$^{a/b}$), 18.4 (C-14$^{a/b}$), 17.8 (C-14$^{a/b}$), 17.6 (C-17$^{a/b}$), 17.5 (C-17$^{a/b}$); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{24}H_{35}N_3O_5+H]^+$: 446.2649 ($[M+H]^+$); found: 446.2647. **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3353 (m, N-H), 3200 (m, N-H), 3061 (w, C-H), 2928 (m; C-H), 2854 (w, C-H), 1741 (m, C=O), 1662 (s, C=O), 1615 (m, C=O), 1576 (m, C=N), 1513 (m, C=C), 1449 (m, C=C), 1380 (s, C-H), 1158 (m, C-O), 762 (m, C-H_{Ar}), 708 (m, C-H_{Ar}).

3.4.5. Methyl (2-(benzoylimino)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentanoyl)-L-alaninate (30)



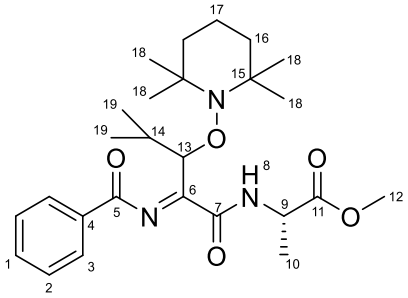
30

The reaction was performed according to the general procedure in section **3.1.**. The product was obtained as a mixture of diastereomers.

Colorless oil (7.50 mg, 16.3 µmol, 54 %, d.r.: 1:1); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.09 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 8.64 (d, $^3J_{H\text{-}H}$ = 7.6 Hz, 1H, H-8^a), 8.41 (d, $^3J_{H\text{-}H}$ = 7.8 Hz, 1H, H-8^b), 7.83 - 7.80 (m, 4H, H-3^a, H-3^b), 7.61 - 7.52 (m, 2H, H-1^a. H-1^b), 7.47 - 7.43 (m, 4H, H-2^a, H-2^b), 4.83 (dd, $^3J_{H\text{-}H}$ = 8.3, 6.2 Hz, 1H, H-13$^{a/b}$), 4.76 (dd, $^3J_{H\text{-}H}$ = 9.1, 5.6 Hz, 1H, H-13$^{a/b}$), 4.63 - 4.47 (m, 2H, H-9^a, H-9^b), 3.72 (s, 3H, H-12$^{a/b}$), 3.72 (s, 3H, H-12$^{a/b}$), 2.26 - 2.15 (m, 2H, H-14^a, H-14^b), 2.05 - 1.93 (m, 2H, H-14^a, H-14^b), 1.62 – 1.57 (m, 2H, 1 x H-17^a, 1 x H-17^b), 1.54 - 1.45 (m, 16H, H-10^a, H-10^b, 2 x H-16^a, 2 x H-16^b, 1 x H-18^a, 1 x H-18^b), 1.34 – 1.24 (s, 12H, 2 x H-16^a, 2 x H-16^b, 1 x H-17^a, 1 x H-17^b, 1 x H-18^a, 1 x H-18^b), 1.16 (s, 12H, 2 x H-18^a, 2 x H-18^b), 1.05 - 1.00 (m, 6H, H-19^a, H-19^b); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 180.0 (C-5$^{a/b}$), 179.8 (C-5$^{a/b}$), 172.89 (C-11$^{a/b}$), 172.85 (C-11$^{a/b}$), 164.8 (C-6$^{a/b}$), 163.7 (C-6$^{a/b}$), 160.8 (C-7a$^{/b}$), 160.2 (C-7$^{a/b}$), 134.0 (2C, C-4$^{a/b}$), 133.2 (C-1^b), 133.1 (C-1^a), 132.4 (C-2$^{a/b}$/C-3$^{a/b}$), 129.1 (C-2$^{a/b}$/C-3$^{a/b}$), 129.0 (C-2$^{a/b}$/C-3$^{a/b}$), 128.94 (2C, C-2$^{a/b}$, C-3$^{a/b}$), 128.89 (2C, C-2$^{a/b}$, C-3$^{a/b}$), 127.8 (C-2$^{a/b}$/C-3$^{a/b}$), 86.9 (C-13$^{a/b}$), 85.3 (C-13$^{a/b}$), 61.4 (C-15$^{a/b}$), 60.9 (C-15$^{a/b}$), 60.8 C-15$^{a/b}$), 60.3 (C-15$^{a/b}$), 52.9 (2C, C-12$^{a/b}$), 49.0 (2C, C-9$^{a/b}$), 40.7 (2C, C-16$^{a/b}$), 34.3 (C-18$^{a/b}$), 34.1 (C-18$^{a/b}$), 33.9 (C-18$^{a/b}$), 33.7 (C-18$^{a/b}$), 30.2 (2C, C-16$^{a/b}$), 26.8 (C-14$^{a/b}$), 26.5 (C-14$^{a/b}$), 24.8 (C-18$^{a/b}$), 20.8 (2C, C-18$^{a/b}$), 20.5 (C-18$^{a/b}$), 18.5 (C-10$^{a/b}$), 18.4 (C-10$^{a/b}$), 17.5 (2C, C-17$^{a/b}$), 10.9 (C-19$^{a/b}$), 10.8 (C-19$^{a/b}$); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{25}H_{37}N_3O_5+H]^+$: 460.2806 ($[M+H]^+$); found: 460.2802. **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3354 (w, N-H), 3201 (w, N-H), 3060 (w, C-H), 2929 (m; C-H), 2874 (w, C-H), 1743 (m, C=O), 1665 (s, C=O),

1611 (m, C=O), 1576 (m, C=N), 1514 (m, C=C), 1449 (m, C=C), 1381 (s, C-H), 1159 (m, C-O), 698 (m, C-H_{Ar}).

3.4.6. Methyl (2-(benzoylimino)-4-methyl-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentanoyl)-*L*-alaninate (31)



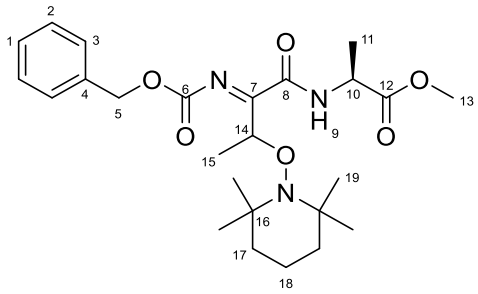
31

The reaction was performed according to the general procedure in section **3.1.**. The product was obtained as a mixture of diastereomers.

Colorless oil (12.0 mg, 25.3 µmol, 70 %, d.r.: 1.5:1.0); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.14 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 9.04 – 8.95 (m, 1H, H-8^b), 7.89 - 7.75 (m, 4H, H-3$^{a/b}$), 7.62 – 7.50 (m, 2H, H-1$^{a/b}$), 7.50 – 7.39 (m, 4H, H-2$^{a/b}$), 6.12 – 5.73 (m, 1H, H-8^a), 5.37 – 5.33 (m, 1H, H-13^a), 4.65 - 4.44 (m, 3H, H-9$^{a/b}$, H-13^b), 3.74 - 3.69 (m, 6H, H-12$^{a/b}$), 2.63 - 2.54 (m, 1H, H-14^b), 2.44 – 2.36 (m, 1H, H-14^a), 1.55 - 1.37 (m, 12H, 2 x H-10$^{a/b}$, 4 x H-16$^{a/b}$, 2 x H-17$^{a/b}$), 1.35 – 1.20 (m, 18H, 4 x H-16$^{a/b}$, 2 x H-17$^{a/b}$, 3 x H-18$^{a/b}$, H-19^b), 1.19 - 1.12 (m, 6H, 2 x H-18$^{a/b}$), 1.08 – 1.06 (m, 3H, 1 x H-18$^{a/b}$), 1.04 (d, $^3J_{H\text{-}H}$ = 6.7 Hz, 3H, H-19^b), 0.94 (dd, $^3J_{H\text{-}H}$ = 7.2, $^4J_{H\text{-}H}$ = 1.1 Hz, 3H, H-19^a), 0.90 – 0.82 (m, 9H, 2 x H-18$^{a/b}$, H-19^a); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 180.5 (C-5$^{a/b}$), 180.2 (C-5$^{a/b}$), 172.9 (C-11$^{a/b}$, 172.8 (C-11$^{a/b}$), 167.1 (C-6$^{a/b}$), 166.1 (C-6$^{a/b}$), 162.3 (C-7$^{a/b}$), 162.1 (C-7$^{a/b}$), 134.3 (2C, C-4$^{a/b}$), 133.2 (C-1$^{a/b}$), 133.1 (C-1$^{a/b}$), 129.1 (2C, C-2$^{a/b}$), 129.0 (2C, C-3$^{a/b}$), 128.9 (2C, C-2$^{a/b}$), 127.8 (2C, C-3$^{a/b}$), 87.7 (C-13$^{a/b}$), 85.2 (C-13$^{a/b}$), 62.7 (C-15$^{a/b}$), 62.4 (C-15$^{a/b}$), 61.0 (2C, C-15$^{a/b}$), 52.8 (2C, C-12$^{a/b}$), 48.9 (C-9$^{a/b}$), 48.8 (C-9$^{a/b}$), 40.8 (2C, C-16$^{a/b}$), 34.3 (C-18$^{a/b}$), 33.5 (C-18$^{a/b}$), 32.0 (C-14$^{a/b}$), 31.4 (C-14$^{a/b}$), 30.2 (2C, C-16$^{a/b}$), 21.2 (C-18$^{a/b}$), 21.1 (C-18$^{a/b}$), 20.6 (C-18$^{a/b}$), 20.3 (C-18$^{a/b}$), 20.01 (C-18$^{a/b}$/C-19$^{a/b}$), 19.95 (C-18$^{a/b}$/C-19$^{a/b}$), 19.8 (C-18$^{a/b}$/C-19$^{a/b}$), 19.21 (C-19$^{a/b}$), 19.16 (C-19$^{a/b}$), 18.6 (C-10$^{a/b}$), 18.4 (C-10$^{a/b}$), 17.5 (C-17$^{a/b}$), 17.4 (C-17$^{a/b}$), 16.6 (C-19$^{a/b}$); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{26}H_{39}N_3O5+H]^+$: 474.2962 ($[M+H]^+$); found: 474.2958. **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3367 (m, N-H), 3181 (m, N-H), 3064 (w, C-H), 2932 (m; C-H),

2874 (w, C-H), 1744 (m, C=O), 1673 (s, C=O), 1624 (m, C=O), 1578 (m, C=N), 1514 (m, C=C), 1450 (m, C=C), 1376 (s, C-H), 1160 (m, C-O), 764 (m, C-H_{Ar}), 701 (m, C-H_{Ar}).

3.4.7. Methyl (2-(((benzyloxy)carbonyl)imino)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butanoyl)-*L*-alaninate (32)



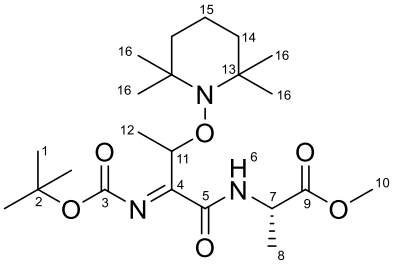
32

The reaction was performed according to the general procedure in section **3.1.**. The product was obtained as a mixture of isomers.

Pale-yellow oil (9.82 mg, 20.6 μmol, 57 %, d.r.: 1:1; additionally, another 1:1 mixture of isomers, presumably of the E/Z-isomers at the C=N double bond, can be observed); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.21 [CAM]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.37 – 7.26 (m, 20H, H-1$^{a/b/c/d}$, H-2$^{a/b/c/d}$, H-3$^{a/b/c/d}$), 5.77 – 5.62 (m, 4H, H-9$^{a/b/c/d}$), 4.92 – 4.73 (m, 4H, H-10$^{a/b/c/d}$), 4.69 – 4.58 (m, 4H, H-5$^{a/b/c/d}$), 4.57 – 4.51 (m, 2H, H-14$^{a/b/c/d}$), 4.49 – 4.44 (m, 2H, H-5$^{a/b/c/d}$), 4.43 – 4.37 (m, 4H, H-5$^{a/b/c/d}$, H-14$^{a/b/c/d}$), 3.74 (s, 3H, H-13$^{a/b/c/d}$), 3.73 (s, 3H, H-13$^{a/b/c/d}$), 3.72 (s, 3H, H-13$^{a/b/c/d}$), 3.71 (s, 3H, H-13$^{a/b/c/d}$), 1.67 – 1.61 (m, 12H, H-11$^{a/b/c/d}$), 1.61 – 1.57 (m, 4H, H-18$^{a/b/c/d}$), 1.48 – 1.40 (m, 16H, H-17$^{a/b/c/d}$), 1.38 – 1.36 (m, 6H, H-15$^{a/b/c/d}$), 1.35 – 1.32 (m, 6H, H-15$^{a/b/c/d}$), 1.32 – 1.29 (m, 4H, H-18$^{a/b/c/d}$), 1.21 – 1.19 (m, 6H, H-19$^{a/b/c/d}$), 1.19 – 1.14 (m, 6H, H-19$^{a/b/c/d}$), 1.15 – 1.12 (m, 6H, H-19$^{a/b/c/d}$), 1.07 (s, 12H, H-19$^{a/b/c/d}$), 1.04 (s, 12H, H-19$^{a/b/c/d}$), 1.00 – 0.95 (m, 6H, H-19$^{a/b/c/d}$); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 171.6 (C-6$^{a/b/c/d}$/C-12$^{a/b/c/d}$), 170.5 (3C, C-6$^{a/b/c/d}$/C-12$^{a/b/c/d}$), 170.4 (C-6$^{a/b/c/d}$/C-12$^{a/b/c/d}$), 170.33 (C-6$^{a/b/c/d}$/C-12$^{a/b/c/d}$), 170.30 (C-6$^{a/b/c/d}$/C-12$^{a/b/c/d}$), 170.23 (C-6$^{a/b/c/d}$/C-12$^{a/b/c/d}$), 155.76 (2C, C-7$^{a/b/c/d}$/C-8$^{a/b/c/d}$), 155.75 (2C, C-7$^{a/b/c/d}$/C-8$^{a/b/c/d}$), 155.57 (2C, C-7$^{a/b/c/d}$/C-8$^{a/b/c/d}$), 155.55 (C-7$^{a/b/c/d}$/C-8$^{a/b/c/d}$), 137.82 (C-4$^{a/b/c/d}$), 137.76 (C-4$^{a/b/c/d}$), 137.72 (C-4$^{a/b/c/d}$), 137.66 (C-4$^{a/b/c/d}$), 128.87 (2C, C-1$^{a/b/c/d}$/C-2$^{a/b/c/d}$/C-3$^{a/b/c/d}$), 128.86 (2C, C-1$^{a/b/c/d}$/C-2$^{a/b/c/d}$/C-3$^{a/b/c/d}$), 128.8 (4C, C-1$^{a/b/c/d}$/C-2$^{a/b/c/d}$/C-3$^{a/b/c/d}$), 128.25 (2C, C-1$^{a/b/c/d}$/C-2$^{a/b/c/d}$/C-3$^{a/b/c/d}$), 128.24 (2C, C-1$^{a/b/c/d}$/C-2$^{a/b/c/d}$/C-3$^{a/b/c/d}$), 128.22 (2C, C-1$^{a/b/c/d}$/C-2$^{a/b/c/d}$/C-3$^{a/b/c/d}$), 128.20 (2C, C-1$^{a/b/c/d}$/C-2$^{a/b/c/d}$/C-3$^{a/b/c/d}$), 128.09 (4C,

C-1$^{a/b/c/d}$/C-2$^{a/b/c/d}$/C-3$^{a/b/c/d}$), 91.3 (C-14$^{a/b/c/d}$), 90.9 (C-14$^{a/b/c/d}$), 80.5 (C-14$^{a/b/c/d}$), 78.3 (C-14$^{a/b/c/d}$), 66.4 (C-5$^{a/b/c/d}$), 66.3 (C-5$^{a/b/c/d}$), 66.22 (C-5$^{a/b/c/d}$), 66.20 (C-5$^{a/b/c/d}$), 61.8 (2C, C-16$^{a/b/c/d}$), 61.64 (C-16$^{a/b/c/d}$), 61.60 (C-16$^{a/b/c/d}$), 59.7 (2C, C-16$^{a/b/c/d}$), 59.61 (C-16$^{a/b/c/d}$), 59.57 (C-16$^{a/b/c/d}$), 53.32 (C-13$^{a/b/c/d}$), 53.25 (C-13$^{a/b/c/d}$), 53.12 (C-13$^{a/b/c/d}$), 53.11 (C-13$^{a/b/c/d}$), 48.6 (C-10$^{a/b/c/d}$), 48.5 (C-10$^{a/b/c/d}$), 48.3 (C-10$^{a/b/c/d}$), 48.2 (C-10$^{a/b/c/d}$), 41.03 (2C, C-17$^{a/b/c/d}$), 40.96 (2C, C-17$^{a/b/c/d}$), 40.7 (2C, C-17$^{a/b/c/d}$), 40.5 (2C, C-17$^{a/b/c/d}$), 34.48 (2C, C-19$^{a/b/c/d}$), 34.46 (2C, C-19$^{a/b/c/d}$), 34.4 (2C, C-19$^{a/b/c/d}$), 34.3 (2C, C-19$^{a/b/c/d}$), 20.87 (2C, C-19$^{a/b/c/d}$), 20.85 (2C, C-19$^{a/b/c/d}$), 20.70 (2C, C-19$^{a/b/c/d}$), 20.66 (2C, C-19$^{a/b/c/d}$), 17.7 (2C, C-18$^{a/b/c/d}$), 17.6 (2C, C-18$^{a/b/c/d}$), 15.23 (C-11$^{a/b/c/d}$), 15.18 (C-11$^{a/b/c/d}$), 15.1 (C-11$^{a/b/c/d}$), 15.0 (C-11$^{a/b/c/d}$), 14.6 (C-15$^{a/b/c/d}$), 14.5 (2C, C-15$^{a/b/c/d}$), 14.4 (C-15$^{a/b/c/d}$); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{25}H_{37}N_3O_6+H]^+$: 476.2755 ($[M+H]^+$); found: 476.2742; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3300 (w, N-H), 2930 (m, C-H), 1727 (s, C=O), 1557 (m, C=N), 1430 (m, C=C), 1363 (m, C-H), 1263 (m), 1105 (m, C-O), 765 (m, C-H_{Ar}), 733 (m, C-H_{Ar}), 698 (m, C-H_{Ar}).

3.4.8. Methyl (2-((tert-butoxycarbonyl)imino)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butanoyl)-*L*-alaninate (33)

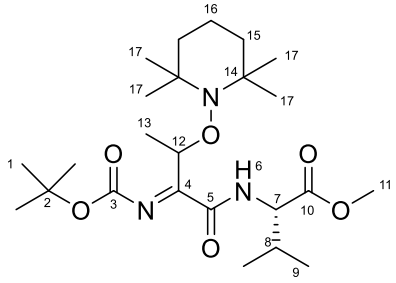


33

The reaction was performed according to the general procedure in section **3.1.**. The product was obtained as a mixture of diastereomers.

Colorless oil (8.56 mg, 19.4 µmol, 54%, d.r.: 2:1); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.19 [UV]; **^{1}H NMR** (500 MHz, CD_3CN, 298 K) δ (ppm) = 8.66 (s, 1H, H-6^b), 7.67 (s, 1H, H-6^a), 4.87 (s, 2H, H-11$^{a/b}$), 4.46 (s, 2H, H-7$^{a/b}$), 3.69 (s, 6H, H-10$^{a/b}$), 1.64 – 1.50 (m, 20H, H-1$^{a/b}$, H-15$^{a/b}$), 1.50 – 1.44 (m, 6H, H-12$^{a/b}$), 1.44 - 1.36 (m, 10H, H-8$^{a/b}$, H-14$^{a/b}$), 1.34 - 1.25 (m, 6H, H-14$^{a/b}$, H-15$^{a/b}$), 1.22 (s, 6H, H-16$^{a/b}$), 1.08 (s, 12H, H-16$^{a/b}$), 1.01 (s, 6H, H-16$^{a/b}$); **^{13}C{^{1}H} NMR** (500 MHz, CD_3CN, 298 K) δ (ppm) = 173.4 (2C, C-9$^{a/b}$), 167.3 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 162.8 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 160.1 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 84.1 (2C, C-2$^{a/b}$), 82.8 (2C, C-11$^{a/b}$), 60.8 (2C, C-13$^{a/b}$), 60.2 (2C, C-13$^{a/b}$), 53.0 (2C, C-10$^{a/b}$), 49.1 (2C, C-7$^{a/b}$), 41.0 (2C, C-14$^{a/b}$), 34.7 (2C, C-16$^{a/b}$), 33.7 (2C, C-16$^{a/b}$), 30.3 (2C, C-14$^{a/b}$), 28.3 (6C, C-1$^{a/b}$), 20.8 (4C, C-16$^{a/b}$), 19.7 (2C, C-12$^{a/b}$), 17.7 (2C, C-8$^{a/b}$/C-15$^{a/b}$), 17.6 (2C, C-8$^{a/b}$/C-15$^{a/b}$); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{22}H_{39}N_3O_6+H]^+$: 442.2912 ($[M+H]^+$); found: 442.2909; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3344 (m, N-H), 2925 (m, C-H), 2854 (m, C-H), 1738 (s, C=O), 1678 (m, C=O), 1624 (m, C=N), 1454 (m, C-H), 1367 (m, C-H), 1261 (m), 1025 (s, C-O).

3.4.9. Methyl (2-((*tert*-butoxycarbonyl)imino)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butanoyl)-*L*-valinate (34)

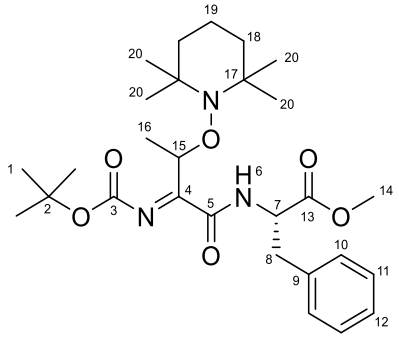


34

The reaction was performed according to the general procedure in section **3.1.**. The product was obtained as a mixture of diastereomers.

Colorless oil (7.00 mg, 14.9 µmol, 41 %, d.r.: 1:1); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.44 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.46 (s, 2H, 2 x H-6$^{a/b}$), 5.00 (s, 1H, H-12$^{a/b}$), 4.88 (s, 1H, H-12$^{a/b}$), 4.55 - 4.44 (m, 2H, 2 x H-7$^{a/b}$), 3.73 (s, 3H, H-11$^{a/b}$), 3.73 (s, 3H, H-11$^{a/b}$), 2.30 - 2.11 (m, 2H, 2 x H-8$^{a/b}$), 1.53 – 1.40 (m, 26H, 6 x H-1$^{a/b}$, 2 x H-16$^{a/b}$, 2 x H-13$^{a/b}$), 1.40 - 1.30 (m, 4H, 4 x H-15$^{a/b}$), 1.25 – 1.17 (m, 6H, 4 x H-15$^{a/b}$, 2 x H-16$^{a/b}$), 1.16 – 1.09 (m, 6H, 2 x H-17$^{a/b}$), 1.05 – 0.97 (m, 12H, 4 x H-17$^{a/b}$), 0.94 (s, 6H, 2 x H-17$^{a/b}$), 0.90 - 0.81 (m, 12H, 4 x H-9$^{a/b}$); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 172.2 (2C, C-10$^{a/b}$), 167.1 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 162.7 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 159.7 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 83.8 (2C, C-2$^{a/b}$), 82.7 (2C, C-12$^{a/b}$), 60.5 (2C, C-14$^{a/b}$), 60.4 (C-14$^{a/b}$), 59.9 (C-14$^{a/b}$), 57.9 (2C, C-7$^{a/b}$), 52.6 (2C, C-11$^{a/b}$), 40.9 (2C, C-15$^{a/b}$), 34.8 (C-17$^{a/b}$), 34.5 (d, 2C, C-17$^{a/b}$), 33.6 (C-17$^{a/b}$), 33.3 (C-17$^{a/b}$), 32.0 (C-8$^{a/b}$), 31.9 (C-8$^{a/b}$), 30.2 (2C, C-15$^{a/b}$), 28.4 (6C, C-1$^{a/b}$), 20.8 (4C, C-17$^{a/b}$), 19.7 (C-13$^{a/b}$), 19.4 (C-13$^{a/b}$), 19.3 (2C, C-9$^{a/b}$), 18.1 (2C, C-9$^{a/b}$), 17.6 (2C, C-16$^{a/b}$); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{24}H_{43}N_3O_6+H]^+$: 470.3225 ($[M+H]^+$); found: 470.3224. **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3345 (w, N-H), 2968 (m, C-H), 2932 (m, C-H), 2874 (w, C-H), 1738 (s, C=O), 1686 (s, C=O), 1514 (m, C=N), 1468 (m, C-H), 1369 (m; C-H), 1247 (m), 1153 (s, C-O).

3.4.10. Methyl (2-((*tert*-butoxycarbonyl)imino)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butanoyl)-*L*-phenylalaninate (35)

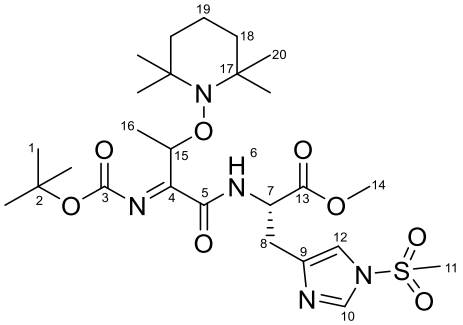


35

The reaction was performed according to the general procedure in section **3.1.**. The product was obtained as a mixture of diastereomers.

Colorless oil (13.1 mg, 25.3 µmol, 70 %, d.r.: 1:1); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.16 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.47 (s, 1H, H-6$^{a/b}$), 7.33 - 7.20 (m, 7H, H-6$^{a/b}$, H-10$^{a/b}$/H-11$^{a/b}$/H-12$^{a/b}$), 7.20 - 7.09 (m, 4H, H-10$^{a/b}$/H-11$^{a/b}$/H-12$^{a/b}$), 5.03 – 4.46 (m, 4H, H-7$^{a/b}$, H-15$^{a/b}$), 3.72 (s, 3H, H-14$^{a/b}$), 3.71 (s, 3H, H-14$^{a/b}$), 3.28 – 2.97 (m, 4H, H-8$^{a/b}$), 1.54 (s, 20H, 6 x H-1$^{a/b}$, 2 x H-19$^{a/b}$), 1.46 (d, 6H, H-16$^{a/b}$), 1.43 - 1.38 (m, 4H, 4 x H-18$^{a/b}$), 1.31 - 1.25 (m, 6H, 4 x H-18$^{a/b}$, 2 x H-19$^{a/b}$), 1.18 (s, 6H, 2 x H-20$^{a/b}$), 1.08 (s, 6H, 2 x H-20$^{a/b}$), 1.04 (s, 6H, 2 x H-20$^{a/b}$), 0.96 (s, 6H, 2 x H-20$^{a/b}$); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 171.8 (2C, C-13$^{a/b}$), 166.7 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 162.2 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 159.5 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 136.5 (2C, C-9$^{a/b}$), 129.70 (2C, C-10$^{a/b}$/C-11$^{a/b}$/C-12$^{a/b}$), 129.67 (2C, C-10$^{a/b}$/C-11$^{a/b}$/C-12$^{a/b}$), 129.1 (2C, C-10$^{a/b}$/C-11$^{a/b}$/C-12$^{a/b}$),129.0 (2C, C-10$^{a/b}$/C-11$^{a/b}$/C-12$^{a/b}$), 127.5 (2C, C-10$^{a/b}$/C-11$^{a/b}$/C-12$^{a/b}$), 83.7 (2C, C-2$^{a/b}$), 82.4 (2C, C-15$^{a/b}$), 60.42 (C-17$^{a/b}$), 60.35 (C-17$^{a/b}$), 60.2 (C-17$^{a/b}$), 59.8 (C-17$^{a/b}$), ~ 53.8 (2C, C-7$^{a/b}$, overlap with deuterated solvent residual signal), 52.8 (2C, C-14$^{a/b}$), 40.8 (2C, C-18$^{a/b}$), 38.2 (2C, C-8$^{a/b}$), 34.6 (C-20$^{a/b}$), 34.2 (C, C-20$^{a/b}$), 33.4 (2C, C-20$^{a/b}$), 30.2 (2C, C-18$^{a/b}$), 28.4 (6C, C-1$^{a/b}$), 20.8 (2C, C-20$^{a/b}$), 20.6 (2C, C-20$^{a/b}$), 19.6 (2C, C-16$^{a/b}$), 17.6 (2C, C-19$^{a/b}$); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{28}H_{43}N_3O_6+H]^+$: 518.3225 ($[M+H]^+$); found: 518.3224. **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3345 (w, N-H), 3031 (w, C-H), 2931 (m, C-H), 2872 (w, C-H), 1730 (s, C=O), 1685 (m, C=O), 1513 (m, C=N), 1498 (m, C=C), 1432 (m, C-H), 1366 (m, C-H), 1245 (m), 1151 (m, C-O), 736 (s, C-H$_{Ar}$), 701 (m, C-H$_{Ar}$).

3.4.11. Methyl N^{α}-(2-((tert-butoxycarbonyl)imino)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butanoyl)-N^{τ}-(methylsulfonyl)-*L*-histidinate (36)

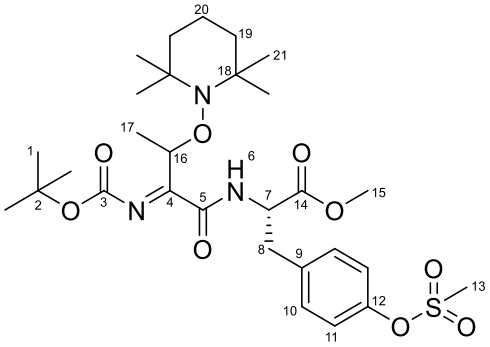


36

The reaction was performed according to the general procedure in section **3.1.**. The product was obtained as a mixture of diastereomers.

Colorless oil (9.10 mg, 15.9 µmol, 53 %, d.r.: 1:1); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.29 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 8.15 – 7.77 (m, 4H, H-6$^{a/b}$, H-10$^{a/b}$), 7.16 – 7.07 (m, 2H, H-12$^{a/b}$), 5.09 – 4.46 (m, 4H, H-7$^{a/b}$, H-15$^{a/b}$), 3.73 (s, 3H, H-14$^{a/b}$), 3.72 (s, 3H, H-14$^{a/b}$), 3.26 (s, 3H, H-11$^{a/b}$), 3.26 (s, 3H, H-11$^{a/b}$), 3.20 – 3.11 (m, 4H, H-8$^{a/b}$), 1.54 (s, 20H, H-1$^{a/b}$, H-19$^{a/b}$), 1.51 – 1.37 (m, 14H, H-16$^{a/b}$, H-18$^{a/b}$), 1.33 – 1.28 (m, 2H, H-19$^{a/b}$), 1.20 (s, 6H, H-20$^{a/b}$), 1.10 (s, 6H, H-20$^{a/b}$), 1.06 (s, 3H, H-20$^{a/b}$), 1.04 (s, 3H, H-20$^{a/b}$), 0.97 (s, 6H, H-20$^{a/b}$); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 171.5 (C-13$^{a/b}$), 171.4 (C-13$^{a/b}$), 167.0 (2C, C-4$^{a/b}$), 162.4 (2C, C-3$^{a/b}$/C-5$^{a/b}$), 159.7 (2C, C-3$^{a/b}$/C-5$^{a/b}$), 140.6 (C-9$^{a/b}$), 140.5 (C-9$^{a/b}$), 137.0 (2C, C-10$^{a/b}$), 115.4 (C-12$^{a/b}$), 115.3 (C-12$^{a/b}$), 83.8 (2C, C-2$^{a/b}$), 82.5 (2C, C-15$^{a/b}$), 60.8 (C-17$^{a/b}$), 60.4 (2C, C-17$^{a/b}$), 59.9 (C-17$^{a/b}$), 53.01 (C-14$^{a/b}$), 52.98 (C-14$^{a/b}$), 52.3 (2C, C-7$^{a/b}$), 44.09 (C-11$^{a/b}$), 44.06 (C-11$^{a/b}$), 40.8 (4C, C-18$^{a/b}$), 34.6 (2C, C-20$^{a/b}$), 33.5 (2C, C-20$^{a/b}$), 30.3 (C-8$^{a/b}$), 30.2 (C-8$^{a/b}$), 28.4 (6C, C-1$^{a/b}$), 20.8 (2C, C-20$^{a/b}$), 20.7 (2C, C-20$^{a/b}$), 19.6 (2C, C-16$^{a/b}$), 17.6 (2C, C-19$^{a/b}$); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{26}H_{43}N_5O_8S+H]^+$: 586.2905 ($[M+H]^+$); found: 586.2887; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3345 (w, N-H), 2978 (m, C-H), 2932 (m, C-H), 1730 (s, C=O), 1678 (m, C=O), 1518 (m, C=N), 1479 (m, C=C), 1371 (s, C-H), 1248 (m), 1177 (s, SO_2), 1156 (s, C-O), 1083 (m, C-N), 771 (m, C-H_{Ar}).

3.4.12. Methyl (2*S*)-2-(2-((tert-butoxycarbonyl)imino)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butanamido)-3-(4-((methylsulfonyl)oxy)phenyl)propanoate (37)

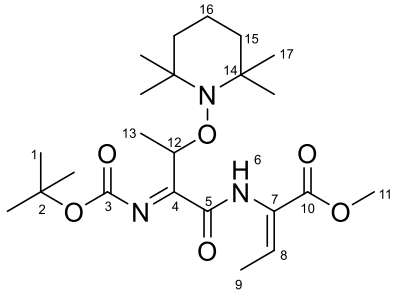


37

The reaction was performed according to the general procedure in section **3.1.**. The product was obtained as a mixture of diastereomers.

Colorless oil (14.5 mg, 23.7 µmol, 66 %, d.r.: 1:1); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.90 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.51 (s, 1H, H-6$^{a/b}$), 7.30 – 7.07 (m, 9H, H-6$^{a/b}$, H-10$^{a/b}$, H-11$^{a/b}$), 5.06 – 4.49 (m, 4H, H-7$^{a/b}$, H-16$^{a/b}$), 3.73 (s, 3H, H-15$^{a/b}$), 3.72 (s, 3H, H-15$^{a/b}$), 3.32 – 3.20 (m, 2H, H-8$^{a/b}$), 3.18 – 3.06 (m, 8H, H-8$^{a/b}$, H-13$^{a/b}$), 1.54 (bs, 20H, H-1$^{a/b}$, H-20$^{a/b}$), 1.49 – 1.36 (m, 14H, H-17$^{a/b}$, H-19$^{a/b}$), 1.33 – 1.25 (m, 2H, H-20$^{a/b}$), 1.18 (s, 6H, H-21$^{a/b}$), 1.09 (s, 6H, H-21$^{a/b}$), 1.03 (s, 6H, H-21$^{a/b}$), 0.96 (s, 6H, H-21$^{a/b}$); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 171.5 (2C, C-14$^{a/b}$), 166.7 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 162.3 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 159.6 (2C, C-3$^{a/b}$/C-4$^{a/b}$/C-5$^{a/b}$), 148.9 (2C, C-12$^{a/b}$), 136.2 (C-9$^{a/b}$), 136.04 (C-9$^{a/b}$), 131.4 (2C, C-10$^{a/b}$), 131.3 (2C, C-10$^{a/b}$), 122.6 (4C, C-11$^{a/b}$), 83.8 (2C, C-2$^{a/b}$), 82.4 (2C, C-16$^{a/b}$), 60.8 (C-18$^{a/b}$), 60.4 (C-18$^{a/b}$), 60.4 (C-18$^{a/b}$), 59.9 (C-18$^{a/b}$), ~ 53.8 (2C, C-7$^{a/b}$, overlap with deuterated solvent residual signal), 52.99 (C-15$^{a/b}$), 52.97 (C-15$^{a/b}$), 40.8 (4C, C-19$^{a/b}$), 37.8 (4C, C-8$^{a/b}$, C-13$^{a/b}$), 34.6 (2C, C-21$^{a/b}$), 33.4 (2C, C-21$^{a/b}$), 28.4 (6C, C-1$^{a/b}$), 20.8 (2C, C-21$^{a/b}$), 20.6 (2C, C-21$^{a/b}$), 19.6 (2C, C-17$^{a/b}$), 14.5 (2C, C-20$^{a/b}$); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{29}H_{45}N_3O_9S+H]^+$: 612.2949 ($[M+H]^+$); found: 612.2934; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3356 (w, N-H), 2978 (w, C-H), 2935 (w, C-H), 1731 (s, C=O), 1677 (m, C=O), 1505 (m, C=N), 1458 (m, C=C), 1368 (s, C-H), 1247 (m), 1176 (m, SO_2), 1151 (s, C-O), 870 (m, C-H_{Ar}), 838 (m, C-H_{Ar}).

3.4.13. Methyl (*Z*)-2-(2-((*tert*-butoxycarbonyl)imino)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butanamido)but-2-enoate (39)



39

The reaction was performed according to the general procedure in section **3.1.**. It is important to note, that the crude NMR of the reaction only shows one regioisomer which corresponds to the C-12-functionalized product. More information on chemoselectivity studies can be found in section **3.4.17.**.

Colorless oil (10.4 mg, 22.9 µmol, 64 %); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.24 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 8.42 (s, 1H, H-6), 6.84 (s, 1H, H-8), 4.95 (s, 1H, H-12), 3.76 (s, 3H, H-11), 1.77 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 3H, H-9), 1.62 – 1.49 (m, 13H, H-1, H-13, H-16), 1.49 – 1.37 (m, 4H, H-15), 1.33 – 1.28 (m, 1H, H-16), 1.24 – 1.17 (m, 3H, H-17), 1.15 – 1.02 (m, 9H, H-17); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 166.7 (C-3), 164.7 (C-10), 160.2 (C-4), 159.2 (C-5), 134.6 (C-8), 125.8 (C-7), 83.8 (C-2), 82.3 (C-12), 60.2 (C-14), 59.7 (C-14), 52.5 (C-11), 40.6 (C-15), 34.4 (C-17), 33.3 (C-17), 28.2 (3C, C-1), 20.6 (C-17), 20.4 (C-17), 19.5 (C-13), 17.4 (C-16), 14.9 (C-9); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{23}H_{39}N_3O_6+H]^+$: 454.2912 ($[M+H]^+$); found: 454.2886; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3359 (w, N-H), 2977 (m, C-H), 2932 (m, C-H), 1725 (s, C=O), 1700 (m, C=O), 1680 (m, C=N), 1500 (m, C-H), 1438 (m, C-H), 1369 (m, C-N), 1246 (m), 1151 (s, C-O).

3.4.14. Screening Regarding the Oxidation of 23 with TEMPO

Initial screening was performed in the LED photo-setup (451 nm). Screening for this reaction was performed with flavin **14**. The NMR-yield (*vs.* internal standard) of product **23** is reported. Other wavelengths were also tested for this reaction (*e. g.* 410 – 420 nm, 440 – 450 nm) but turned out to be less productive. Entry #5 turned out to work best for this catalytic system.

#	Catalyst	Catalyst loading	Solvent	Molarity	Time	NMR-yield
1	**14**	20 mol%	ACN	18 mM	24h	20%
2	**14**	10 mol%	ACN	18 mM	24h	10%
3	**14**	1 mol%	ACN	18 mM	24h	2%
4	**14**	20 mol%	ACN	18 mM	16h	16%
5	**14**	20 mol%	DCM	18 mM	24h	60%
6	**14**	20 mol%	CF_3Ph	18 mM	24h	28%
7	**14**	20 mol%	DCM	72 mM	24h	13%
8	**14**	20 mol%	DCM	36 mM	24h	24%
9	**14**	20 mol%	DCM	9 mM	24h	25%
10	**14**	20 mol%	DCM	4.5 mM	24h	8%

3.4.15. Attempted Conversion of 23 with TEMPO and 21

To exclude background reaction of TEMPO and **21** with substrate **23**, the corresponding reactions were set up without the addition of flavin catalyst **14** (LED photo-setup (451 nm)). Both reactions did not yield product **24**.

#	Catalyst	Solvent[a]	Time	Reactant	NMR-yield	Remaining Substrate (NMR)
1	None	DCM	24h	TEMPO	0%	> 95 %
2	None	DCM	24h	**21**	0%	> 90%

[a]: 18 mM.

3.4.16. Attempted Conversion of (*Z*)-40 with TEMPO and 21

To exclude background reaction of TEMPO and **21** with substrate **(*Z*)-40**, the corresponding reactions were set up without the addition of flavin catalyst **14** (LED photo-setup (451 nm)). Both reactions did not yield product **25**.

#	Catalyst	Solvent[a]	Time	Reactant	NMR-yield	Remaining Substrate (NMR)
1	None	DCM	16h	TEMPO	0%	> 95 %
2	None	DCM	16h	**21**	0%	≈ 90 %

[a]: 18 mM.

3.4.17. Studies regarding the chemoselectivity of the reaction

To check for chemoselectivity, a competition experiment between otherwise structurally identical α,β-unsaturated methyl ester **38** and α,β-unsaturated (*N*,*N*)-dimethyl amide **25** was investigated. First, the two substrates were investigated in separate catalyses. These reactions were performed according to the general procedure in section **3.1.**. The NMR yield of the TEMPO-functionalized amide **25** amounted to 79 % while the NMR yield for the functionalization of the ester amounted to 66 %.

For the competition experiment, the ester (1.00 equiv.) and the amide (1.00 equiv.) were placed in the same photo vial, dissolved in DCM (2 mL, 18.0 mM w. r. t. ester) and combined with TEMPO (2.00 equiv.) and the flavin catalyst (0.20 equiv.). The sample was irradiated with blue LED light (λ = 451 nm, 1 W) under rapid stirring. After 16 hours, the solution was dried *in vacuo* and dissolved in CD_2Cl_2 followed by the addition of trimethylbenze-1,3,5-tricarboxylate (3.00 mg, 12.0 µmol, 0.33 equiv.) as internal NMR standard. The NMR yield was calculated according to the procedure in section **3.1.** and section **3.2.1.**. The NMR yield for the functionalization of the amide amounted to 60 % while the yield for the functionalization of the ester amounted to 6 %, giving a chemoselectivity of 10:1 in favor of the functionalized amide (**figure SI-04**). The isolated yield of the TEMPO-functionalized amide **25** was 57 %. The product of the ester functionalization could not be isolated due to the small amount of product. These encouraging foundings provided the motivation for the synthesis of substrate **SI-30** and its use in the catalytic transformation with TEMPO (see section **3.4.12.**).

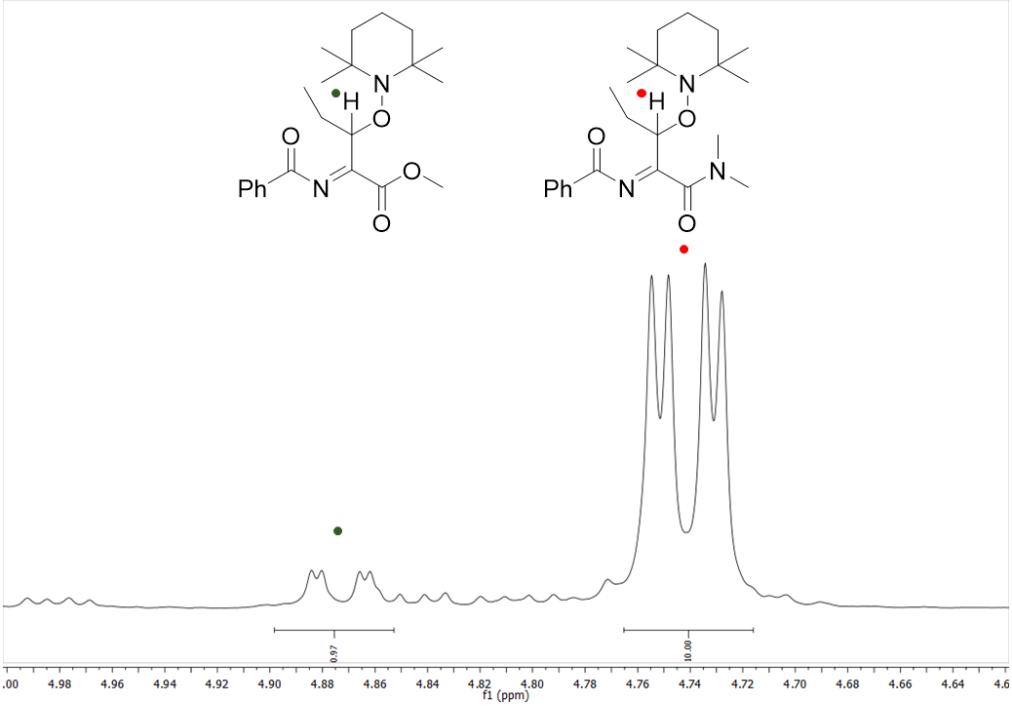
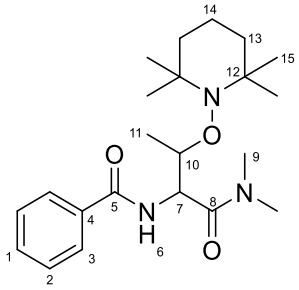


Figure SI-04: Crude ^{1}H NMR spectrum of the competition experiment showing the 10:1 ratio between the TEMPO-functionalized amide and ester substrate.

3.5. Follow-Up Reactions

3.5.1. *N*-(1-(Dimethylamino)-1-oxo-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butan-2-yl)benzamide (43)



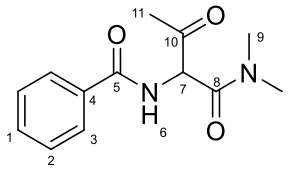
43

N-(1-(Dimethylamino)-1-oxo-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butan-2-ylidene)benzamide (**25**) (28.0 mg, 72.3 µmol, 1.00 equiv.) was dissolved in DCM (anhydrous, 4.2 mL, 18.0 mM), sodium borohydride (54.7 mg, 1.45 mmol, 20.0 equiv.) was added and the reaction mixture was stirred at 45 °C for four hours. The reaction was quenched cautiously with water afterwards and was extracted with DCM (3 x 10 mL). The combined organic phases were dried with Na_2SO_4 and concentrated *in vacuo* to yield *N*-(1-(dimethylamino)-1-oxo-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butan-2-yl)benzamide (**43**). The product was obtained as a mixture of diastereomers.

White solid (25.3 mg, 64.9 µmol, 90 %, d.r.: 1.5:1.0); **TLC** (silica, PE/EtOAc 1:1): R_f = 0.46 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.84 – 7.80 (m, 2H, H-3^a), 7.79 – 7.75 (m, 2H, H-3^b), 7.55 – 7.49 (m, 2H, H-1$^{a/b}$), 7.47 – 7.42 (m, 4H, H-2$^{a/b}$), 7.28 (d, $^3J_{H\text{-}H}$ = 8.1 Hz, 1H, H-6^a), 6.88 (d, $^3J_{H\text{-}H}$ = 9.1 Hz, 1H, H-6^b), 5.22 – 5.14 (m, 2H, H-7$^{a/b}$), 4.45 – 4.36 (m, 1H, H-10^a), 4.31 – 4.21 (m, 1H, H-10^b), 3.26 (s, 3H, H-9^b), 3.18 (s, 3H, H-9^a), 2.98 (s, 3H, H-9^b), 2.97 (s, 3H, H-9^a), 1.48 – 1.41 (m, 8H, H-13$^{a/b}$), 1.34 – 1.28 (m, 10H, H-11$^{a/b}$, H-14$^{a/b}$), 1.18 – 1.03 (m, 24H, H-15$^{a/b}$); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 171.8 (C-8^b), 169.9 (C-8^a), 166.7 (2C, C-5$^{a/b}$), 134.8 (C-4^a), 134.7 (C-4^b), 131.9 (C-1^b), 131.8 (C-1^a), 128.9 (2C, C-2^a), 128.8 (2C, C-2^b), 127.4 (2C, C-3^b), 127.4 (2C, C-3^a), 80.4 (C-10^b), 78.3 (C-10^a), 61.3 (2C, C-12$^{a/b}$), 59.5 (2C, C-12$^{a/b}$), 53.3 (C-7$^{a/b}$), 52.6 (C-7$^{a/b}$), 41.0 (C-13$^{a/b}$), 40.7 (C-13$^{a/b}$), 40.6 (C-13$^{a/b}$), 40.5 (C-13$^{a/b}$), 37.9 (C-9^b), 37.7 (C-9^a), 35.92 (C-9^b), 35.89 (C-9^a), 34.6 (2C,

C-15$^{a/b}$), 34.3 (2C, C-15$^{a/b}$), 30.1 (2C, C-14$^{a/b}$), 20.8 (2C, C-15$^{a/b}$), 20.4 (2C, C-15$^{a/b}$), 17.6 (C-11^{b}), 16.5 (C-11^{a}); **HR-MS** (ESI^{+}): *m/z* = calc. for $[C_{22}H_{35}N_3O_3+H]^+$: 390.2751 ($[M+H]^+$); found: 390.2738; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3309 (w, N-H), 2972 (w, C-H), 2929 (m, C-H), 2871 (w, C-H), 1631 (s, C=O), 1513 (m, C=C), 1484 (m, C=C), 1401 (m, C-H), 1376 (m, C-H), 1361 (m, C-N), 1133 (m, C-O), 1083 (m, C-O), 932 (m), 711 (m, C-H_{Ar}), 694 (m, C-H_{Ar}).

3.5.2. *N*-(1-(Dimethylamino)-1,3-dioxobutan-2-yl)benzamide (44)

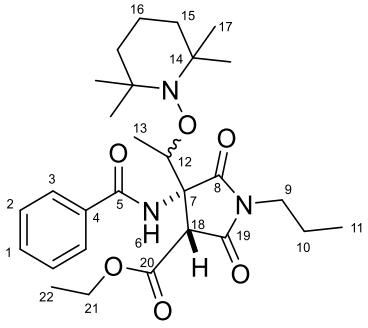


44

3-Chlorobenzoperoxoic acid (77%, 38.0 mg, 169 µmol, 3.0 equiv.) was dissolved in DCM (anhydrous, 2 mL, 28.0 mM) and added as a solution to *N*-(1-(dimethylamino)-1-oxo-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butan-2-yl)benzamide (**43**) (22.0 mg, 56.5 µmol, 1.00 equiv.) at 0 °C. The reaction was stirred at 0 °C for 45 minutes and quenched with Na_2SO_3 solution (10%, 10 mL). The mixture was extracted with DCM (3 x 10 mL), the combined organic phases were dried with Na_2SO_4, concentrated *in vacuo* and purified by column chromatography (silica, PE/EtOAc 6:4) to yield *N*-(1-(dimethylamino)-1,3-dioxobutan-2-yl)benzamide (**44**).

White solid (7.30 mg, 29.4 µmol, 52 %); **TLC** (silica, PE/EtOAc 6:4): R_f = 0.14 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.89 – 7.83 (m, 2H, H-3), 7.69 (d, $^3J_{H\text{-}H}$ = 6.5 Hz, 1H, H-6), 7.59 – 7.53 (m, 1H, H-1), 7.51 – 7.43 (m, 2H, H-2), 5.56 (d, $^3J_{H\text{-}H}$ = 6.5 Hz, 1H, H-7), 3.21 (s, 3H, H-9), 3.00 (s, 3H, H-9), 2.19 (s, 3H, H-11); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 202.3 (C-10), 167.1 (C-5), 166.1 (C-8), 133.9 (C-4), 132.6 (C-1), 129.2 (C-2), 127.7 (C-3), 61.7 (C-7), 38.1 (C-9), 36.6 (C-9), 26.5 (C-11).; **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{13}H_{16}N_2O_3+H]^+$: 249.1234 ($[M+H]^+$); found: 249.1215; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3304 (w, N-H), 2928 (w, C-H), 1723 (m, C=O), 1634 (s, C=O), 1510 (m, C=C), 1483 (m, C=C), 1402 (m, C-H), 1356 (m, C-H), 1328 (m, C-N), 1140 (m, C-O), 714 (m, C-H_{Ar}), 694 (m, C-H_{Ar}).

3.5.3. Ethyl 4-benzamido-2,5-dioxo-1-propyl-4-(1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)ethyl)pyrrolidine-3-carboxylate (45)



45

A vial equipped with a stir bar was charged with (*Z*)-*N*-(1-oxo-1-(propylamino)but-2-en-2-yl)benzamide (**SI-17**) (8.87 mg, 36.0 μmol, 1.00 equiv.), the flavin photocatalyst (**14)** (2.46 mg, 7.20 μmol, 0.20 equiv.) and TEMPO (16.9 mg, 108 μmol, 3.00 equiv.). Subsequently the vial was sealed with a septum and the atmosphere was changed by evacuating and backfilling the vial with Ar for three times. Then the solid components were dissolved in DCM (anhydrous, 2.0 mL, 18.0 mM). The solution was irradiated with blue LED light (451 nm, 1W) under rapid stirring. After four hours, sodium 1,3-diethoxy-1,3-dioxopropan-2-ide (26.2 mg, 0.62 mL, 0.23 M in THF, 4.00 equiv.) was added under Ar atmosphere at 0°C and stirred at room temperature for two hours. (Sodium 1,3-diethoxy-1,3-dioxopropan-2-ide was prepared in a separate flask by adding sodium hydride to diethyl malonate.) The reaction was quenched with $NaHCO_3$ solution (sat., 10 mL) and extracted with DCM (3 x 10 mL). The organic phases were dried with Na_2SO_4, concentrated *in vacuo* and purified by column chromatography (silica, PE/EtOAc 9:1) to yield ethyl 4-benzamido-2,5-dioxo-1-propyl-4-(1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)ethyl)pyrrolidine-3-carboxylate (**45**).

White solid (11.0 mg, 21.2 μmol, 59%); **TLC** (silica, PE/EtOAc 9:1): R_f = 0.18 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.75 - 7.72 (m, 2H, H-3), 7.57 - 7.53 (m, 1H, H-1), 7.48 - 7.43 (m, 2H, H-2), 7.03 (s, 1H, H-6), 4.92 - 4.82 (m, 1H, H-12), 4.32 (s, 1H, H-18), 4.02 (q, $^3J_{H\text{-}H}$ = 7.1, 2H, H-21), 3.62 - 3.49 (m, 2H, H-9), 1.66 (*virt.* h, $^3J_{H\text{-}H} \approx {}^3J_{H\text{-}H}$ = 7.4 Hz, 2H, H-10), 1.60 – 1.54 (m, 1H, H-16) 1.49 - 1.36 (m, 2H, H-15), 1.30 (d, $^3J_{H\text{-}H}$ = 6.5 Hz, 3H, H-13), 1.30 – 1.27 (m, 4H, H-16, H-17), 1.26 - 1.24 (m, 2H, H-15), 1.21 (s, 3H, H-17), 1.09 (t,

$^{3}J_{H\text{-}H}$ = 7.1 Hz, 3H, H-22), 1.00 - 0.96 (m, 6H, 2 x H-17), 0.94 (t, $^{3}J_{H\text{-}H}$ = 7.4 Hz, 3H, H-11); **$^{13}C\{^{1}H\}$ NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 175.0 (C-8), 171.4 (C-19), 167.0 (C-5), 166.3 (C-20), 133.6 (C-4), 132.7 (C-1), 129.2 (2C, C-2), 127.5 (2C, C-3), 79.7 (C-12), 65.8 (C-7), 62.6 (C-21), 61.8 (C-14), 59.9 (C-14), 41.7 (C-9), 41.2 (C-18), 40.6 (C-15), 35.2 (C-17), 34.1 (C-17), 30.2 (C-15), 21.4 (C-10), 21.0 (2C, C-17), 17.6 (C-16), 14.2 (C-22), 13.7 (C-13), 11.6 (C-11); **HR-MS** (ESI$^+$): *m/z* = calc. for $[C_{28}H_{41}N_3O_6+H]^+$: 516.3068 ($[M+H]^+$); found:.516.3068; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3433 (w, N-H), 2962 (m, C-H), 2930 (m, C-H), 2873 (m, C-H), 1714 (s, C=O), 1671 (m, C=O), 1516 (m, C=C), 1482 (m, C=C), 1407 (m, C-H), 1366 (m, C-H), 1261 (s, C-O), 1093 (m), 1023 (m), 800 (m, C-H_{Ar}), 713 (m, C-H_{Ar}).

Relevant NOE-contact between H-12 and H-18 that indicates the pyrrolidine-2,5-dione relative configuration (**figure SI-05**):

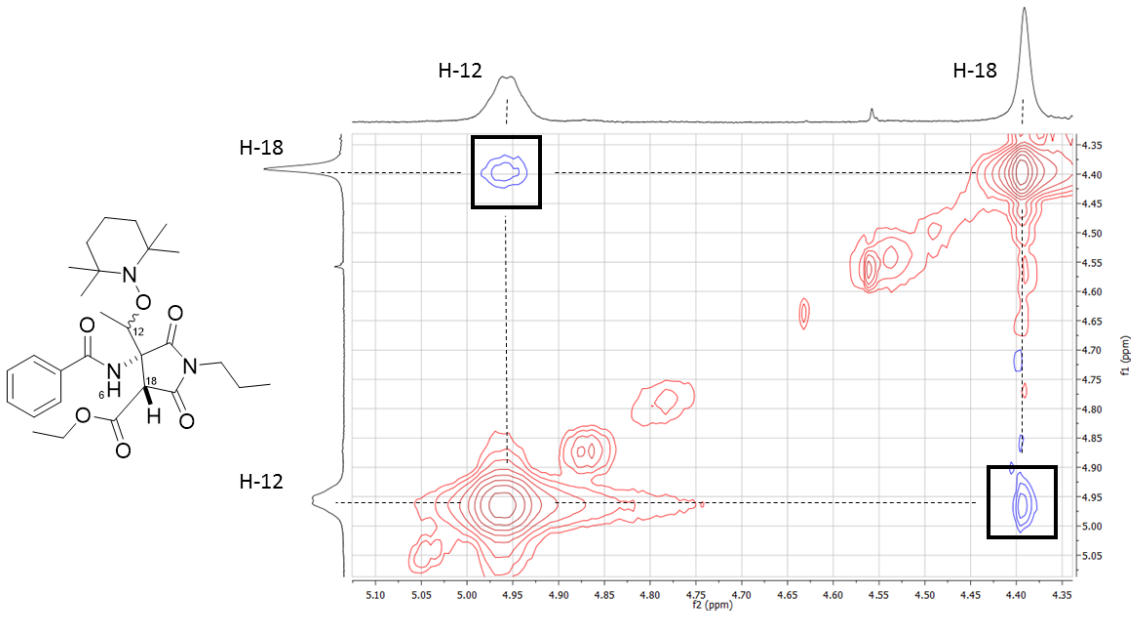


Figure SI-05: NOE-contact between H-12 and H-18.

There is no NOE contact between H-6 and H-18 indicating that the shown diastereomer exists almost exclusively (**figure SI-06**). Based on these two NOE observations, we made the assignment of the pyrrolidin-2,5-dione structure.

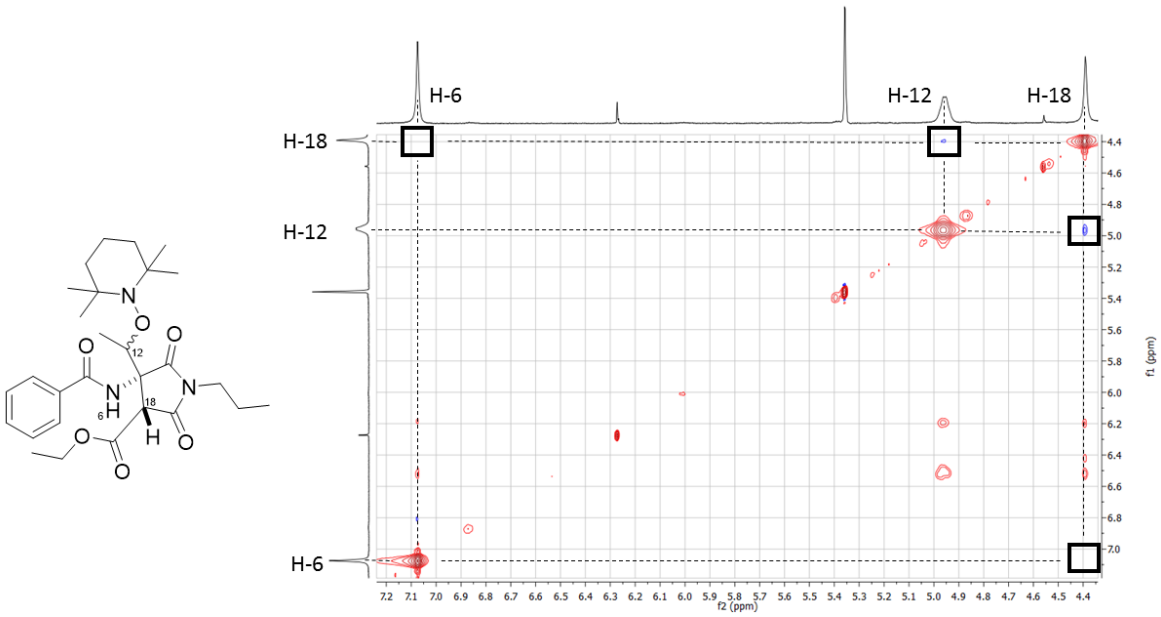
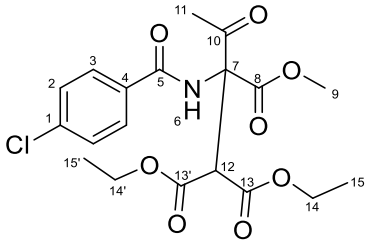


Figure SI-06: NOE-contact between H-12 and H-18 and absence of NOE-contact between H-6 and H-18.

3.5.4. 1,1-Diethyl 2-methyl 2-(4-chlorobenzamido)-3-oxobutane-1,1,2-tricarboxylate (46)



46

A vial equipped with a stir bar was charged with methyl (*Z*)-2-(4-chlorobenzamido)but-2-enoate (**23**) (10.3 mg, 36.0 µmol, 1.00 equiv.), the flavin photocatalyst (**14)** (2.46 mg, 7.20 µmol, 0.20 equiv.) and TEMPO (16.9 mg, 108 µmol, 3.00 equiv.). Subsequently the vial was sealed with a septum and the atmosphere was changed by evacuating and backfilling the vial with Ar for three times. Then the solid components were dissolved in DCM (anhydrous, 2.0 mL, 18.0 mM). The solution was irradiated with blue LED light (λ = 451 nm, 1W) under rapid stirring. After 24 hours, sodium diethylmalonate (26.2 mg, 0.62 mL, 0.23 M in THF, 4.00 equiv.) was added under Ar atmosphere at 0°C and stirred at room temperature for two hours. The vial was opened and 3-chlorobenzoperoxoic acid (77%, 145 mg, 0.65 mmol, 18.0 equiv.) was added and the reaction was stirred for 24 hours at room temperature. The reaction was quenched with Na_2SO_3 solution (10%, 10 mL) and extracted with DCM (3 x 10 mL). The organic phases were washed with $NaHCO_3$ solution (sat.), dried with Na_2SO_4, concentrated *in vacuo* and purified by column chromatography (silica, 1st column: PE/EtOAc 8:2 → 2nd column: DCM/EtOAc 9:1) to yield 1,1-diethyl 2-methyl 2-(4-chlorobenzamido)-3-oxobutane-1,1,2-tricarboxylate (**46**).

White solid (6.21 mg, 14.5 µmol, 40%); **TLC** (silica, PE/EtOAc 8:2): R_f = 0.29 [UV]; **^{1}H NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 7.81 - 7.73 (m, 2H, H-3), 7.58 (s, 1H, H-6), 7.51 - 7.44 (m, 2H, H-2), 4.70 (s, 1H, H-12), 4.17 (q, $^3J_{H-H}$ = 7.1 Hz, 2H, H-14/H-14'), 4.14 - 3.97 (m, 2H, H-14/H-14'), 3.78 (s, 3H, H-9), 2.25 (s, 3H, H-11), 1.22 (t, $^3J_{H-H}$ = 7.1 Hz, 3H, H-15/H-15'), 1.13 (t, $^3J_{H-H}$ = 7.1 Hz, 3H, H-15/H-15'); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 197.6 (C-10), 167.9 (C-8), 167.7 (C-13/C-13'), 166.8 (C-13/C-13'), 166.5 (C-5), 139.0 (C-1), 132.1 (C-4), 129.5 (2C, C-2), 129.3 (2C, C-3), 72.1 (C-7), 62.8 (2C, C-14, C-14'), 54.7 (C-12), ~ 53.4 (C-9, overlap with deuterated solvent residual signal), 25.7 (C-11), 14.2 (C-15/C-15'),

14.0 (C-15/C-15'); **HR-MS** (ESI^+): *m/z* = calc. for $[C_{19}H_{22}ClNO_8+Na]^+$: 450.0926 ($[M+Na]^+$); found: 450.0927; **IR**: (ATR): $\tilde{\nu}$ [cm^{-1}] = 3420 (w, N-H), 2981 (m, C-H), 2856 (w, C-H), 1736 (s, C=O), 1670 (m, C=O), 1513 (m, C=C), 1480 (s, C=C), 1370 (m, C-H), 1310 (m, C-O), 1228 (m, C-O), 1094 (m, C-Cl), 855 (m, C-Cl), 758 (m, C-H_{Ar}).

4. Emission Spectra and Triplet Energy Measurement

4.1. General Information

UV/Vis absorption spectra were measured on a Perkin Elmer Lambda 35 UV/Vis Spectrometer in quartz cuvettes. Emission spectra where recorded on a Horiba Scientific FlouroMax-4P Spectrofluorometer equipped with a continuous Xe source for steady state spectra and a Xe flashlight source for the observation of phosphorescence spectra. Spectra were recorded in quartz tubes (4 mm internal diameter) in a small quartz Dewar vessel that was filled with liquid nitrogen for recording spectra at cryogenic temperatures (77 K). Uvasol® ethanol and potassium iodide were purchased from Sigma Aldrich. All solutions including saturated solutions of KI in ethanol were degassed prior to use. All solutions were handled under dry nitrogen to exclude oxygen as triplet quencher.

4.2. Characterization of Flavin 14

Flavin **14** was dissolved in ethanol to give a 70 µM solution. The absorption spectrum (d = 10 mm) is shown in **figure SI-07**, normalized to the absorption maximum at λ = 330 nm. Luminescence of a 70 µM solution in ethanol after excitation at λ = 455 nm was recorded in a quartz tube (4 mm internal diameter) and is shown normalized to the emission-maximum at λ = 525 nm in **figure SI-07**. The emission is attributed to fluorescence. A defined crossing of the emission and the absorption spectrum can be observed which is therefore the 0←0 transition from the S_1 state to the ground state. Therefore, a S_1 energy of 246 kJ/mol can be calculated.

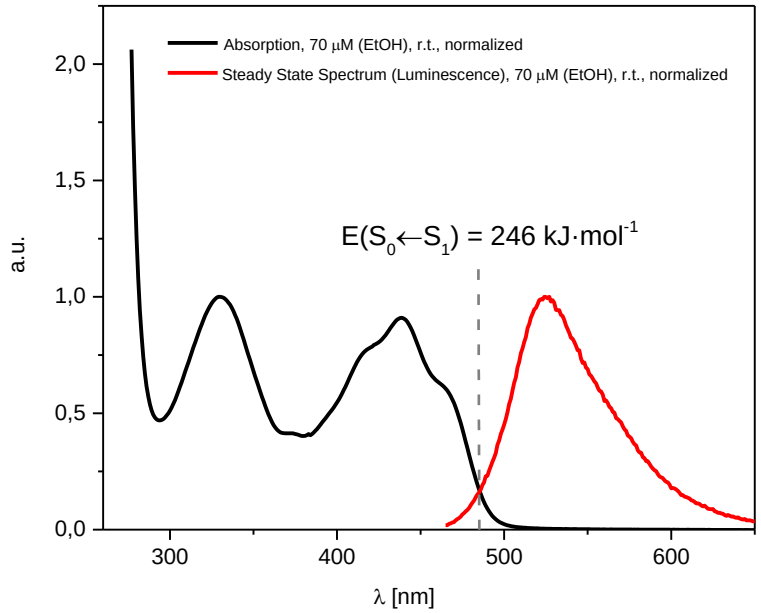


Figure SI-07: Recorded UV/Vis of **14** in ethanol (c = 70 µM) normalized to $A_{330\ nm}$; recorded luminescence of **14** in ethanol (c = 70 µM) at ambient conditions, normalized to $I_{525\ nm}$.

At room temperature neither in ethanol (orange line) nor in a saturated solution of KI in ethanol (petrol line) a signal that could be attributed to phosphorescence was detected. Moreover, after cooling an ethanol solution of **14** to 77 K, the detected band of fluorescence did not alter its appearance and no additional signal was detected. Therefore, the heavy-atom induced (room temperature) phosphorescence method[18] was applied which leads to an increased intersystem crossing rate by adding a heavy-atom containing salt in excess to the solution. By coordination of the heavy-atom anion to electron-donating functional groups of the molecule, an increased quantum yield in the phosphorescence is observed. Indeed, using a saturated solution of KI in ethanol led already under steady state conditions to the detection of a weak additional red-shifted emission band after excitation at λ = 592 nm (blue line). The highly intense signal under pulsed conditions (green line) can be assigned to phosphorescence due to the complete bleaching of the corresponding fluorescence signal. Tentatively assigning the most blue shifted point of inflection of the phosphorescence emission in the pulsed spectrum ($\lambda_{max} \cong 583$ nm) to the 0←0 transition of

[18] A. Segura-Carretero *et al.*, *Anal. Chim. Acta* **2000**, *417*, 19.

the phosphorescence allows to give an estimate for the triplet energy of 205 ± 2 kJ/mol for **14** in ethanol/KI (**figure SI-08**).

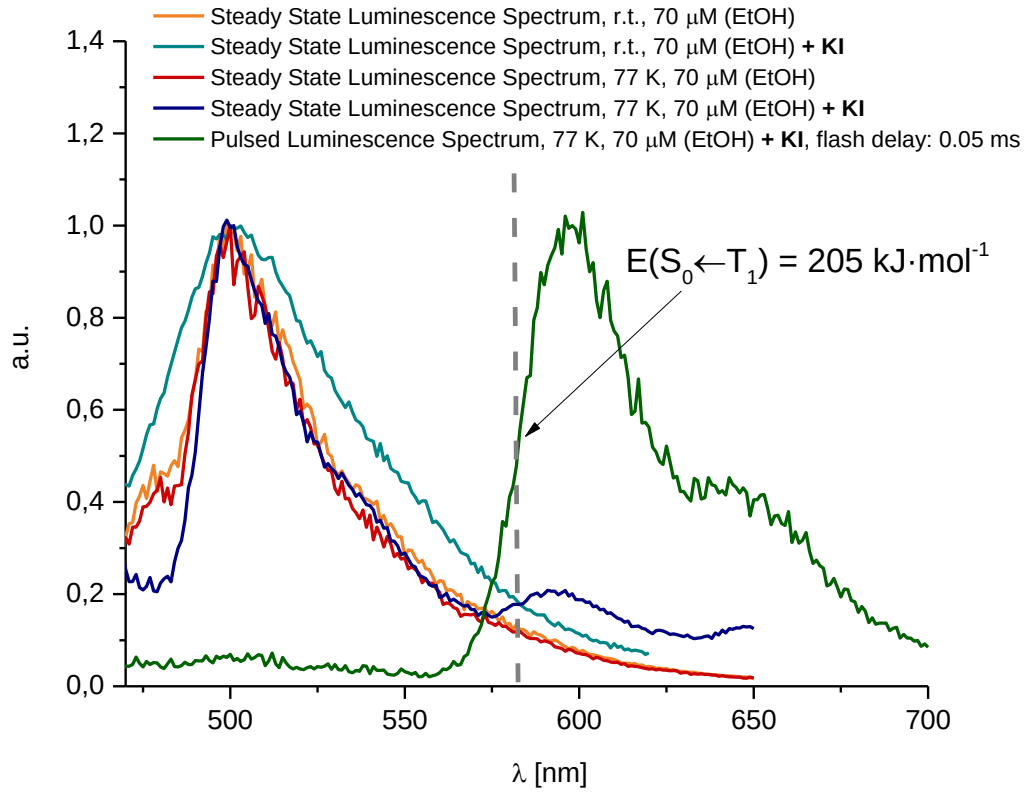


Figure SI-08: Normalized steady state spectra of **14** in ethanol and ethanol/KI (c = 70 µM) at room temperature and 77 K and normalized time resolved spectrum of **14** in ethanol/KI (c = 70 µM) after 0.05 ms delay.

4.3. Characterization of Flavin SI-09

Flavin **SI-09** was dissolved in ethanol to give a 70 µM solution. The absorption spectrum (d = 10 mm) is shown in **figure SI-09**, normalized to the absorption maximum at λ = 443 nm. Luminescence of a 70 µM solution in ethanol after excitation at λ = 460 nm was recorded in a quartz tube (4 mm internal diameter) and is shown normalized to the emission-maximum at λ = 509 nm in **figure SI-09**. The emission is attributed to fluorescence. A defined crossing of the emission and the absorption spectrum can be observed which is therefore the 0←0 transition from the S_1 state to the ground state. Therefore, a S_1 energy of 244 kJ/mol can be calculated

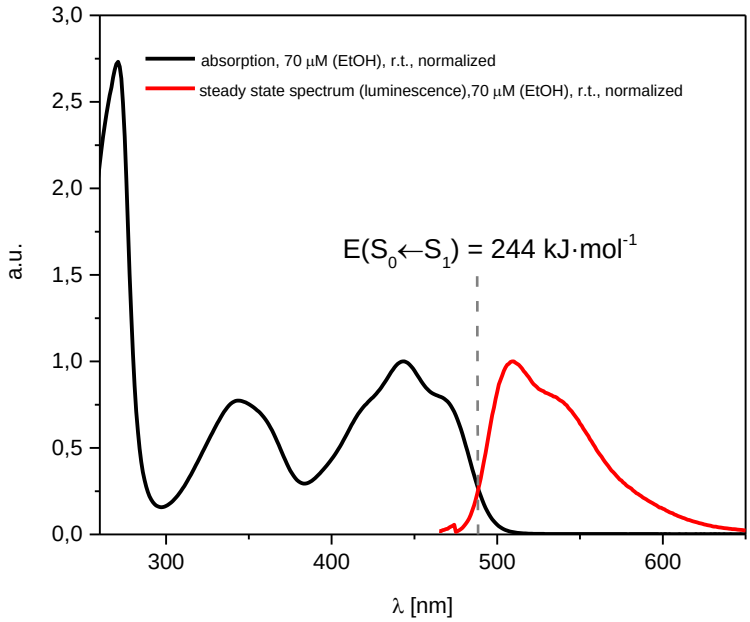


Figure SI-09: Recorded UV/Vis of **SI-09** in ethanol (c = 70 µM) normalized to $A_{443\ nm}$; recorded luminescence of **SI-09** in ethanol (c = 70 µM) at ambient conditions, normalized to $I_{509\ nm}$.

At room temperature neither in ethanol (orange line) nor in a saturated solution of KI in ethanol (petrol line) a signal that could be attributed to phosphorescence was detected after excitation at λ = 460 nm. After cooling an ethanol solution of **SI-09** to 77 K, the detected fluorescence showed a slight blue shift as well as a broadening of the emission band. Applying the aforementioned heavy-atom induced phosphorescence method, led already under steady state conditions to the detection of a strong red-shifted emission band after excitation at λ = 595 nm (blue line). Additionally, a tremendous decrease in intensity of the formerly strong fluorescence band could be seen, underlining the effectiveness of the addition of KI to the solution. The intense signal under pulsed conditions (green line) can be clearly assigned to phosphorescence due to the complete bleaching of the already under steady-state conditions weak fluorescence signal. Tentatively assigning the most blue shifted point of inflection of the phosphorescence emission in the pulsed spectrum ($\lambda_{max} \cong 583$ nm) to the 0←0 transition of the phosphorescence allows to give an estimate for the triplet energy of 205 ± 2 kJ/mol for **SI-09** in ethanol/KI (**figure SI-10**).

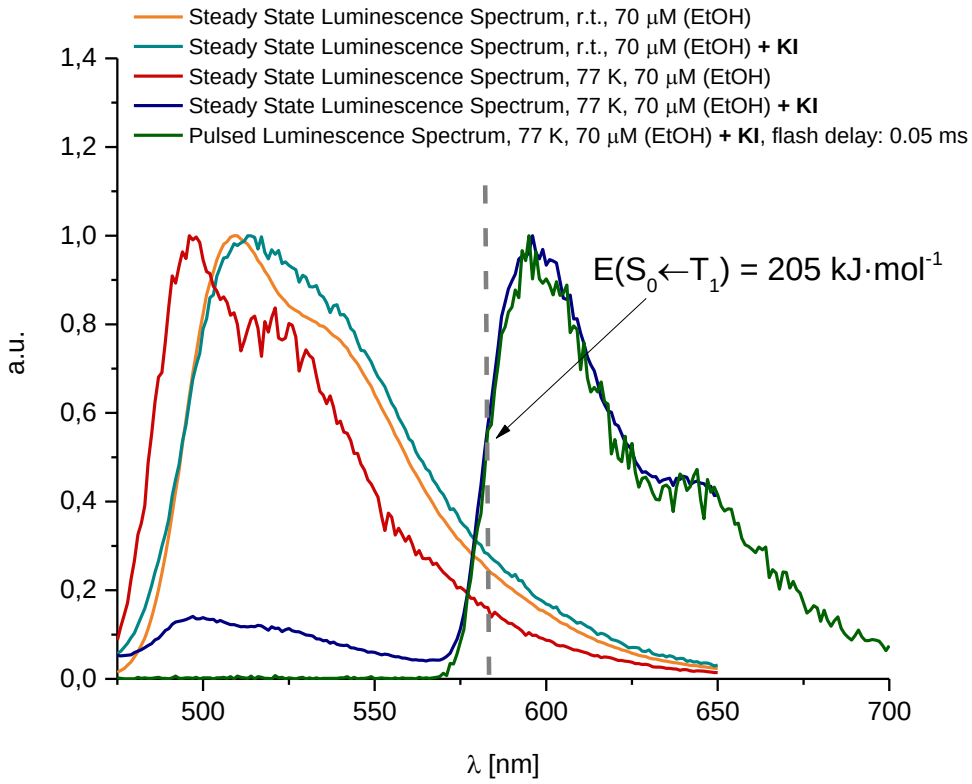


Figure SI-10: Normalized steady state spectra of **SI-09** in ethanol and ethanol/KI (c = 70 µM) at room temperature and 77 K and normalized time resolved spectrum of **SI-09** in ethanol/KI (c = 70 µM) after 0.05 ms delay.

5. Adduct NMR-Studies

5.1. 1,3-Cycloheptadiene Flavin Adduct Studies (19)

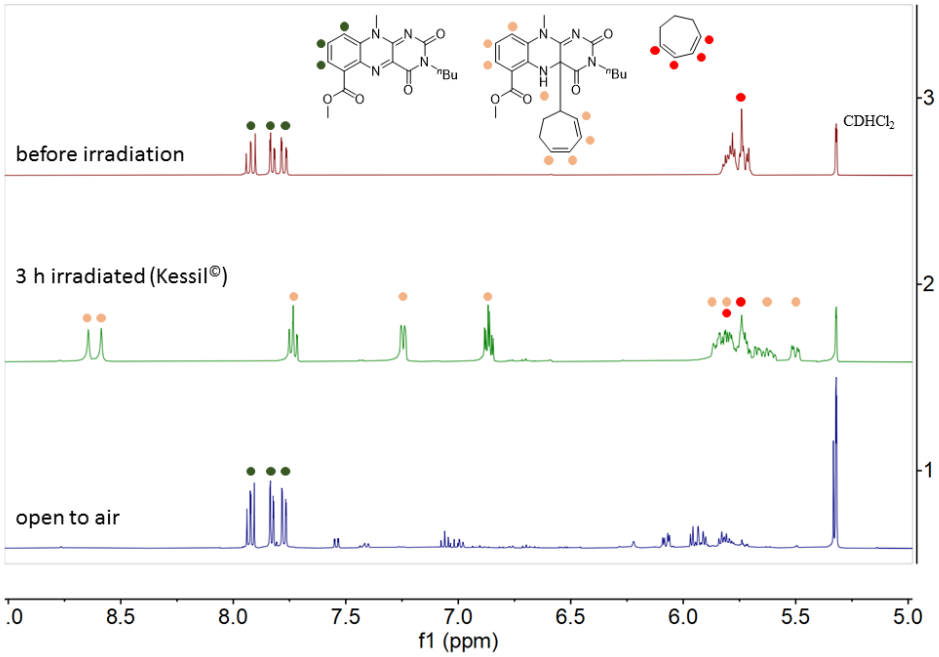
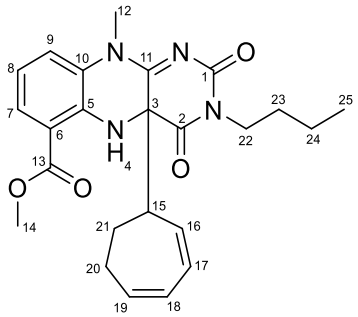


Figure SI-11: ^{1}H NMR spectrum of 1,3-cycloheptadiene and flavin **14** before irradiation, after 3 hours of irradiation and again after opening the NMR tube to air.



19

The catalyst (**14**) (6.16 mg, 18.0 µmol, 1.00 equiv.) is added to a *J. Young* NMR tube, the tube is evacuated and backfilled with Ar three times and CD_2Cl_2 (0.5 mL, 36 mM) is added. 1,3-Cycloheptadiene (2.42 µL, 21.6 µmol, 1.20 equiv.) is added, the tube is sealed and irradiated under Ar atmosphere for three hours (Kessil Tuna Blue©). Catalyst **14** is converted completely to the

adduct **19** (**figure SI-11**). Afterwards the tube is opened to react with O_2 and the catalyst is regenerated (**figure SI-11**).

Analysis of the adduct (set of two diastereomers in a ratio ~ 1:1 (labelled as "a" and "b"); spectra contain small amount of 1,3-cycloheptadiene which was used in slight excess (**figure SI-12** and **SI-13**):

^{1}H NMR (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 8.64 (s, 1H, H-4$^{a/b}$), 8.59 (s, 1H, H-4$^{a/b}$), 7.73 (dd, $^3J_{H\text{-}H}$ = 8.0, $^4J_{H\text{-}H}$ = 1.3 Hz, 2H, H-7^a, H-7^b), 7.36 - 7.16 (m, 2H, H-9^a, H-9^b), 6.86 (t, $^3J_{H\text{-}H}$ = 8.0 Hz, 2H, H-8^a, H-8^b), 5.89 - 5.82 (m, 2H, H-16$^{a/b}$, H-17$^{a/b}$), 5.81 – 5.76 (m, 2H, H-18$^{a/b}$), 5.72 – 5.70 (m, 1H, H-17$^{a/b}$), 5.66 (ddd, *J* = 11.3, 6.7, 2.3 Hz, 1H, H-19$^{a/b}$), 5.61 (ddd, *J* = 11.0, 6.7, 2.2 Hz, 1H, H-19$^{a/b}$), 5.50 (dd, $^3J_{H\text{-}H}$ = 12.0, 4.1 Hz, 1H, H-16$^{a/b}$), 3.93 (s, 3H, H-14$^{a/b}$), 3.92 (s, 3H, H-14$^{a/b}$), 3.90 – 3.81 (m, 2H, H-22$^{a/b}$), 3.79 – 3.68 (m, 2H, H-22$^{a/b}$), 3.65 (s, 6H, H-12^a, H-12^b), 2.93 - 2.87 (m, 1H, H15$^{a/b}$), 2.87 - 2.83 (m, 1H, H-15$^{a/b}$), 2.41 – 2.36 (m, 1H, H-20$^{a/b}$), 2.31 – 2.26 (m, 1H, H-20$^{a/b}$), 2.20 – 2.08 (m, 1H, H-20$^{a/b}$), 2.05 – 1.94 (m, 2H, H-20$^{a/b}$, H-21$^{a/b}$), 1.90 – 1.85 (m, 1H, H-21$^{a/b}$), 1.76 - 1.66 (m, 1H, H-21$^{a/b}$), 1.60 – 1.54 (m, 5H, H-21$^{a/b}$, H-23$^{a/b}$),1.40 – 1.29 (m, 4H, H-24$^{a/b}$), 0.93 (*virt.* q, $^3J_{H\text{-}H}$ = 7.3 Hz, 6H, H-25$^{a/b}$); **^{13}C{^{1}H} NMR** (126 MHz, CD_2Cl_2, 298 K): δ (ppm) = 168.24 (C-13$^{a/b}$), 168.20 (C-13$^{a/b}$), 167.8 (C-1$^{a/b}$/C-2$^{a/b}$), 167.7 (C-1$^{a/b}$/C-2$^{a/b}$), 161.8 (C-11$^{a/b}$), 161.7 (C-11$^{a/b}$), 156.3 (d, 2C, C-1$^{a/b}$/C-2$^{a/b}$), 137.1 (C-5$^{a/b}$), 136.9 (C-5$^{a/b}$), 135.9 (C-18$^{a/b}$), 134.8 (C-18$^{a/b}$), 129.6 (C-10$^{a/b}$), 129.4 (C-10$^{a/b}$), 129.1 (2C, C-6$^{a/b}$), 128.5 (C-16$^{a/b}$), 128.2 (C-16$^{a/b}$), 127.8 (2C, C-7$^{a/b}$), 127.5 (2C, C-17$^{a/b}$), 125.00 (C-19$^{a/b}$), 124.95 (C-19$^{a/b}$), 120.9 (C-9$^{a/b}$), 120.8 (C-9$^{a/b}$), 118.32 (C-8$^{a/b}$), 118.27 (C-8$^{a/b}$), 113.6 (C-6$^{a/b}$), 113.4 (C-6$^{a/b}$), 59.5 (d, 2C, C-3$^{a/b}$), 52.7 (d, 2C, C-14$^{a/b}$), 48.4 (C-15$^{a/b}$), 48.3 (C-15$^{a/b}$), 41.9 (C-22$^{a/b}$), 41.8 (C-22$^{a/b}$), 32.8 (C-12$^{a/b}$), 32.7 (C-12$^{a/b}$), 30.73 (C-23$^{a/b}$), 30.66 (C-23$^{a/b}$), 29.9 (C-20$^{a/b}$), 29.2 (C-20$^{a/b}$), 28.0 (C-21$^{a/b}$), 27.3 (C-21$^{a/b}$), 20.7 (2C, C-24$^{a/b}$), 14.1 (2C, C-25$^{a/b}$); **HR-MS** (ESI$^+$): for the adduct: *m/z* calculated for $[C_{24}H_{28}N_4O_4+H]^+$: 437.2183 ($[M+H]^+$); found: 437.2175; the semiquinone radical, which forms upon homolysis of the weak flavin substrate σ-bond is also observed: *m/z* calculated for $[C_{17}H_{19}N_4O_4+H]^{\cdot+}$: 344.1479 ($[M+H]^{\cdot+}$); found: 344.1470;

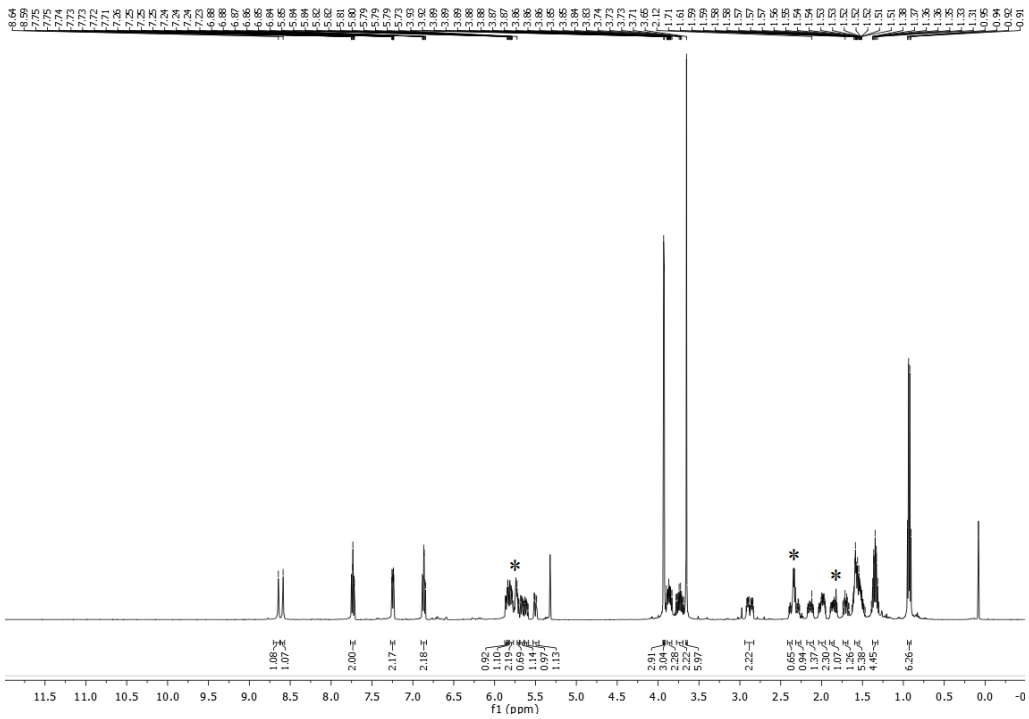


Figure SI-12: ^{1}H NMR spectrum of the flavin 1,3-cycloheptadiene adduct (contains small amount of residual 1,3-cycloheptadiene). The adduct is observed as a mixture of two diastereomers.

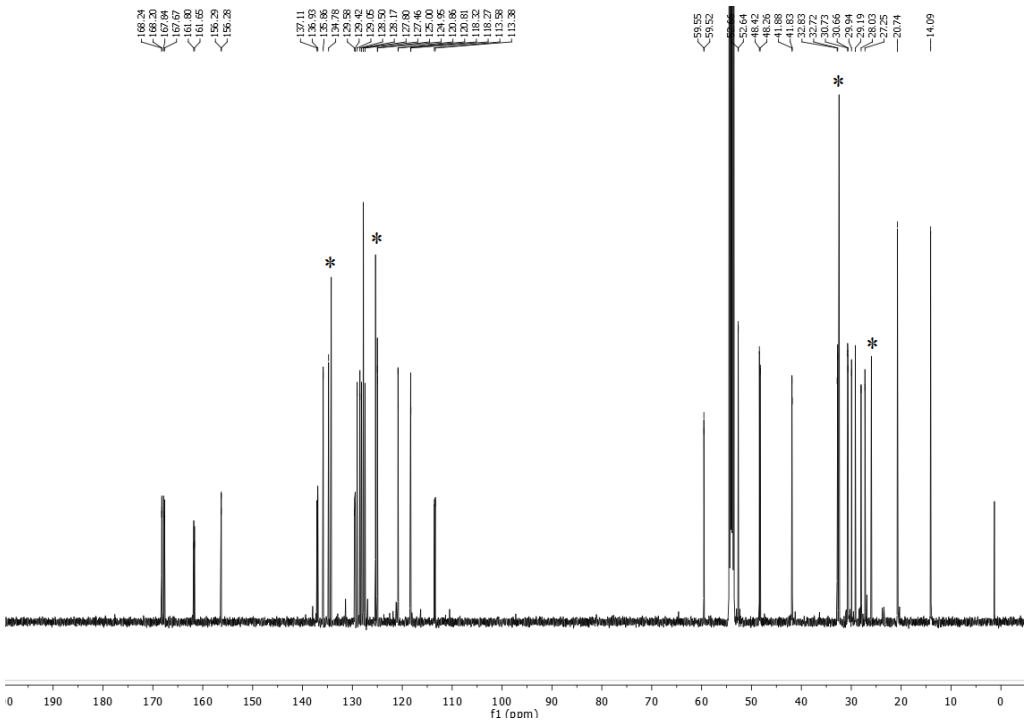


Figure SI-13: $^{13}C\{^{1}H\}$ NMR spectrum of the flavin 1,3-cycloheptadiene adduct (contains small amount of residual 1,3-cycloheptadiene). The adduct is observed as a mixture of two diastereomers.

Besides the adduct-characteristic chemical shifts, 2D-NMR spectra show important contacts within the molecule to assure the formation of the adduct. The HMBC spectrum shows contacts between the signal at 8.64 ppm/8.59 ppm and the aromatic moiety (**figure SI-14**). This proves the existence of the H-4:

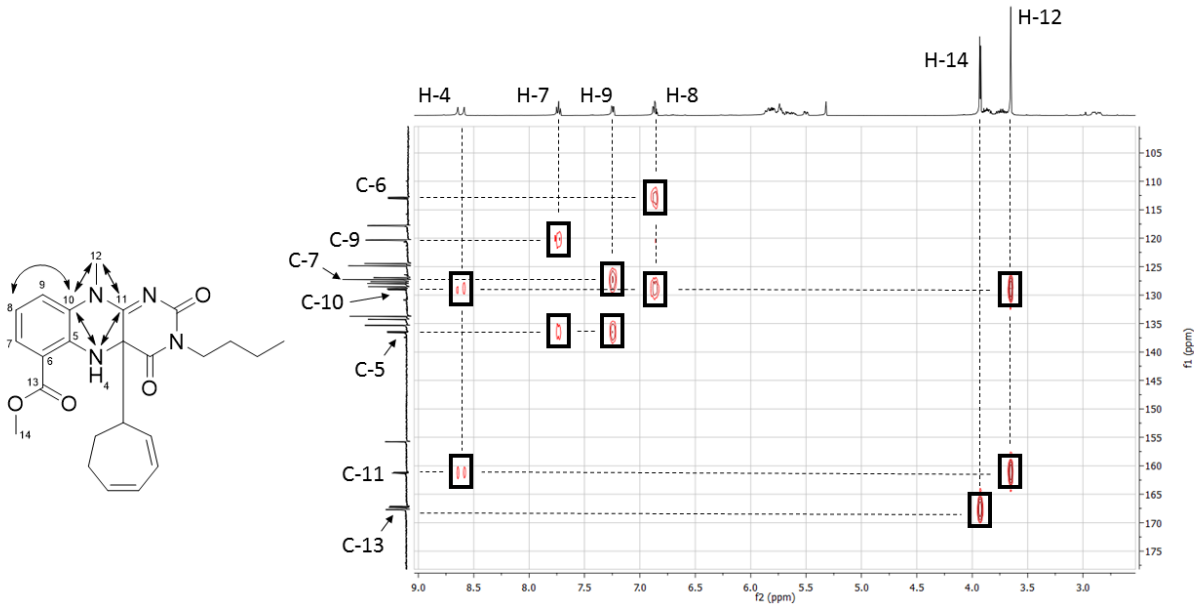


Figure SI-14: HMBC contacts within adduct **19** (for the sake of clarity not all contacts within the molecule have been marked with arrows).

The COSY spectrum shows the neighborhood of H-15$^{a/b}$ and H-16$^{a/b}$ as well as the neighborhood of the olefinic protons (can only be surmised due to overlapping of the signals) (**figure SI-15**). The contact between H-15$^{a/b}$ and H-16$^{a/b}$ is important to verify the NOE-contact of H4 and H-16$^{a/b}$ (**figure SI-16**).

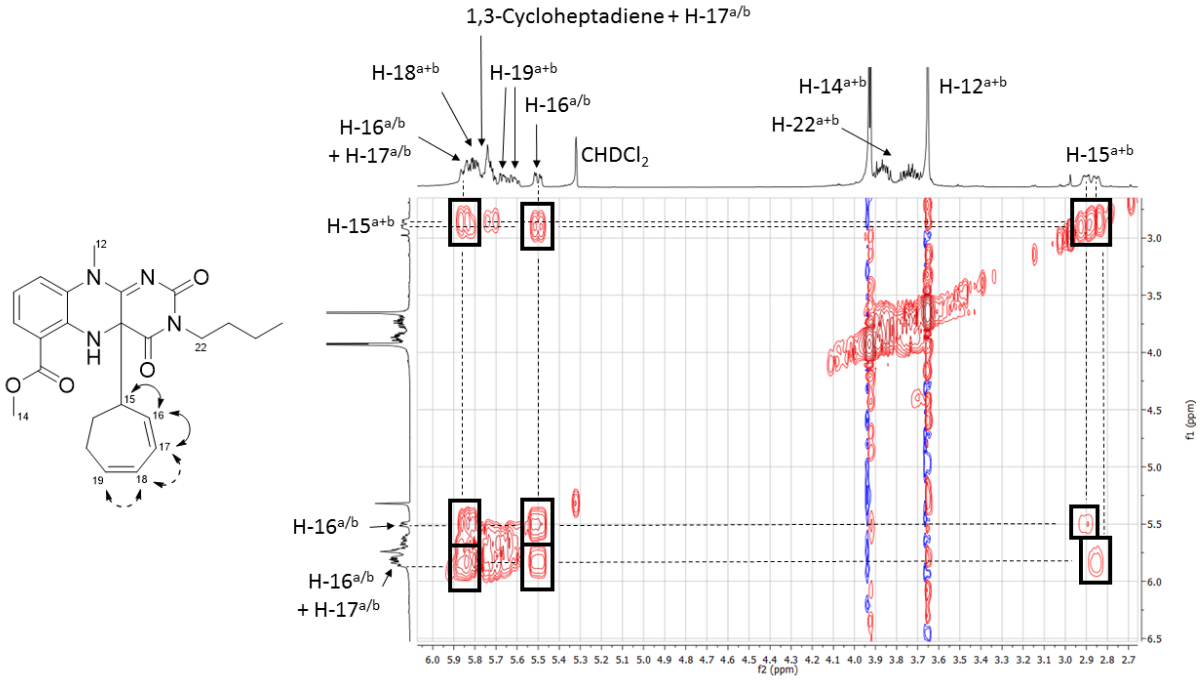


Figure SI-15: COSY contacts within adduct **19**.

The NOE-contact between H4 and H-16 in both adduct diastereomers corroborates the spatial proximity of the flavin core and a shifted 1,3-cycloheptadiene moiety (**figure SI-16**).

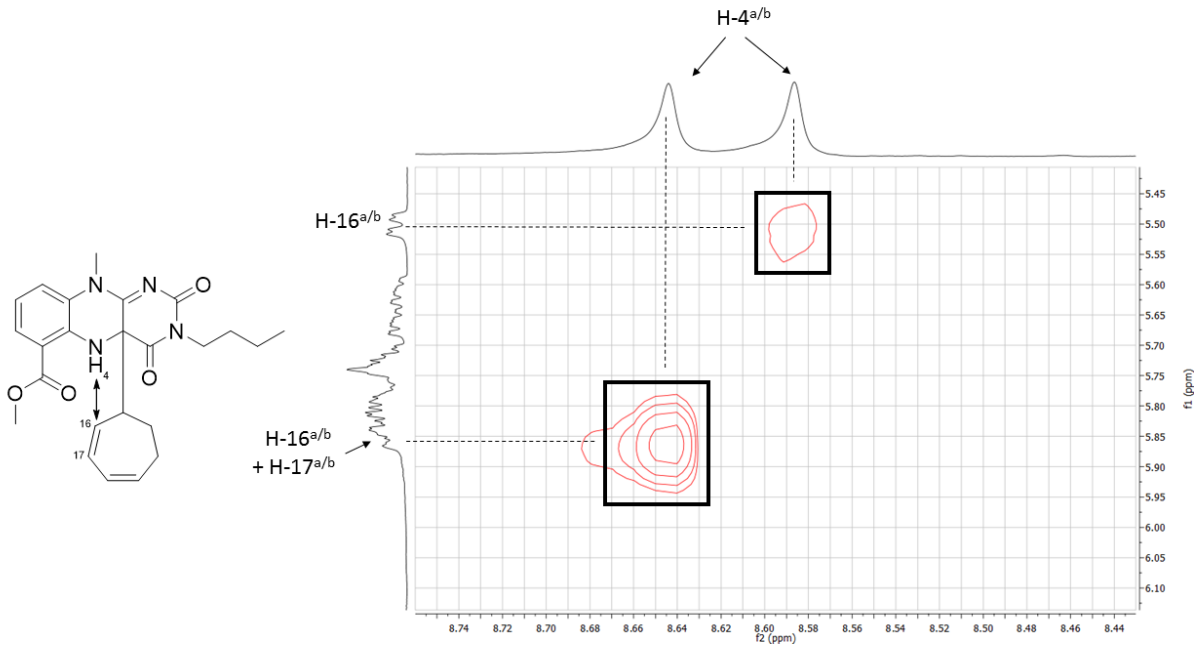


Figure SI-16: NOE contact within adduct **19** showing the spatial proximity between the flavin core and a shifted 1,3-cycloheptadiene moiety.

5.2. Intercepting the Cycloheptadien Flavin Adduct with TEMPO

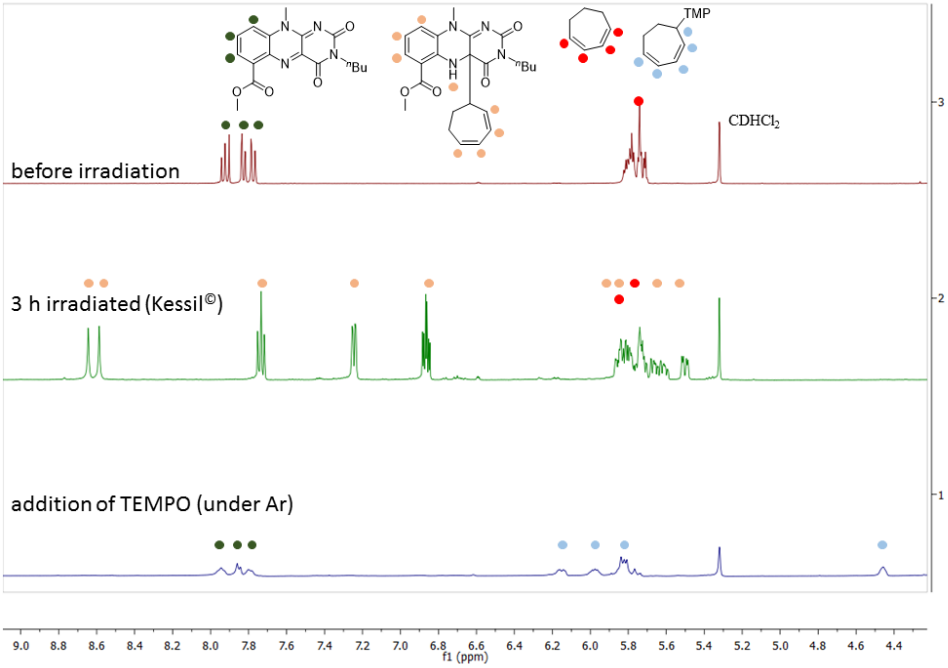
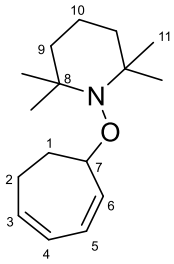


Figure SI-17: ^{1}H NMR spectrum of 1,3-cycloheptadiene and flavin **14** before irradiation, after three hours of irradiation and again after adding TEMPO to the NMR tube.

The catalyst (**14**) (6.16 mg, 18.0 µmol, 1.00 equiv.) is added to a *J. Young* NMR tube, evacuated three times and dissolved in CD_2Cl_2 (0.5 mL, 36 mM). 1,3-Cycloheptadiene (2.42 µL, 21.6 µmol, 1.20 equiv.) is added, the tube sealed and irradiated under Ar atmosphere for three hours (Kessil Tuna Blue©) (**figure SI-17**). Afterwards TEMPO is added under Ar atmosphere and let to react for one hour (**figure SI-17**). The crude sample is then purified by column chromatography (silica, PE/EtOAc 9:1) to isolate 1-(cyclohepta-2,4-dien-1-yloxy)-2,2,6,6-tetramethylpiperidine (**SI-32**) (**figure SI-18** and **SI-19**).



SI-32

TLC (silica, PE/EtOAc 9:1): R_f = 0.83 [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 6.17 - 6.10 (m, 1H, H-6), 5.99 – 5.90 (m, 1H, H-3), 5.86 – 5.77 (m, 2H, H-4, H-5), 4.44 (dt, $^3J_{H\text{-}H}$ = 6.6, 3.4 Hz, 1H, H-7), 2.40 – 2.22 (m, 2H, H-2), 2.16 – 2.07 (m, 1H, H-1), 1.91 – 1.83 (m, 1H, H-1), 1.61 – 1.53 (m, 1H, H-10), 1.48 – 1.43 (m, 4H, H-9), 1.38 – 1.31 (m, 1H, H-9), 1.14 (s, 12H, H-11); **^{13}C{^{1}H} NMR** (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 135.6 (C-3), 134.8 (C-6), 124.5 (C-4/C-5), 124.2 (C-4/C-5), 81.3 (C-7), 60.0 (C-8), 59.6 (C-8), 40.3 (C-9), 34.3 (C-11), 30.7 (C-1), 26.0 (C-2), 20.4 (C-11), 17.2 (C-10).

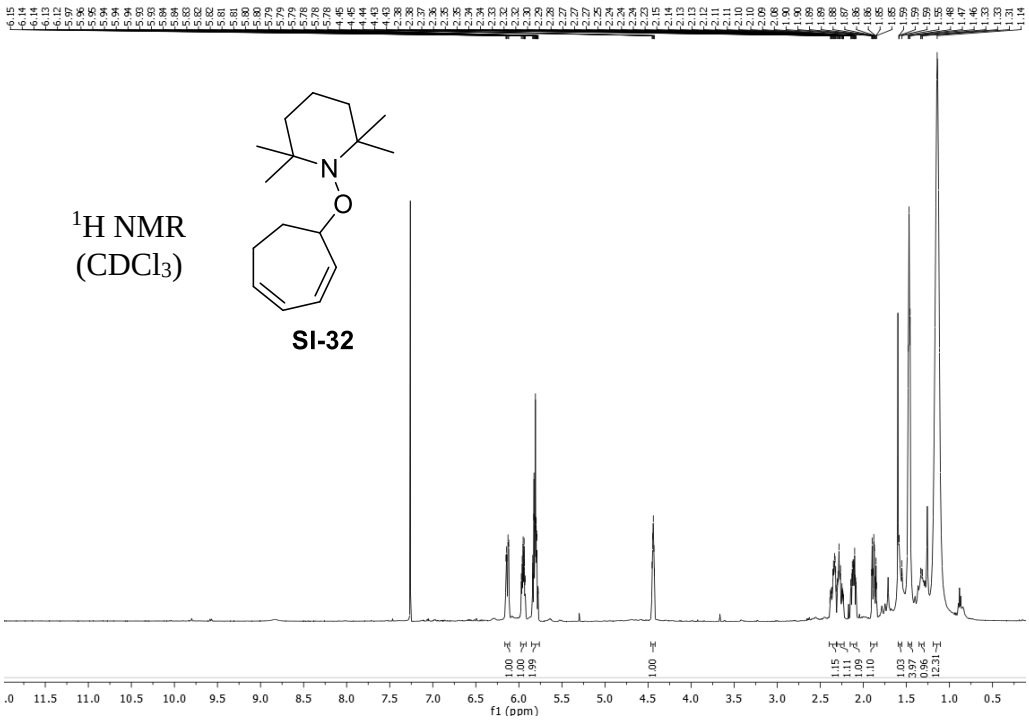


Figure SI-18: ^{1}H NMR spectrum of **SI-32**.

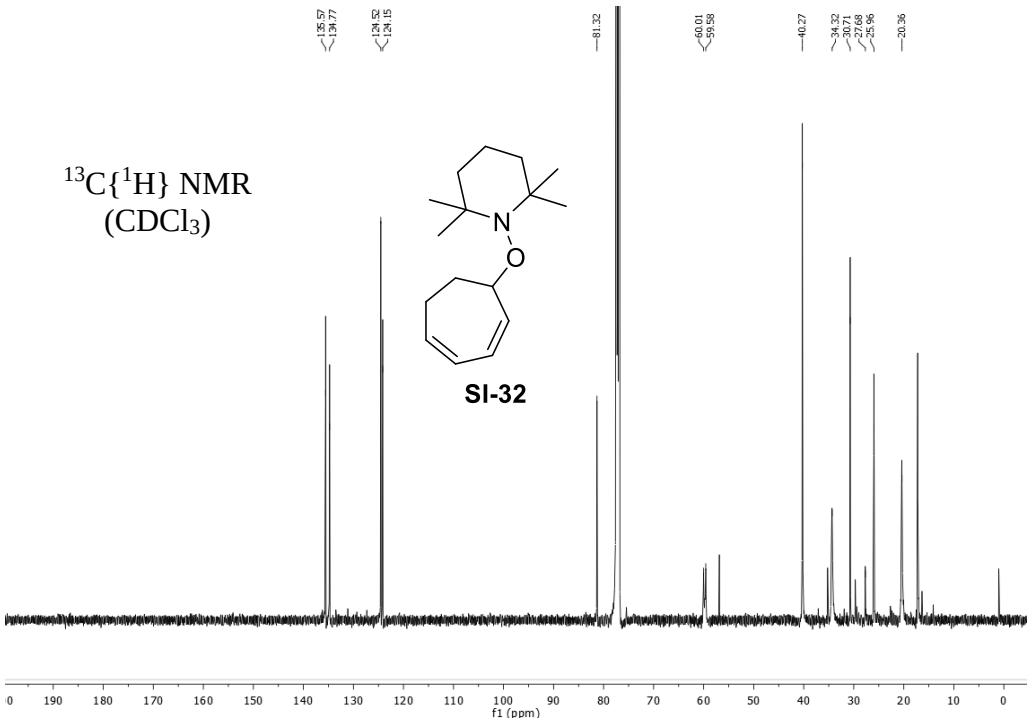
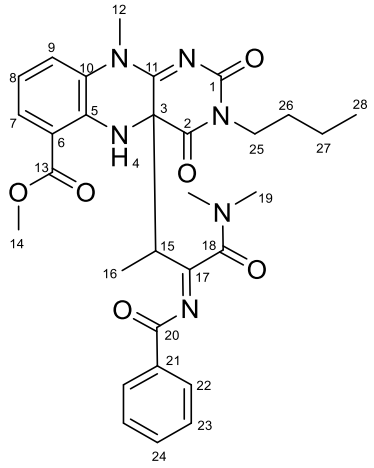


Figure SI-19: $^{13}C\{^{1}H\}$ NMR spectrum of **SI-32**.

5.3. Dehydrobutyrine Flavin Adduct Studies

5.3.1. (*Z*)-40 Flavin Adduct studies



42

The flavin **14** (6.16 mg, 18.0 µmol, 1.00 equiv.) is added to a *J. Young* NMR tube, the tube evacuated and backfilled with Ar three times and CD_2Cl_2 (0.5 mL, 36 mM) is added. Then, **(*Z*)-40** (4.18 mg, 18.0 µmol, 1.00 equiv.) is added, the tube sealed and irradiated under Ar atmosphere for 15 minutes (LED 451 nm).

Analysis of the adduct **42** (set of two diastereomers in a ratio ~ 1.5:1 (labelled as "a" and "b"); some signals could not be assigned due to incomplete conversion) (**figure SI-20** and **SI-21**):

^{1}H NMR (500 MHz, CD_2Cl_2, 298 K) δ (ppm) = 8.63 (s, 1H, H-4$^{a/b}$), 8.34 (s, 1H, H-4$^{a/b}$), 7.73 (dd, $^3J_{H\text{-}H}$ = 8.1 Hz, $^4J_{H\text{-}H}$ = 1.3 Hz, 1H, H-7$^{a/b}$), 7.63 – 7.53 (m, 2H, H-24^a, H-24^b), 7.45 – 7.41 (m, 4H, H-22$^{a/b}$/H-23$^{a/b}$), 7.31 (dd, $^3J_{H\text{-}H}$ = 8.1 Hz, $^4J_{H\text{-}H}$ = 1.2 Hz, 1H, H-9$^{a/b}$), 7.28 (dd, $^3J_{H\text{-}H}$ = 8.1 Hz, $^4J_{H\text{-}H}$ = 1.2 Hz, 1H, H-9$^{a/b}$), 6.94 (t, $^3J_{H\text{-}H}$ = 8.1 Hz, 1H, H-8$^{a/b}$), 6.86 (t, $^3J_{H\text{-}H}$ = 8.1 Hz, 1H, H-8$^{a/b}$), 3.91 (s, 3H, H-14$^{a/b}$), 3.83 (s, 3H, H-14$^{a/b}$), 3.69 - 3.65 (m, 7H, H-12$^{a/b}$, H-12$^{a/b}$, H-15$^{a/b}$), 3.31 (q, $^3J_{H\text{-}H}$ = 7.1 Hz, 1H, H-15$^{a/b}$), 1.38 (d, $^3J_{H\text{-}H}$ = 7.1 Hz, 3H, H-16$^{a/b}$), 1.22 (d, $^3J_{H\text{-}H}$ = 7.1 Hz, 3H, H-16$^{a/b}$); **^{13}C{^{1}H} NMR** (126 MHz, CD_2Cl_2, 298 K): δ (ppm) = 168.6 (C-17$^{a/b}$), 168.2 (C-13$^{a/b}$), 168.1 (C-17$^{a/b}$), 167.9 (C-13$^{a/b}$), 160.3 (C-11$^{a/b}$), 158.9 (C-11$^{a/b}$), 134.0 (C-24$^{a/b}$), 133.9 (C-24$^{a/b}$), 129.7 (C-10$^{a/b}$), 129.1 (2C, C-22$^{a/b}$/C-23$^{a/b}$), 129.0 (2C, C-22$^{a/b}$/C-23$^{a/b}$), 128.6 (C-10$^{a/b}$),

127.8 (C-7$^{a/b}$), 127.7 (C-7$^{a/b}$), 121.1 (C-9$^{a/b}$), 121.0 (C-9$^{a/b}$), 119.0 (C-8$^{a/b}$), 118.2 (C-8$^{a/b}$), 59.8 (C-3$^{a/b}$), 56.7 (C-3$^{a/b}$), 52.7 (C-14$^{a/b}$), 52.5 (C-14$^{a/b}$), 45.9 (C-15$^{a/b}$), 45.0 (C-15$^{a/b}$), 42.3 (C-25$^{a/b}$), 42.1 (C-25$^{a/b}$), 33.1 (C-12$^{a/b}$), 32.8 (C-12$^{a/b}$), 14.2 (C-16$^{a/b}$), 14.1 (C-16$^{a/b}$), 14.0 (C-28$^{a/b}$), 13.4 (C-28$^{a/b}$); **HR-MS** (ESI$^+$): *m/z* calculated for $[C_{30}H_{34}N_6O_6+Na]^+$: 597.2432 ($[M+Na]^+$); found: 597.2426.

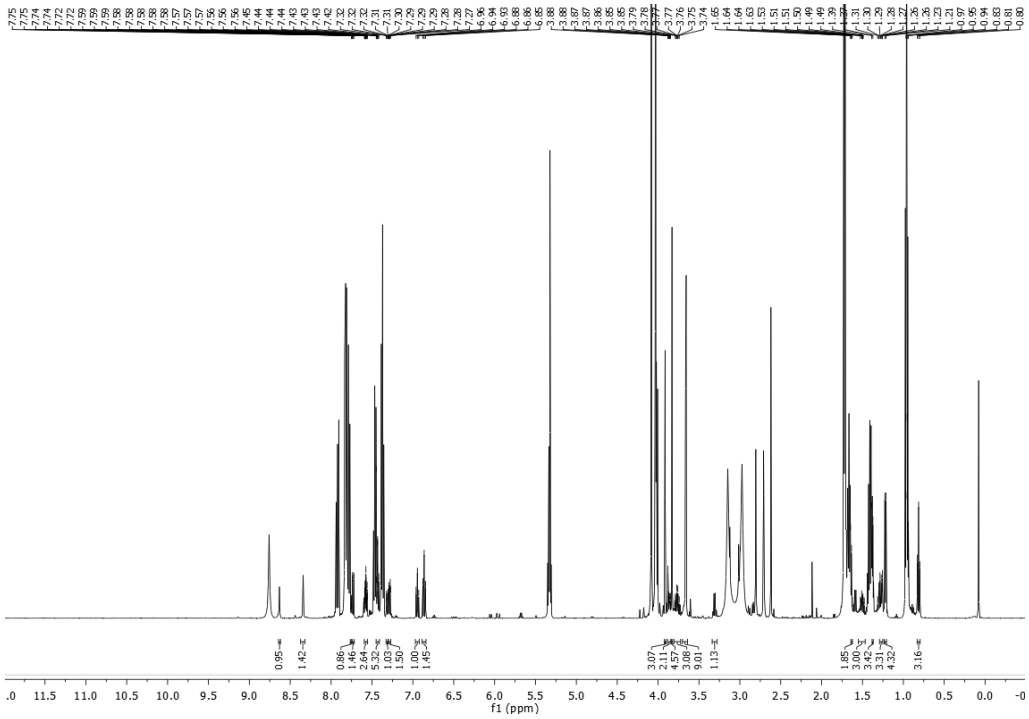


Figure SI-20: ^{1}H NMR spectrum of the flavin **(*Z*)-40** adduct (contains amount of unreacted flavin **14** and **(*Z*)-40**). The adduct is observed as a mixture of two diastereomers.

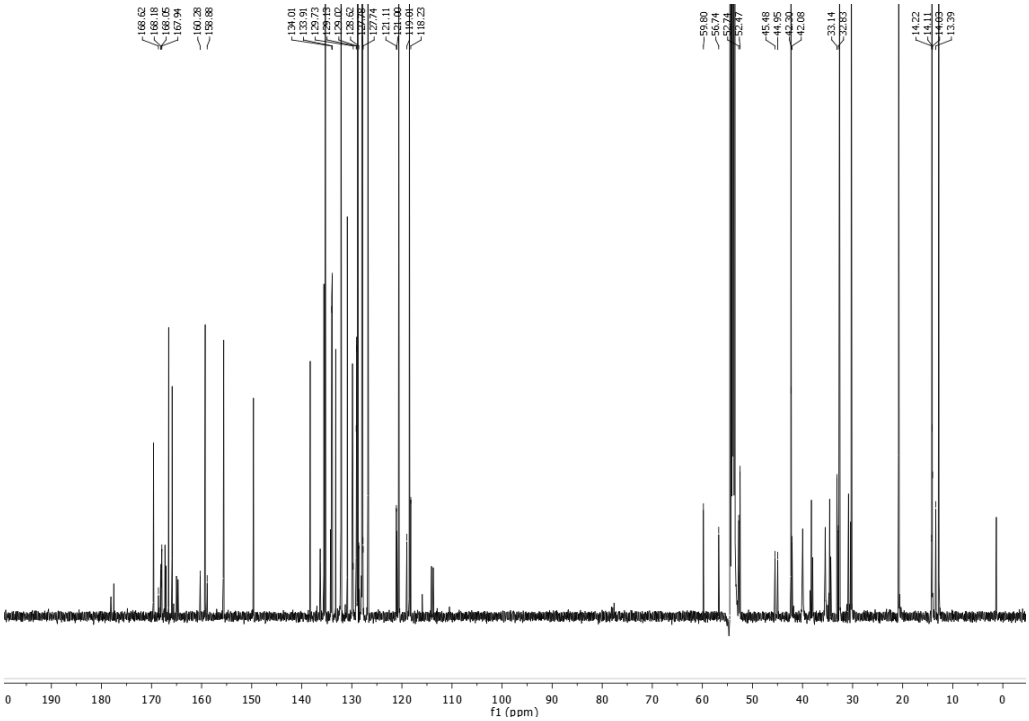


Figure SI-21: $^{13}C\{^{1}H\}$ NMR spectrum of the flavin **(*Z*)-40** adduct (contains amount of unreacted flavin **14** and **(*Z*)-40**). The adduct is observed as a mixture of two diastereomers.

Besides the adduct-characteristic chemical shifts, 2D-NMR spectra show important contacts within the molecule to assure the formation of the adduct. The HMBC spectrum shows contacts between the signal at 1.38 ppm/1.22 ppm (H-16$^{a/b}$) and C-3$^{a/b}$ (and C-15$^{a/b}$) (**figure SI-22**).The signal at 1.38 ppm is difficult to detect, since it overlaps with the signal of unreacted flavin **14** (green). Nevertheless, the COSY spectrum shows the neighborhood between the signal at 1.38 ppm and 3.31 ppm (H-15$^{a/b}$) (**figure SI-26**).

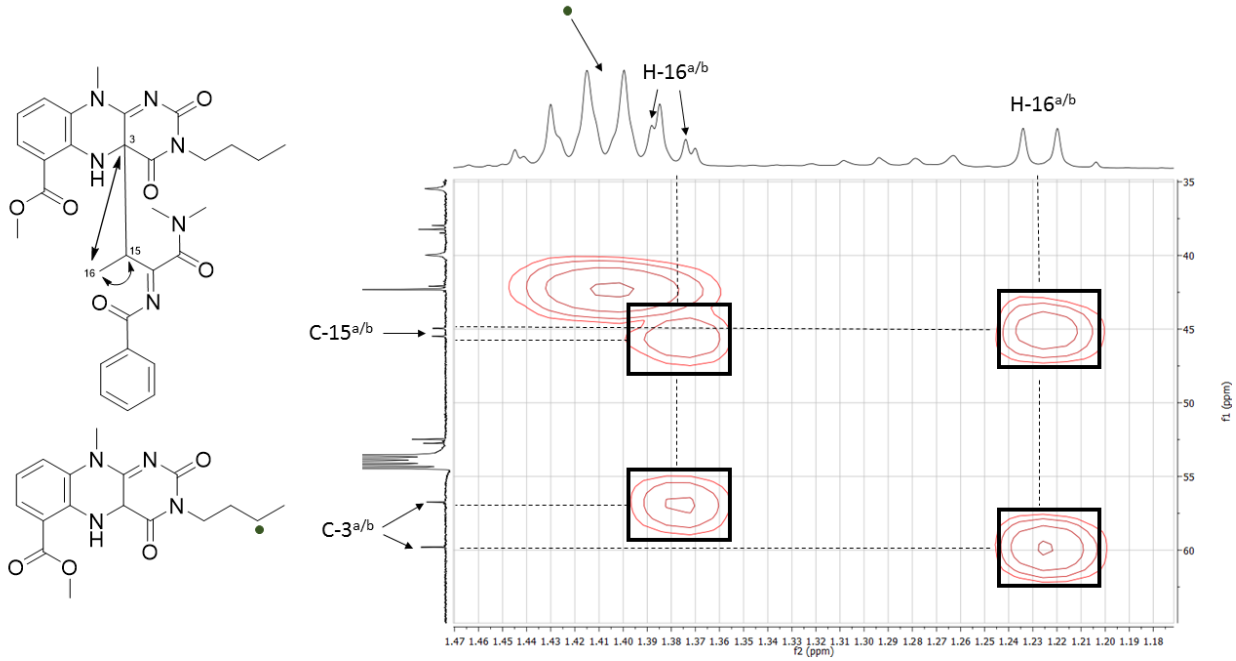


Figure SI-22: HMBC contacts between H-16$^{a/b}$ and C-15$^{a/b}$/C-3$^{a/b}$ within adduct **42**.

The HMBC spectrum, furthermore, shows the contact between H15$^{a/b}$/H-16$^{a/b}$ and C-17$^{a/b}$ indicating a strongly shifted acylimine (**figure SI-23**). The contact between the signal at 8.63 ppm/8.34 ppm and C-10$^{a/b}$/C-11$^{a/b}$ can also be observed (**figure SI-24**). This corroborates the existence of the H4. C-10$^{a/b}$/C-11$^{a/b}$ couple to further protons within the flavin core (H-12$^{a/b}$ and H-8$^{a/b}$) (**figure SI-25**).

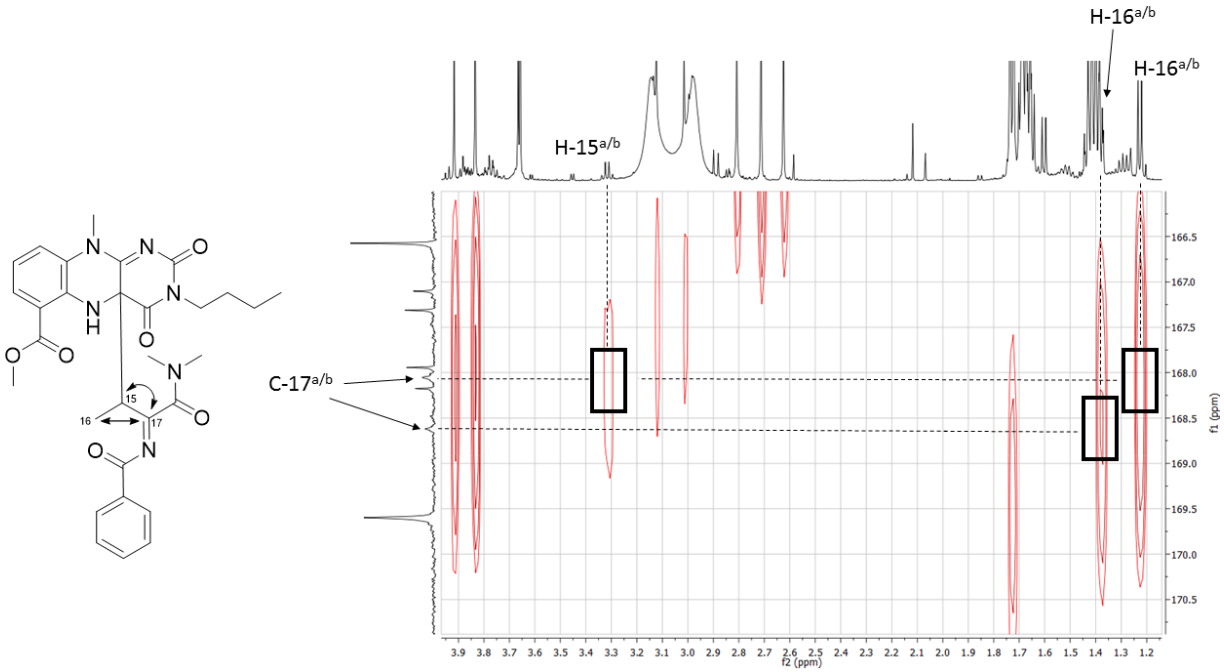


Figure SI-23: HMBC contacts between H-15$^{a/b}$/H-16$^{a/b}$ and C-17$^{a/b}$ within adduct **42**.

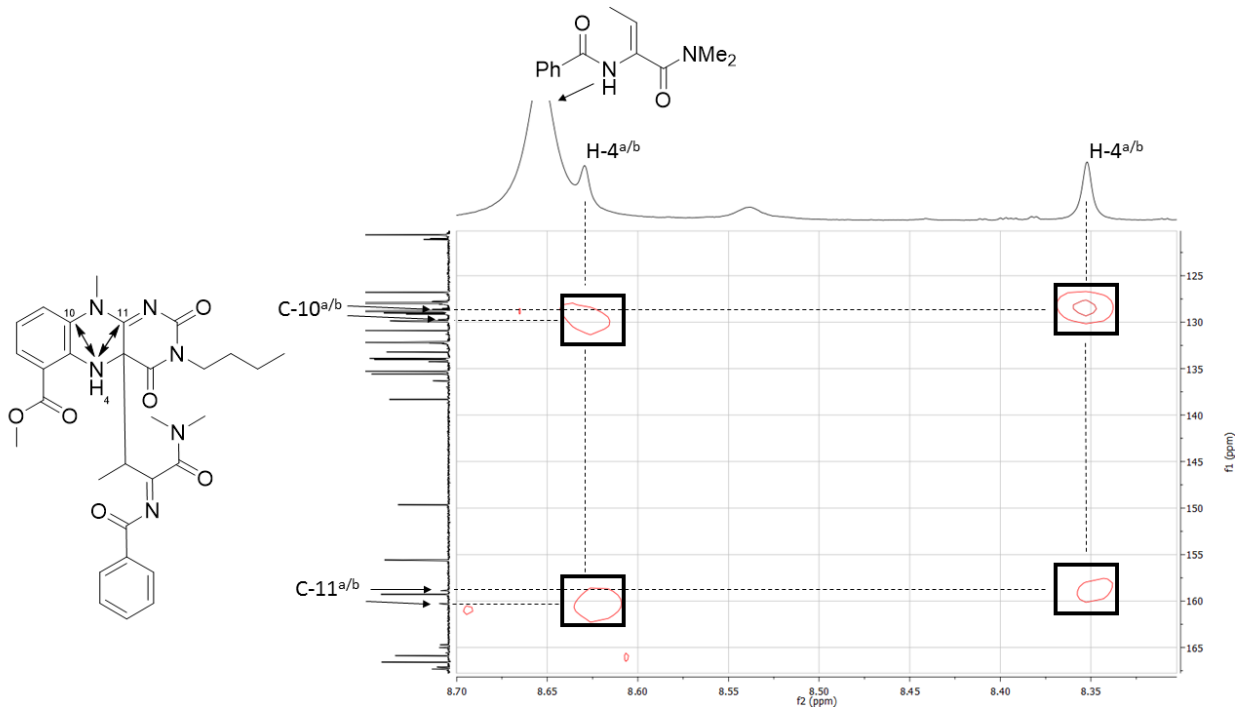


Figure SI-24: HMBC contacts between H-14$^{a/b}$ and C-10$^{a/b}$/C-11$^{a/b}$ within adduct **42**.

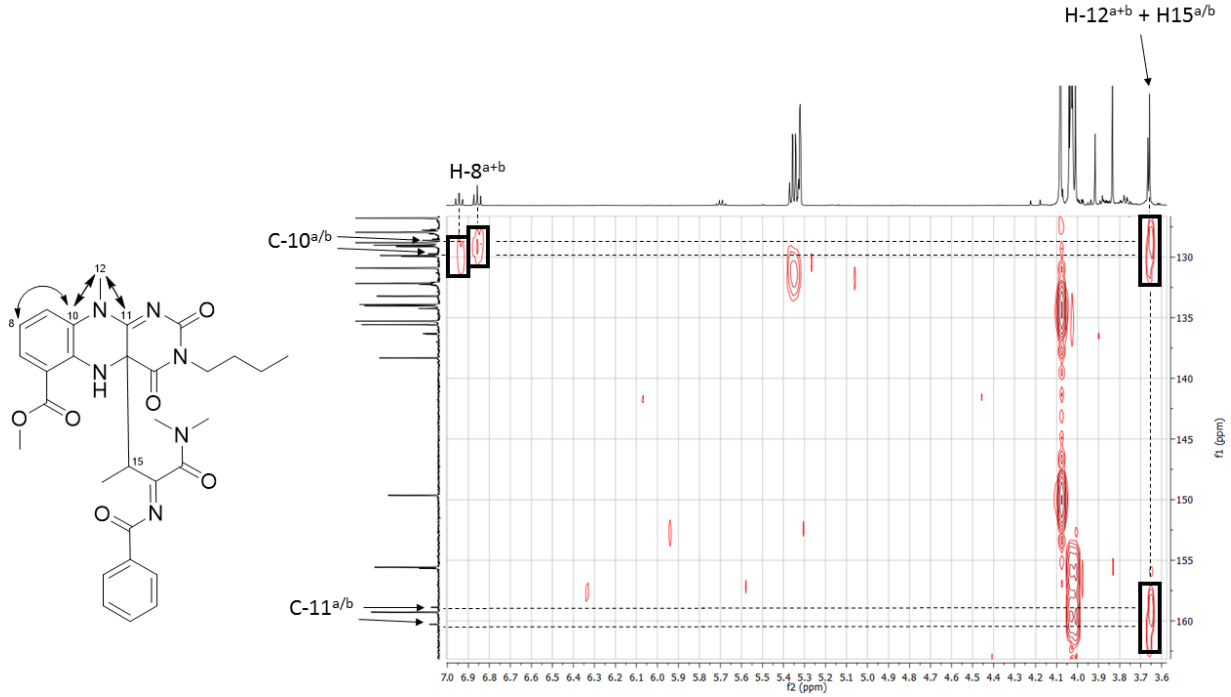


Figure SI-25: HMBC contacts between H-8$^{a/b}$ and C-10$^{a/b}$ as well as H-12$^{a/b}$ and C-10$^{a/b}$/C-11$^{a/b}$ within adduct **42**.

The COSY spectrum shows the neighborhood of the signals at 3.69 - 3.65 ppm/3.31 ppm (C-15$^{a/b}$) and 1.38 ppm/1.22 ppm (C-16$^{a/b}$). The COSY spectrum also corroborates the overlap between H-12$^{a/b}$ and H-15$^{a/b}$ (**figure SI-26**).

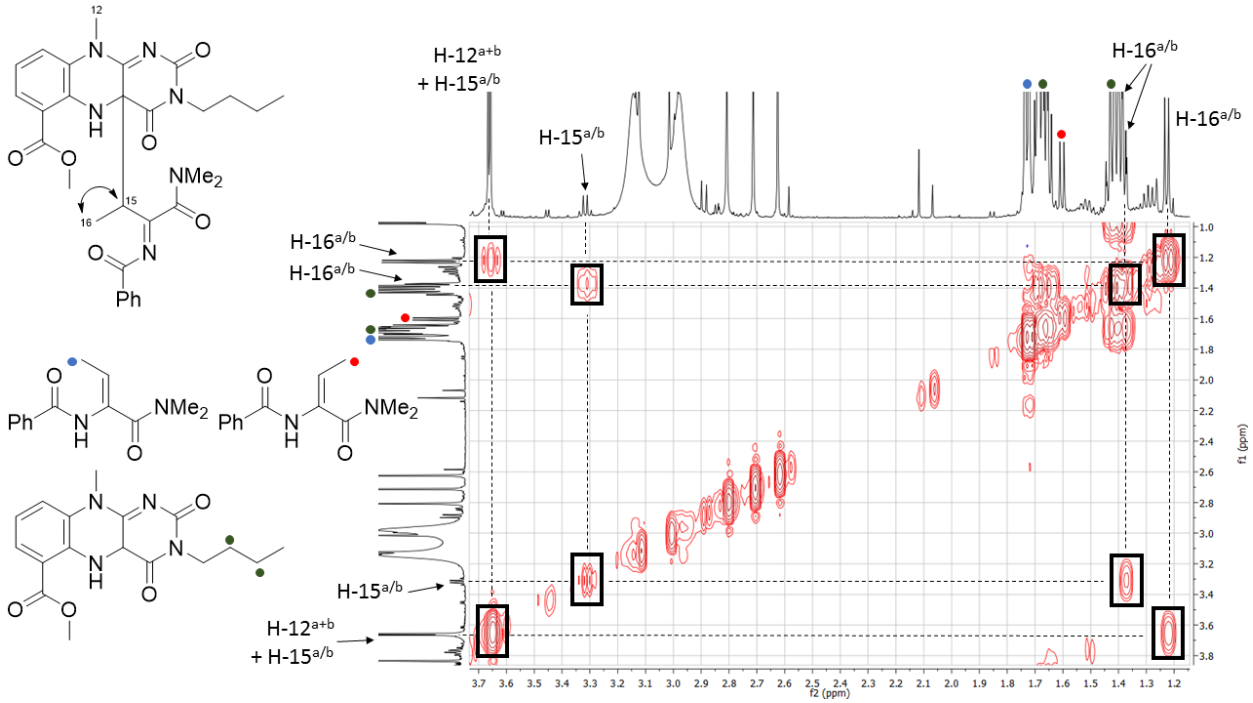


Figure SI-26: COSY contacts between H-15$^{a/b}$ and H-16$^{a/b}$ within adduct **42**.

Moreover, the NOE-contact between H4 and H-16 proves the spatial proximity of the flavin core and oxidized dehydrobutyrine, indicating the existence of the adduct (**figure SI-27**).

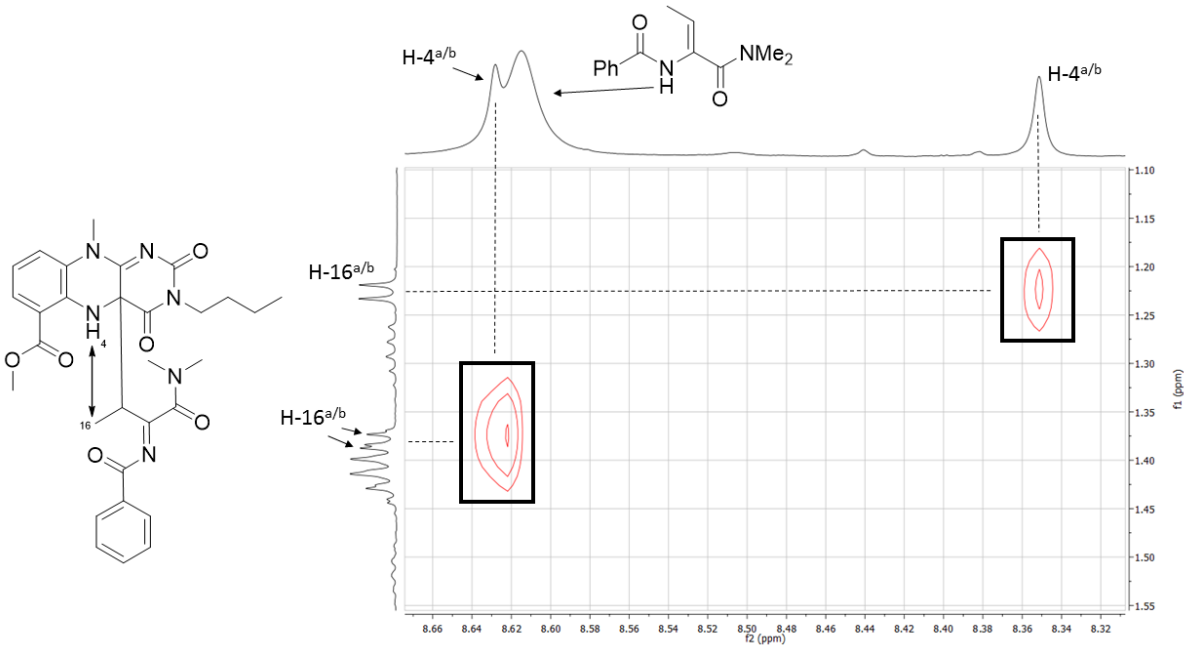


Figure SI-27: NOE contact within adduct **42** showing the spatial proximity between the flavin core and **(*Z*)-40**.

5.3.2. Interpretation of the (*Z*)-40 Flavin Adduct studies

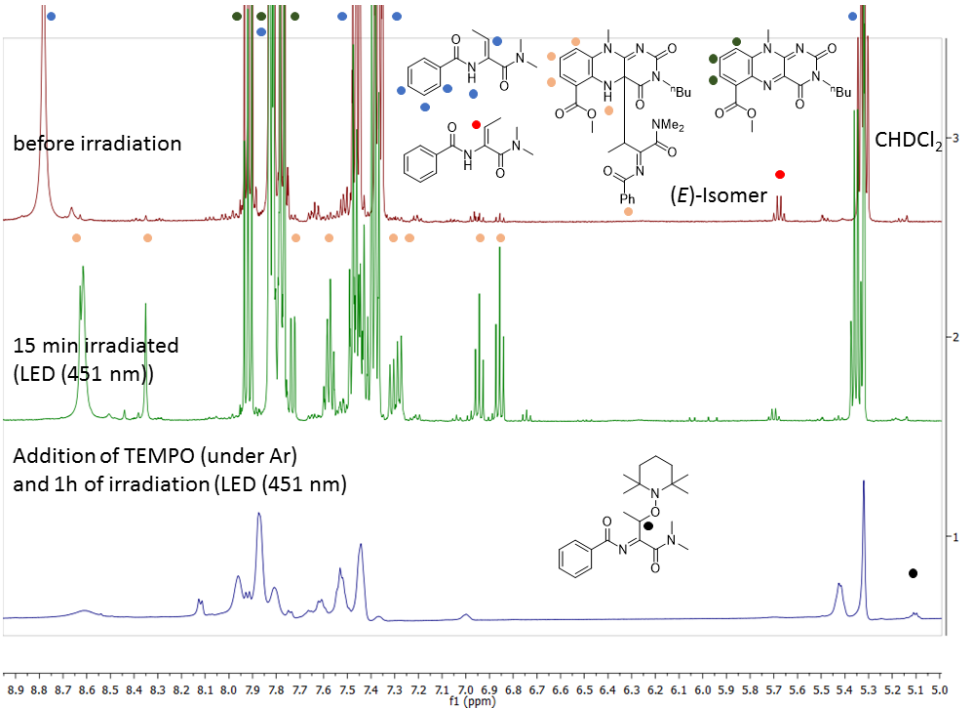


Figure SI-28: ^{1}H NMR spectrum of **(*Z*)-40** and flavin **14** before irradiation, after 15 minutes of irradiation and again after adding TEMPO to the NMR tube and irradiating for one hour.

The catalyst (**14**) (6.16 mg, 18.0 µmol, 1.00 equiv.) is added to a *J. Young* NMR tube, the tube is evacuated and backfilled with Ar three times and CD_2Cl_2 (0.5 mL, 36 mM) is added. **(*Z*)-40** (4.18 mg, 18.0 µmol, 1.00 equiv.) is added, the tube is sealed and irradiated under Ar atmosphere for 15 minutes (LED; λ = 451 nm) (**figure SI-28**). Adduct is formed as two diastereomers under these conditions and the *E*/*Z* ratio remains unaltered (*E*/*Z* ratio before and after irradiation equals 1:30). Afterwards TEMPO is added under Ar atmosphere and let to react for one hour under irradiation (LED; λ = 451 nm) (**figure SI-28**). The formation of the hydroxylamine-functionalized product **25** can be observed concomitant to the consumption of the adduct **SI-33**.

5.3.3. Interpretation of the (*Z*)-41 Flavin Adduct Studies

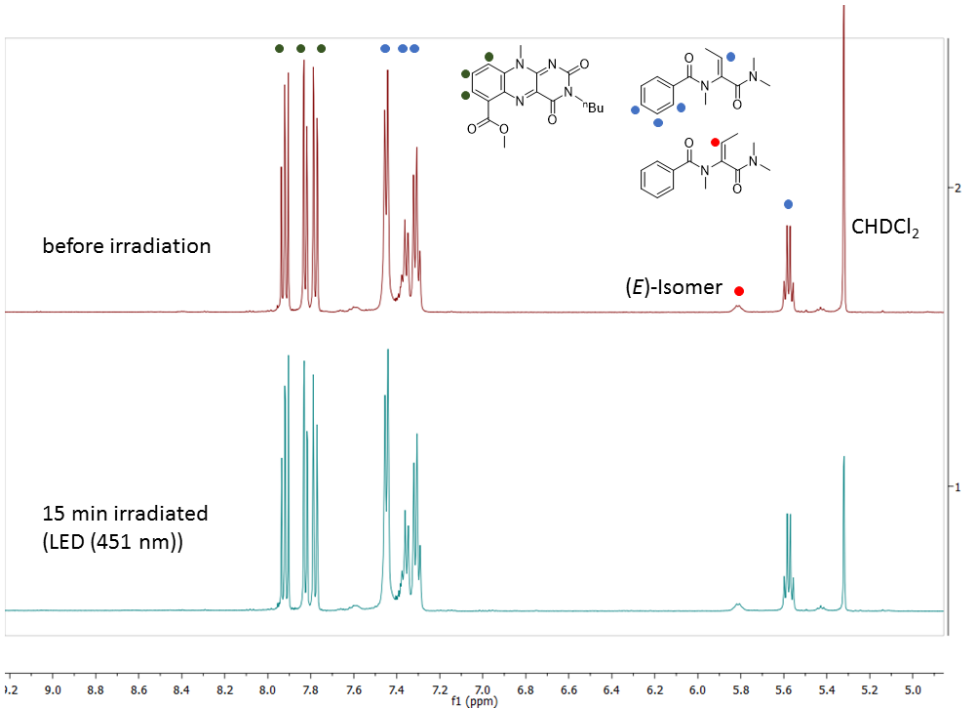


Figure SI-29: ^{1}H NMR spectrum of **(*Z*)-41** and flavin **14** before irradiation, and after 15 minutes of irradiation.

The catalyst (**14**) (6.16 mg, 18.0 µmol, 1.00 equiv.) is added to a *J. Young* NMR tube, the tube is evacuated and backfilled with Ar three times and CD_2Cl_2 (0.5 mL, 36 mM) is added. **(*Z*)-41** (4.43 mg, 18.0 µmol, 1.00 equiv.) is added, the tube is sealed and irradiated under Ar atmosphere for 15 minutes (LED; λ = 451 nm). No adduct is formed under these conditions and no *E*/*Z*-isomerization takes place (*E*/*Z* ratio before and after irradiation equals 1:7) (**figure SI-29**).

To check for reactivity after longer irradiation time, **(*Z*)-41** is used as a substrate in a catalytic reaction with TEMPO and flavin catalyst **14** according to the general procedure in **3.1.**. After 16 hours of irradiation no product and no *E*/*Z* isomerization is observed. The characteristic α-hydroxylamine proton is not detected and no new signals arise (**figure SI-30**). The crude NMR spectrum of the catalytic reaction of **(*Z*)-41** is depicted as well (**figure SI-31**).

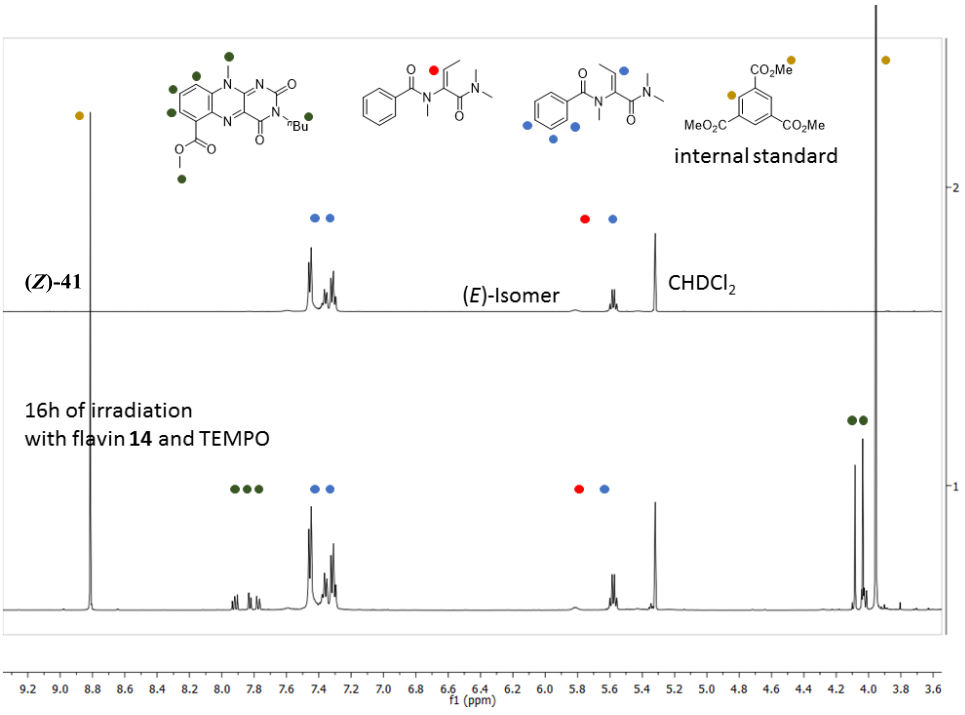


Figure SI-30: ^{1}H NMR spectrum of **(*Z*)-41** (top) and of crude reaction after 16 hours of irradiation with flavin **14** and TEMPO (bottom).

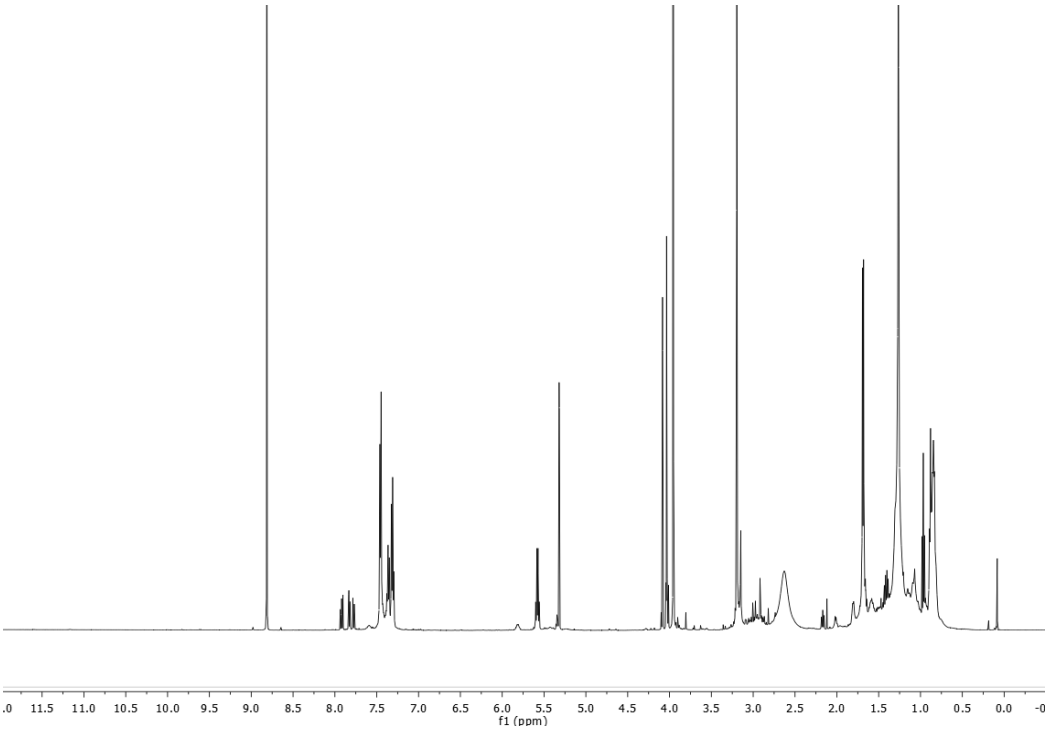


Figure SI-31: Full crude ^{1}H NMR spectrum of the catalytic reaction of **(*Z*)-41**.

5.3.4. Interpretation of the (*E*)-40 Flavin Adduct Studies

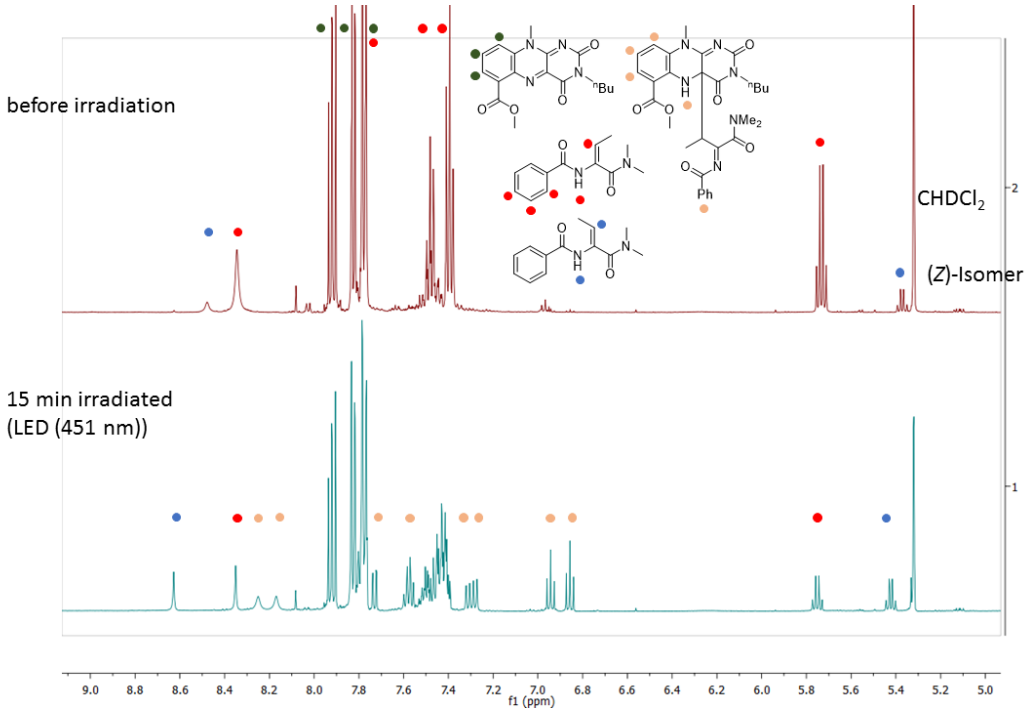


Figure SI-32: ^{1}H NMR spectrum of **(*E*)-40** and flavin **14** before irradiation, and after 15 minutes of irradiation.

The catalyst (**14**) (6.16 mg, 18.0 µmol, 1.00 equiv.) is added to a *J. Young* NMR tube, the tube is evacuated and backfilled with Ar three times and CD_2Cl_2 (0.5 mL, 36 mM) is added. **(*E*)-40** (4.18 mg, 18.0 µmol, 1.00 equiv.) is added, the tube is sealed and irradiated under Ar atmosphere for 15 minutes (LED; λ = 451 nm). Adduct is formed as two diastereomers under these conditions and additionally, *E*/*Z*-isomerization takes place (*E*/*Z* ratio before irradiation equals 6:1 and after irradiation 1:1) (**figure SI-32**).

5.3.5. Interpretation of the (*E*)-41 Flavin Adduct Studies

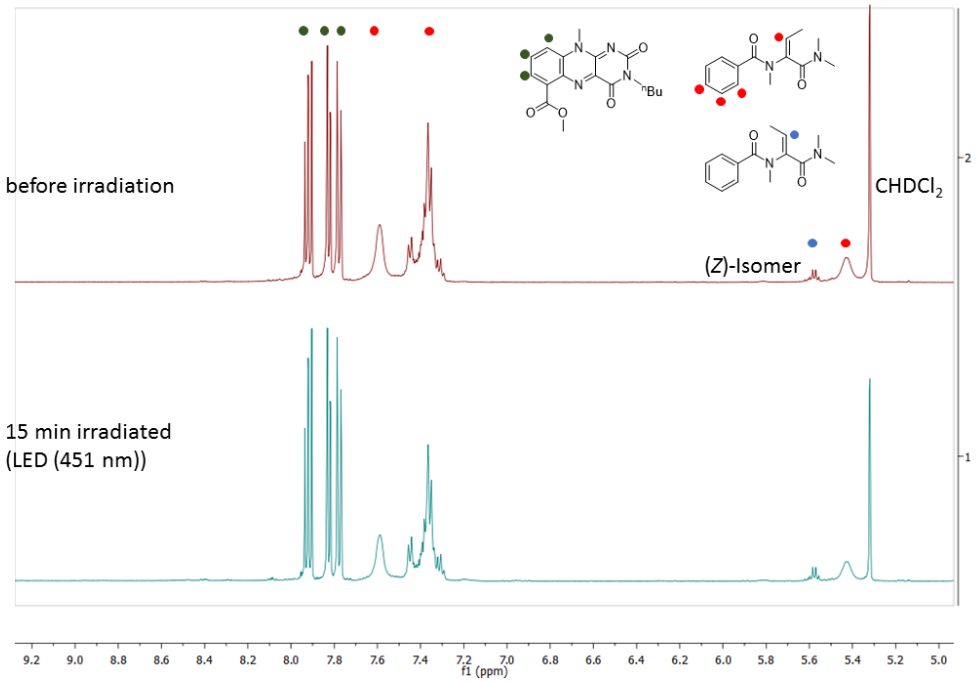


Figure SI-33: ^{1}H NMR spectrum of **(*E*)-41** and flavin **14** before irradiation, and after 15 minutes of irradiation.

The catalyst (**14**) (6.16 mg, 18.0 µmol, 1.00 equiv.) is added to a *J. Young* NMR tube, the tube is evacuated and backfilled with Ar three times and CD_2Cl_2 (0.5 mL, 36 mM) is added. **(*E*)-41** (4.43 mg, 18.0 µmol, 1.00 equiv.) is added, the tube is sealed and irradiated under Ar atmosphere for 15 minutes (LED; λ = 451 nm). No adduct is formed under these conditions and additionally, no *E*/*Z*-isomerization takes place (*E*/*Z* ratio before irradiation and after irradiation equals 6:1) (**figure SI-33**).

6. Cyclic Voltammetry

We first recorded the cyclic voltammogram of RFTA(Me) in CH_3CN (scan rate of 0.1 V s^{-1}) and determined a half-wave potential for the reversible transformation of $E_{1/2}$ = -0.86 V *vs.* SCE (**figure SI-34**). This is in accordance with the reported value of $E_{1/2}$ = -0.82 V *vs.* SCE by Cibulka *et al.* for RFTA(Me).[19]

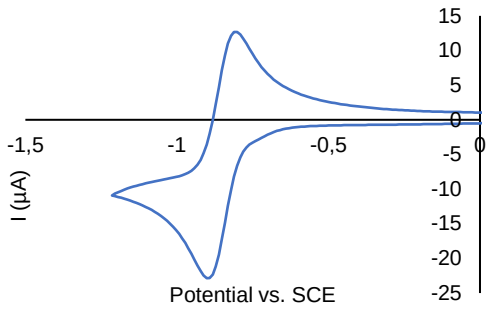


Figure SI-34: Cyclic voltammogram of 1 mM RFTA(Me) in 0.1 M $TBAPF_6/CH_3CN$ with a scan rate of 0.1 V s^{-1}.

The cyclic voltammogram of flavin **14** (CH_3CN, scan rate of 0.1 V s^{-1}) shows two separate oxidation waves under analogous conditions (**figure SI-35**). The half-wave potential was determined with the peak potentials of wave 1 and wave 2, which correspond to the reversible transformation.[20] This resulted in a more positive half-wave potential of $E_{1/2}$ = -0.72 V *vs.* SCE compared to RFTA(Me), which can be rationalized by the electron-withdrawing ester substituent.

[19] M. März *et al., Org. Biomol. Chem.* **2018**, *16*, 6809.
[20] S. L. J. Tan, R. D. Webster, *J. Am. Chem. Soc.* **2012**, *134*, 5954.

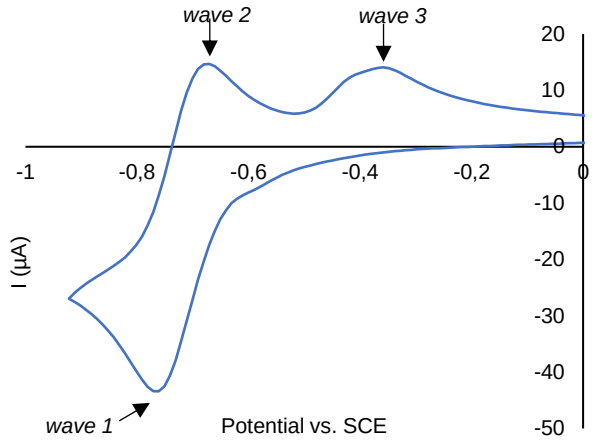
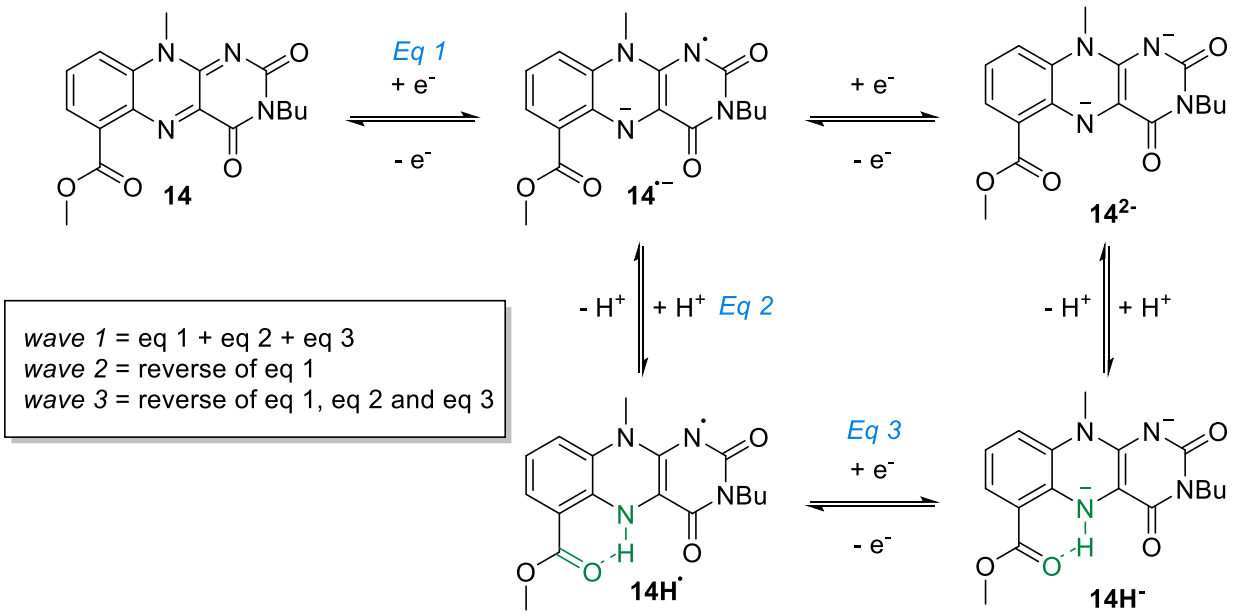


Figure SI-35: Cyclic voltammogram of 1 mM **14** in 0.1 M $TBAPF_6/CH_3CN$ with a scan rate of 0.1 Vs^{-1}.

The occurrence of two oxidation waves is well-known for riboflavin and other N3-unsubstituted flavins. This can be rationalized by a competing and irreversible reduction of the flavin in the presence of a proton source yielding the neutral semiquinone (instead of the anionic semiquinone). Even though the protonation of an anionic semiquinone to a neutral semiquinone is chemically reversible, this process is of irreversible nature since it occurs prior to the re-oxidation of the anionic semiquinone.[20,21,22] In comparison to riboflavin, protonation of the radical anion **14**$^{\bullet-}$ is expected to be significantly favored since a stabilizing hydrogen-bond interaction occurs between the C6-ester group and the N5-proton (**scheme SI-01**). In analogy to N3-unsubstituted riboflavin, we assign the reduction wave (wave 1) to a one-electron reduction to the semiquinone anion **14**$^{\bullet-}$ followed by protonation to **14**H$^{\bullet}$ and the second one-electron reduction of neutral semiquinone **14**H$^{\bullet}$ (which has a more positive redox potential) to anionic hydroquinone **14**H^{-} (**scheme SI-01**). As reduction of **14**$^{\bullet-}$ to **14**$^{2-}$ occurs at more negative potentials,[20] this transformation is unfavored at the applied potentials. After reversing the direction of the scan, two oxidation waves appear, which can be assigned to one- and two-electron oxidations of **14**$^{\bullet-}$ (wave 2) and **14**H^{-} (wave 3). Thus, at scan rates of 0.1 Vs^{-1} protonation of **14**$^{\bullet-}$ is highly favored, while deprotonation is disfavored due to the stabilizing hydrogen bond interactions in **14**H$^{\bullet}$. Under similar conditions wave 3 is not visible in the CV of N3 methylated RFTA, even at low scan rates of 0.05 Vs^{-1}

[20] S. L. J. Tan, R. D. Webster, *J. Am. Chem. Soc.* **2012**, *134*, 5954.
[21] A. Niemz *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 887.
[22] S. L. J. Tan e*t al.*, *J. Phys. Chem. B* **2015**, *119*, 14053.

indicating that the deprotonation from [RFTA(Me)]H$^{\cdot}$ to [RFTA(Me)]$^{\cdot-}$ occurs rapidly. Thus, only [RFTA(Me)]$^{\cdot-}$ is present on the electrode surface and wave 2 is observed exclusively, which is supported by literature.[22]



Scheme SI-01: Partial electrochemical reduction and protonation mechanism of flavin **14**.

This occurrence of two separate oxidation waves is not observed for N3-alkylated flavins. Since flavin **14** is also methylated at that N3-position, we wondered where the proton came from. As the residual water content (2.6 mM, measured by Karl Fischer titration) exceeds the concentration of **14** (1 mM) it is possible that the proton transfer occurs between **14**$^{\cdot-}$ and water. To confirm this hypothesis, CVs with the addition of different amounts of water (**figure SI-36**) were measured. More positive half-wave potentials of **14** were observed with increasing amounts of added water, which could be explained by hydrogen-bonding interactions between the flavin and water in analogy to similar observations with quinones.[23,24] However, the shape of the cyclic voltammograms remained unaltered.

[22] S. L. J. Tan et *al.*, *J. Phys. Chem. B* **2015**, *119*, 14053.
[23] M. Tessensohn *et al.*, *J. Phys. Chem. C* **2013**, *117*, 1081.
[24] M. Quan *et al.*, *J. Am. Chem. Soc.* **2007**, *129*, 12847.

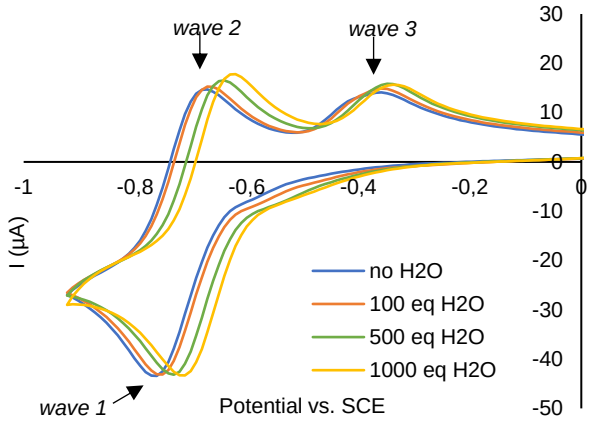


Figure SI-36: CV spectra of 1 mM **14** in 0.1 M $TBAPF_6/CH_3CN$ with a scan rate of 0.1 Vs^{-1} with successive water addition.

We then recorded cyclic voltammograms with a water content of 2000 equiv. at different scan rates (**figure SI-37**). The intensity of wave 3 decreased at higher scan rates while the intensity of wave 2 increased significantly. At higher scan rates, the rapid re-oxidation of anionic **14**$^{\bullet -}$ (wave 2) outcompetes the protonation of the radical anion, which would lead to the formation of neutral **14**H$^{\bullet}$ and wave 3. Similar studies were conducted with riboflavin.[20] Since more **14**$^{\bullet -}$ is present on the electrode surface, the intensity of wave 2 increases relative to wave 3.

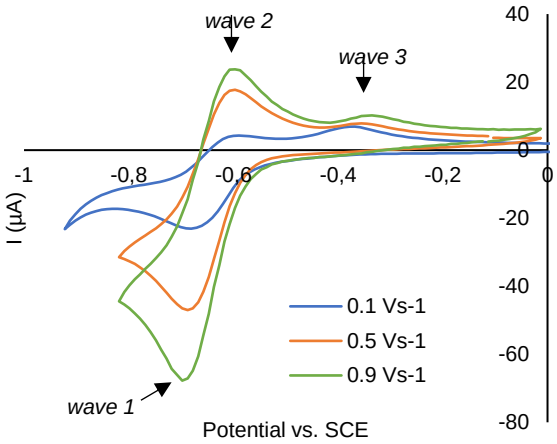


Figure SI-37: CV spectra of 1 mM **14** in 0.1 M $TBAPF_6/CH_3CN$ with different scan rates after addition of 2000 equiv of water.

[20] S. L. J. Tan, R. D. Webster, *J. Am. Chem. Soc.* **2012**, *134*, 5954.

When using acetic acid as a better proton source, the protonation of **14**$^{\bullet-}$ to **14**H$^{\bullet}$ is expected to be faster.[21] Indeed, with increasing amounts of acetic acid, the anionic semiquinone **14**$^{\bullet-}$ on the electrode surface is fully protonated resulting in the disappearance of wave 2 (**figure SI-38**). This corroborates our assignment of the three waves for flavin **14**.

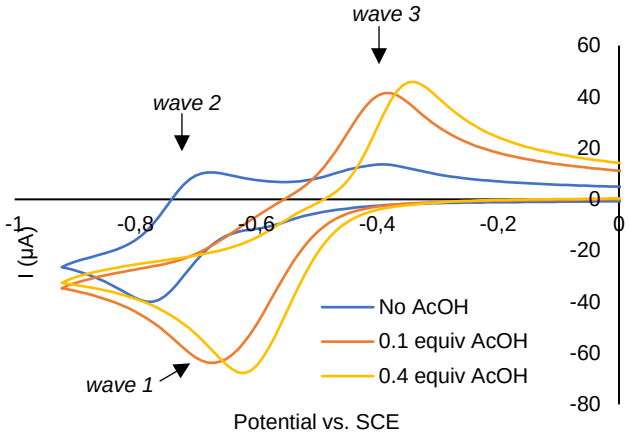
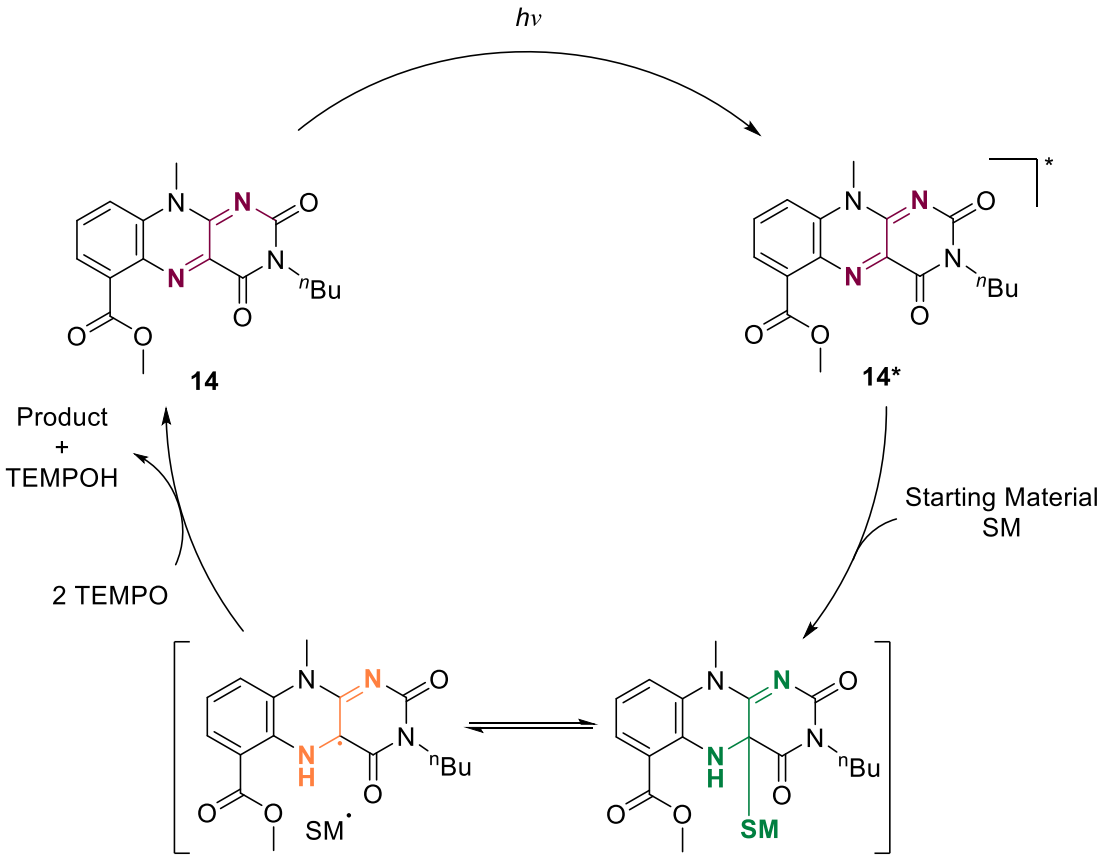


Figure SI-38: CV spectra of 1 mM **14** in 0.1 M $TBAPF_6/CH_3CN$ with a scan rate of 0.5 Vs^{-1} with successive addition of AcOH (100 mM in MeCN).

[21] A. Niemz *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 887.

7. Proposed Catalytic Cycle

A plausible reaction mechanism commences with flavin excitation and subsequent reaction with the starting material (SM). This generates a C-centred SM radical, which can undergo reversible C-C bond formation with the flavin semiquinone (at C-4a). One equivalent of TEMPO then reacts with the substrate and forms the desired product. The flavin catalyst is re-oxidised by a second equivalent of TEMPO, which is converted to TEMPOH (**scheme SI-02**).

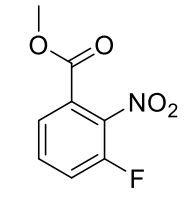


Scheme SI-02: Proposed catalytic cycle of the functionalization of dehydroamino acids.

8. NMR Data

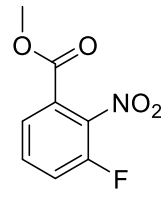
8.1. Compound SI-01

^{1}H NMR
($CDCl_3$)



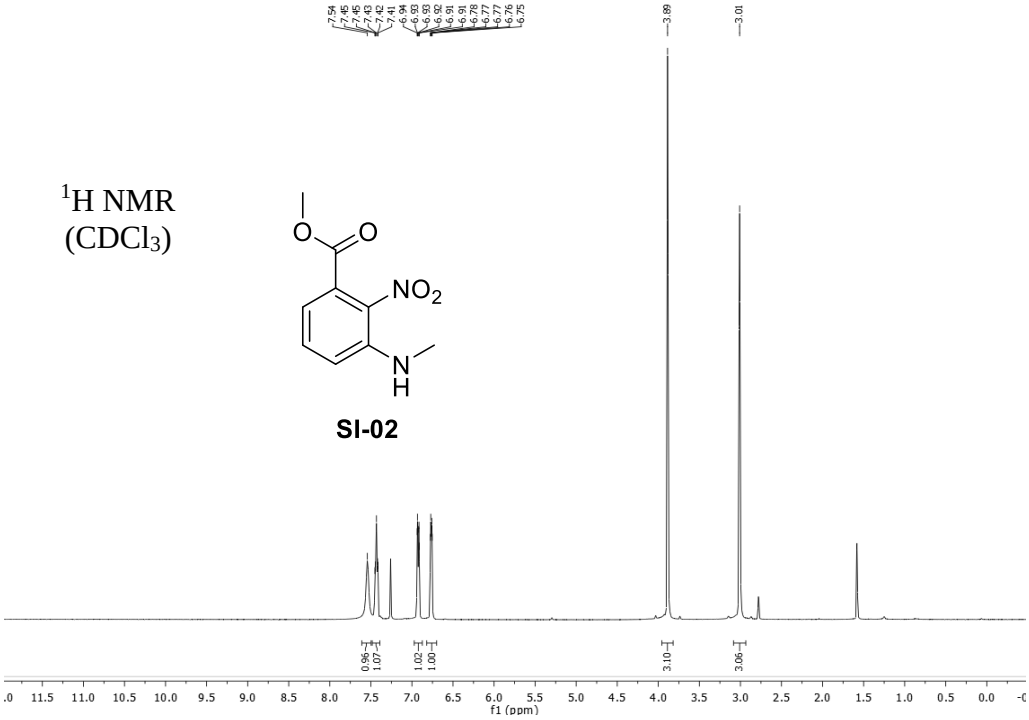
SI-01

^{13}C{^{1}H} NMR
($CDCl_3$)



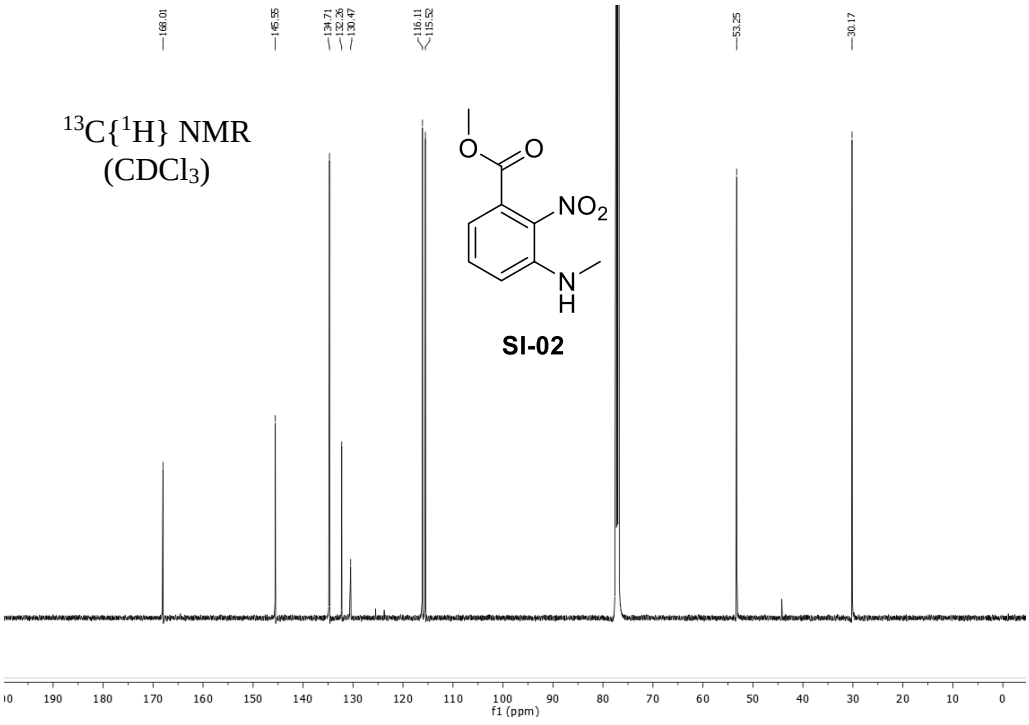
SI-01

8.2. Compound SI-02



^{1}H NMR
($CDCl_3$)

SI-02

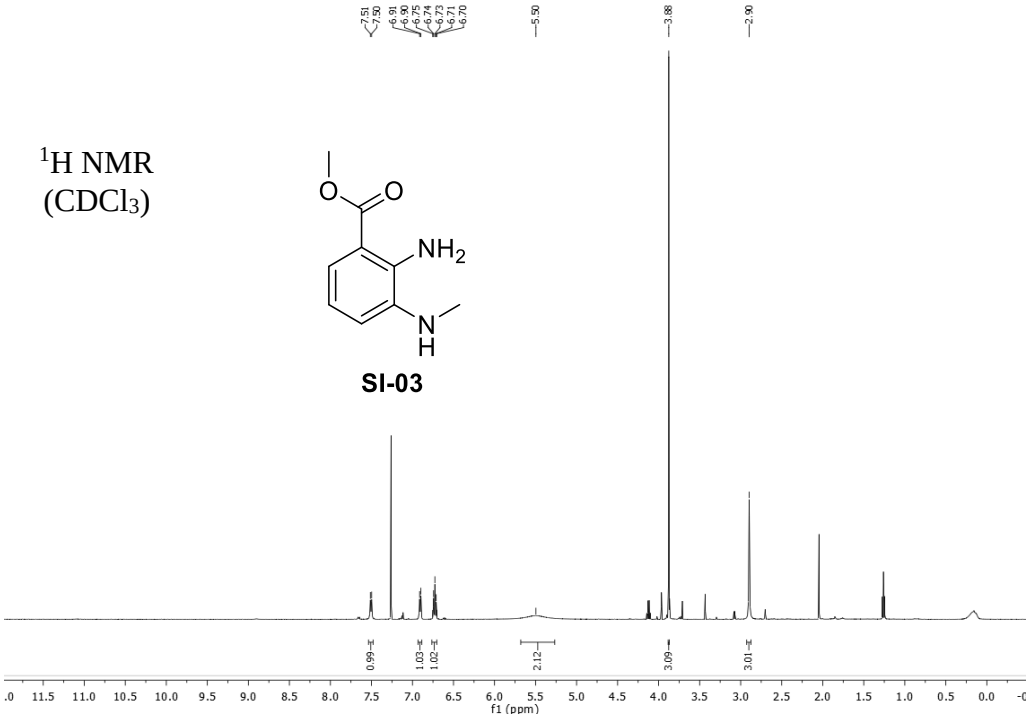


^{13}C{^{1}H} NMR
($CDCl_3$)

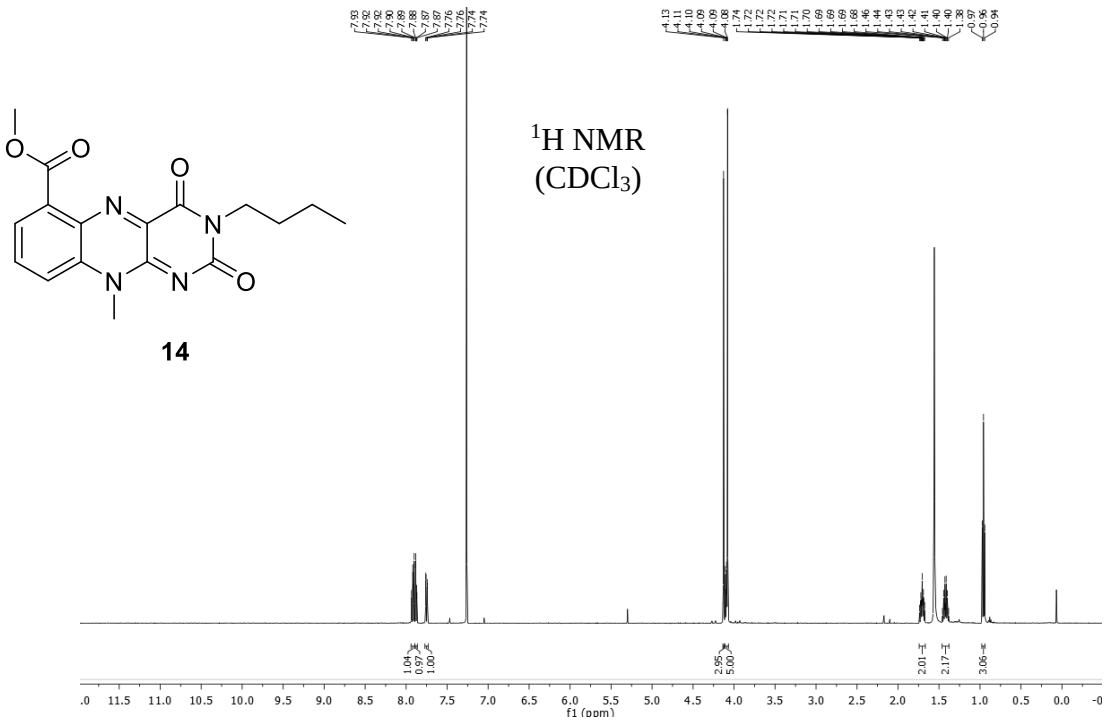
SI-02

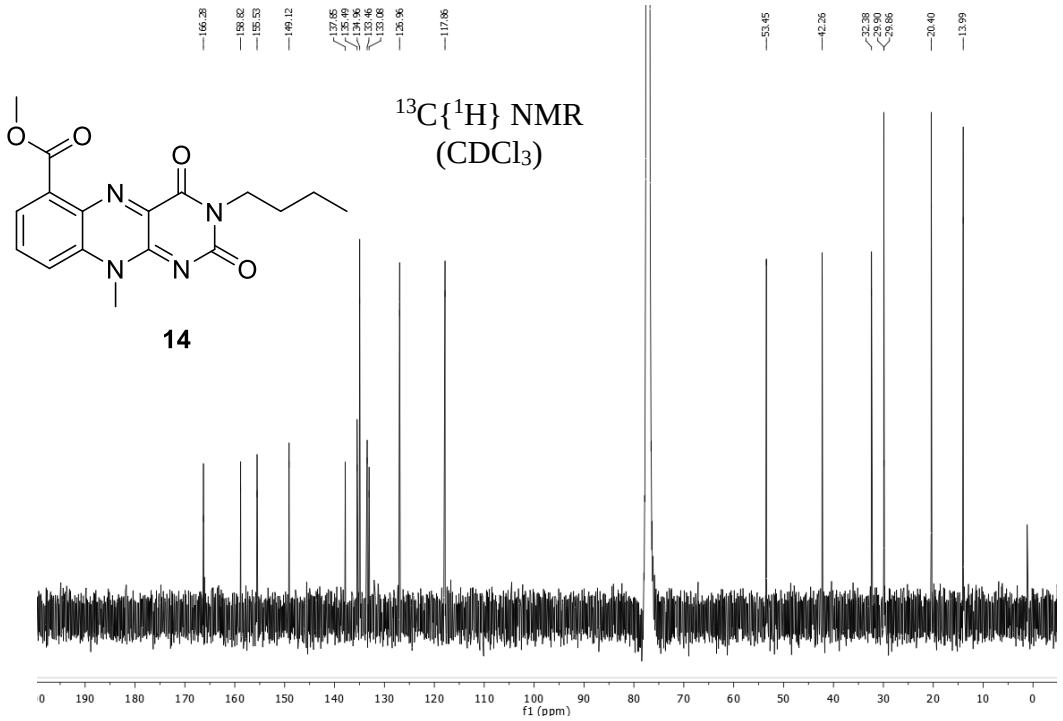
8.3. Compound SI-03

^{1}H NMR
($CDCl_3$)



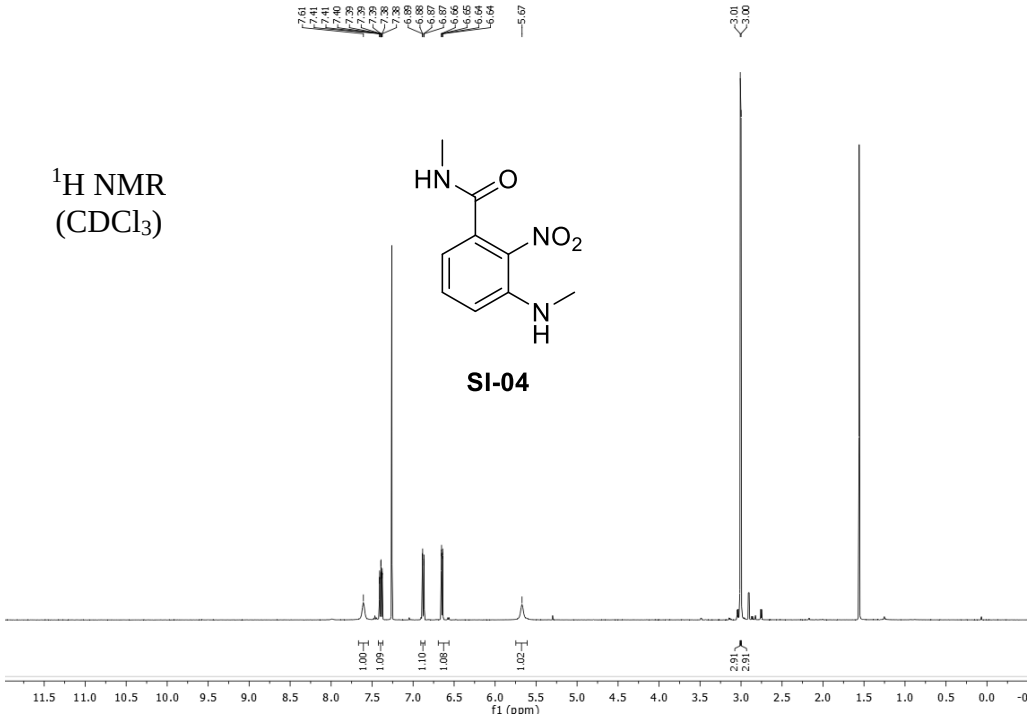
8.4. Compound 14





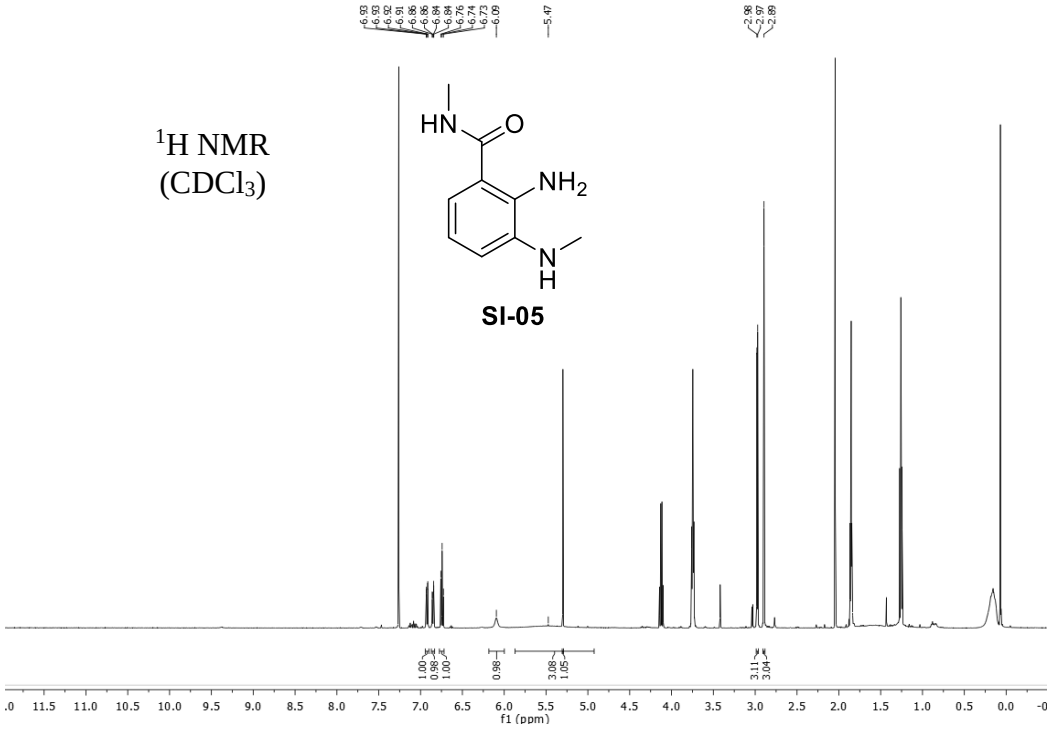
8.5. Compound SI-04

^{1}H NMR
($CDCl_3$)



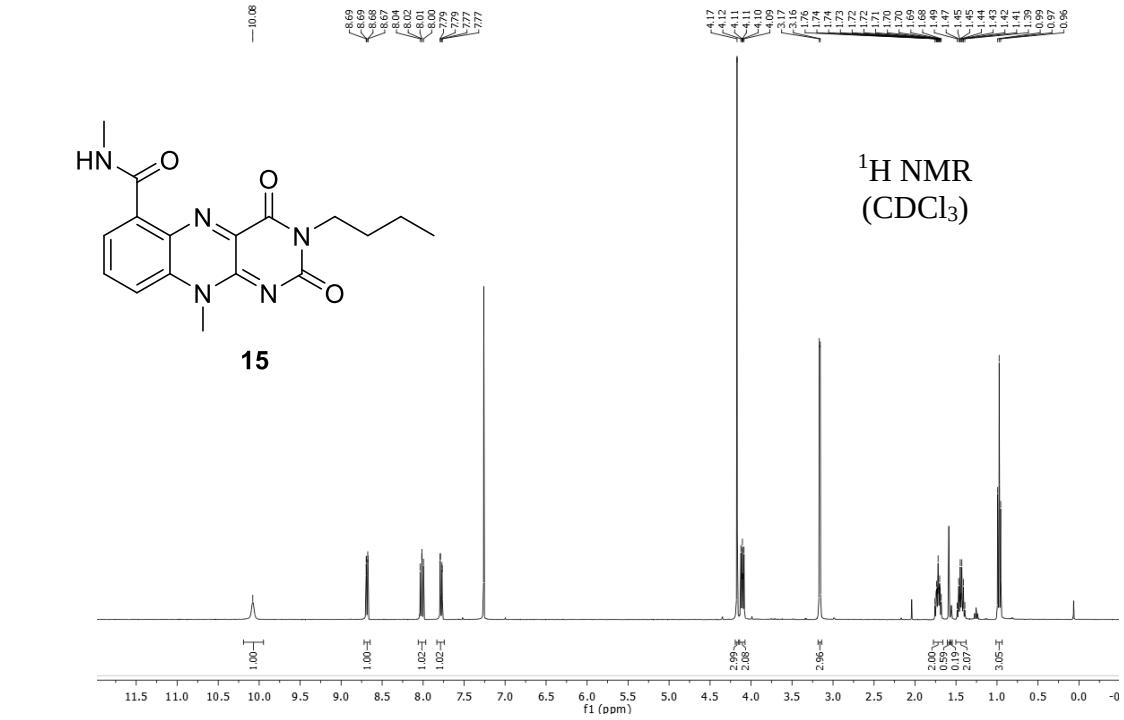
8.6. Compound SI-05

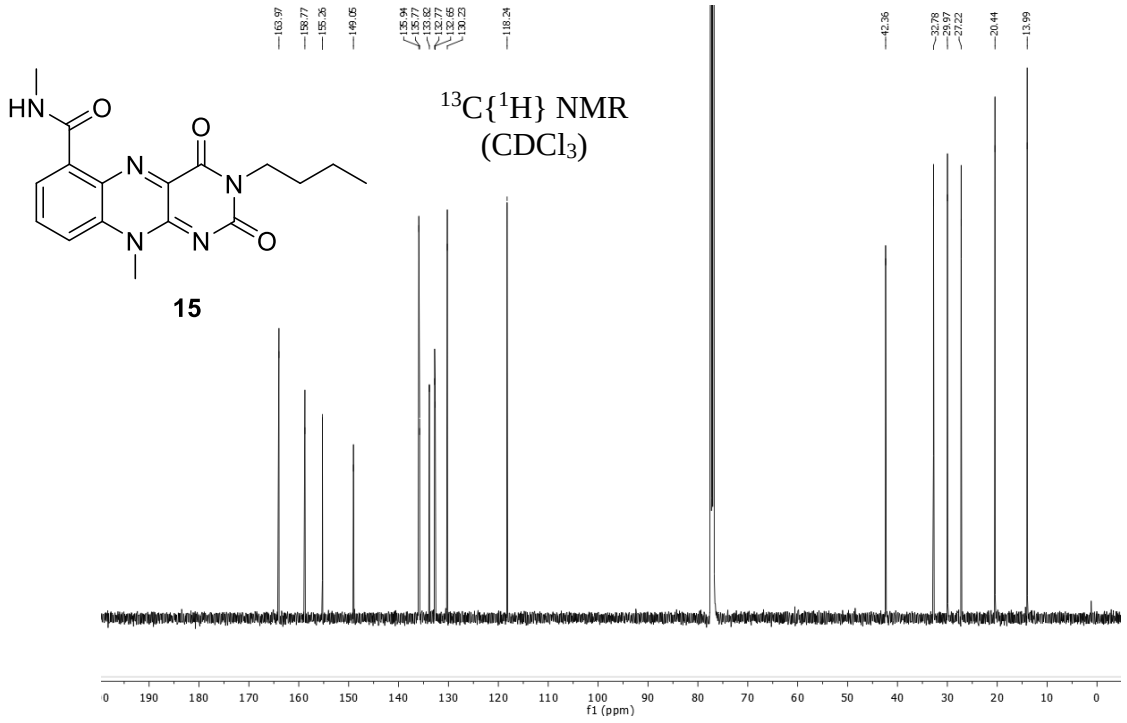
^{1}H NMR
($CDCl_3$)



This spectrum contains significant amount of EtOAc. The material was used for the next step without further purification and the residual solvent was tolerated.

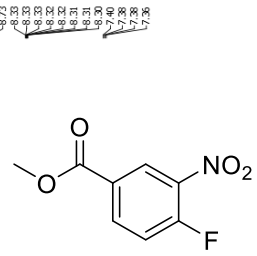
8.7. Compound 15





8.8. Compound SI-06

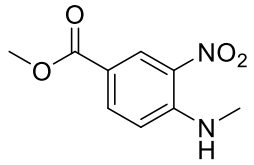
^{1}H NMR
($CDCl_3$)



SI-06

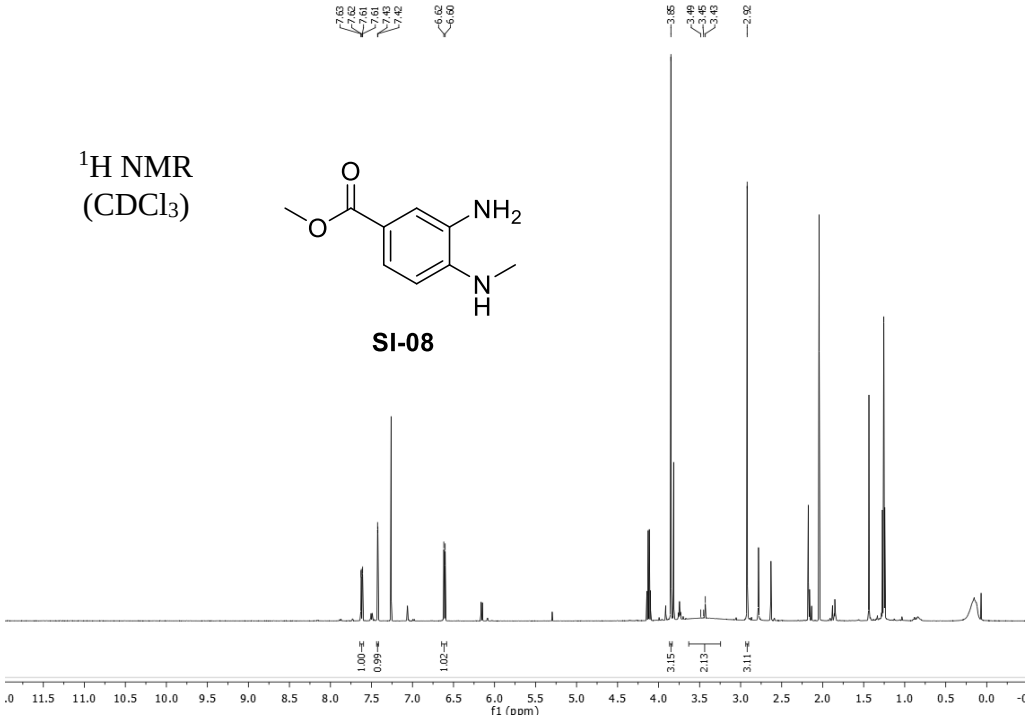
8.9. Compound SI-07

^{1}H NMR
($CDCl_3$)



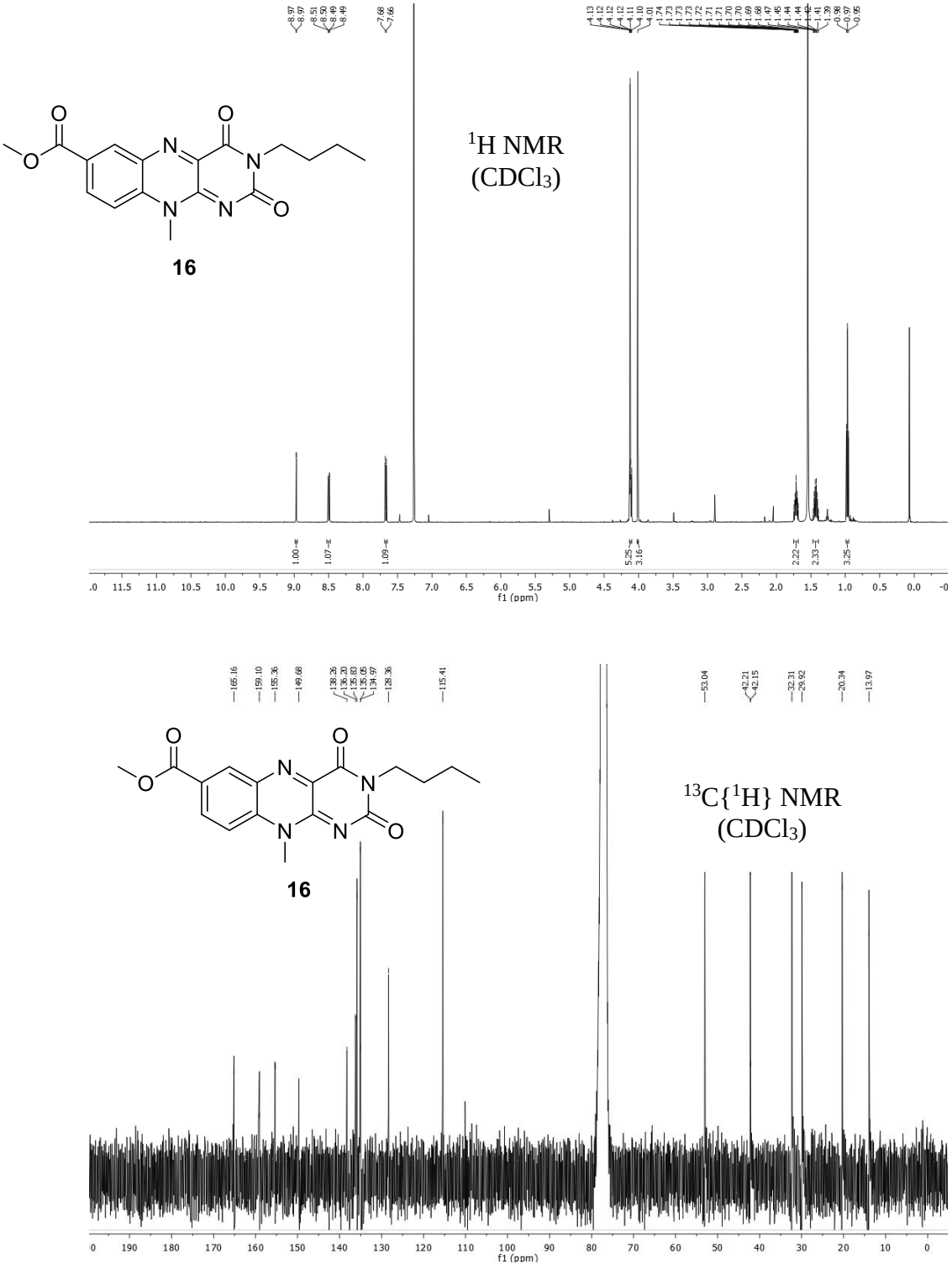
SI-07

8.10. Compound SI-08



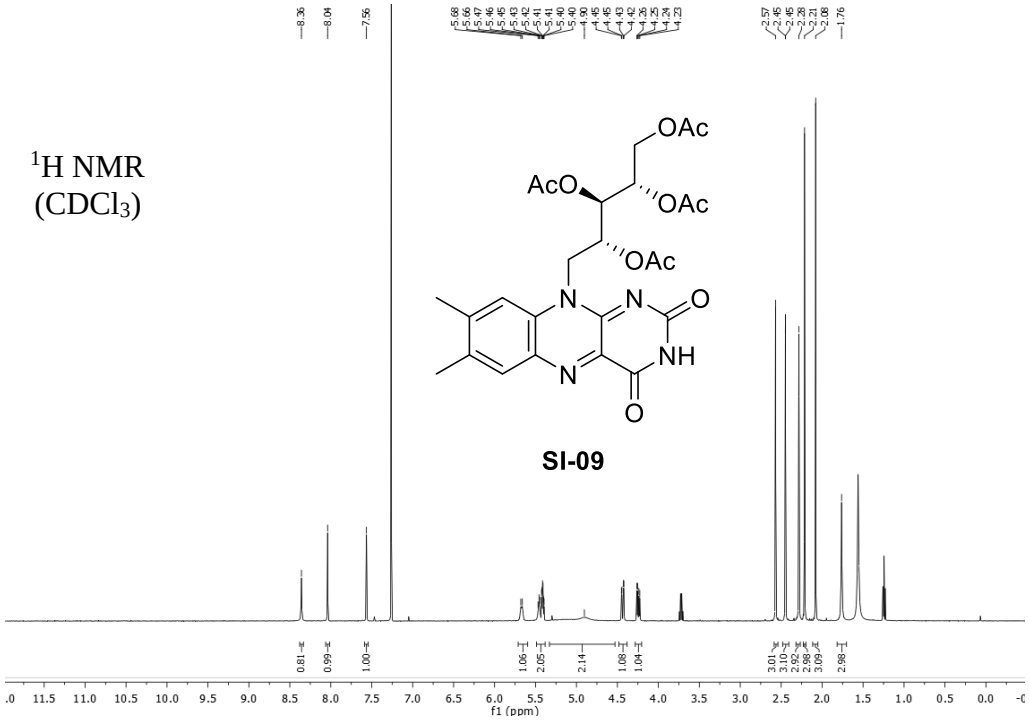
This spectrum contains significant amount of EtOAc. The material was used for the next step without further purification and the residual solvent was tolerated.

8.11. Compound 16



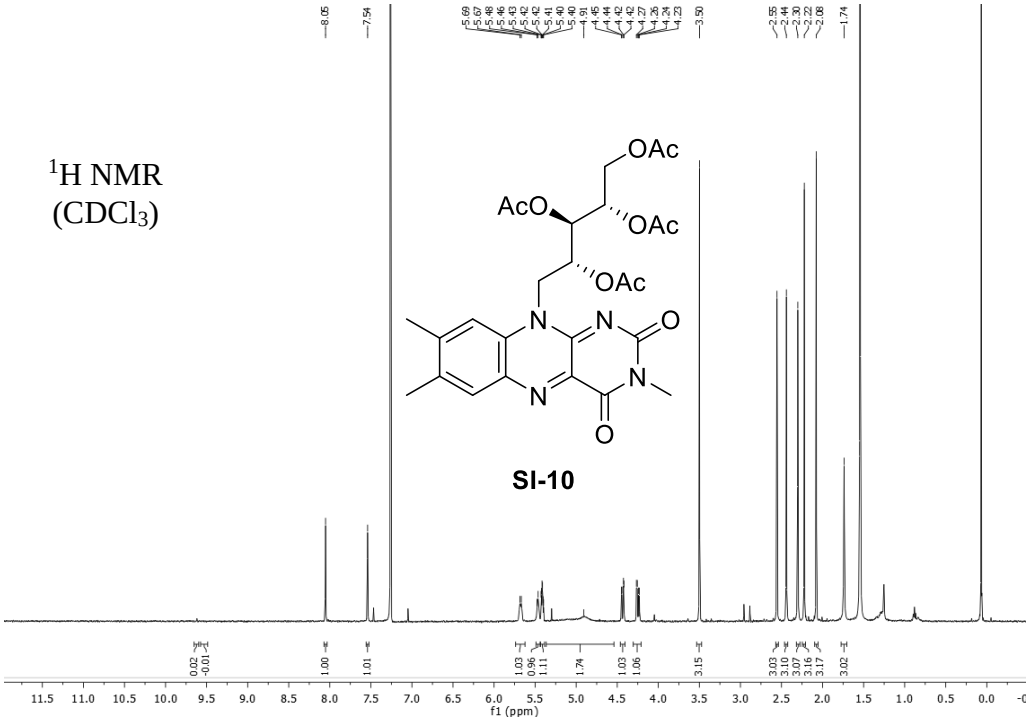
8.12. Compound SI-09

^{1}H NMR
($CDCl_3$)

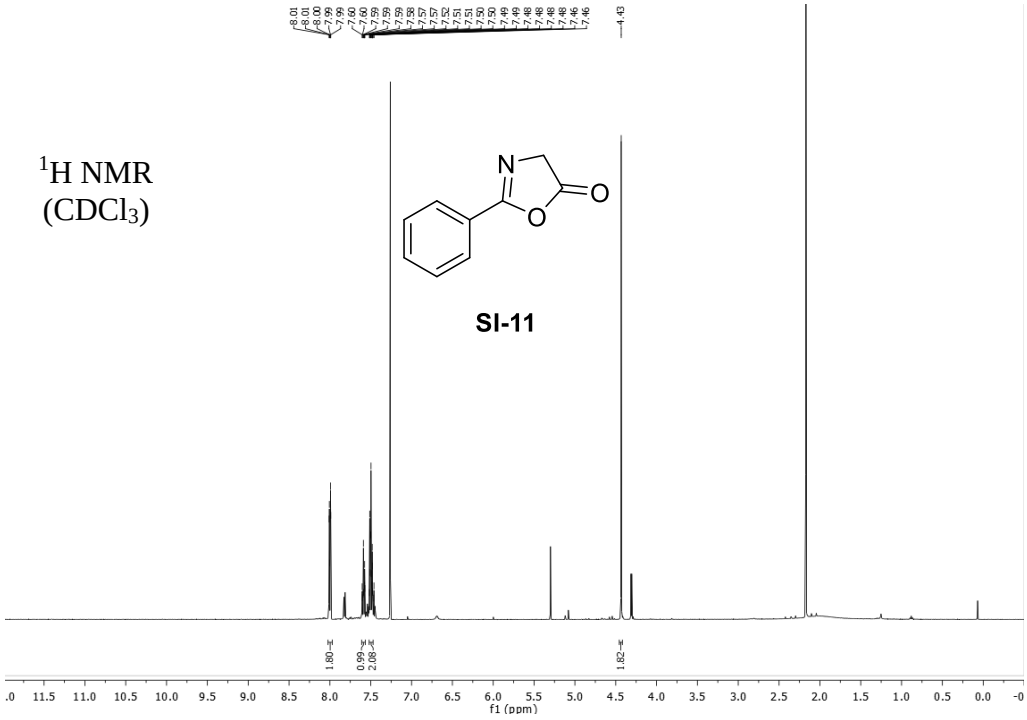


8.13. Compound SI-10

^{1}H NMR
($CDCl_3$)

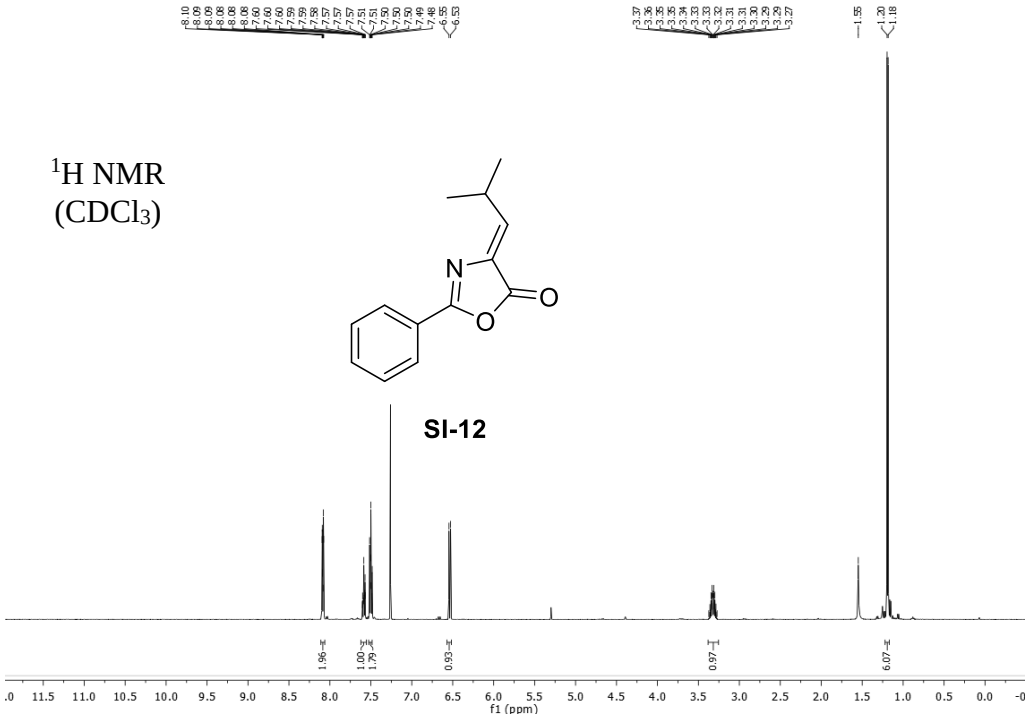


8.14. Compound SI-11

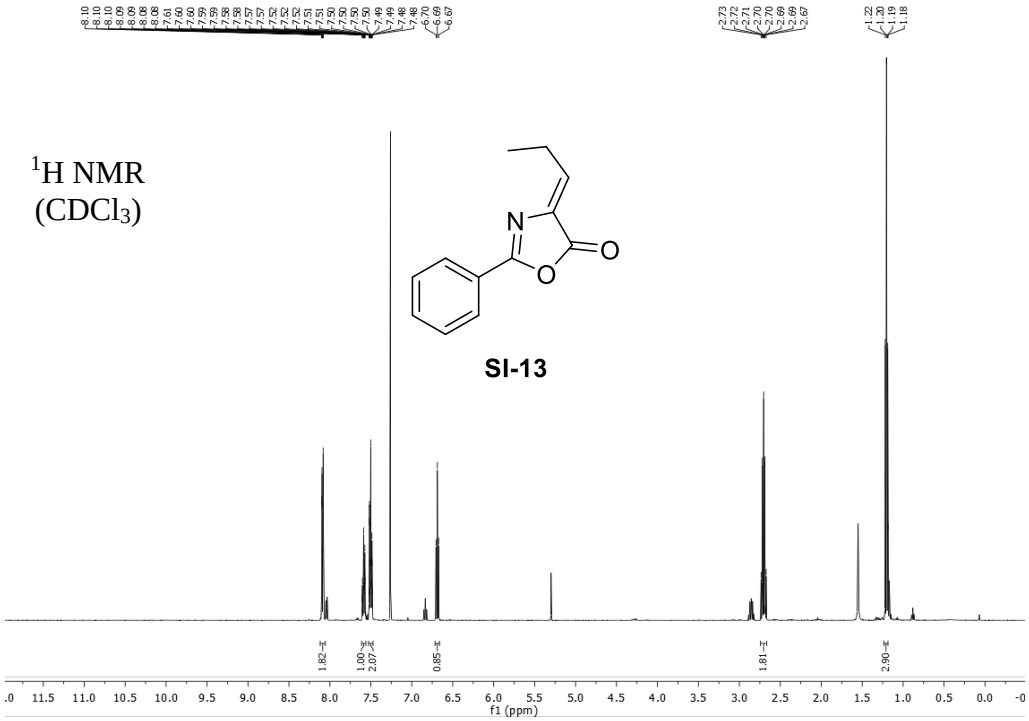


8.15. Compound SI-12

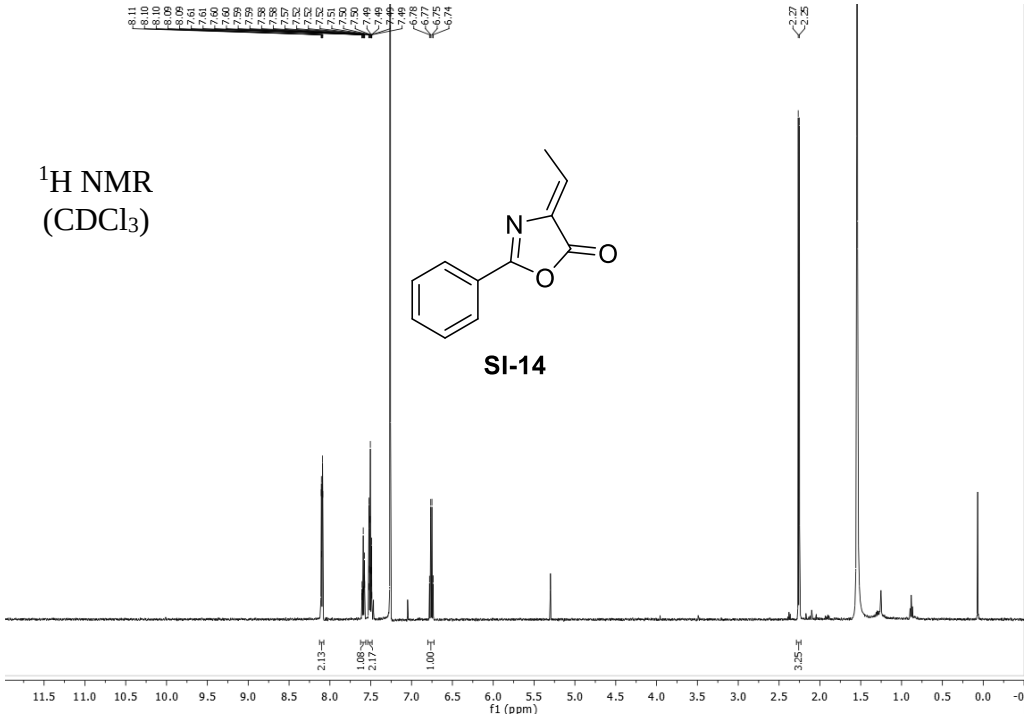
^{1}H NMR
($CDCl_3$)



8.16. Compound SI-13

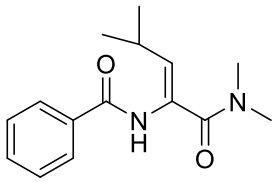


8.17. Compound SI-14



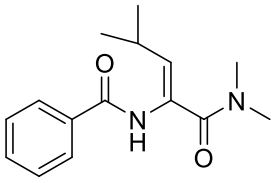
8.18. Compound SI-15

^{1}H NMR
(DMSO-d_6)



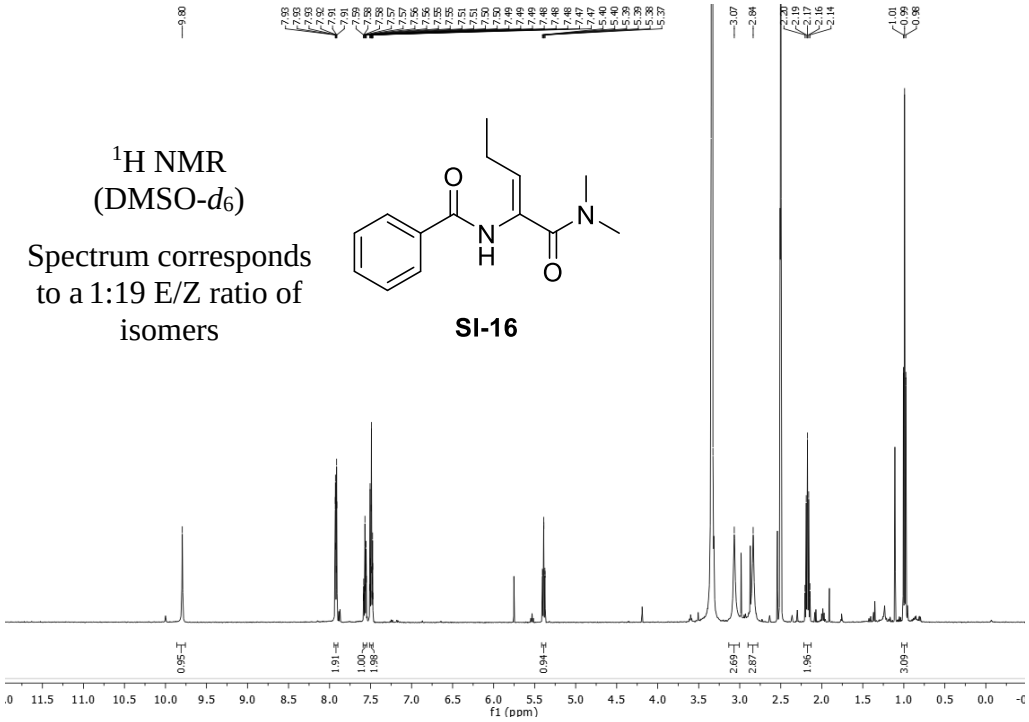
SI-15

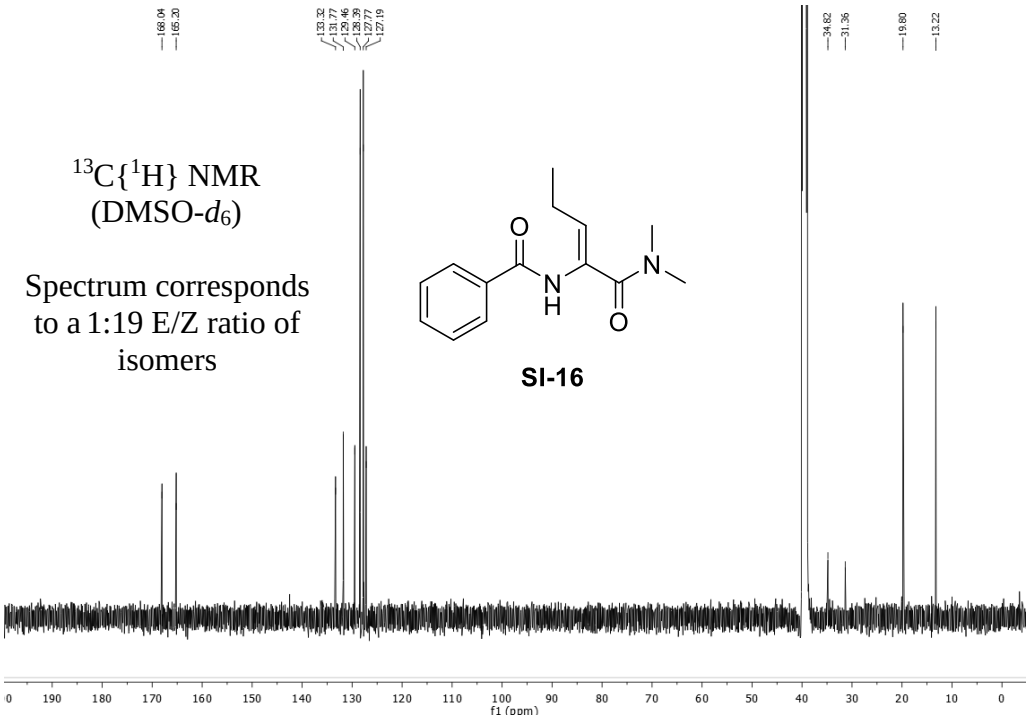
^{13}C{^{1}H} NMR
(DMSO-d_6)



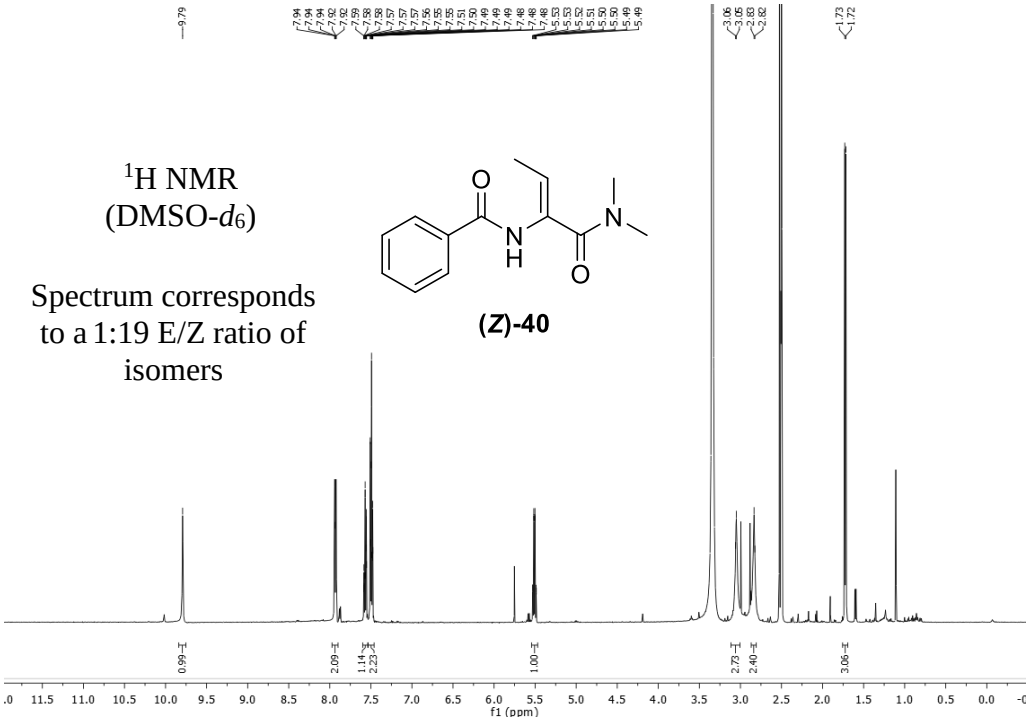
SI-15

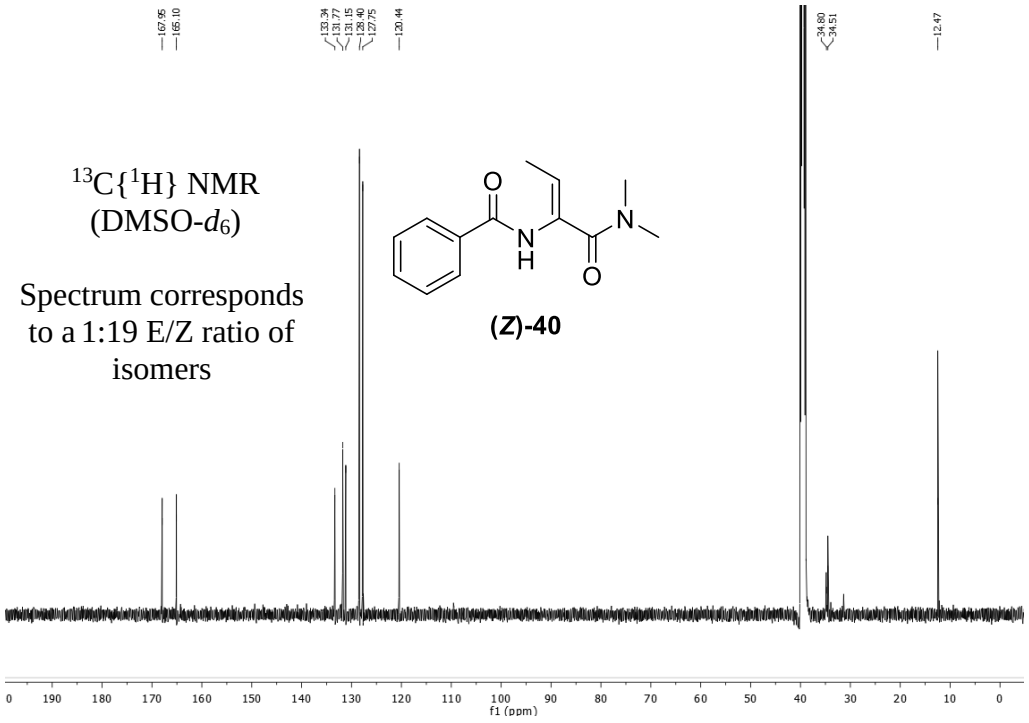
8.19. Compound SI-16





8.20. Compound (*Z*)-40

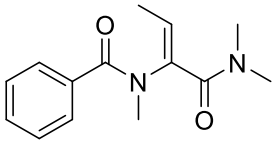




8.21. Compound (*Z*)-41

^{1}H NMR
(DMSO-d_6)

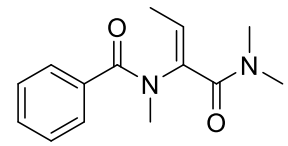
Spectrum corresponds to a 1:7 E/Z ratio of isomers



(*Z*)-41

^{13}C{^{1}H} NMR
(DMSO-d_6)

Spectrum corresponds to a 1:7 E/Z ratio of isomers

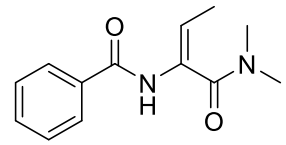


(*Z*)-41

8.22. Compound (*E*)-40

^{1}H NMR
(DMSO-d_6)

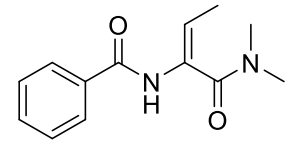
Spectrum corresponds to a 6:1 E/Z ratio of isomers



(*E*)-40

^{13}C{^{1}H} NMR
(DMSO-d_6)

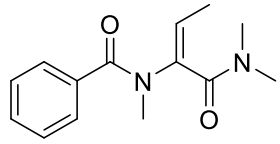
Spectrum corresponds to a 6:1 E/Z ratio of isomers



(*E*)-40

8.23. Compound (*E*)-41

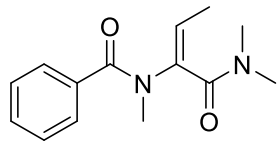
^{1}H NMR
(DMSO-d_6)



(***E***)-**41**

Spectrum corresponds to a 6:1 E/Z ratio of isomers

^{13}C{^{1}H} NMR
(DMSO-d_6)

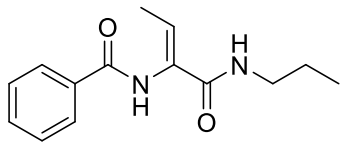


(***E***)-**41**

Spectrum corresponds to a 6:1 E/Z ratio of isomers

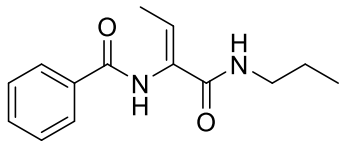
8.24. Compound SI-17

^{1}H NMR
(DMSO-d_6)



SI-17

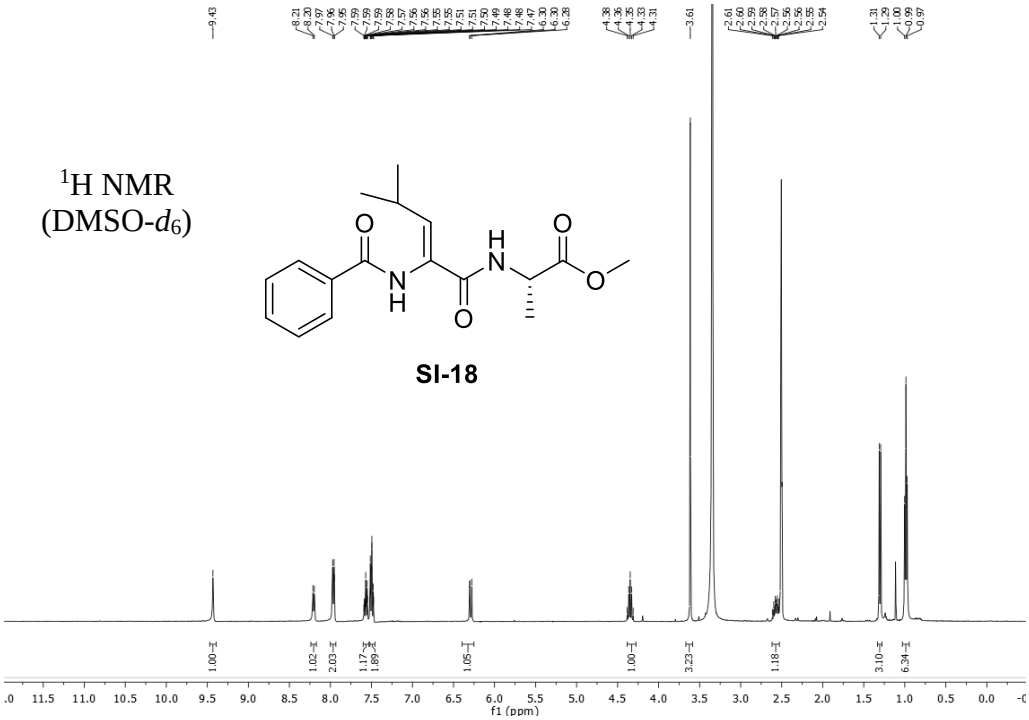
^{13}C{^{1}H} NMR
(DMSO-d_6)



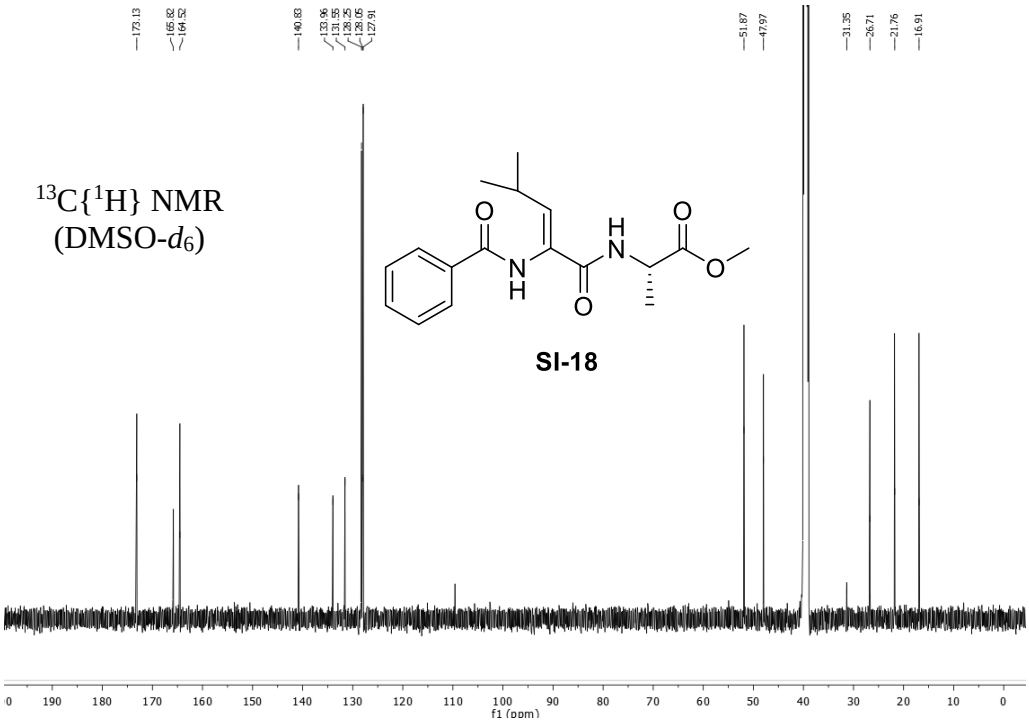
SI-17

8.25. Compound SI-18

^{1}H NMR
(DMSO-d_6)

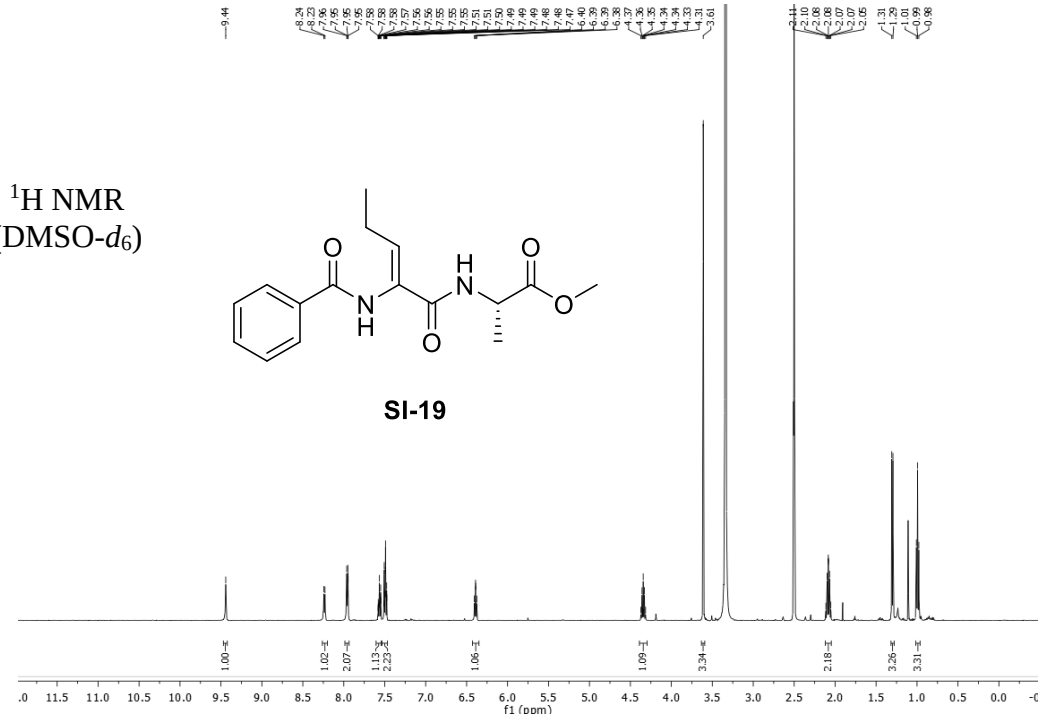


^{13}C{^{1}H} NMR
(DMSO-d_6)

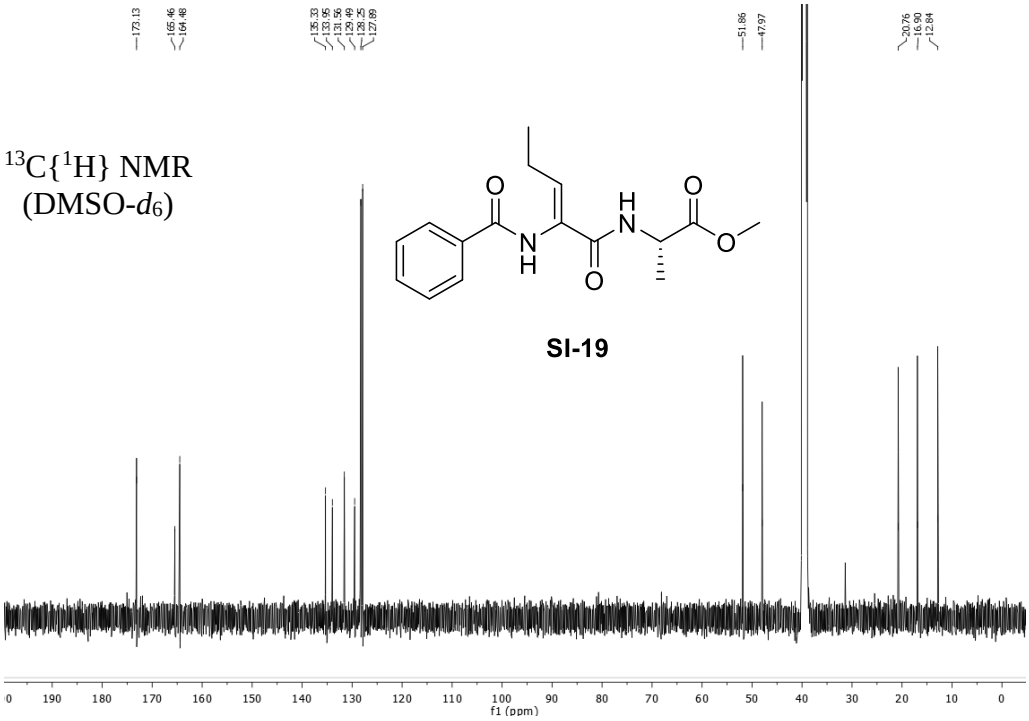


8.26. Compound SI-19

^{1}H NMR
(DMSO-d_6)

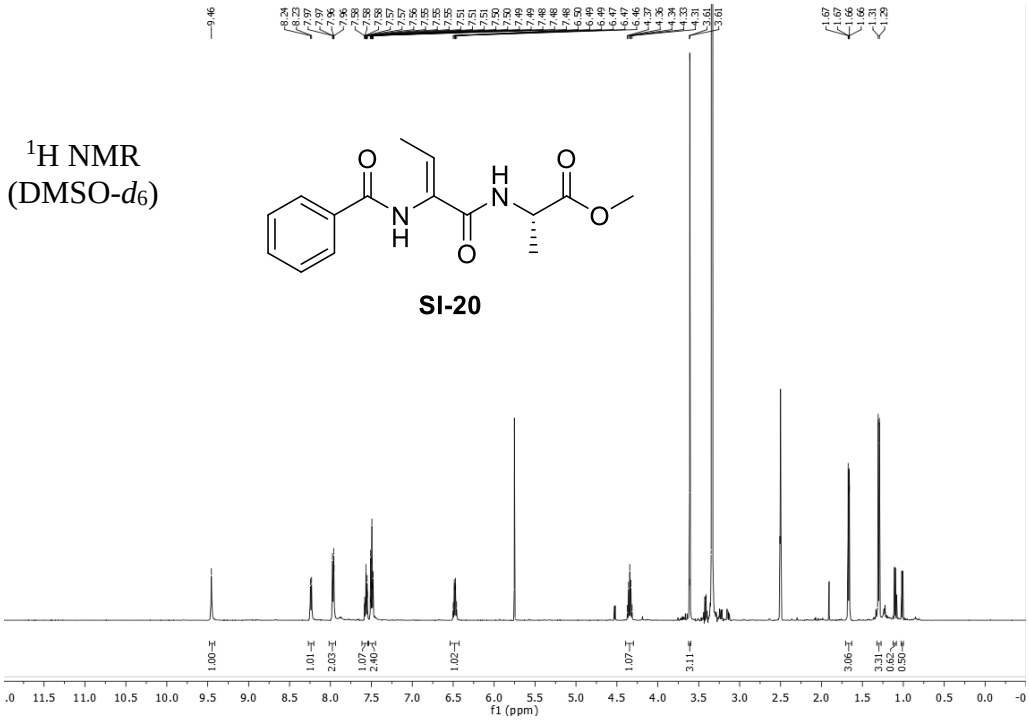


^{13}C{^{1}H} NMR
(DMSO-d_6)

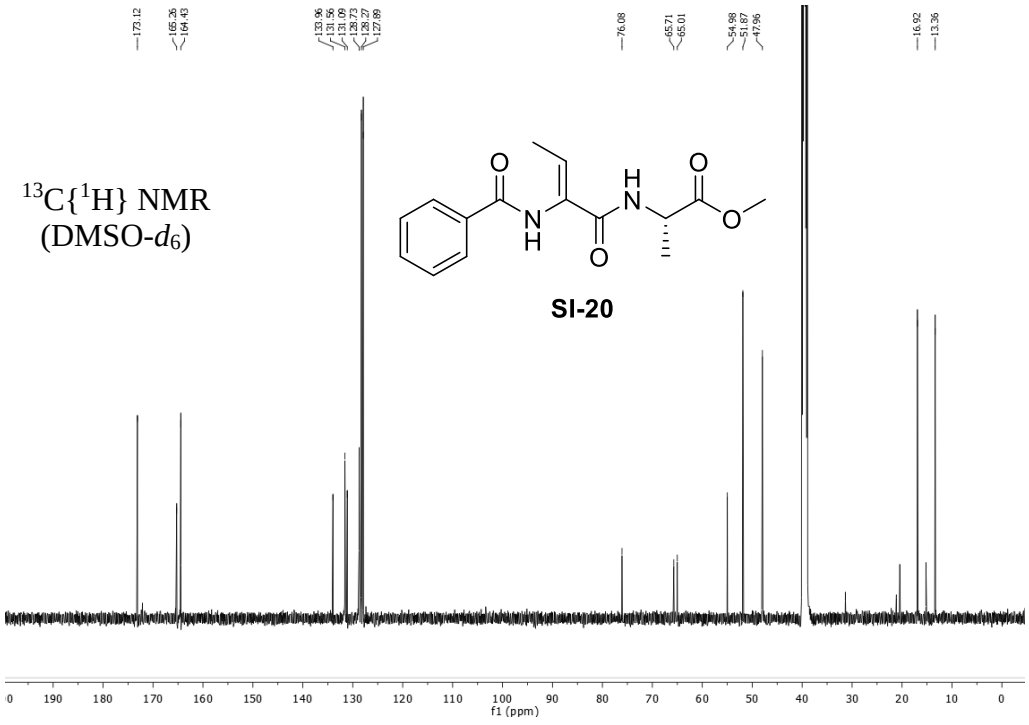


8.27. Compound SI-20

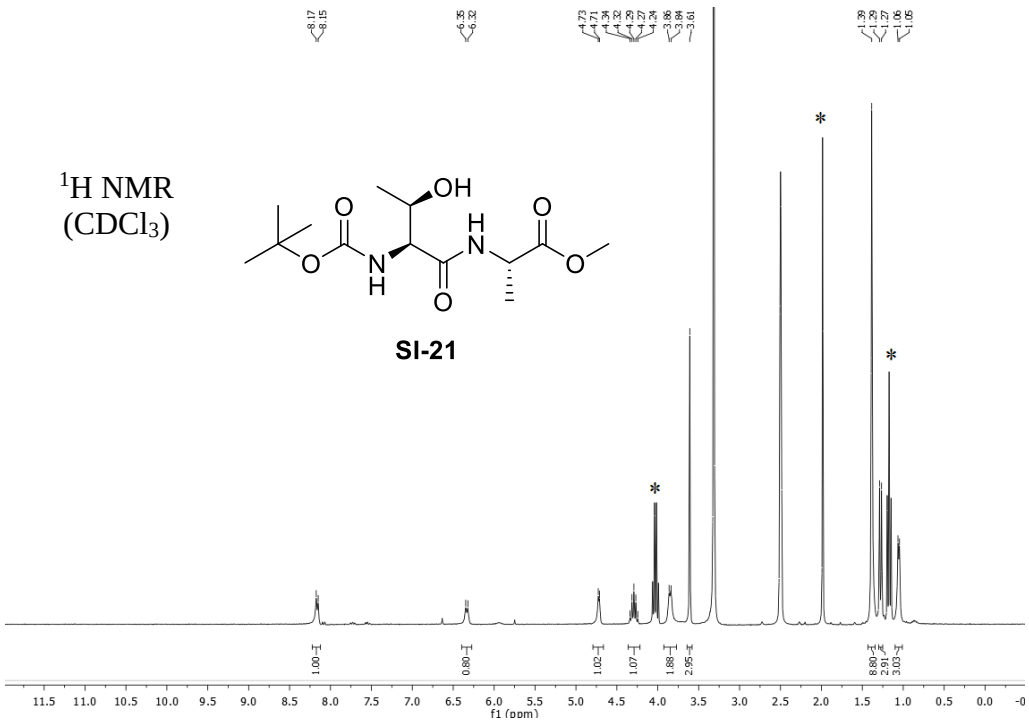
^{1}H NMR
(DMSO-d_6)



^{13}C{^{1}H} NMR
(DMSO-d_6)



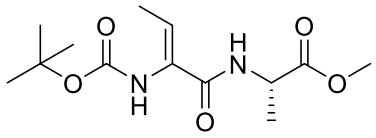
8.28. Compound SI-21



This spectrum contains significant amount of EtOAc. The material was used for the next step without further purification and the residual solvent was tolerated.

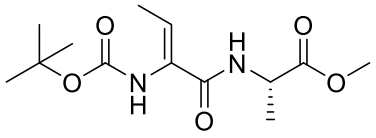
8.29. Compound SI-22

^{1}H NMR
(DMSO-d_6)



SI-22

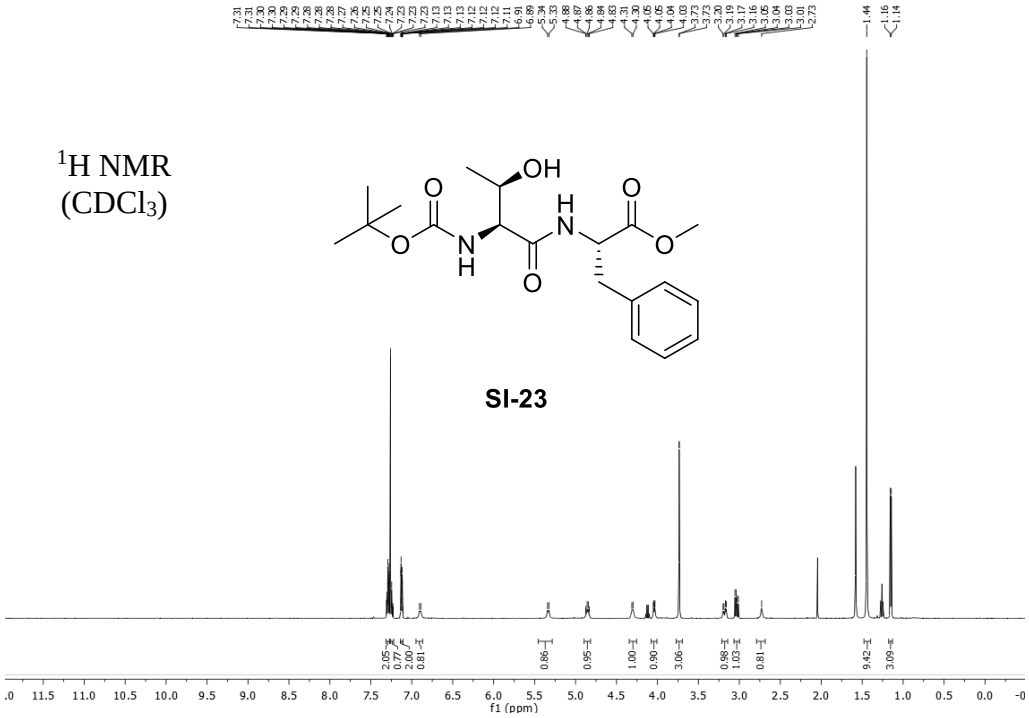
^{13}C{^{1}H} NMR
(DMSO-d_6)



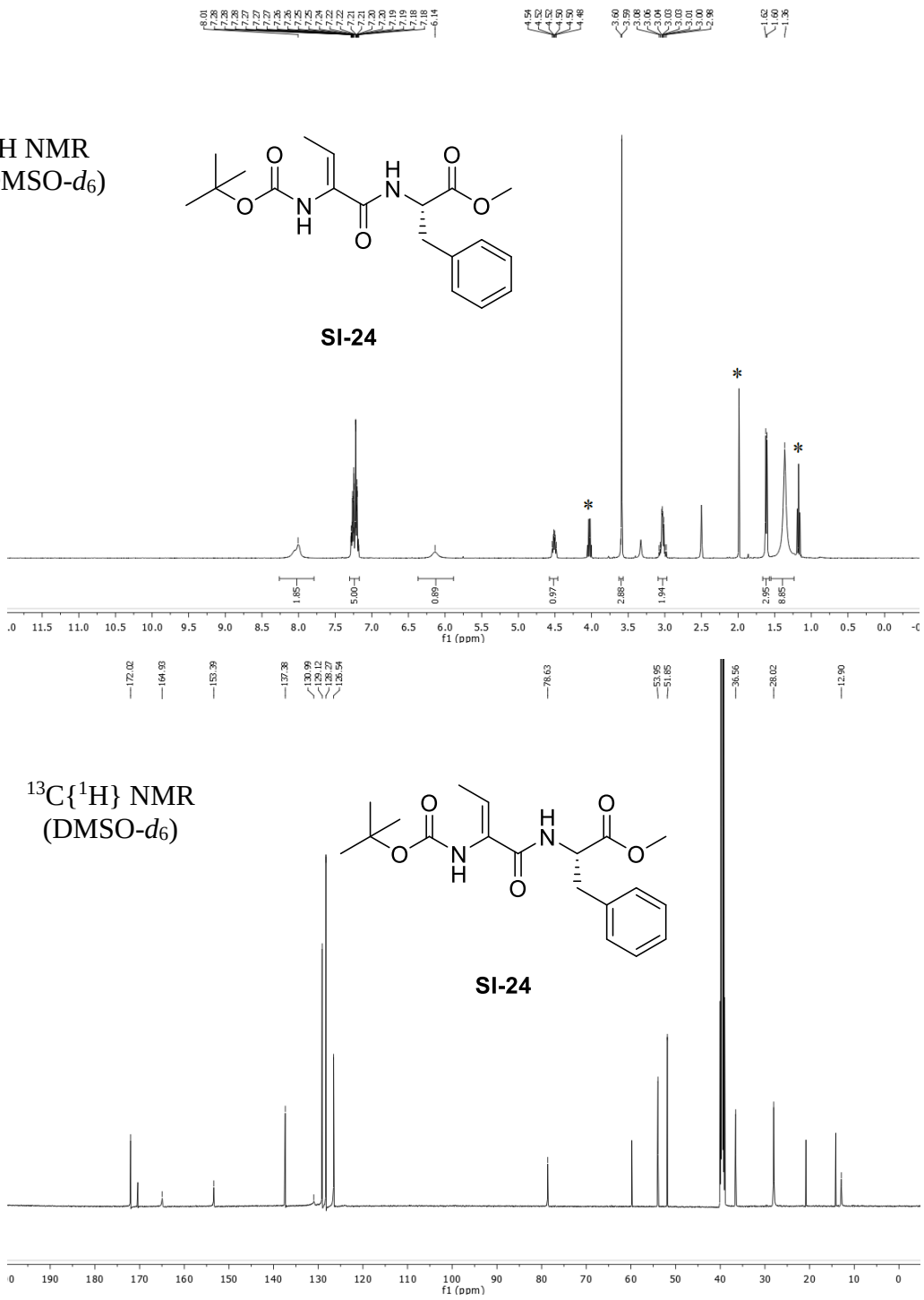
SI-22

8.30. Compound SI-23

^{1}H NMR
($CDCl_3$)



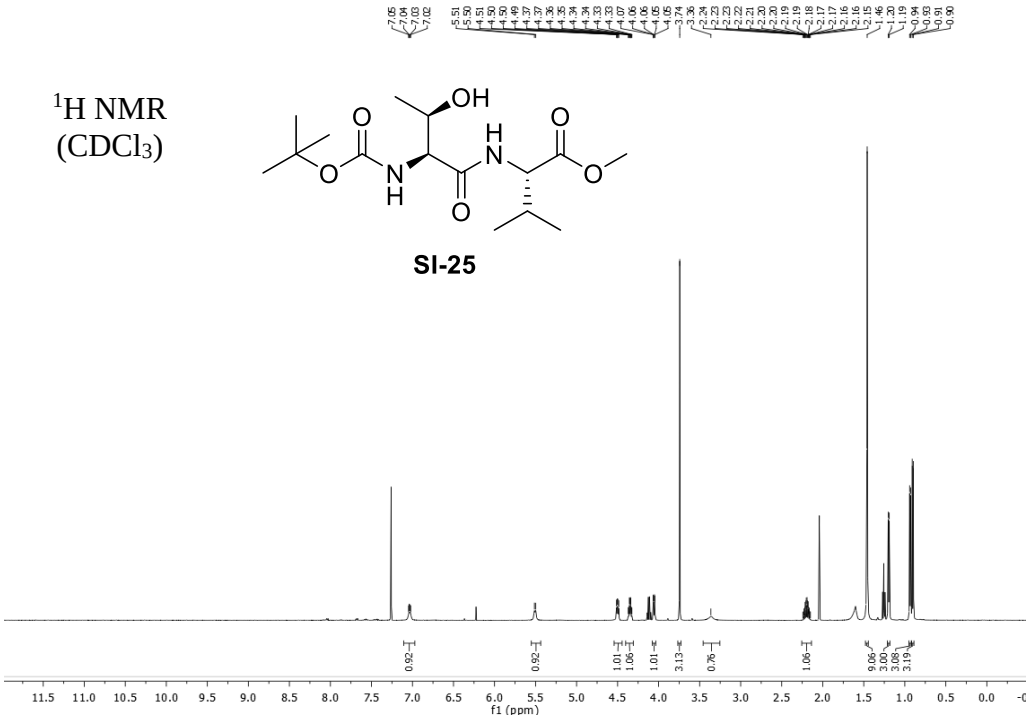
8.31. Compound SI-24



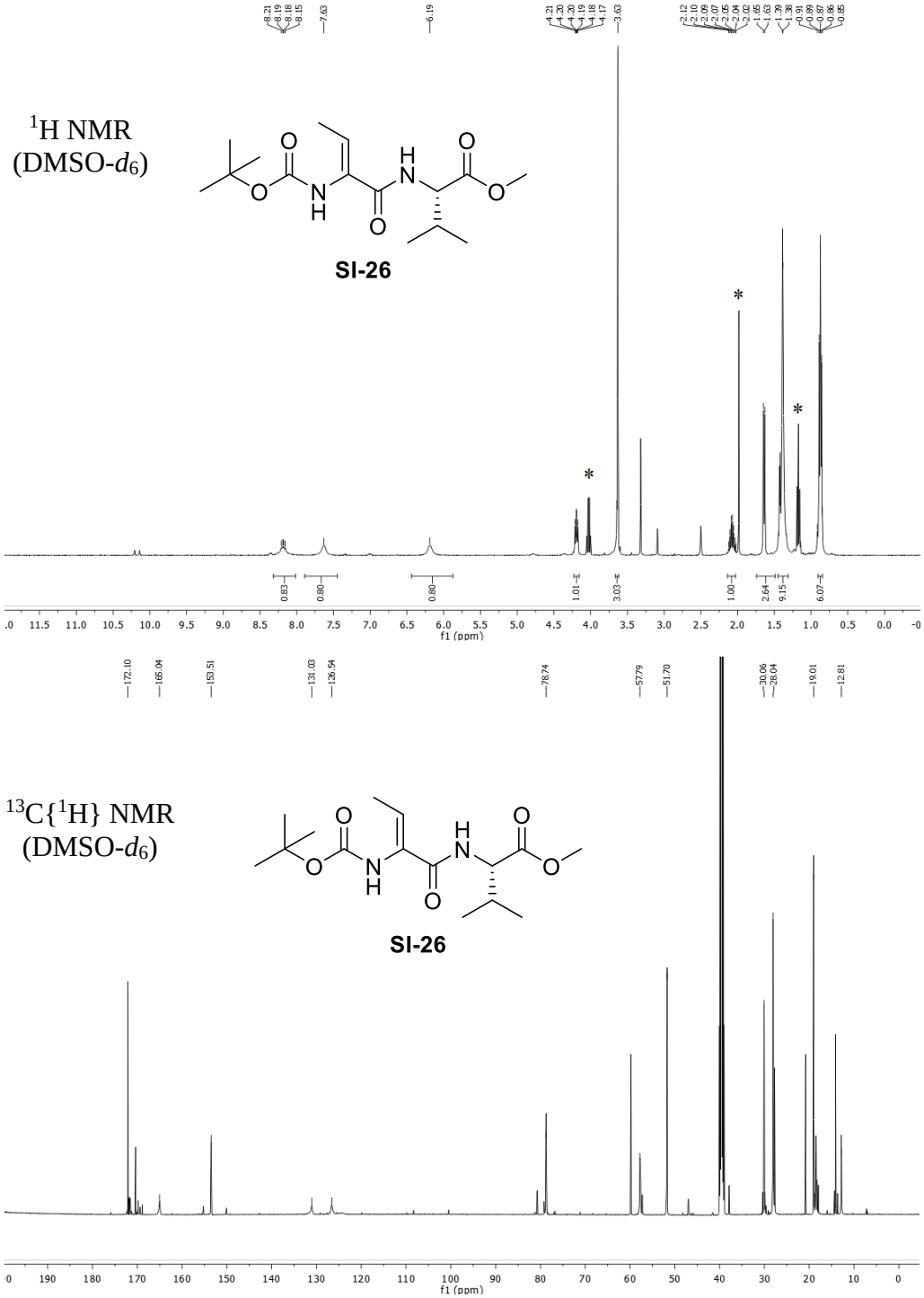
The spectra contain small amounts of residual EtOAc that evaded removal by drying. The reported isolated yielded was corrected accordingly.

8.32. Compound SI-25

^{1}H NMR
($CDCl_3$)

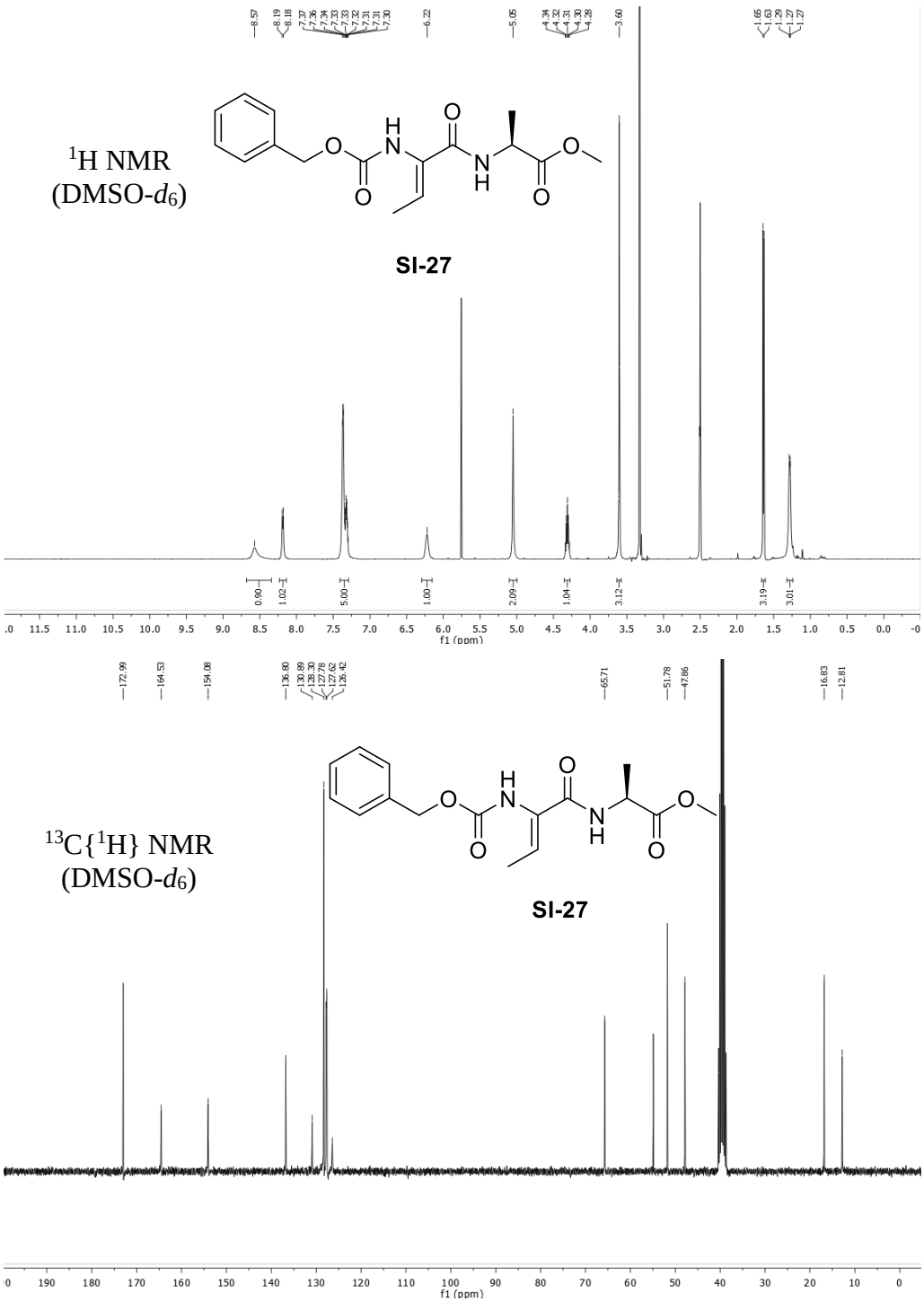


8.33. Compound SI-26



The spectra contain small amounts of residual EtOAc that evaded removal by drying. The reported isolated yielded was corrected accordingly.

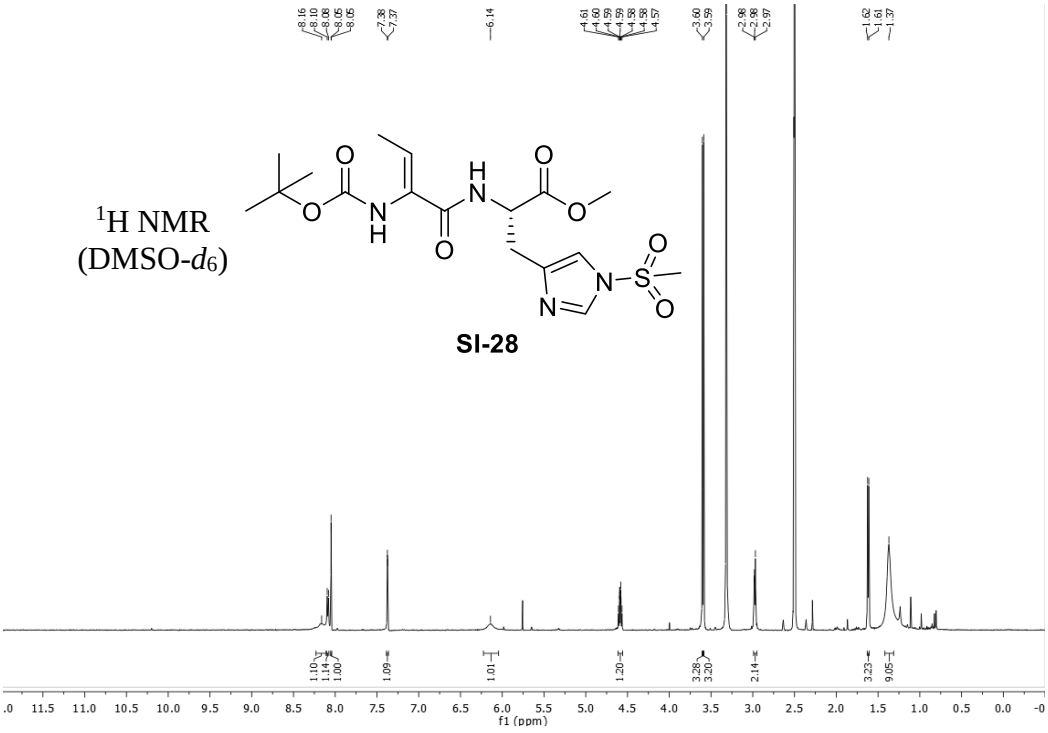
8.34. Compound SI-27



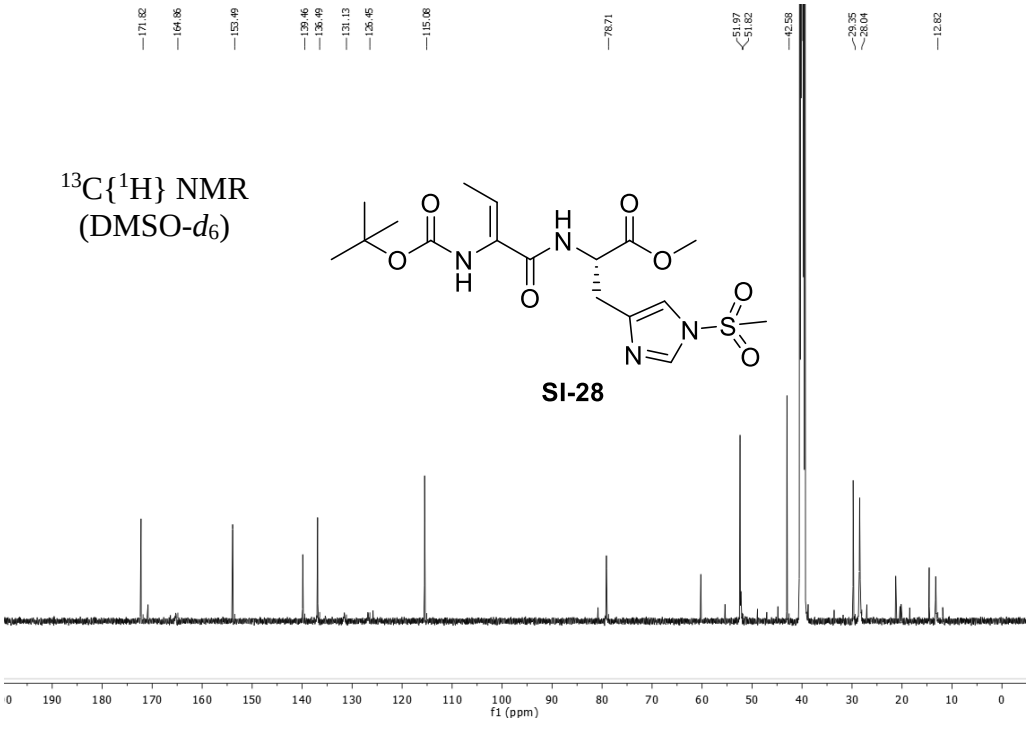
The spectra contain small amounts of residual DCM that evaded removal by drying. The reported isolated yielded was corrected accordingly.

8.35. Compound SI-28

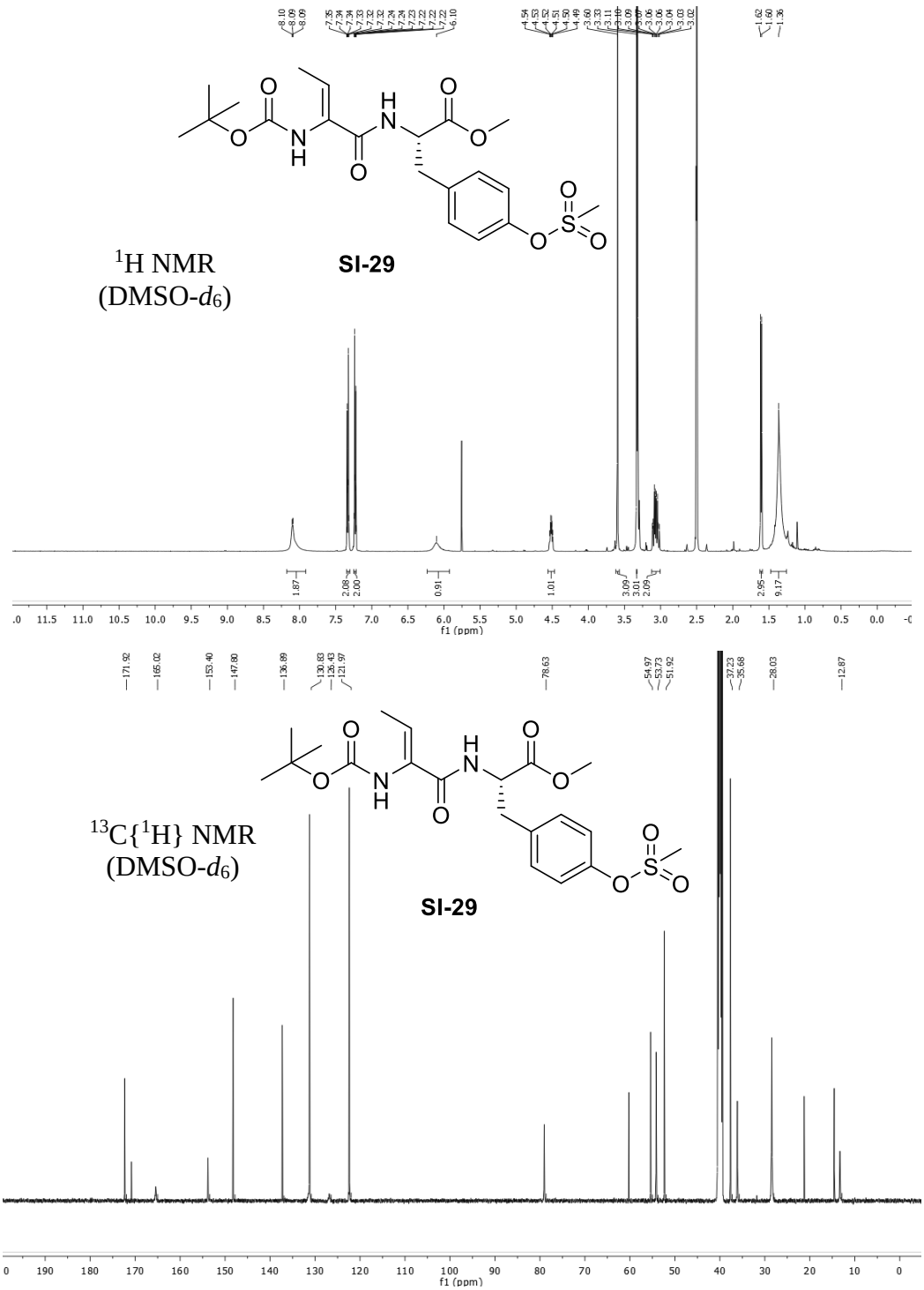
^{1}H NMR
(DMSO-d_6)



^{13}C{^{1}H} NMR
(DMSO-d_6)



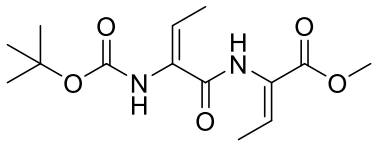
8.36. Compound SI-29



The spectra contain small amounts of residual DCM that evaded removal by drying. The reported isolated yielded was corrected accordingly.

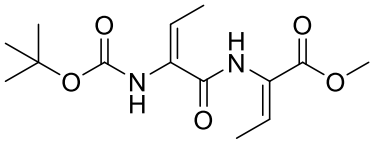
8.37. Compound SI-30

^{1}H NMR
(DMSO-d_6)



SI-30

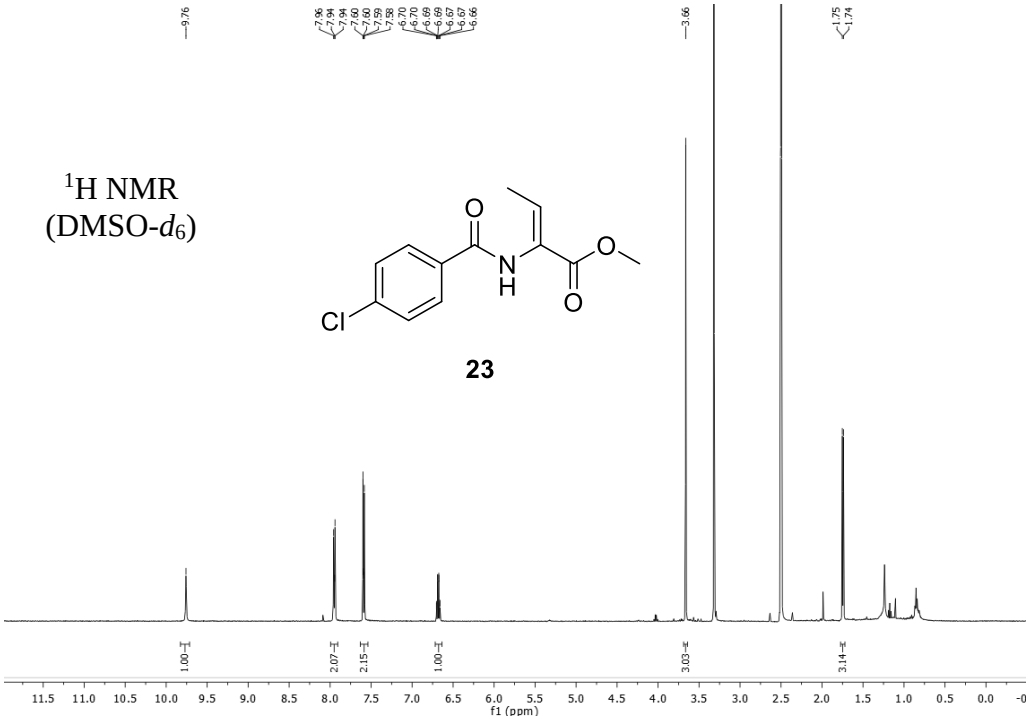
^{13}C{^{1}H} NMR
(DMSO-d_6)



SI-30

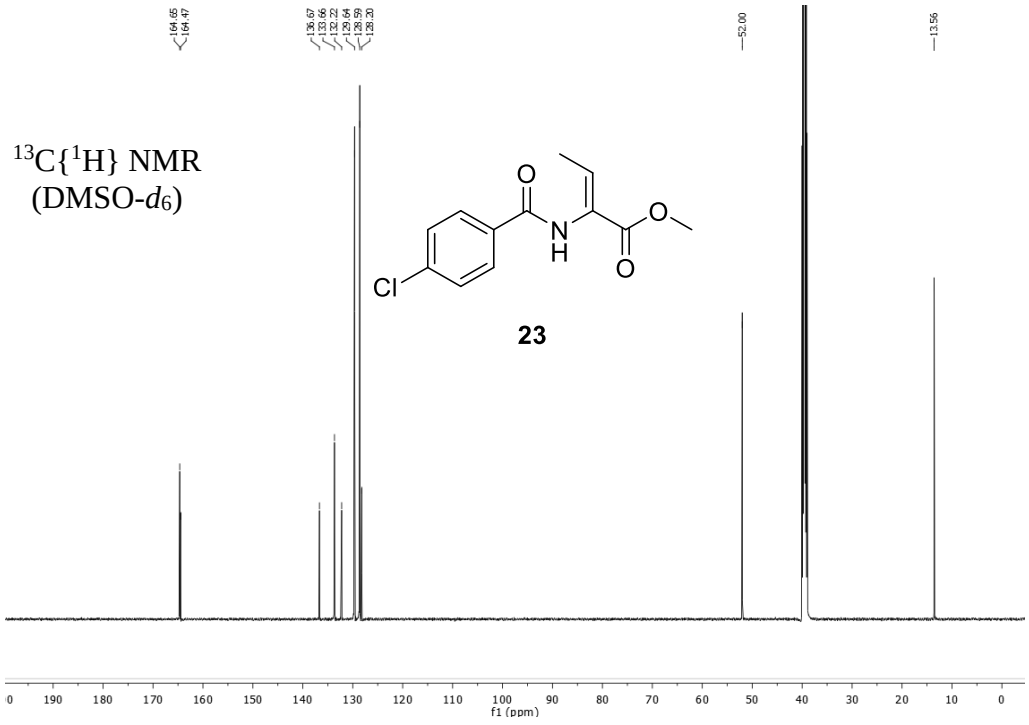
8.38. Compound 23

^{1}H NMR
(DMSO-d_6)



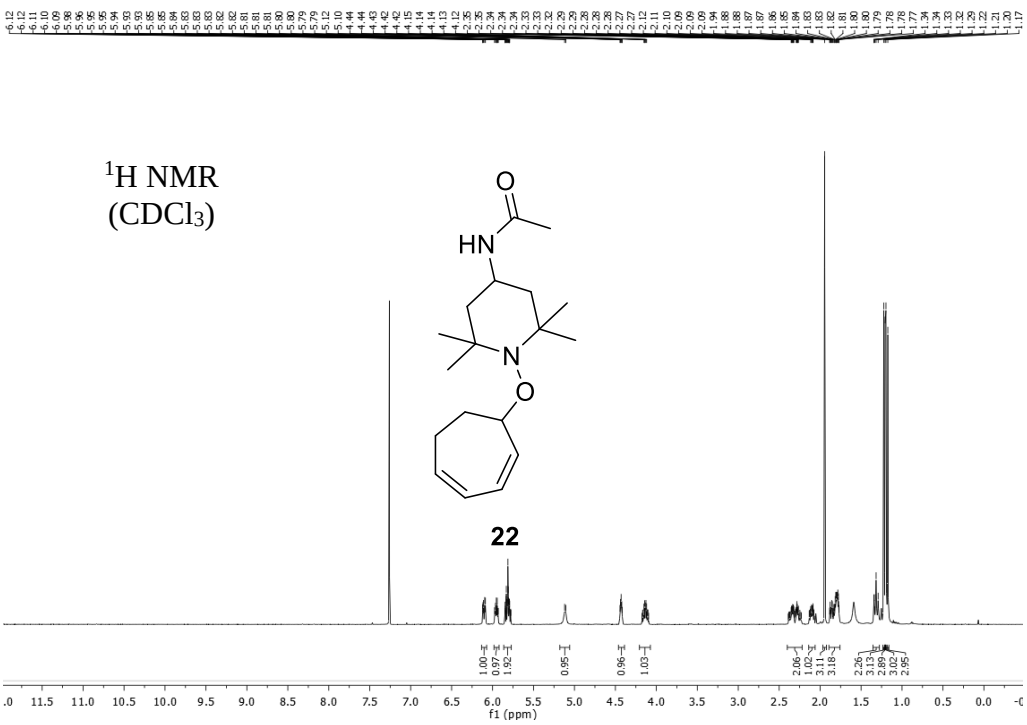
23

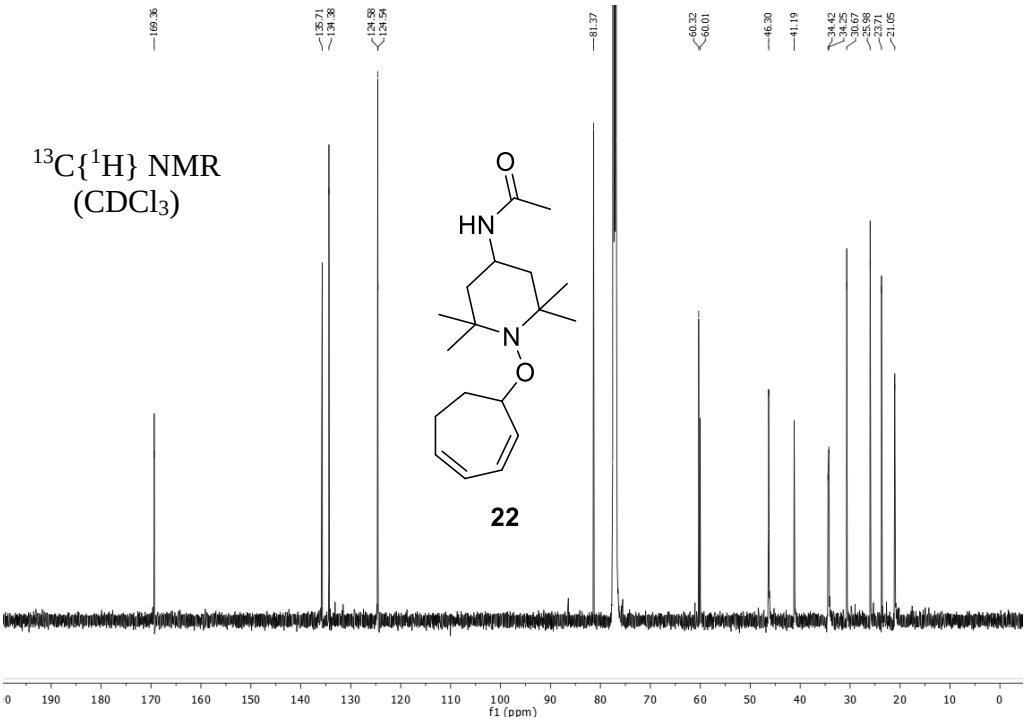
^{13}C{^{1}H} NMR
(DMSO-d_6)



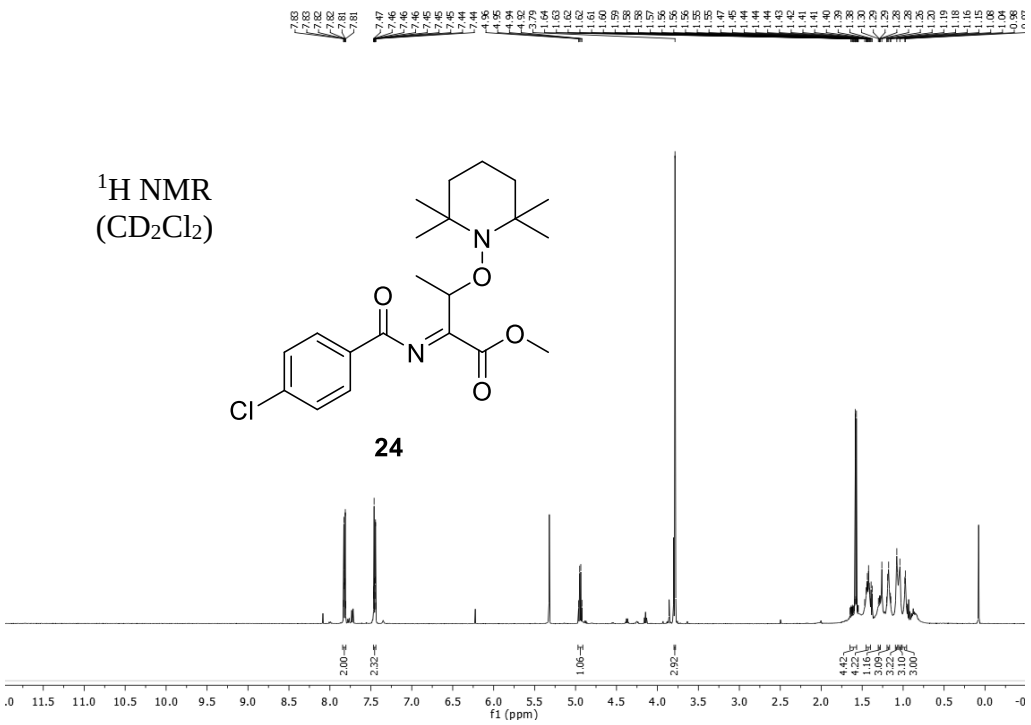
23

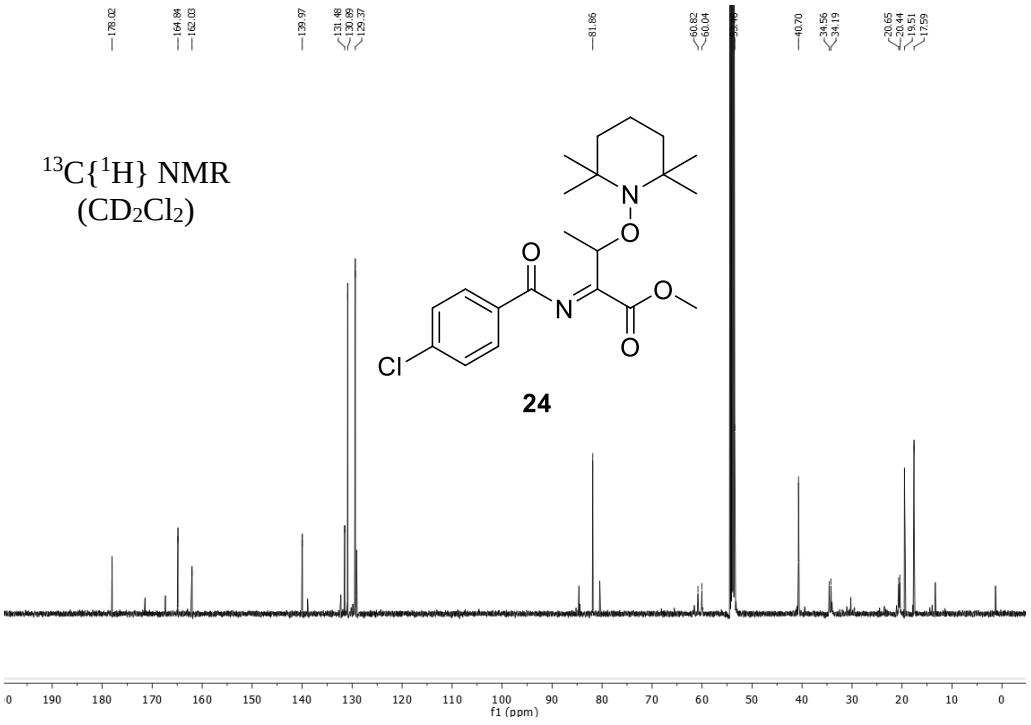
8.39. Compound 22





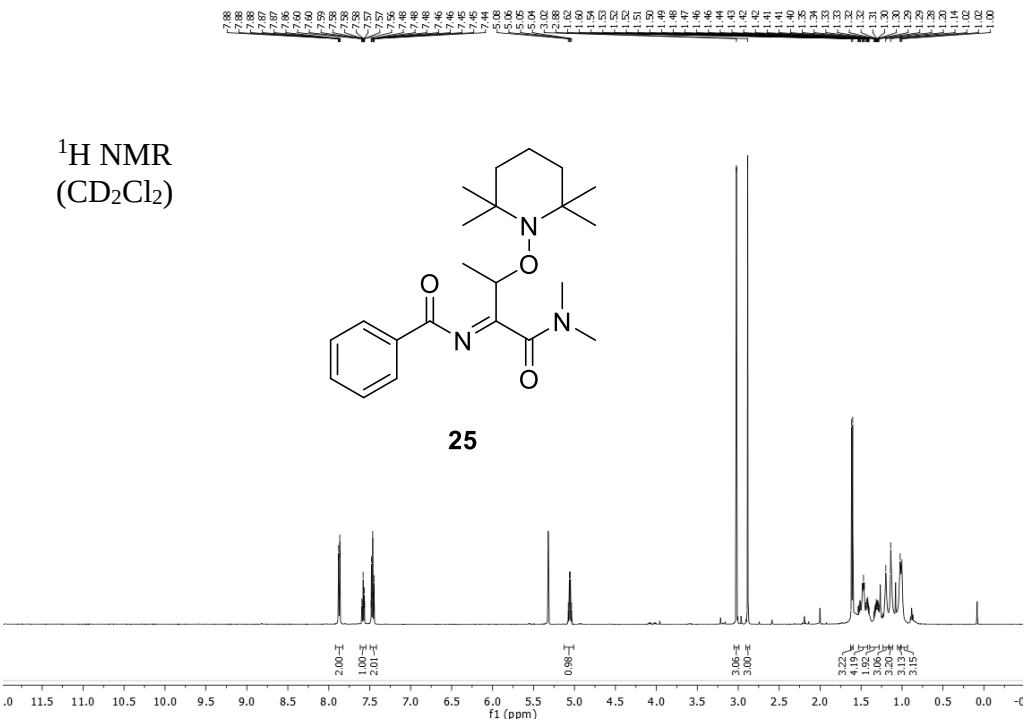
8.40. Compound 24



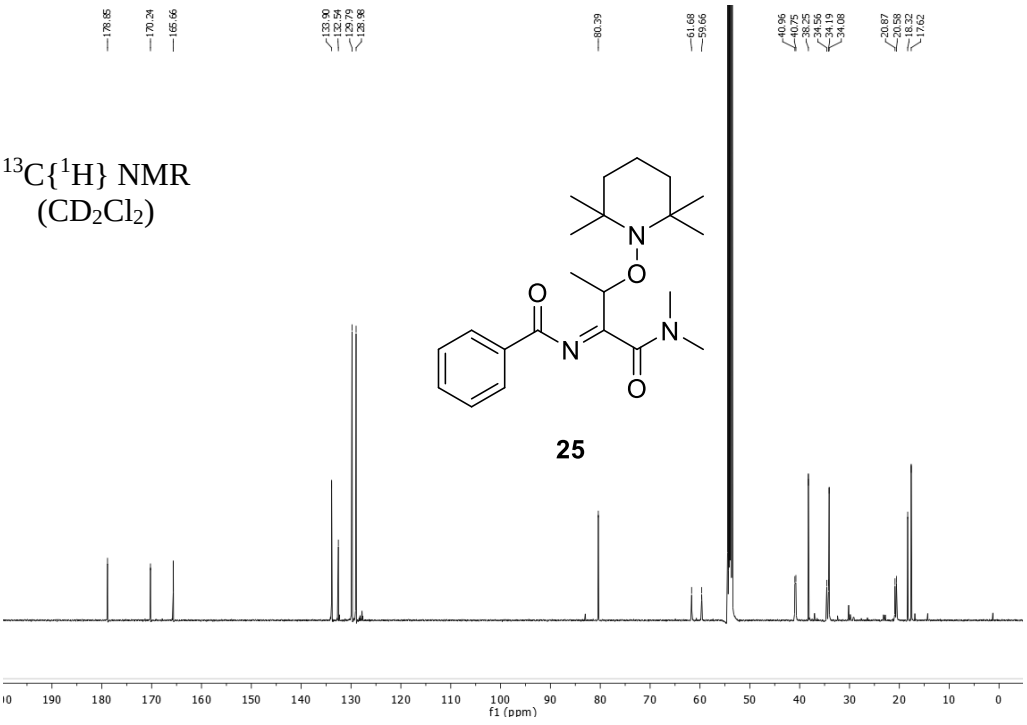


8.41. Compound 25

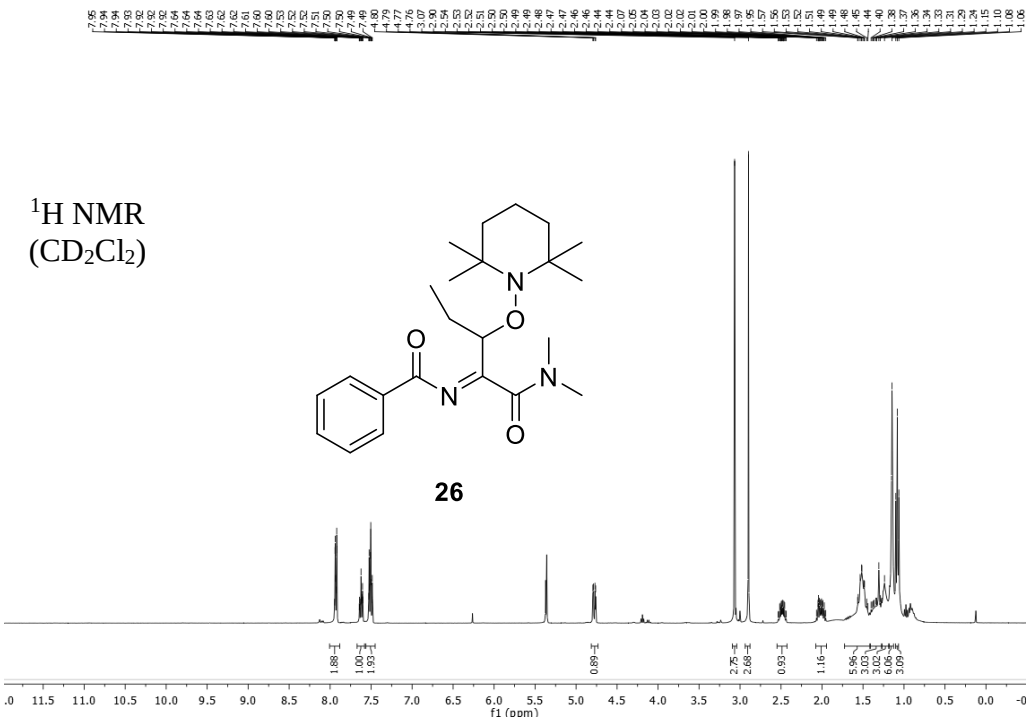
^{1}H NMR
(CD_2Cl_2)

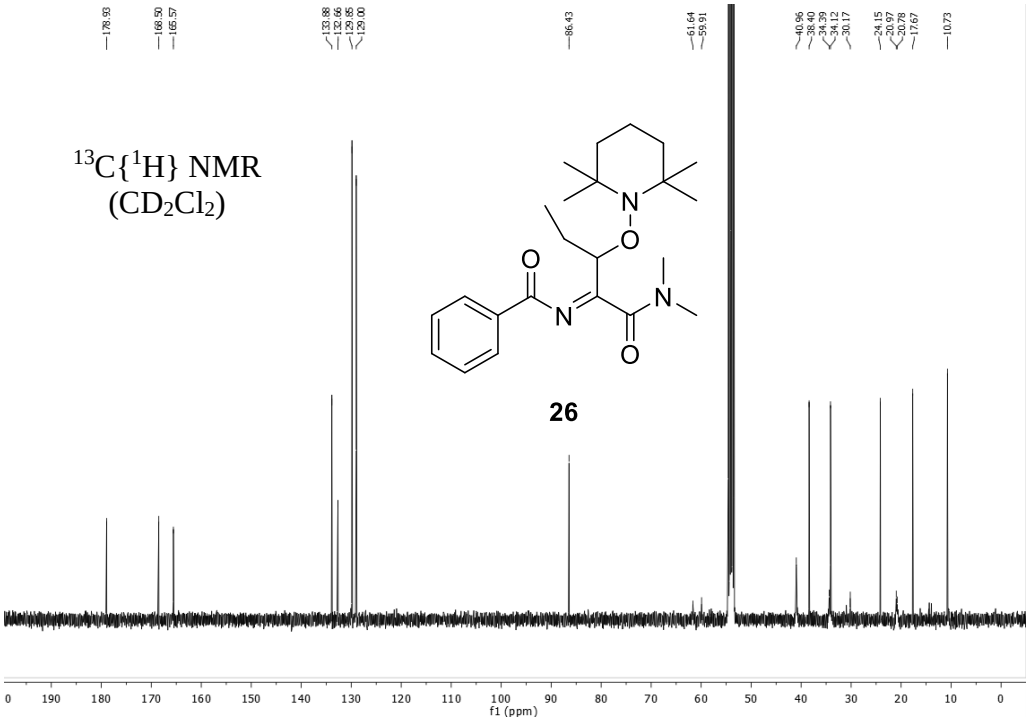


^{13}C{^{1}H} NMR
(CD_2Cl_2)

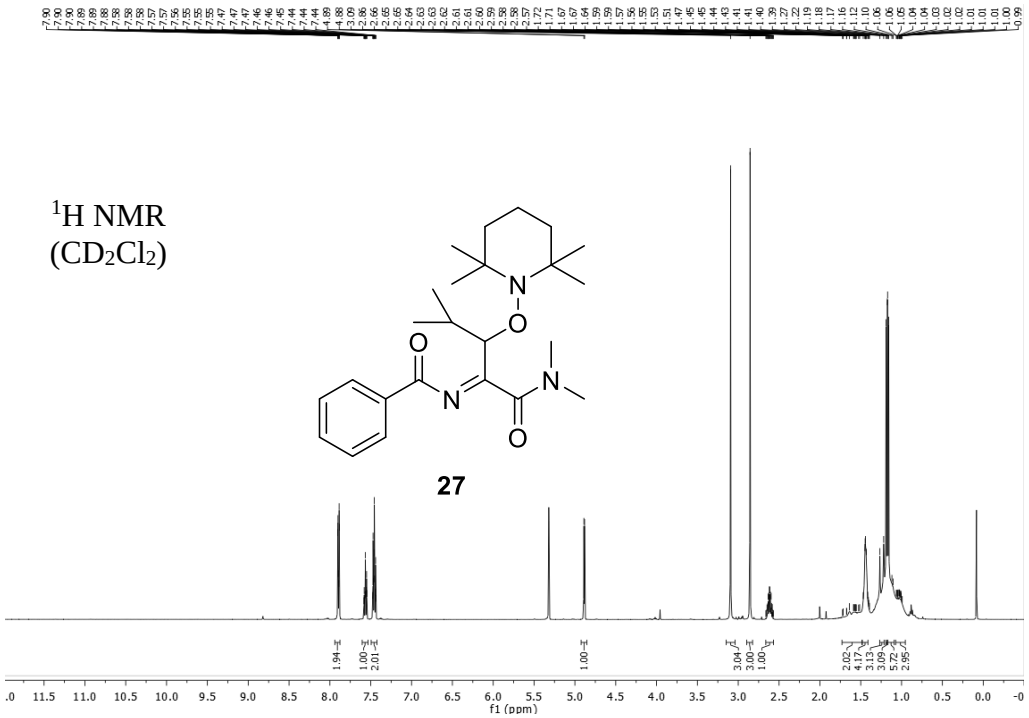


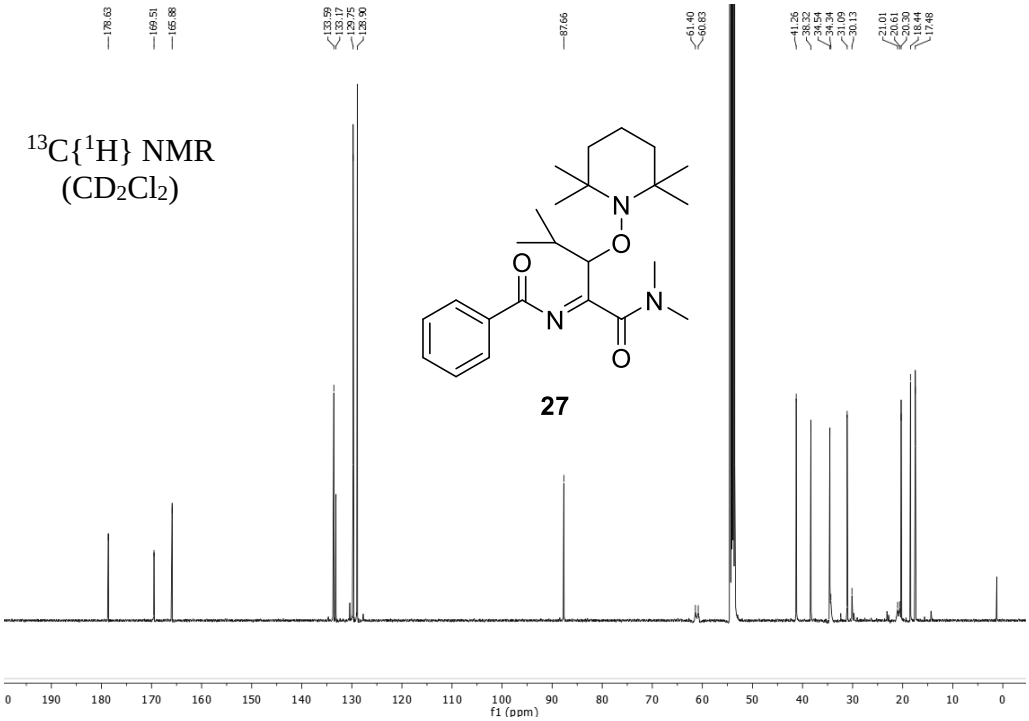
8.42. Compound 26



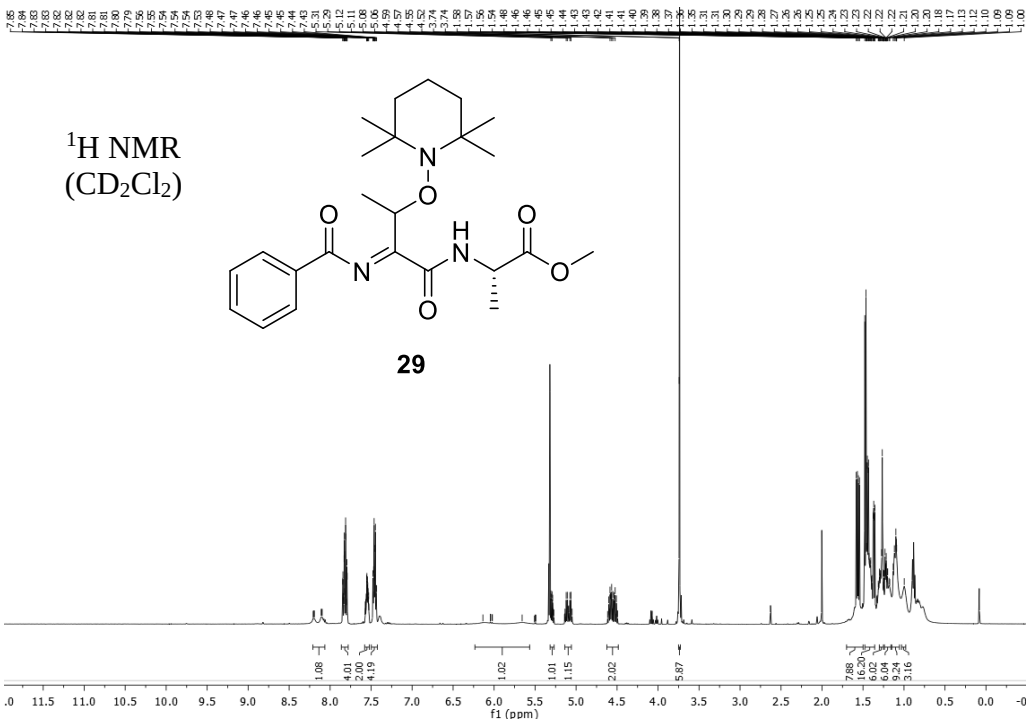


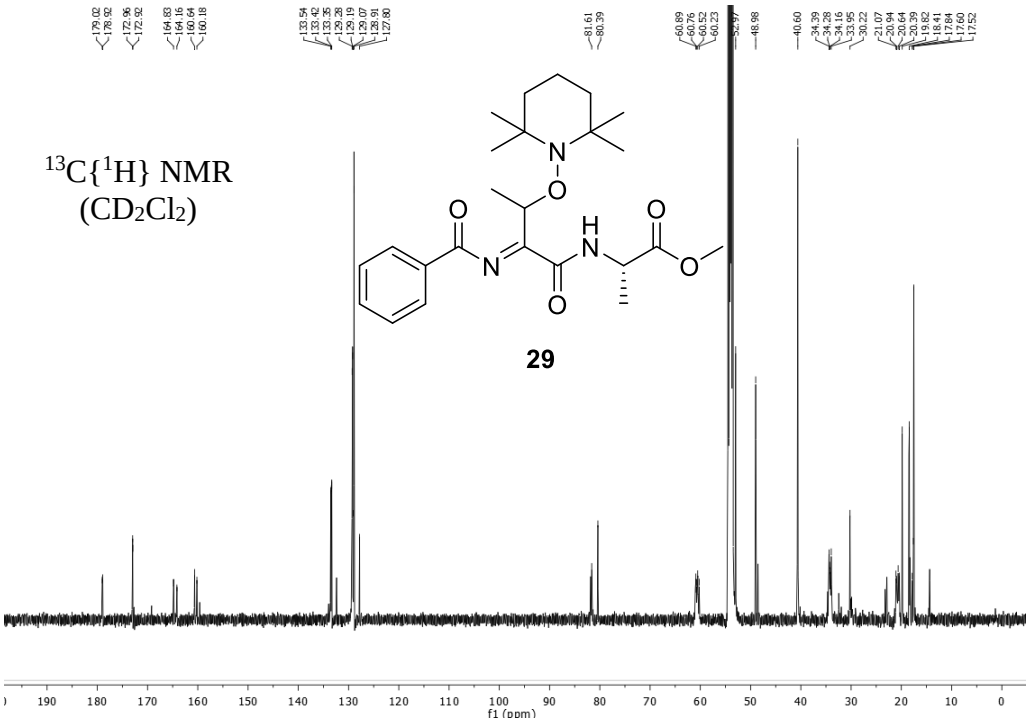
8.43. Compound 27





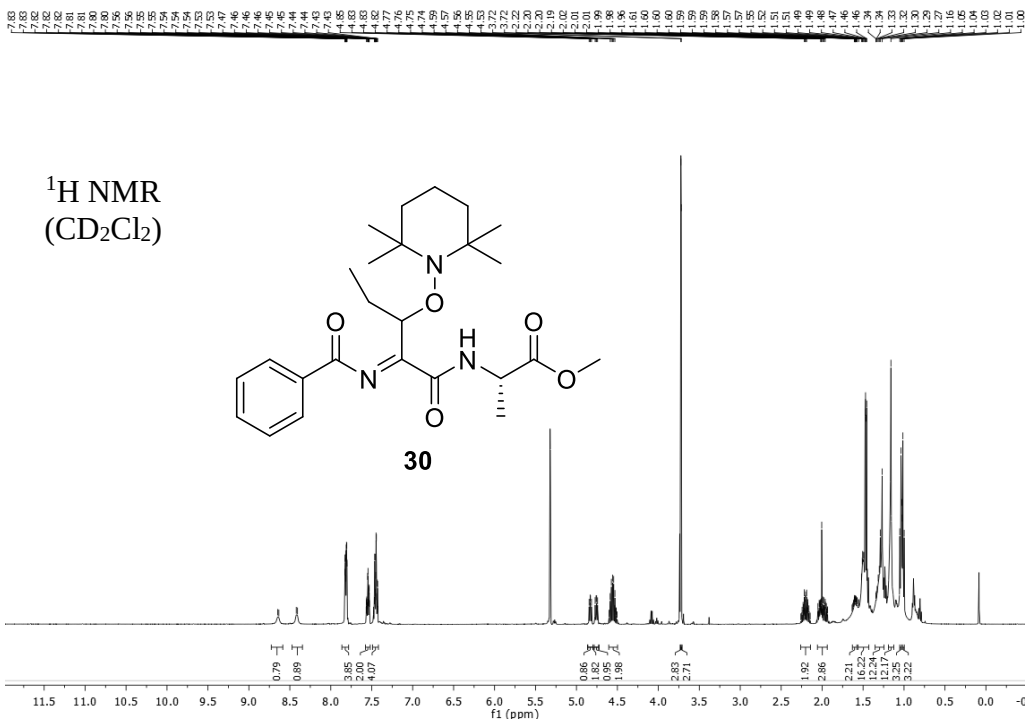
8.44. Compound 29

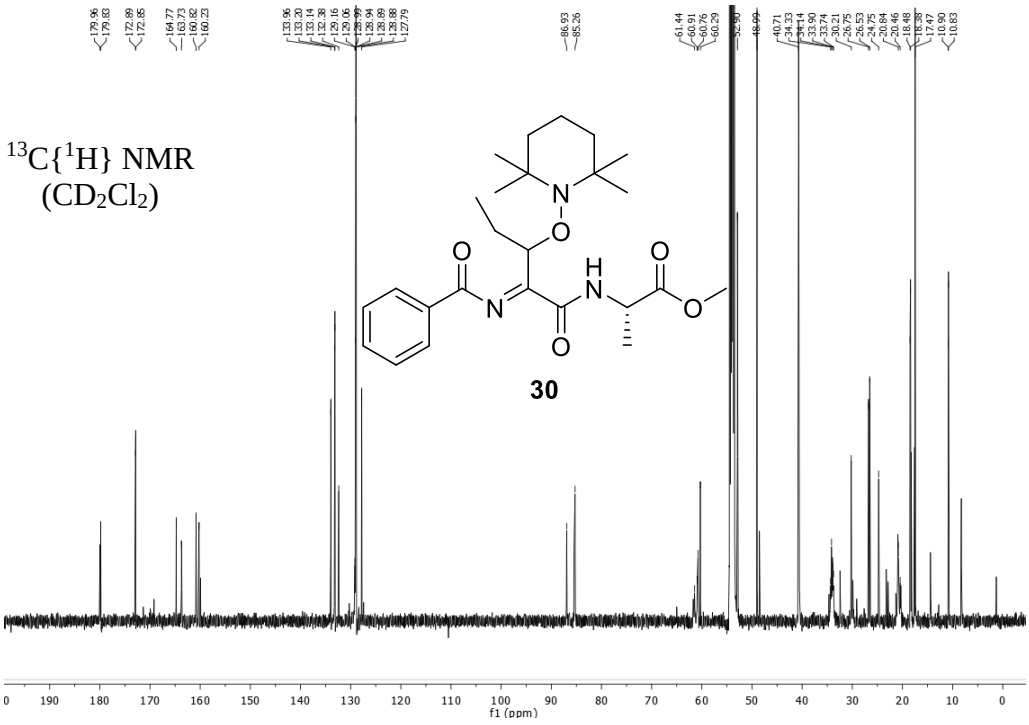




The product was obtained as a mixture of two diastereomers (dr 1:1).

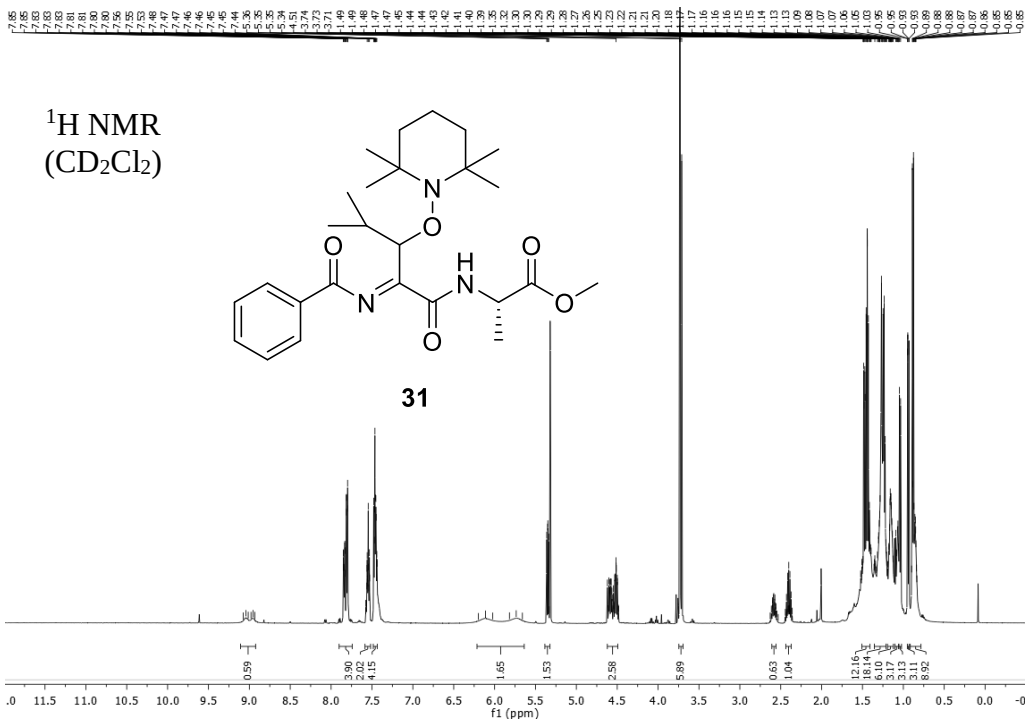
8.45. Compound 30

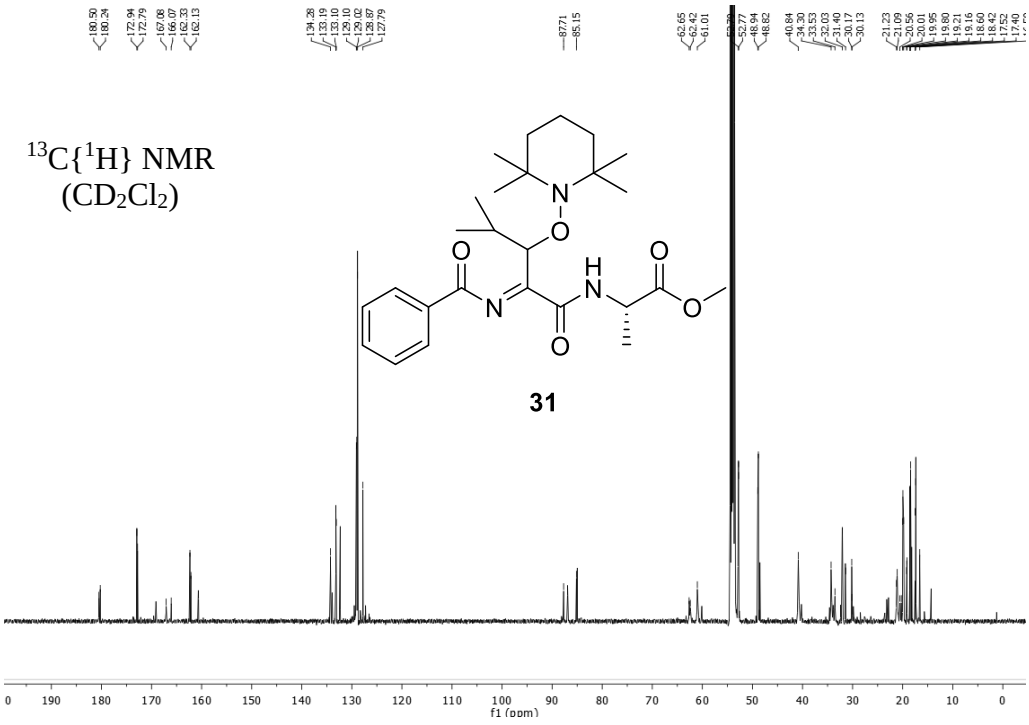




The product was obtained as a mixture of two diastereomers (dr 1:1).

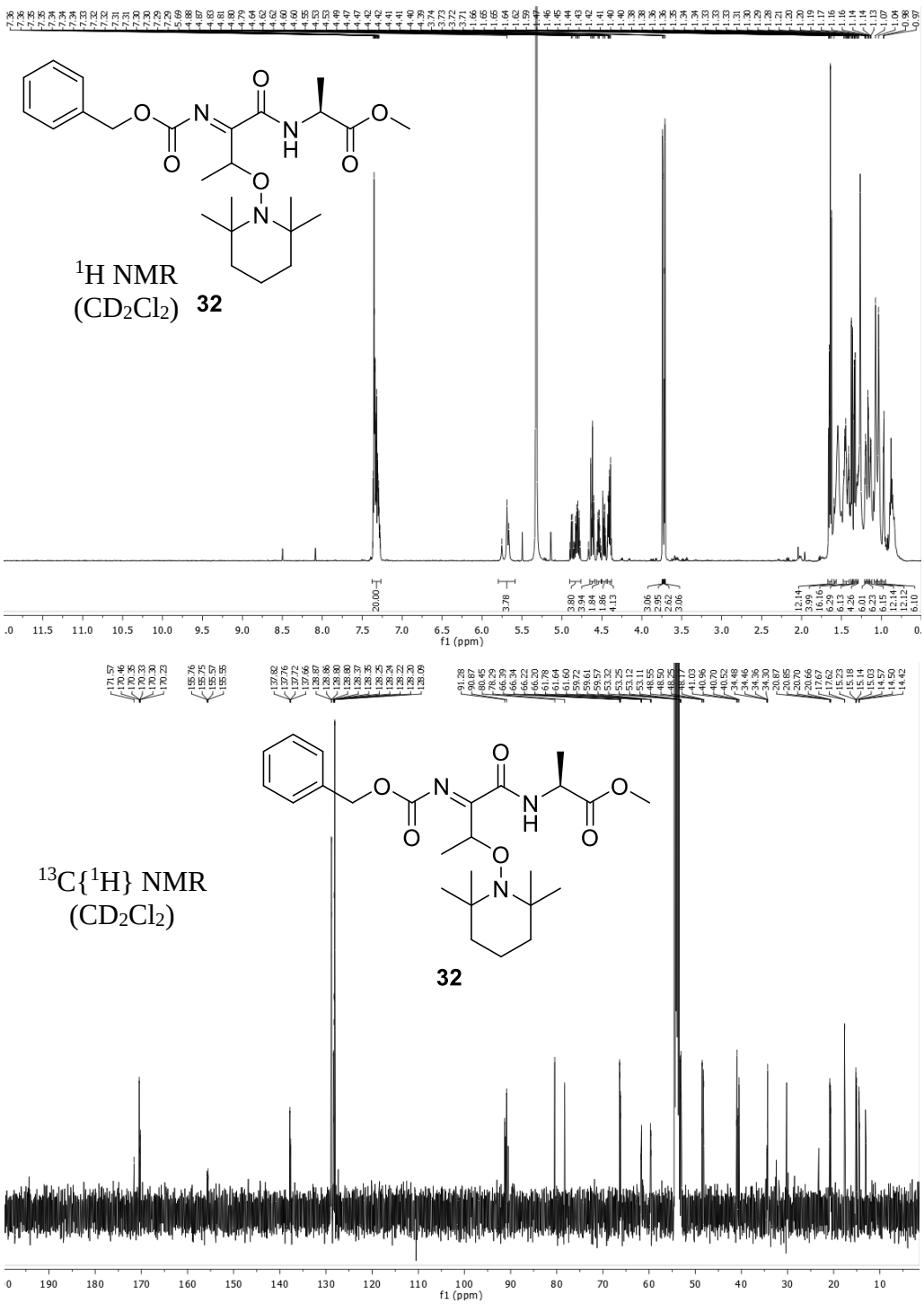
8.46. Compound 31





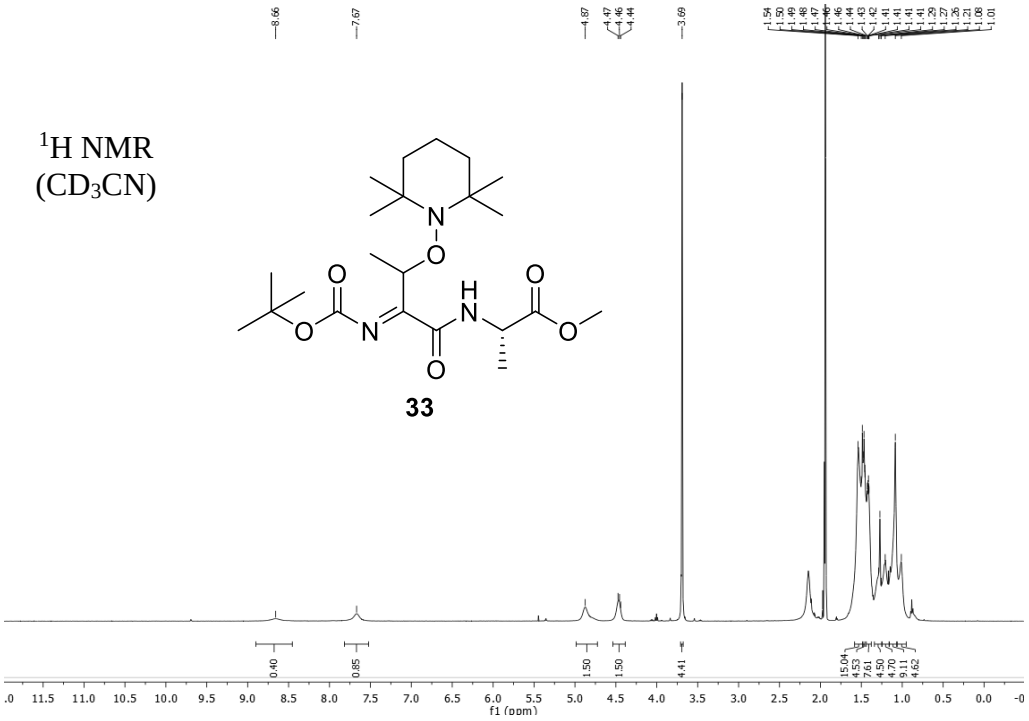
The product was obtained as a mixture of two diastereomers (dr 1.5:1).

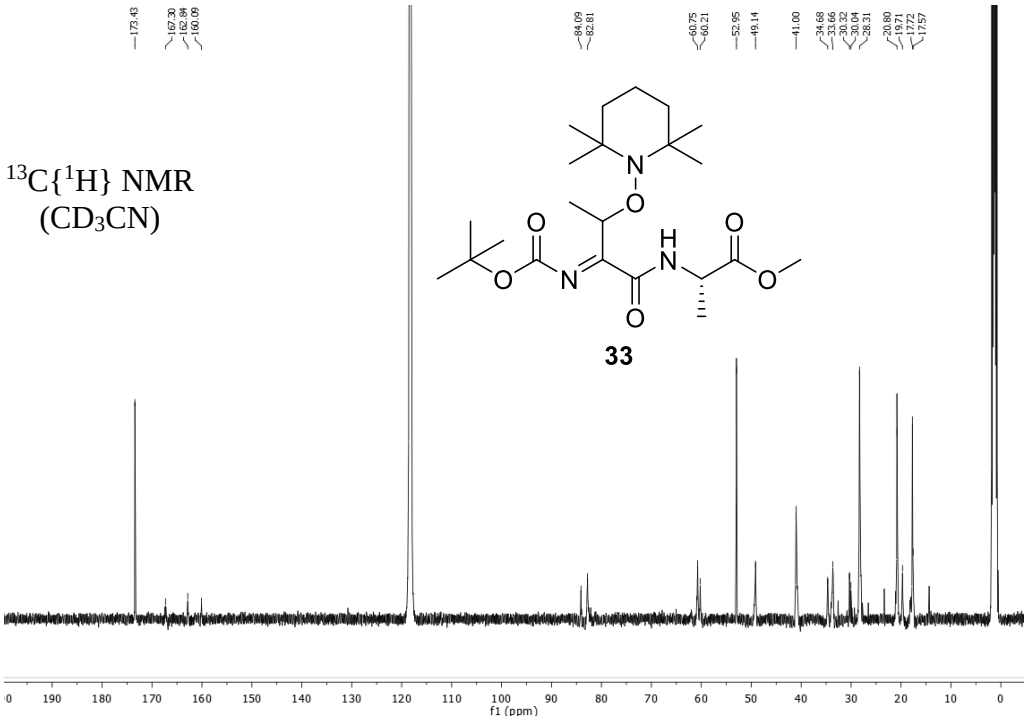
8.47. Compound 32



The product was obtained as a mixture of four isomers (1:1:1:1).

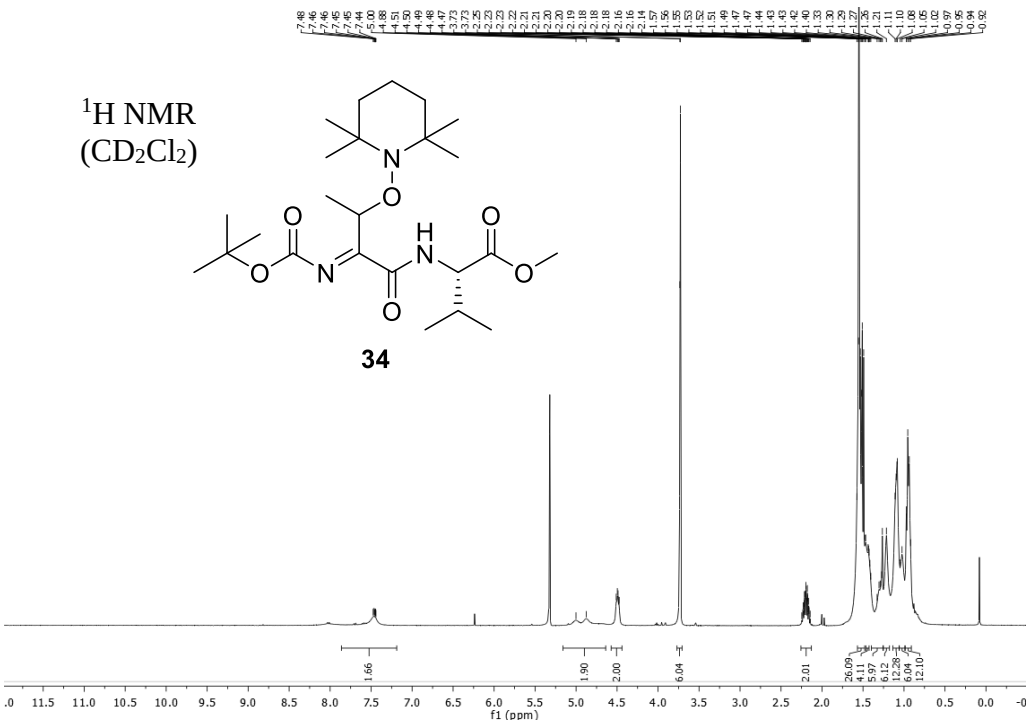
8.48. Compound 33

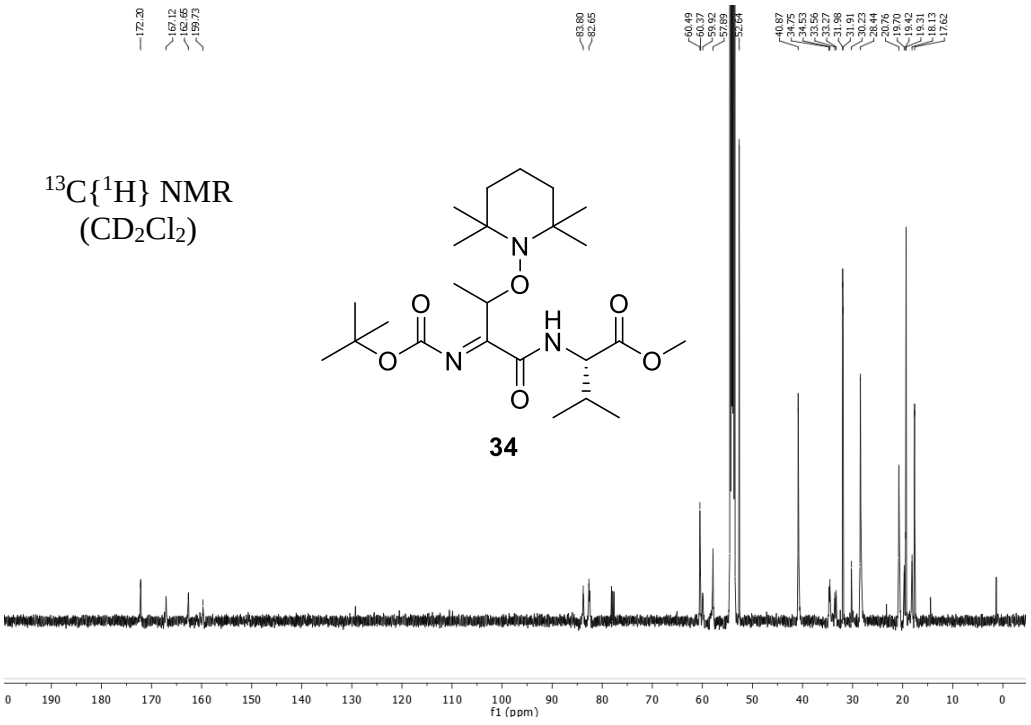




The product was obtained as a mixture of two diastereomers (dr 2:1).

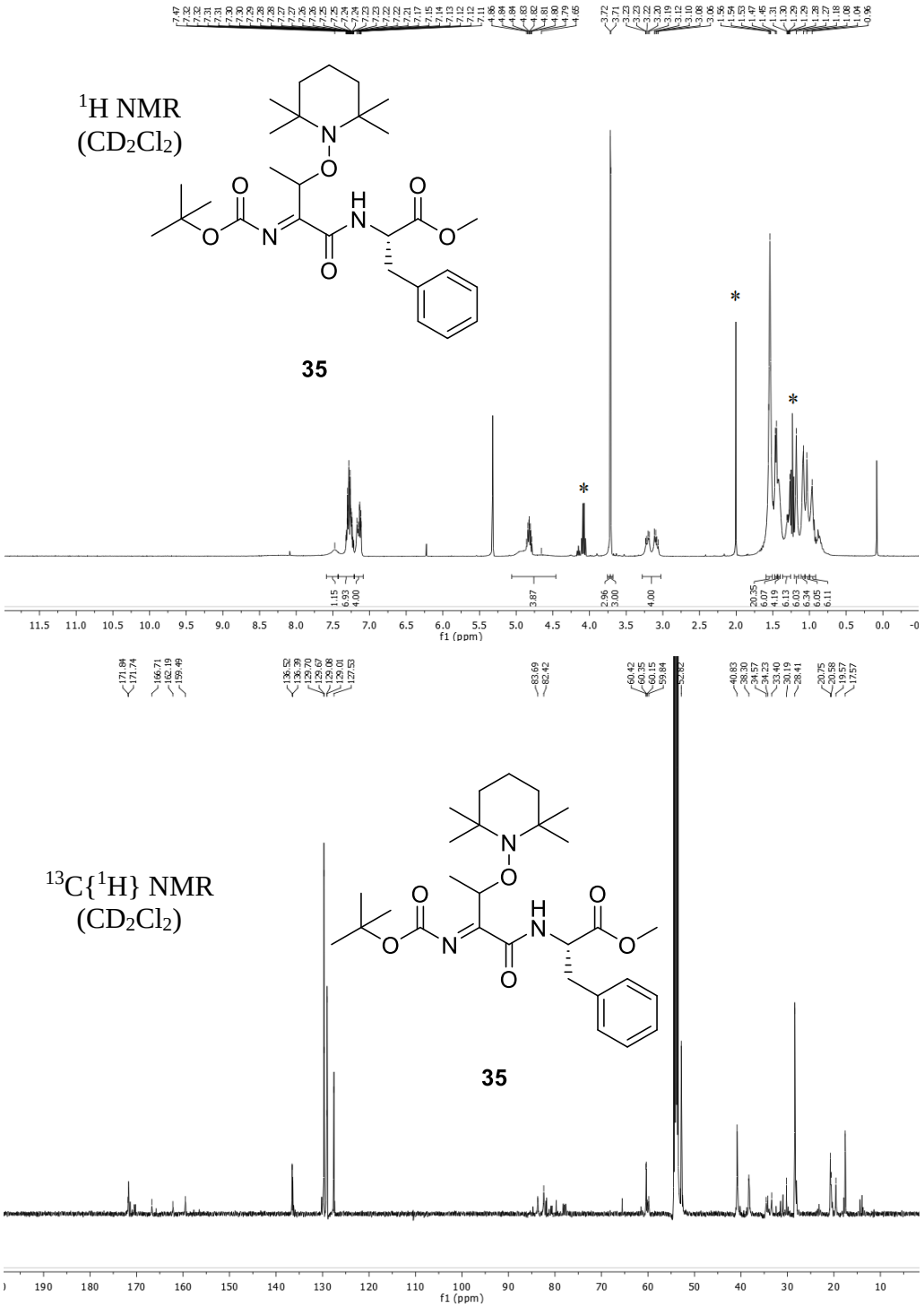
8.49. Compound 34





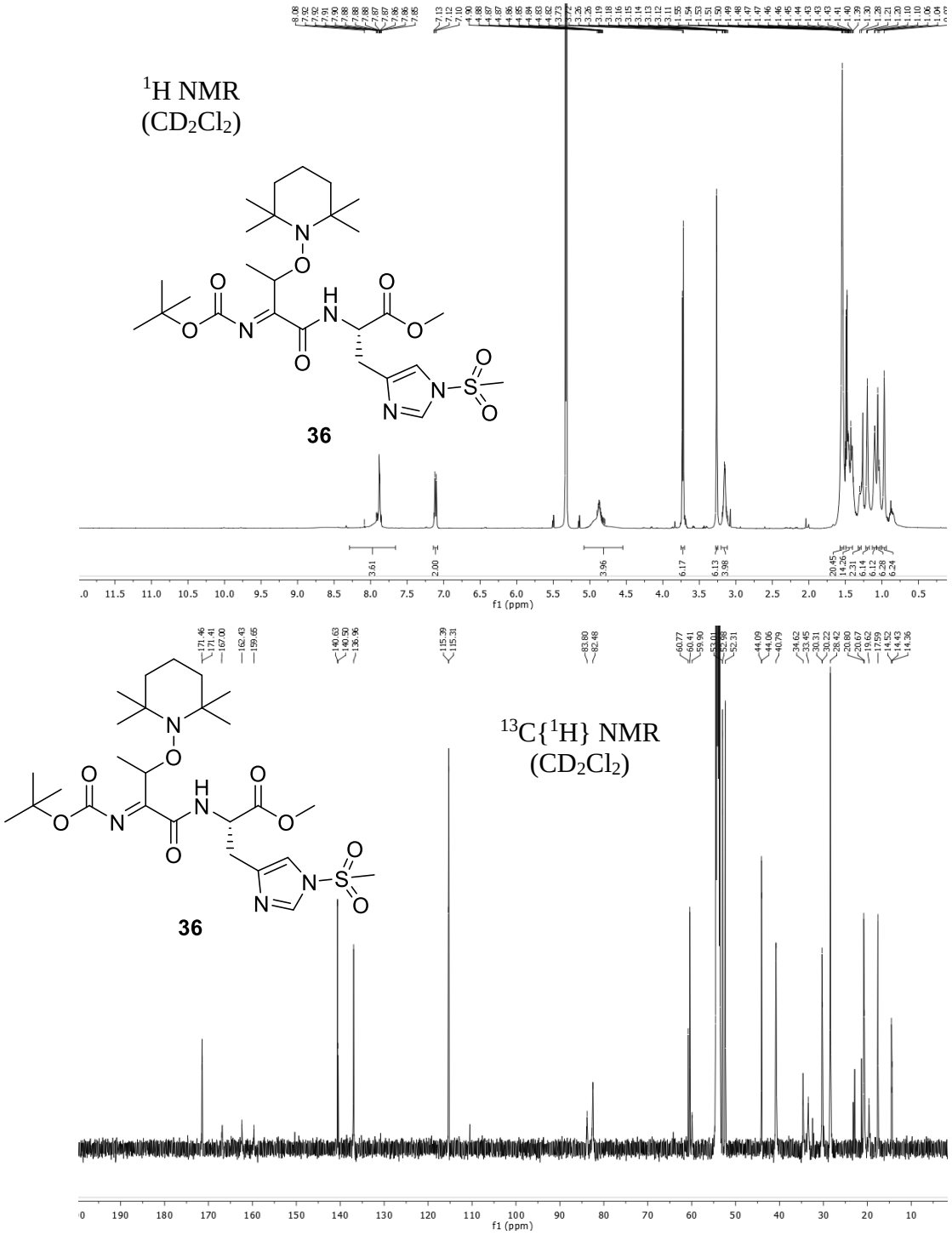
The product was obtained as a mixture of two diastereomers (dr 1:1).

8.50. Compound 35



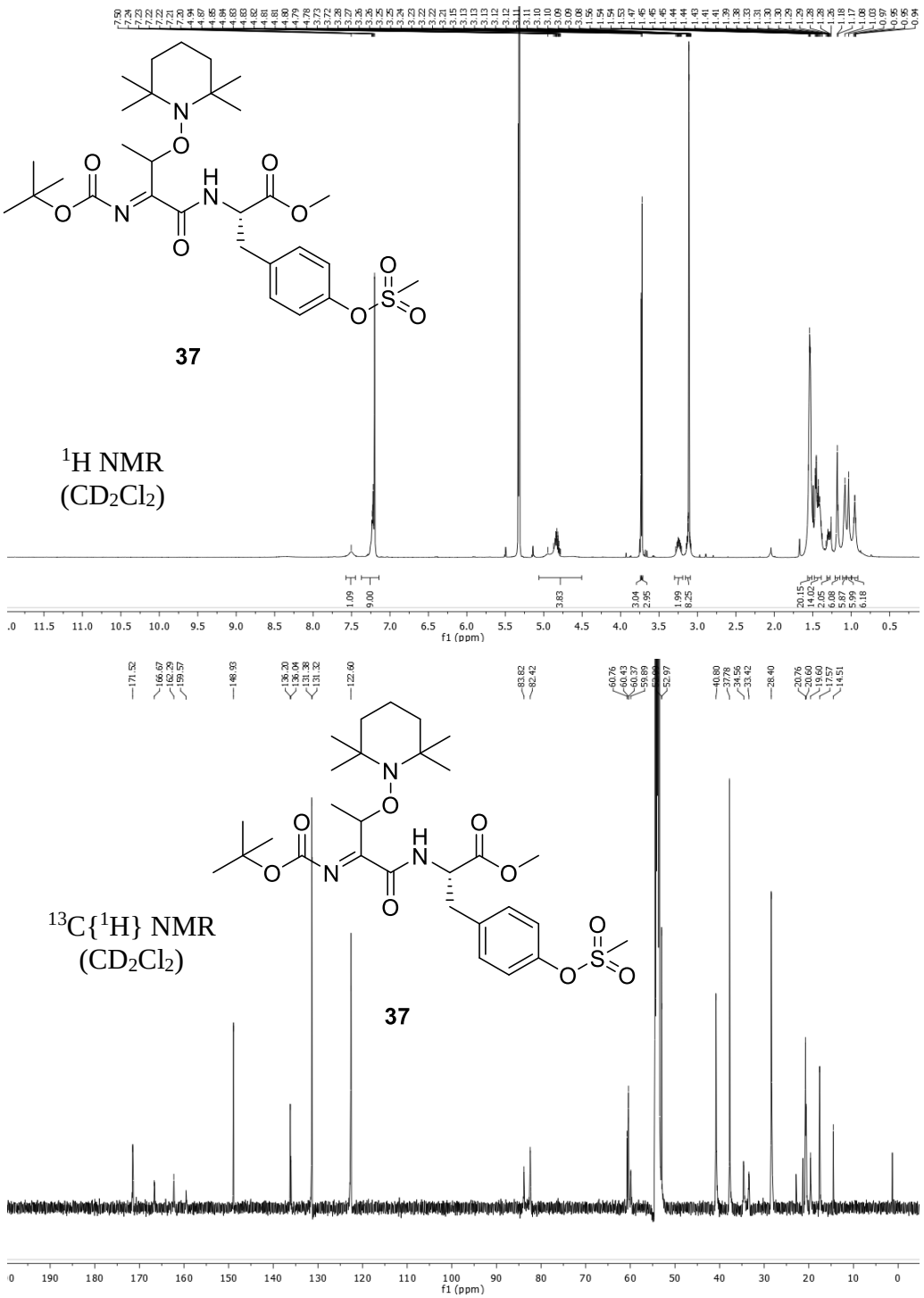
The spectra contain small amounts of residual EtOAc that evaded removal by drying. The reported isolated yielded was corrected accordingly. The product was obtained as a mixture of two diastereomers (dr 1:1).

8.51. Compound 36



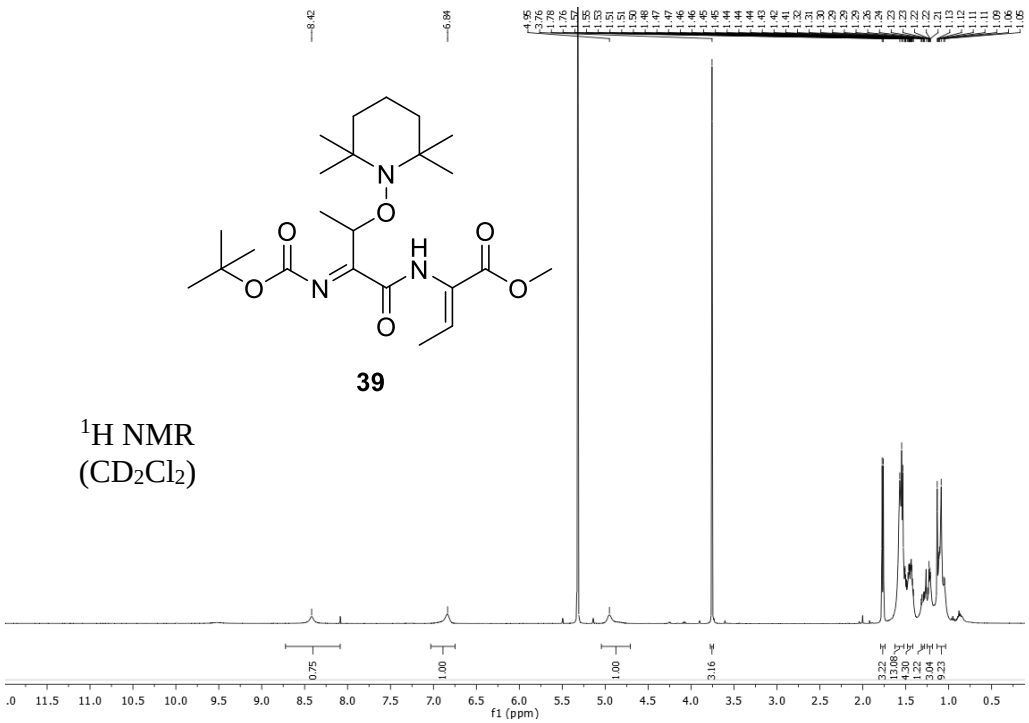
The product was obtained as a mixture of two diastereomers (dr 1:1).

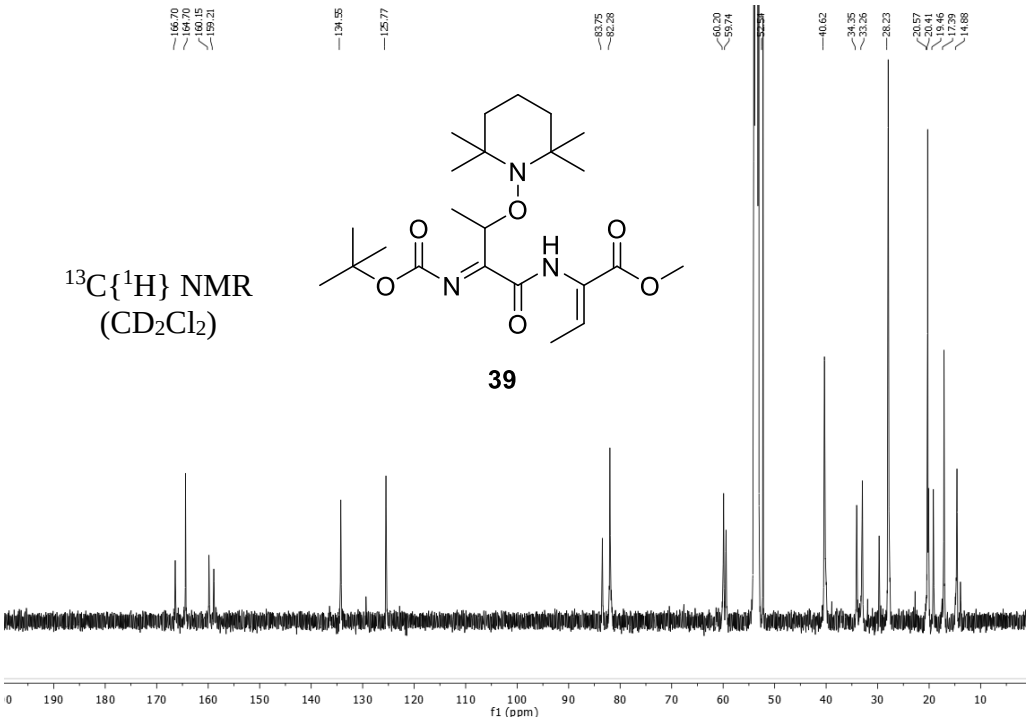
8.52. Compound 37



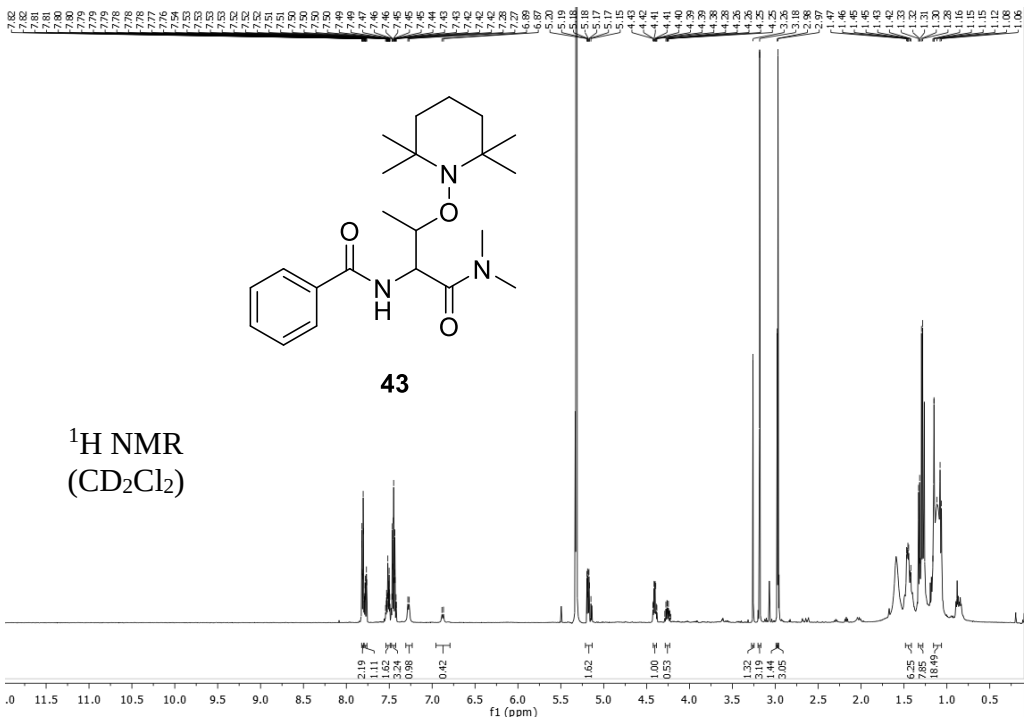
The product was obtained as a mixture of two diastereomers (dr 1:1).

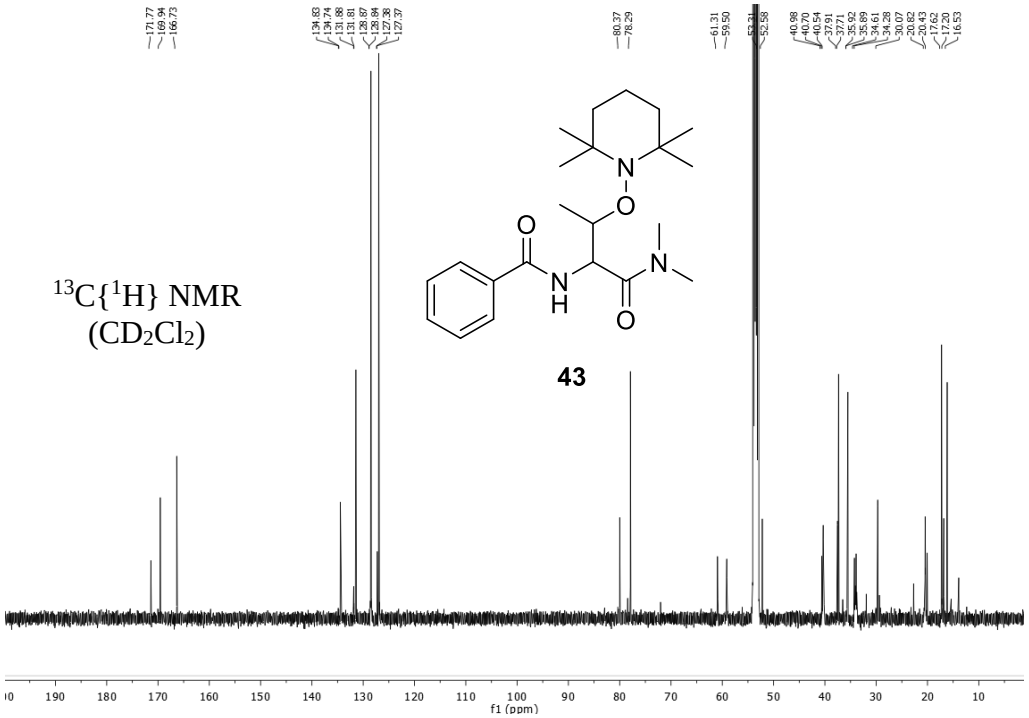
8.53. Compound 39





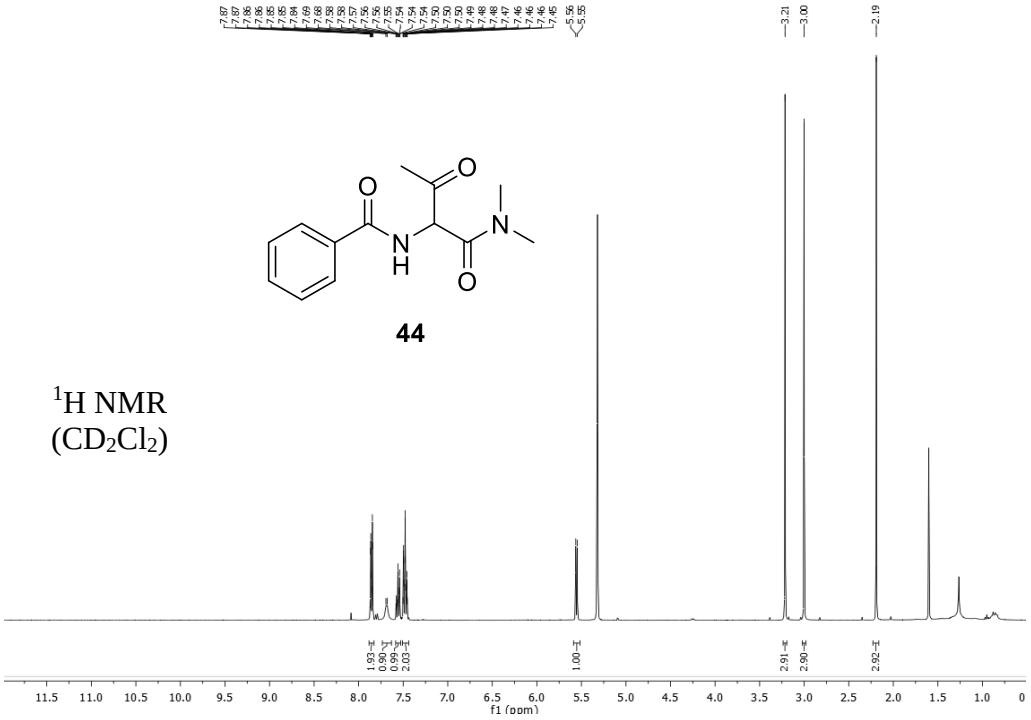
8.54. Compound 43

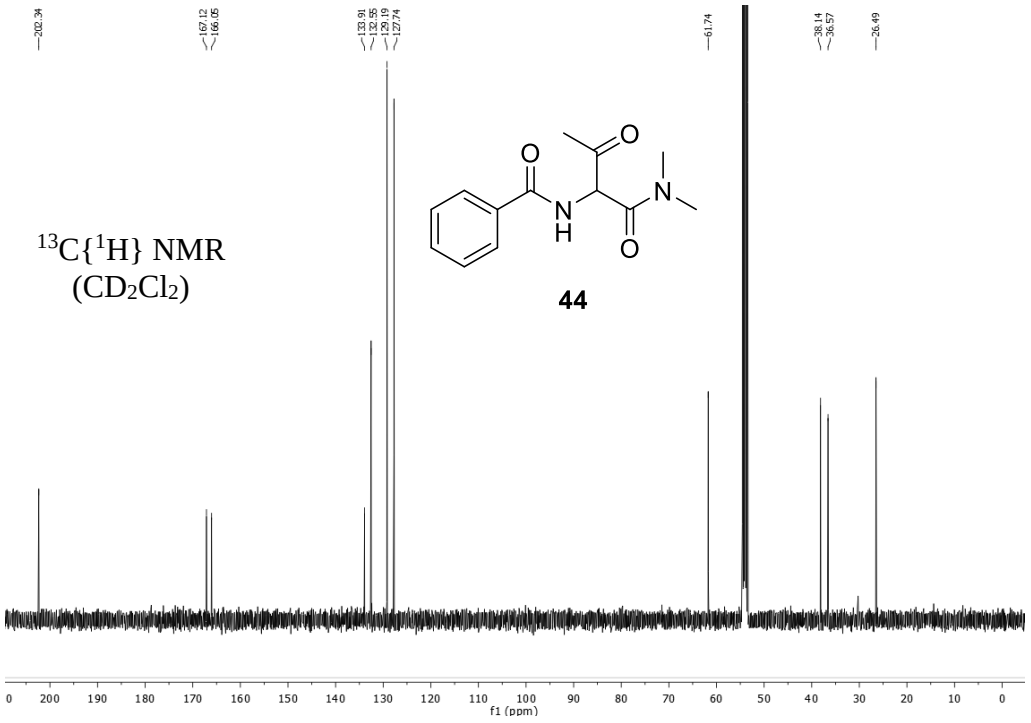




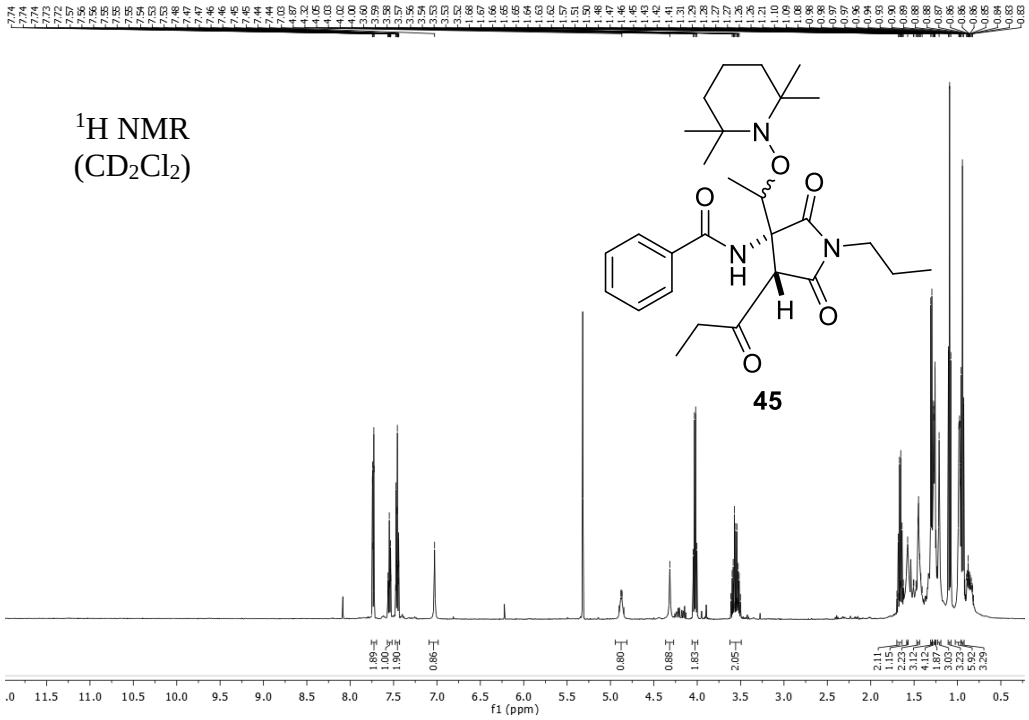
The product was obtained as a mixture of two diastereomers (dr 1.5:1.0).

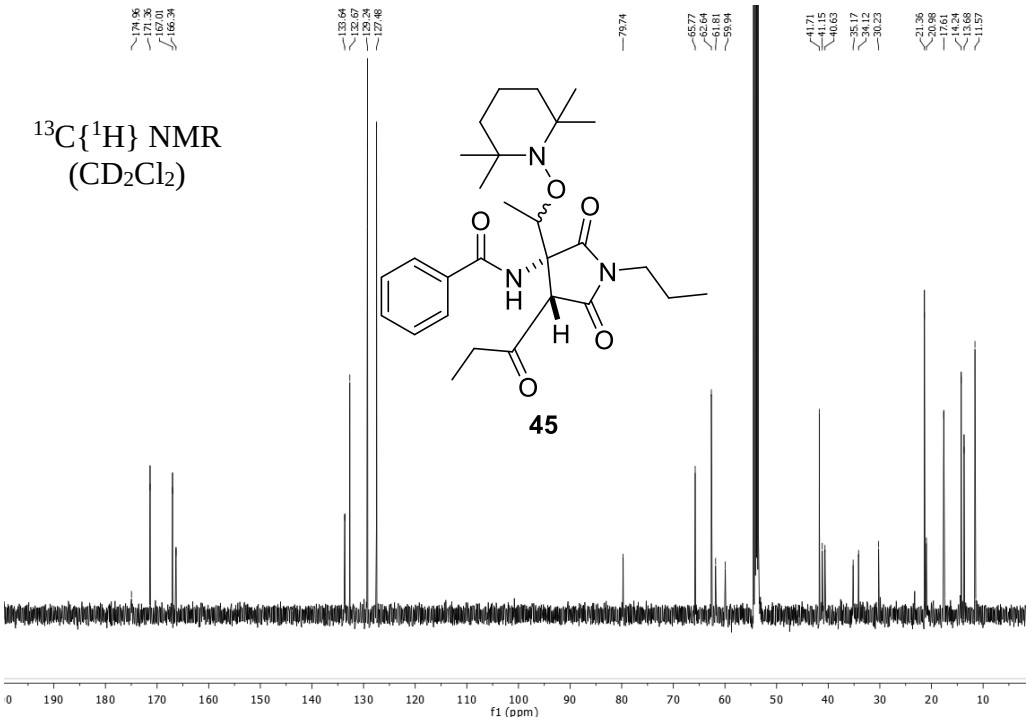
8.55. Compound 44





8.56. Compound 45





8.57. Compound 46