SUPPORTING INFORMATION

Enantioselective Lewis Acid Catalysis in Intramolecular [2+2] Photocycloaddition Reactions: A Mechanistic Comparison between Representative Coumarin and Enone Substrates

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General Information

All reactions, sensitive to air or moisture, were carried out in flame-dried glassware under positive pressure of argon using standard *Schlenk* techniques. Photochemical experiments were performed in flame-dried irradiation tubes (*Duran* glass, outer diameter: 1 cm, glass thickness 1.5 mm, volume: 12 mL for room temperature irradiation, 15 mL for low temperature irradiation) under positive pressure of argon. Irradiation experiments were performed in an RPR-100 photochemical reactor (Southern New England Ultra Violet Company, Branford, CT, USA) equipped with fluorescence lamps (Philips black light blue 8 W, λ_{max} = 366 nm). For the photoreactions dry dichloromethane (dried over 4Å molecular sieves) was used and degassed by three freeze-pump-thaw-cycles. Flash chromatography was performed on silica gel 60 (Merck, 230-400 mesh) with the eluent mixtures given for the corresponding procedures. Thin layer chromatography (TLC) was performed on silica coated glass plates (silca gel 60 F 254). Compounds were detected by UV (λ = 254 nm, 366 nm) or staining with a basic $KMnO_4$ solution. All solvents for chromatography were distilled prior to use. Analytical HPLC was performed using a chiral stationary phase (Daicel ChiralCell, Chemical Industries, flow rate: 1.0 mL/min, type and eluent is given for the corresponding compounds) and UV-detection. IR: JASCO IR-4100. MS / HRMS: ThermoFisher Scientific DFS High Resolution MS (EI, 70 eV); LTQ FT Ultra (ESI). UV/vis: Perkin Elmer Lambda 35 UV/vis spectrometer. ^{1}H and ^{13}C: Bruker AV-250, AV-360 and AV-500 recorded at 300 K. Chemical shifts are reported relative to the residual proton signal of the deuterated solvent ($CHCl_3$: $\delta(^{1}H)$ = 7.26 ppm) or the Deuterium coupled signal of the ^{13}C-signal ($CDCl_3$: $\delta(^{13}C)$ = 77.0 ppm) as reference. Apparent multiplets which occur as a result of accidental equality of coupling constants to those of magnetically non-equivalent protons are marked as virtual (*virt.*). The relative configuration of chiral products and the multiplicity of the ^{13}C-NMR signals were determined by two-dimensional NMR spectra (COSY, NOESY, HSQC, HMBC). Optical rotations were determined using a Perkin-Elmer 241 MC polarimeter (sodium vapour lamp). Conversions were determined by GC analysis using an *Agilent* HP 6890 Series GC system with flame ionisation detector and hydrogen as carrier gas (pressure 160 kPa) using an HP-5 column (poly-dimethyl/diphenyl-siloxane, 95/5).

1. Spectroscopic Data

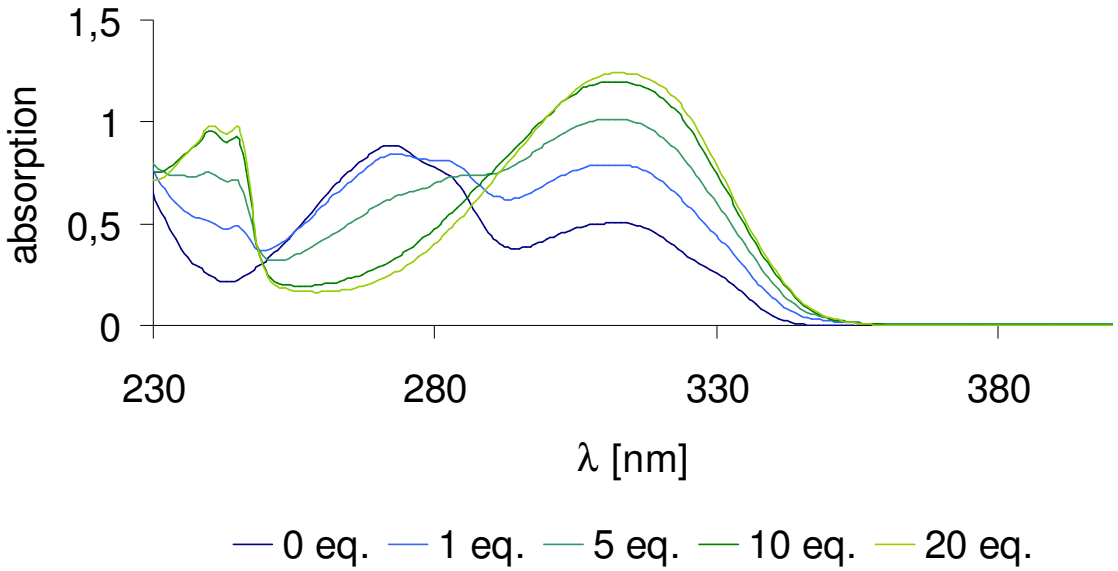


Figure S1. UV-vis spectra of **2a** in the presence of different equivalents of $EtAlCl_2$ (c = 0.8 mM in CH_2Cl_2).

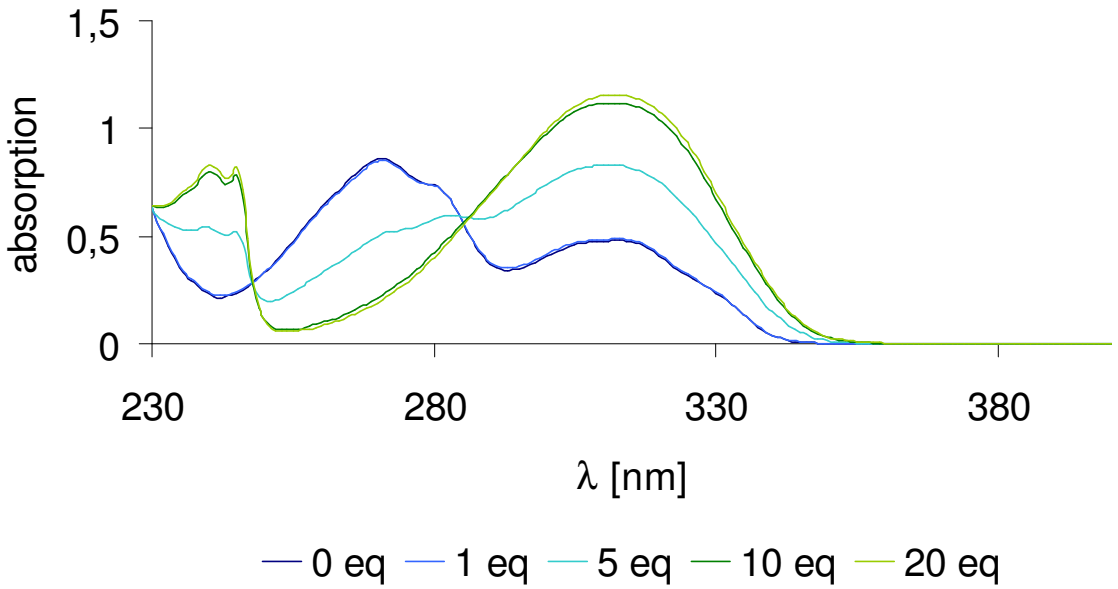


Figure S2. UV-vis spectra of 4-methylcoumarin in the presence of different equivalents of $EtAlCl_2$ (c = 0.8 mM in CH_2Cl_2).

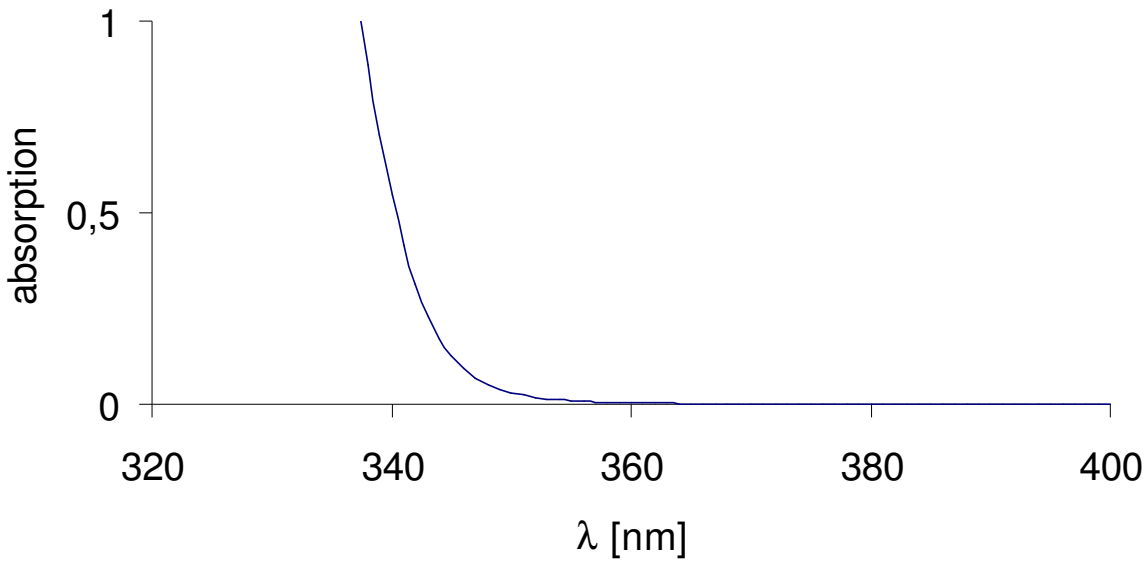


Figure S3. UV-vis spectrum of **2a** at higher concentration (c = 8 mM in CH_2Cl_2).

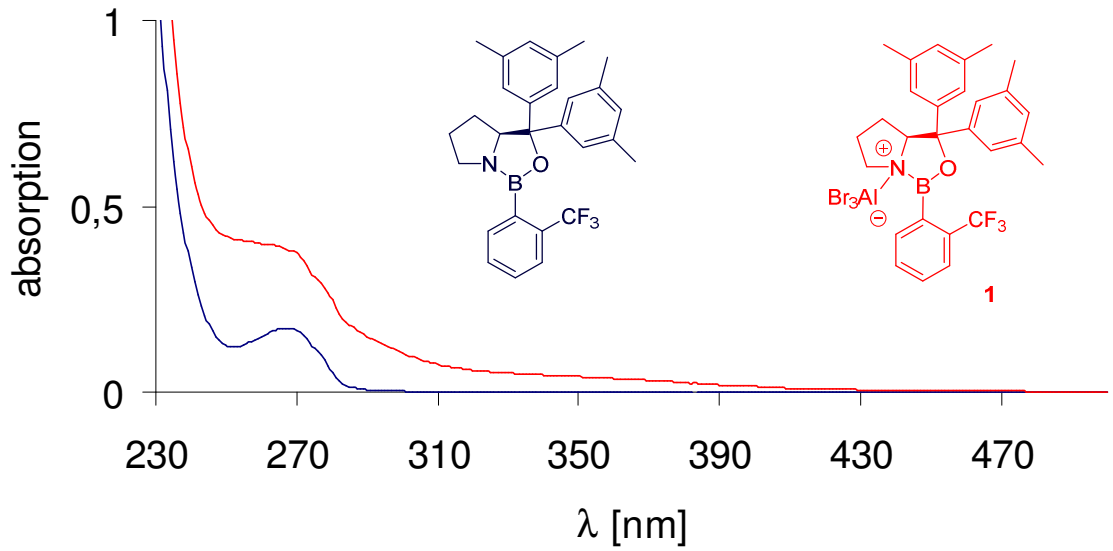


Figure S4. UV-vis spectrum of **1** and its non-activated form (c = 0.8 mM in CH_2Cl_2).

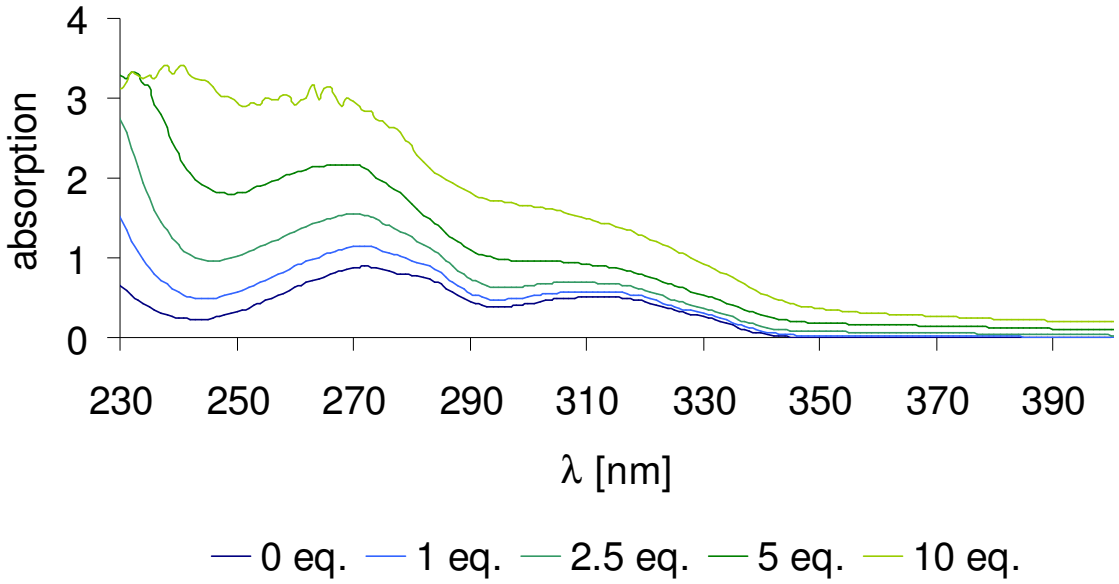


Figure S5. UV-vis spectra of **2a** in the presence of different equivalents of **1** (c = 0.8 mM in CH_2Cl_2).

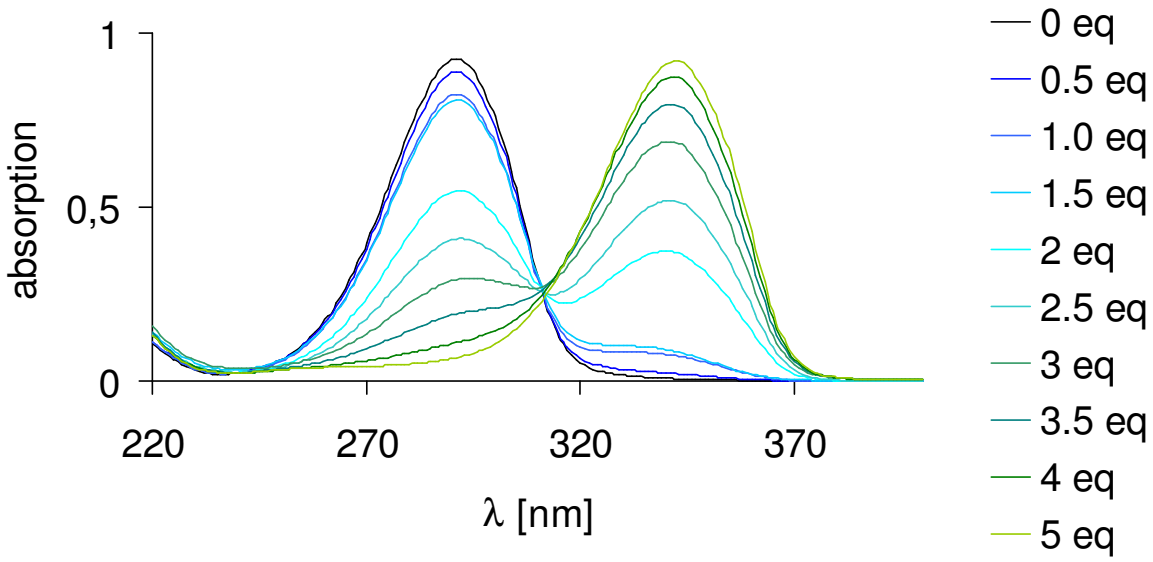


Figure S6. UV-vis spectra of **3a** in the presence of different equivalents of $EtAlCl_2$ (c = 0.5 mM in CH_2Cl_2).

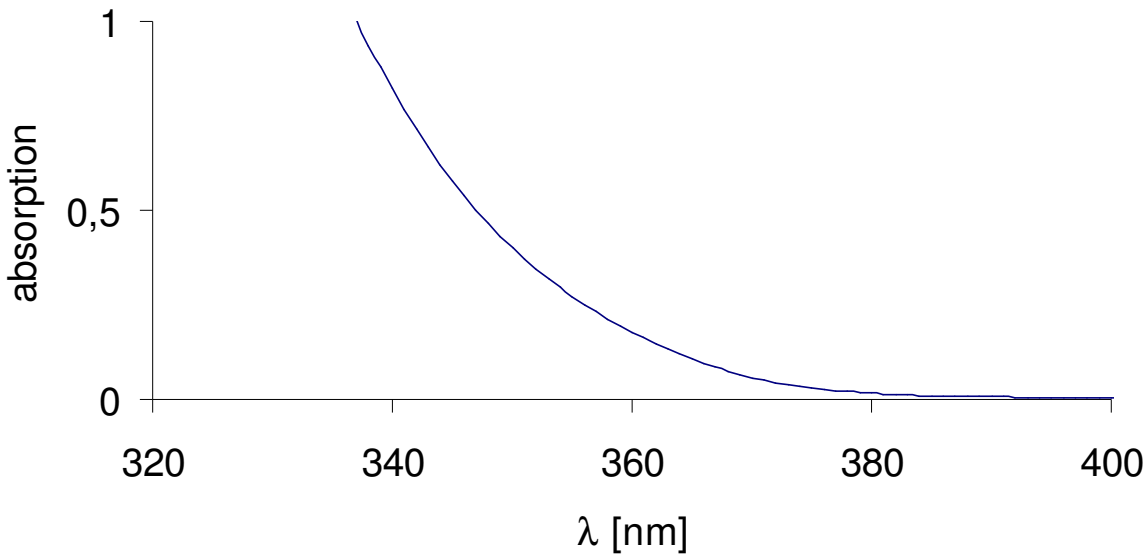


Figure S7. UV-vis spectrum of **3a** at higher concentration (c = 5 mM in CH_2Cl_2).

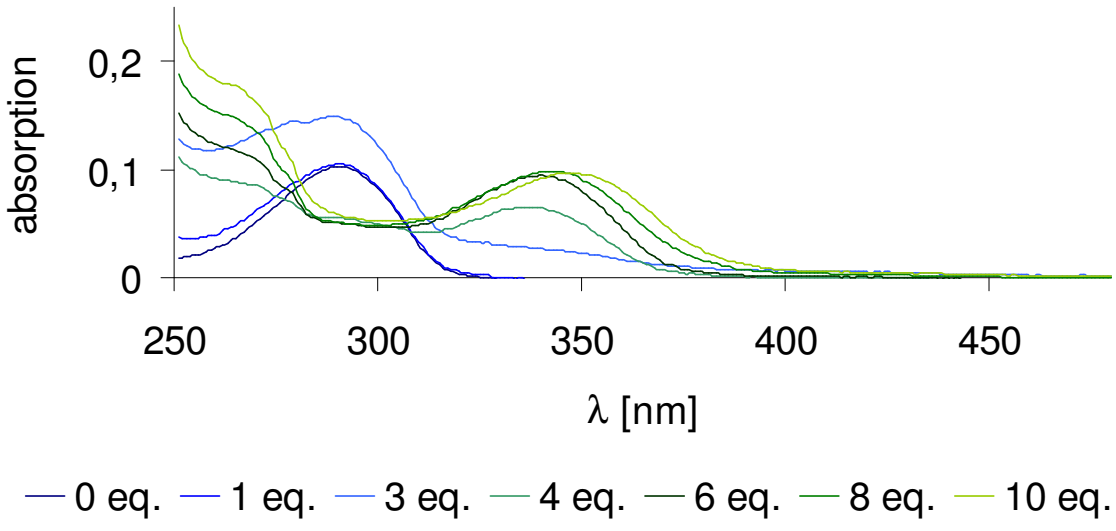


Figure S8. UV-vis spectra of **3a** in the presence of different equivalents of **1** (c = 0.5 mM in CH_2Cl_2).

2. Quantum yield determination

To determine the extinction coefficient of the Fe^{2+}/phen complex experimentally, $FeSO_4$ solutions in 0.05 M aqueous H_2SO_4 with different concentrations of $FeSO_4$ were mixed with ~ 5 eq. 1,10-phenanthroline and the UV-vis spectra recorded. The exctinction coefficents were determined at λ = 510 nm using the Beer-Lambert-Law (Figure S9).

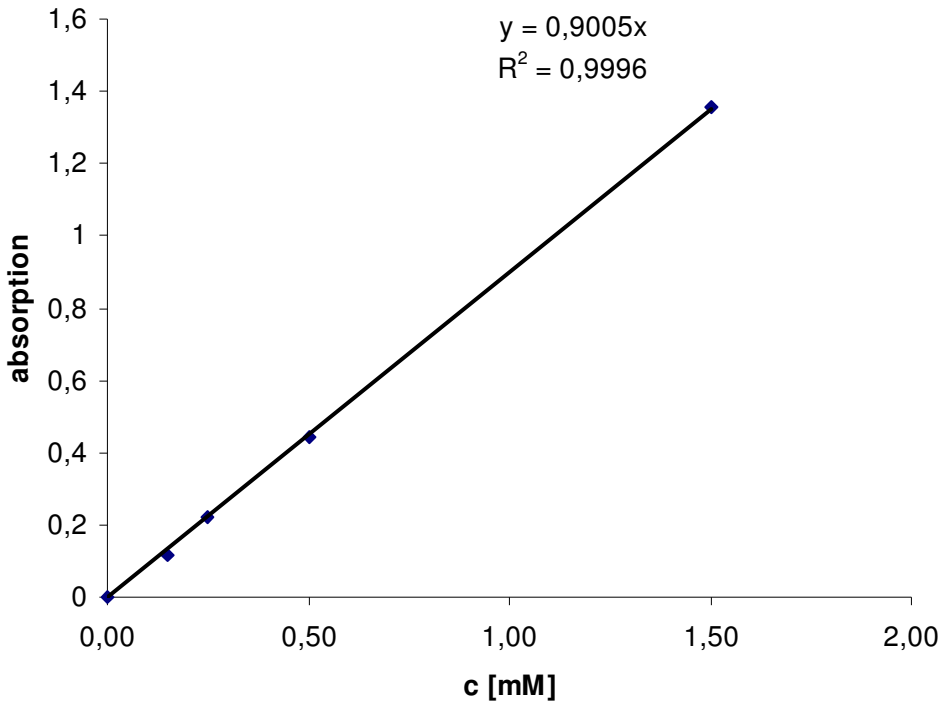


Figure S9. Determination of the exctinction coefficient of the Fe^{2+}/phen solutions.

The $K_3[Fe(C_2O_4)]_3]\cdot 3H_2O$ solutions in 0.05 M aqueous H_2SO_4 (c = 150 mM) were prepared in the dark and the irradiation sample was prepared by charging a phototube used for the low temperature photoreactions (see general information) with 5 mL ferrioxalate solution. The tube was irradiated at λ = 366 using the complete cooling equipment (at room temperature) and stopped after 0.5 min, 1 min, 2 min, 3 min and 4 min. An 100 µL aliquot was added to ~ 20 mg 1,10-phenanthroline in 900 µL 0.05 M aqueous H_2SO_4 in the dark and after shaking the UV-vis spectrum of the sample was recorded. Each data point was obtained by irradiation of one 5 mL-sample which was discarded after the aliquot was measured. It can be determined that all photons entering the solution ($\varepsilon_{366nm} \approx 770\ M^{-1}\cdot cm^{-1}$) were absorbed by the ferrioxalate within the irradiation time the experiment was performed. By determination of its conversion and the known quantum yield (Φ = 1.21)[1] of the photoinduced reduction to Fe^{2+} ions at λ = 366 nm using the calibration data from Figure S9 the numbers of photons entering the reaction solution can be derived. Using the time dependent concentration of Fe^{2+} ions, the formal concentration of photons entering the reaction solution per minute was determined (Figure S10). Thus, the formal photon concentration per time dc(γ)/dt was determined to be 4.01 mM/min.

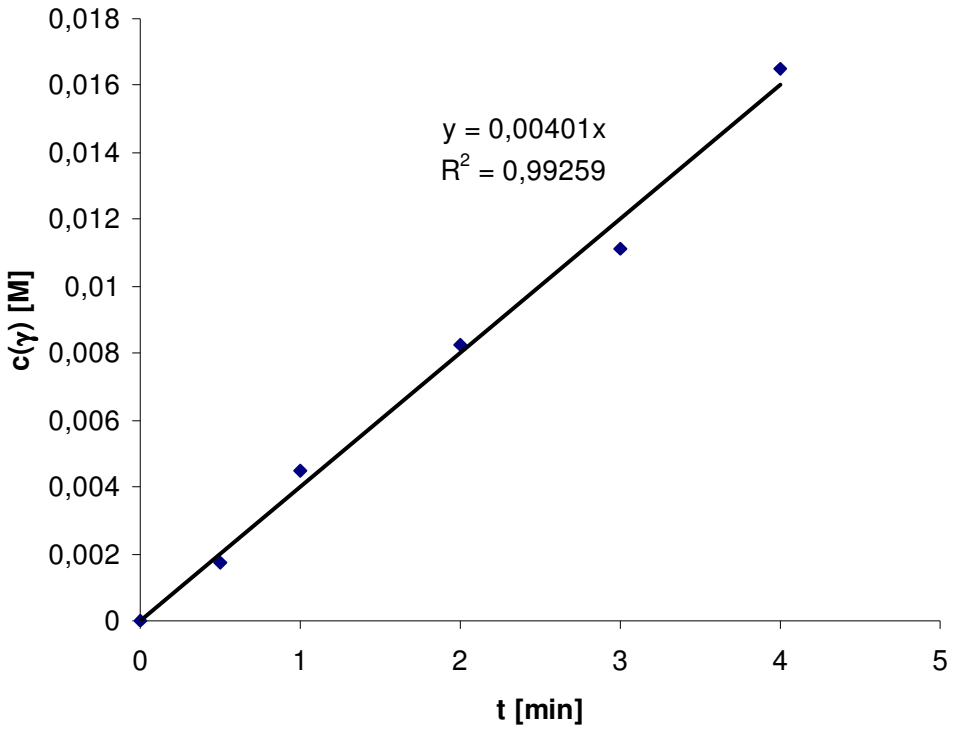
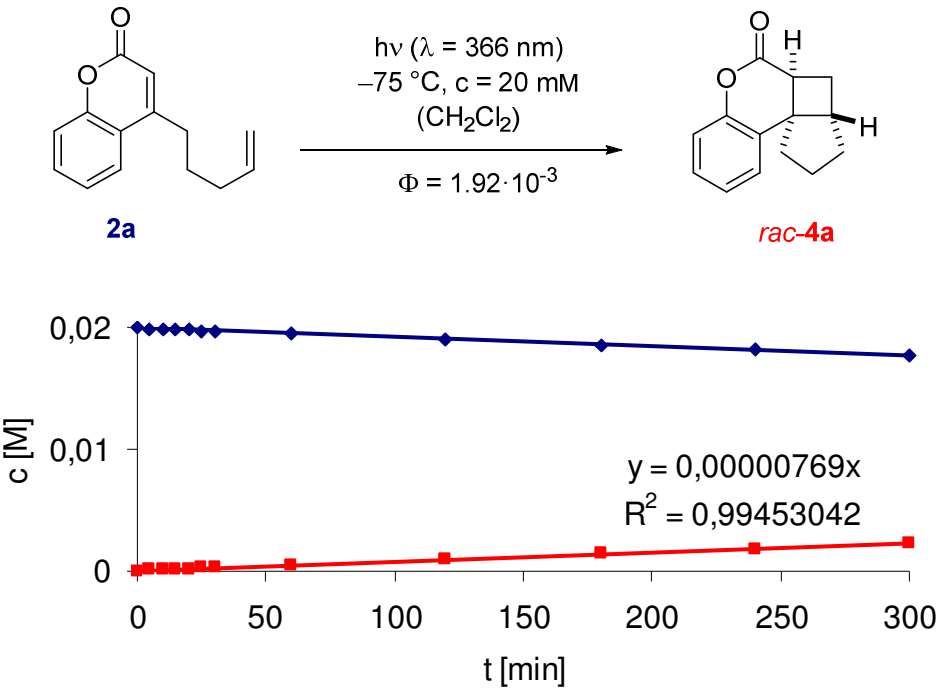


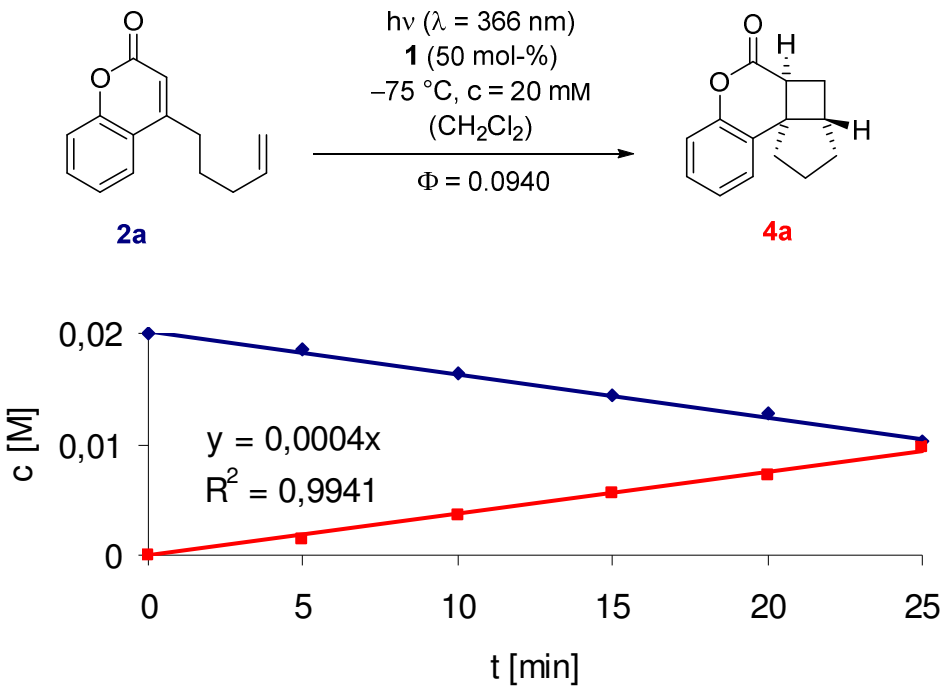
Figure S10. Determination of the photon flux of the equipment used for the photoreactions.

The product formation was determined by performing the photoreaction under the standard conditions for the enantioselective Lewis acid-catalyzed [2+2] photocycloaddition (5 mL reaction volume). For each data point an 100 µL aliquot was diluted with 900 µL dichloromethane and the conversion was determined by GC analysis (dodecane as internal standard). Using the rate constants for the product formation and the time dependent formal photon concentration, the quantum yields of the photoreactions can be estimated.[1] The procedure is valid as long as all photons entering the solution are absorbed. This can be assumed for the Lewis acid-catalyzed [2+2] photocycloadditions (see extinction coefficents of the Lewis acid-substrate complexes in the article). Since the absorption of the substrates in the absence of the Lewis acid is lower at around λ = 366 nm, the calculated quantum yields in these cases are only lower limits. The k value for the first order-reaction of **3a** (see Figure S3) was estimated by assuming zero order-kinetics when the photoreaction was initiated (using the time interval from 0 to 8 min).

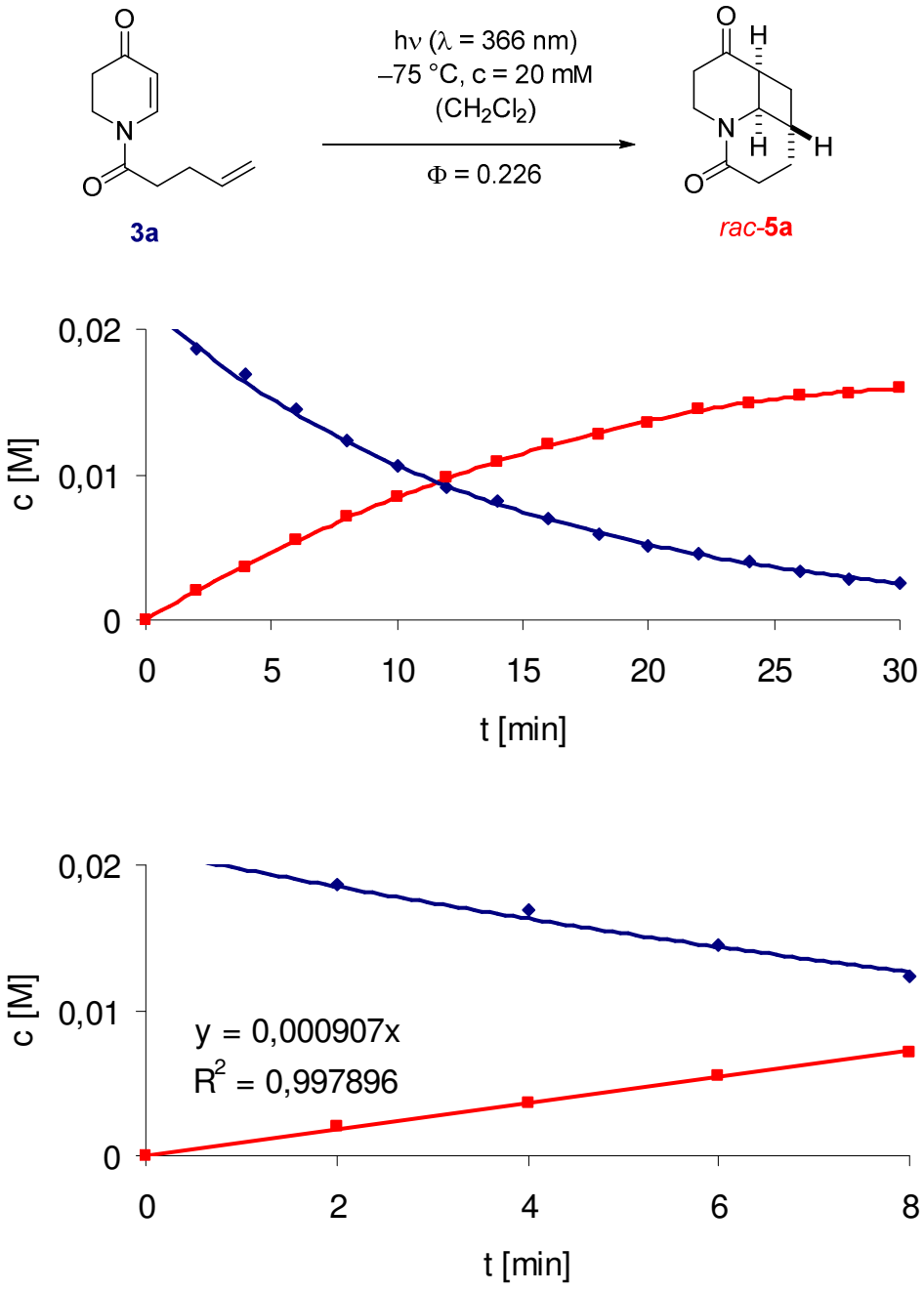


Scheme S1. Product formation of the racemic reaction of **2a**.

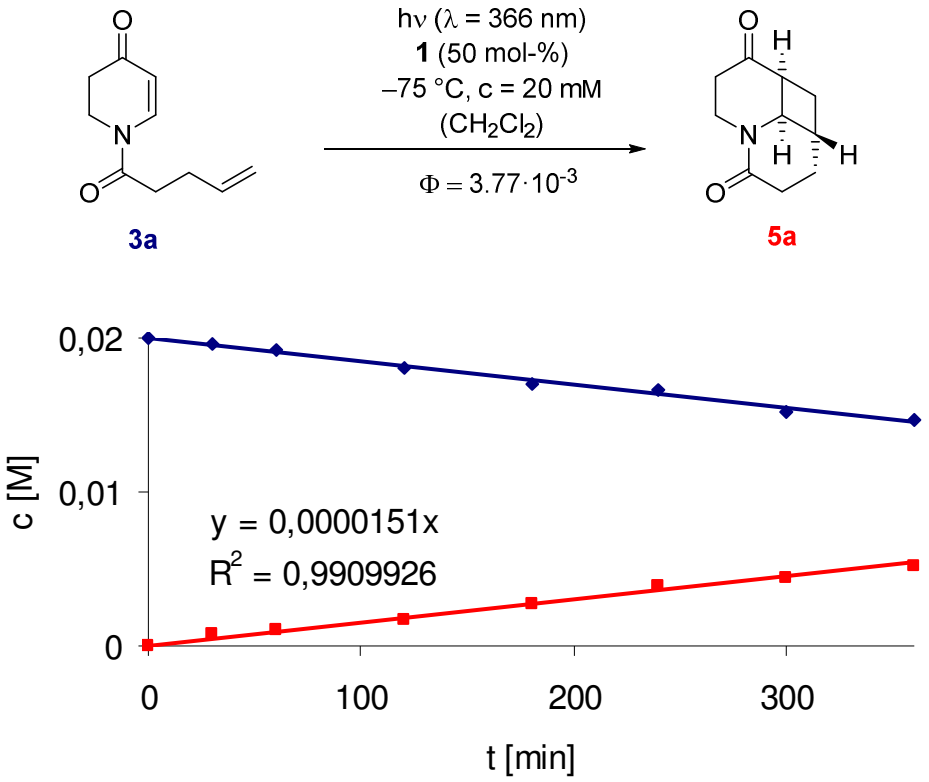
[1] Φ = dn(product)/dn(γ) = dc(product)/dc(γ) = [dc(product)/dt]/[dc(γ)/dt] = k(product)/[dc(γ)/dt]



Scheme S2. Product formation of the enantioselective reaction of **2a**.



Scheme S3. Product formation of the racemic reaction of **3a**.



Scheme S4. Product formation of the enantioselective reaction of **3a**.

3. Investigation of the Substrate-Lewis-Acid Equilibrium

The association of the Lewis-Acid to the dihydropyridone substrate was investigated using UV titration experiments. In our hands, best results are obtained in UV or NMR titration, when the samples are prepared individually from two stock solutions (*vide infra*) rather than diluting one sample further and further.[2] The titration was performed twice to explore the reproducibility in these extremely moisture-sensitive experiments.

A 0.5 mM stock solution of substrate **3** (in the following **A**) containing 10 mM of the Lewis acid $EtAlCl_2$ (**B**) in dichloromethane[3] was added to appropriate amounts of a 0.5 mM solution of the substrate in dichloromethane to give the desired concentrations of **B** in the solution of constant concentration of **A** using microliter syringes (Hamilton, Bonaduz). All samples and stock-solutions where prepared in carefully flame-dried glassware (*Schlenk*-flasks) under Argon atmosphere. The individual samples were transferred from the *Schlenk*-flasks into flow-cuvettes (Hellma-Analytics) as shown in Figure 1. The cuvette and the tubings were rinsed after each titration step using anhydrous dichloromethane and subsequently dried with a stream of dry Argon.

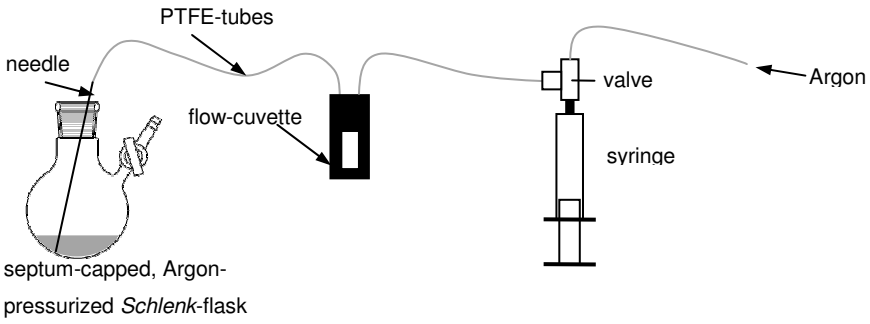


Figure S11: Setup used for the UV-titration under anhydrous conditions.

Although every operation in the described titrations has been done with maximum effort to exclude any exposure of the solutions to water, both titration sets showed a reproducible offset of the expected titration curves at approximately 0.7 mM (see Figure S12). This offset is interpreted as residual water content, leading to the hydrolysis of the Lewis acid. This interpretation was substantiated by Karl-Fischer titration, indicating a water content of the solvent of approximately 5 ppm; additional tiny amounts of water, introduced during the handling with the microliter-syringes, lead to the observed 9.5 ppm (*m*/*m* in dichloromethane).

[2] A detailed description can be found in the Supporting-Information of *Org. Biomol. Chem.* **2011**, *9*, 3516-3529.
[3] Dichloromethane (p.a.) was purified using a MBraun SPS-System and further dried over 4 Å molecular sieves for 5 days

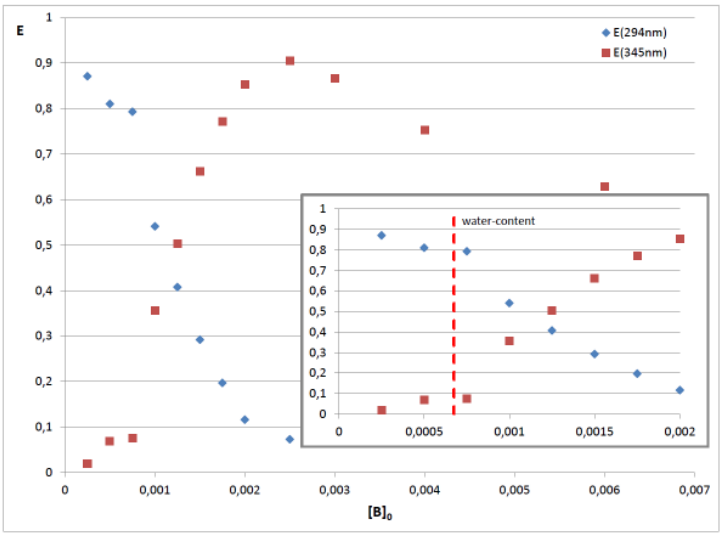
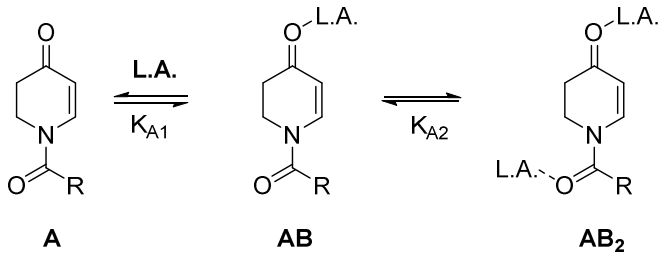


Figure S12: Overview of the full titration set; determination of the residual water content.

In a first attempt, the obtained datasets were analyzed based on the observation that the newly formed absorption band of the complex vanishes upon addition of an increased excess of Lewis acid, suggesting a subsequent 1:2 complex formation with reduced absorbance in the observed spectral window.



Scheme S5: Proposed association equilibrium.

The equations describing the dependence of each concentration as a function of the initial concentrations of substrate ($[\mathbf{A}]_0$), Lewis acid ($[\mathbf{B}]_0$) and the two association constants (K_{A1}, K_{A2}) where solved leading to a cubic equation in $[\mathbf{B}]$[2,3]. Analyzing the titration data based on this assumption using a global least square fit over both datasets gave a best fit for

$$K_{A1}=4424\ \text{Lmol}^{-1} \qquad K_{A2}=163\ \text{Lmol}^{-1}$$

with the absorption coefficients for **A** being known ($\varepsilon_A(294\ \text{nm})=18112\ \text{Lmol}^{-1}\text{cm}^{-1}$, $\varepsilon_A(345\ \text{nm})=0\ \text{Lmol}^{-1}\text{cm}^{-1}$) and the coefficients for the complexes as a result of the fit process ($\varepsilon_{AB}(345\ \text{nm})=22647\ \text{Lmol}^{-1}\text{cm}^{-1}$, $\varepsilon_{AB}(294\ \text{nm})=\varepsilon_{AB2}(294\ \text{nm})=\varepsilon_{AB2}(294\ \text{nm})=0\ \text{Lmol}^{-1}\text{cm}^{-1}$). Attempts to obtain a spectral signature and an estimate for the extinction coefficients of the complex $\mathbf{AB_2}$ failed due to the instability of the solutions at the necessary high concentrations of the Lewis acid ($[\mathbf{B}]_0$>100 mM; *vide infra*). Fitting both sets individually gave only slightly different values (Set 1: $K_{A1}=4519\ \text{Lmol}^{-1}$, $K_{A2}=159\ \text{Lmol}^{-1}$; Set 2: $K_{A1}=4361\ \text{Lmol}^{-1}$, $K_{A2}=165\ \text{Lmol}^{-1}$).

At concentrations of $[\mathbf{B}]_0$>5 mM precipitates were slowly formed at room temperature over time both in the stock solution ($[\mathbf{B}]_0$=10 mM) and the prepared samples. Consequently the obtained values for $[\mathbf{B}]_0$>5 mM have not been taken into account as well as two other pairs of values (one from each titration set) which showed significant deviations **both** in the absorbance at 294 nm and 345 nm, indicating an error in the preparation of the sample (error in the volumes or exposure to moisture).

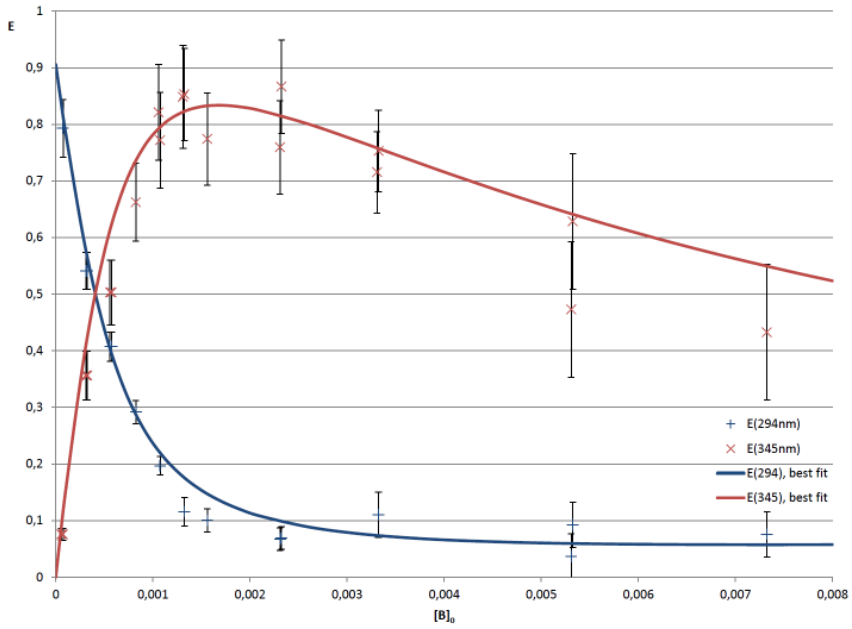


Figure S13: Best-Fit for the simple $\mathbf{AB_2}$-Equilibrium – see Scheme S6.

The stability of the fit was analyzed using a Monte-Carlo approach.[2,4,5] The global fit was repeated 1000 times with datasets, that have been artificially scattered by randomly chosen values (normal distribution) which are derived from the maximum signal residual of the initial nonlinear parameter optimization. The obtained values have been judged by standard statistical methods to give the confidence interval (95% confidence level) for the best fit of the initial dataset.

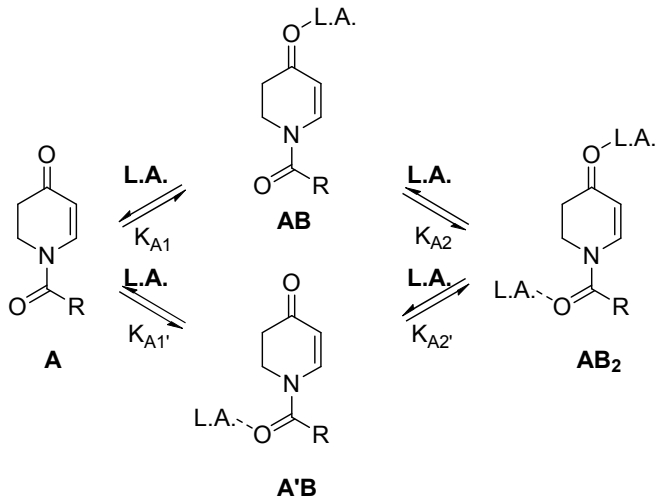
Mean values (Monte-Carlo):	K_{A1}=4472 $Lmol^{-1}$	K_{A2}=174 $Lmol^{-1}$
Confidence-interval:	383 $Lmol^{-1}$	39 $Lmol^{-1}$

Both, the signal residuals of the best fit and the statistical evaluation of the Monte-Carlo analysis show a slight systematic error on the substrate band remains with the assumption of this complex equilibrium (see Scheme S5). Therefore, the alternative order of complexation events was additionally taken into account (see Scheme S6). Solving the stoichiometric

[4] J. S. Alper, R. I. Gelb, *J. Phys. Chem.* **1990**, *94*, 4741-4151.
[5] for a detailed *how-to* see http://www.graphpad.com/manuals/prism4/regressionbook.pdf

equations leads again to a cubic equation in [**B**].[6] Using this equation allows a fit without a systematic error on the substrate band at the price of fitting six to ten parameters.

Analyzing the sensitivity of the fit for all possibly ten parameters (K_{A1}, $K_{A1'}$, K_{A2}, $K_{A2'}$, ε_{AB}(294 nm), ε_{AB}(345 nm), $\varepsilon_{A'B}$(294 nm), $\varepsilon_{A'B}$(345 nm), ε_{AB2}(294 nm), ε_{AB2}(294 nm)) showed, that only K_{A1}, K_{A2} and ε_{AB}(345 nm) influence the outcome of the fit to a significant excess. The parameters $K_{A1'}$, $K_{A2'}$, and $\varepsilon_{A'B}$(345 nm) show a significantly reduced sensitivity and the remaining extinction coefficients (ε_{AB}(294 nm), $\varepsilon_{A'B}$(294 nm), ε_{AB2}(294 nm) and ε_{AB2}(294 nm)) result in all fit attempts in very low values of less than 100 $Lmol^{-1}cm^{-1}$ without any effect on the fit quality.



Scheme 6: Full association equilibrium.

The data was therefore analyzed optimizing the reduced set of parameters giving

K_{A1}=4258 $Lmol^{-1}$ K_{A2}=125 $Lmol^{-1}$

$K_{A1'}$=214 $Lmol^{-1}$ $K_{A2'}$=874 $Lmol^{-1}$

with the absorption coefficients for complexes ε_{AB}(345 nm)=22997 $Lmol^{-1}cm^{-1}$, $\varepsilon_{A'B}$(345 nm)=1500 $Lmol^{-1}cm^{-1}$ and ε_{AB2}(294 nm)=1685 $Lmol^{-1}cm^{-1}$.

The Monte-Carlo analysis gives for the K_{A1} and K_{A2} reasonable error levels with

mean values (Monte-Carlo): K_{A1}=4269 $Lmol^{-1}$ K_{A2}=139 $Lmol^{-1}$

and confidence-intervals: 389 $Lmol^{-1}$ 35 $Lmol^{-1}$

For $K_{A1'}$ and $K_{A2'}$ the errors are massively underestimated in the Monte-Carlo-Analysis due to the lack of sensitivity in the fit-process. Both parameters can be varied by ±75% with effects on the other parameters well within the above given confidence intervals. This massive lack

[6] $(K_{A1}\cdot K_{A2}+K_{A1'}\cdot K_{A2'})\cdot[B]^3 + (2\cdot[A]_0\cdot(K_{A1}\cdot K_{A2}+K_{A1'}\cdot K_{A2'})-[B]_0\cdot(K_{A1}\cdot K_{A2}+K_{A1'}\cdot K_{A2'})+K_{A1}+K_{A1'})\cdot[B]^2 + ([A]_0\cdot(K_{A1}+K_{A1'})-[B]_0\cdot(K_{A1}+K_{A1'})+1)\cdot[B] - [B]_0 = 0$

of precision is obvious from the fact, that these values are a pure result of the nonlinear fit procedure without an underlying spectral signature assigned to the respective species.

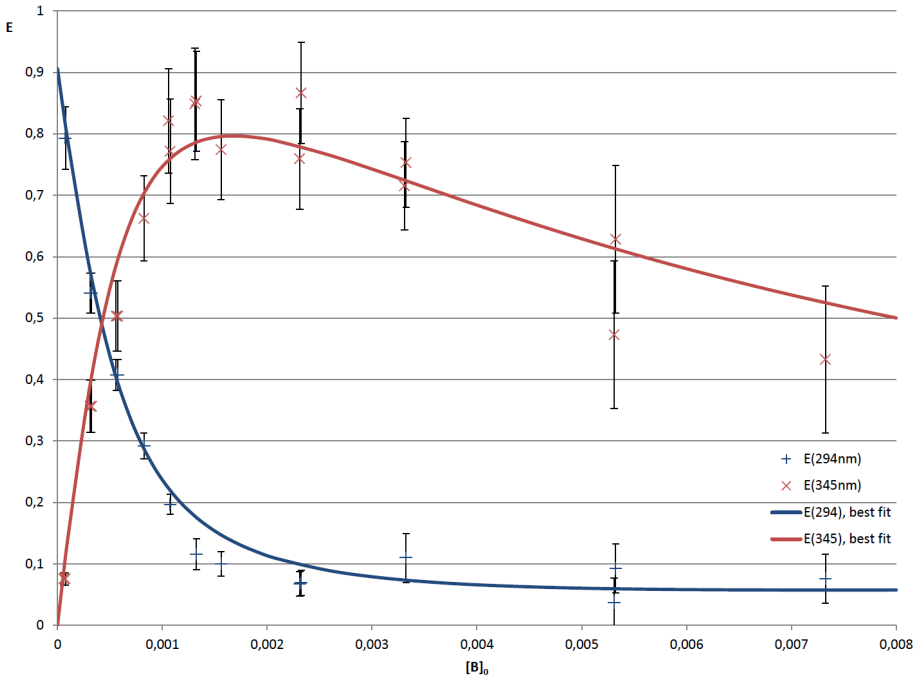


Figure S14: Best fit for the full **AB_2**-Equlibrium – see Scheme S6

Using the full association equilibrium, the analysis was repeated for the full spectral range obtained in this titration (250-400 nm). Spectral signatures $\varepsilon_{AB}(\lambda)$, $\varepsilon_{A'B}(\lambda)$ and $\varepsilon_{AB2}(\lambda)$ can be suggested by iteratively optimizing the spectra and the equilibrium constants. For spectrum of the complex a self-consistent solution is obtained which reproduces the absorption coefficient obtained during the single line fit at 394 nm. The spectra of **A'B** and **AB_2** have again massive uncertainties (no stable self-consistent solution) due to the described problems. Association constants derived from the full spectral range are:

K_{A1}=4658 $Lmol^{-1}$ K_{A2}=155 $Lmol^{-1}$

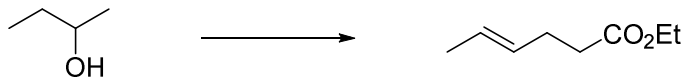
$K_{A1'}$=124 $Lmol^{-1}$ $K_{A2'}$=830 $Lmol^{-1}$

The uncertainty of $K_{A1'}$ and $K_{A2'}$ which depends now also on the optimized spectral signature $\varepsilon_{A'B}(\lambda)$ leads now in turn to a larger uncertainty of the equilibrium constants of the dominating equilibrium (K_{A1} and K_{A2}) delivering values spread over the whole confidence interval of the above described approaches with only slight differences in the fit quality. A full Monte-Carlo analysis of this approach was not performed but the errors can be estimated to be significantly larger than in the *classical* approach using the absorbances at the absorption maxima.

Summary: The analysis of two attempts to determine the equilibrium constants for the association of the Lewis acid $EtAlCl_2$ to the dihydropyridone substrate is possible using the absorbance at the absorption maxima of the substrate (294 nm) and the formed complex (345 nm). As a result, a dominating coordination was found with moderate precision (±10%) which was assigned to a coordination of the Lewis acid to the carbonyl oxygen of the ketone (see NMR studies described in the article). The best fit for the respective association constant was found to be in the range of 4300-4400 $Lmol^{-1}$. A subsequent coordination event leads to a decrease in the absorption at the complex band and was assigned to a second association step (complexation of the amide carbonyl group). The association constant of this equilibrium was determined to be in the range of 150 $Lmol^{-1}$ with an uncertainty of close to 25%. More accurate values cannot be obtained for this equilibrium due to the instability of titration samples with high excess of Lewis acid. The titration data has been tested towards a complexation of the Lewis acid to the substrates amide carbonyl moiety (prior to the complexation of the substrates ketone carbonyl moiety). The analysis suggests in a conclusive way for the inverse order of complexation events the inverse order of association constants with best fits for $K_{A1'}\approx200$ $Lmol^{-1}$ and $K_{A2'}\approx900$ $Lmol^{-1}$, both with very large uncertainties of at least ±75% due to the lack of a corresponding spectral signature in the observed spectral window.

4. Synthetic Procedures and Analytical Data

(*E*)-Ethyl hex-4-enoate



$C_8H_{14}O_2$
MW = 142.20

To a solution of 2.16 g of butan-2-ol (30.0 mmol, 1.0 eq.) in 16.4 mL triethyl orthoacetate (14.6 g, 90.0 mmol, 3.0 eq.) 20 µL acetic acid was added. The reaction mixture was stirred at 135 °C for 18 hours, cooled to room temperature and diluted with 60 mL pentane. 60 mL Water was added and the biphasic mixture was vigorously stirred for three days. The layers were separated and the aqueous layer was extracted three times with 80 mL pentane. The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed was carefully removed with reduced pressure. The volatile ester was obtained as slightly yellow liquid in 52% yield (2.33 g, 16.4 mmol).

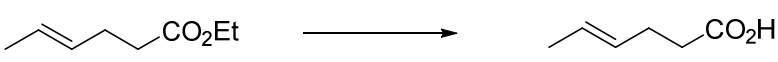
TLC: R_f = 0.88 (P:EE = 9:1, [$KMnO_4$]).

^{1}H-NMR (360 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.25 (t, ^3J = 7.1 Hz, 3H, C*H*$_3$CH$_2$), 1.64 (d, ^3J = 4.8 Hz, 3H, C*H*$_3$CH=CH), 2.20-2.50 (m, 4H, CH$_2$C*H*$_2$), 4.12 (q, ^{3}J = 7.1 Hz, 2H, CH$_3$C*H*$_2$), 5.30-5.60 (m, 2H, C*H*=C*H*).

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.3 (q, *C*H$_3$CH$_2$), 17.9 (q, *C*H$_3$CH=CH), 27.9 (t, *C*H$_2$CH$_2$CO), 34.4 (t, CH$_2$*C*H$_2$CO), 60.2 (t, CH$_3$*C*H$_2$), 126.1 (d, CH$_3$*C*H=CH), 129.2 (d, CH$_3$CH=*C*H), 173.3 (s, CO).

The data obtained matched those reported in the literature.[1]

(*E*)-Hex-4-enoic acid



$C_6H_{10}O_2$
MW = 114.14

To a solution of 2.30 g (*E*)-Ethyl hex-4-enoic ester (16.2 mmol, 1.0 eq.) in 15 mL methanol and 15 mL water was added 3.40 g lithium hydroxide monohydrate (81.0 mmol, 5.0 eq.) and the mixture was stirred for 40 hours at room temperature. The mixture was acidified with concentrated HCl solution (pH = 1) and was extracted three times with 30 mL dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography

(P:EE = 4:1 / 0:1) to afford the volatile title compound as colourless liquid in 79% yield (1.46 g, 12.8 mmol).

TLC: R_f = 0.32 (P:EE = 4:1, [$KMnO_4$]).

^{1}H-NMR (360 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.65 (dd, ^3J = 5.9 Hz, ^4J = 1.2 Hz, 3H, CH_3), 2.25-2.36 (m, 2H, C$H_2$$CH_2$CO), 2.36-2.45 (m, 2H, CH_2CH_2CO), 5.35-5.57 (m, 2H, CH=CH).

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 17.9 (q, *C*H_3CH=CH), 27.5 (t, *C*$H_2$$CH_2$CO), 34.0 (t, CH_2*C*H_2CO), 125.1 (d, CH_3*C*H=CH), 128.8 (d, CH_3CH=*C*H), 179.2 (s, CO).

The data obtained matched those reported in the literature.[2]

4-Hexynoic acid

5.00 g 5-Hexynoic acid (44.6 mmol, 1.0 eq.) was dissolved in 50 mL water and 42.0 g potassium hydroxide (749 mmol, 60 eq.) was added and the mixture was stirred at 170 °C for three hours. After cooling to room temperature and then to 0 °C, the solution was acidified with concentrated HCl solution to a pH value of 12 and the solution was extracted three times with 50 mL dichloromethane. The aqueous layer was acidified with concentrated HCl solution to a pH value of 1 (crystallization of the product starts) and extracted three times with 60 mL dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (P:EE = 9:1 / 0:1) to afford the title compound as colourless, crystalline solid in 93% yield (4.63 g, 41.3 mmol).

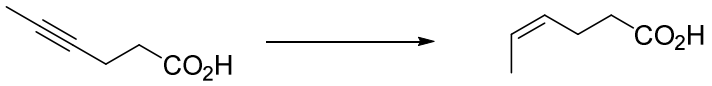
TLC: R_f = 0.43 (P:EE = 4:1, [$KMnO_4$]).

^{1}H-NMR (360 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.77 (t, ^5J = 2.5 Hz, 3H, CH_3), 2.40-2.53 (m, 2H, $CCCH_2$), 2.53-2.63 (m, 2H, $CCCH_2C$*H*$_2$).

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 3.41 (q, CH_3), 14.4 (t, CC*C*H_2), 33.7 (*C*H_2CO), 76.6 (s, CC), 76.9 (s, CC), 178.3 (s, CO).

The data obtained matched those reported in the literature.[3]

(*Z*)-Hex-4-enoic acid



$C_6H_{10}O_2$
MW = 114.14

To a solution of 2.00 g Hex-4-ynoic acid (17.8 mmol, 1.0 eq.) in 20 mL ethyl acetate, 4.23 mL quinoline (4.61 g, 35.7 mmol, 2.0 eq.) and 200 mg palladium on calcium carbonate (*Lindlar*-catalyst, 5 mass-% palladium) were added. The reaction vessel was carefully evacuated and flushed with hydrogen. The procedure was repeated twice and the suspension was vigorously stirred at room temperature for six hours with a hydrogen atmosphere. The suspension was filtered over a short pad of celite, washed with 80 mL ethyl acetate and the solution was washed three times with 50 mL 1 N NaOH solution. The combined aqueous layer were acidified with concentrated HCl solution (pH = 1) and extracted four times with 100 mL dichloromethane. The combined organic layers were dried over Na2SO4, filtered and the solvent was removed *in vacuo*. The residue was purified by column chromatography (P:EE = 9:1 / 0:1) to afford the title compound as slightly yellow liquid in 99% yield (2.00 g, 17.6 mmol).

TLC: R_f = 0.38 (P:EE = 4:1, [$KMnO_4$]).

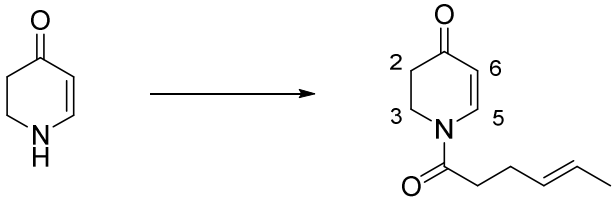
IR (ATR): $\tilde{\nu}$ = 3220 cm^{-1} (w, OH), 3018 (w, $CH{=}CH_2$), 2960 (w, sp^3-CH_2), 2922 (w, sp^3-CH_2), 2874 (sp^3-CH), 1705 (m, $CH{=}CH_2$).

^{1}H-NMR (360 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.64 (d, ^3J = 8.0 Hz, 3H, CH_3), 2.29-2.50 (m, 4H, CH_2CH_2), 5.30-5.65 (m, 2H, CH=CH).

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 12.7 (q, CH_3), 22.2 (t, $COCH_2CH_2$), 33.9 (t, $COCH_2$), 125.7 (d, $CH_3CH{=}CH$), 127.9 (d, $CH_3CH{=}CH$), 179.3 (s, CO_2H).

MS (EI, 70 eV): *m/z* (%) = 114 (67) $[M]^+$, 68 (58) $[C_5H_8]^+$, 55 (100) $[C_4H_7]^+$.

(*E*)-1-(Hex-4-enoyl)-2,3-dihydropyridin-4(1*H*)-one



$C_{11}H_{15}NO_2$
MW = 193.25

Formation of the carboxylic chloride:

To a solution of 543 mg of (*E*)-hex-4-enoic acid (4.76 mmol, 1.1 eq.) in 9 mL dry tetrahydrofuran three drops of dry *N*,*N*-dimethylformamide and 449 µL oxalyl dichloride (665 mg, 5.24 mmol, 1.2 eq.) were added. The solution was stirred for four hours at room temperature and was used for the next step without work-up or purification.

Acylation of 4-dihydropyridone:

1.00 g Benzyl 4-oxo-3,4-dihydropyridine-1(2*H*)-carboxylate (4.32 mmol, 1.0 eq.) was dissolved in 9 mL dry tetrahydrofuran and 100 mg palladium on charcoal (10 mass-% palladium) were added. The reaction vessel was carefully evacuated and flushed with hydrogen and the procedure was repeated twice. The suspension was stirred for two hours at room temperature in a hydrogen atmosphere until complete conversion was achieved (TLC control). The vessel was carefully evacuated and flushed with argon. 1.80 mL Triethylamine (1.32 g, 13.0 mmol, 3.0 eq.) and 52.8 mg *N*,*N*-dimethylaminopyridine (0.432 mmol, 0.1 eq.) were added and the mixture was cooled to 0 °C. The carboxylic chloride solution was added dropwise within 10 minutes and the mixture was allowed to warm to room temperature within 16 hours. The suspension was filtered over a short pad of celite, the pad was washed with 70 mL ethyl acetate, washed with 50 mL 1 N HCl solution and with 50 mL saturated $NaHCO_3$ solution. The organic layer was dried over Na_2SO_4, filtered and the solvent was removed *in vacuo*. The residue was purified by column chromatography (P:EE = 1:1) to afford the title compound as slightly yellow oil in 69% yield (576 mg, 2.98 mmol).

TLC: R_f = 0.09 (P:EE = 4:1, [UV], [$KMnO_4$]).

IR (ATR): $\tilde{\nu}$ = 3071 cm^{-1} (w, sp_2-CH), 2916 (w, sp^3-CH_2), 2855 (w, sp^3-CH_2), 1689 (m, $CH=CH_2$), 1662 (s, $CONR_2$), 1591 (s, sp^2-CH), 1292 (s), 1174 (s), 966 (w, $CH=CH_2$).

^{1}H-NMR (360 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.65 (d, ^3J = 5.7 Hz, 3H, CH_3), 2.39 (td, ^3J = 4.1 Hz, ^3J = 8.0 Hz, 2H, $COCH_2CH_2$), 2.50-2.70 (m, 4H, H-2, $COCH_2$), 4.07 (br s, 2H, H-3*), 5.37 (br s, 1H, H-6*), 5.35-5.65 (m, 2H, $CH=CH(CH_3)$), 7.43-8.30 (m, 1H, H-5*).

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 17.8 (q, CH_3), 27.6 (t, $COCH_2CH_2$), 33.4 (t, $COCH_2CH_2$), 35.8 (t, C-2), 40.6 (t, C-3), 107.6 (d, C-6*), 126.9 (d, $CH=CH(CH_3)$), 128.7 (d, $CH=CH(CH_3)$), 142.3 (d, C-5), 171.0 (s, CON), 193.3 (s, C-1).

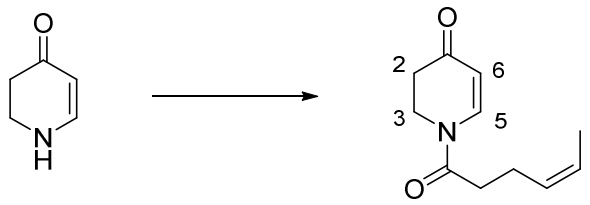
* signal broadening due to coalescence

MS (EI, 70 eV): *m/z* (%) = 193 (26) $[M]^+$, 178 (43) $[M-CH_3]^+$, 141 (18), 97 (76) $[C_6H_9O]^+$, 69 (100) $[C_5H_9]^+$, 55 (58) $[C_4H_7]^+$, 41 (37) $[C_3H_5]^+$.

HRMS (EI, 70 eV): cal. ($C_{11}H_{15}O_2N$): 193.1097; fnd.: 193.1090

cal. ($C_{10}{}^{13}CH_{15}O_2N$): 194.1131; fnd.: 194.1131.

(*Z*)-1-(Hex-4-enoyl)-2,3-dihydropyridin-4(1*H*)-one



$C_{11}H_{15}NO_2$
MW = 193.25

Formation of the carboxylic chloride:

To a solution of 543 mg of (*Z*)-hex-4-enoic acid (4.76 mmol, 1.1 eq.) in 9 mL dry tetrahydrofuran three drops of dry *N*,*N*-dimethylformamide and 449 µL oxalyl dichloride (665 mg, 5.24 mmol, 1.2 eq.) were added. The solution was stirred for four hours at room temperature and was used for the next step without work-up or purification.

Acylation of 4-dihydropyridone:

1.00 g Benzyl 4-oxo-3,4-dihydropyridine-1(2*H*)-carboxylate (4.32 mmol, 1.0 eq.) were dissolved in 9 mL dry tetrahydrofuran and 100 mg palladium on charcoal (10 mass-% palladium) were added. The reaction vessel was carefully evacuated and flushed with hydrogen and the procedure was repeated twice. The suspension was stirred for two hours at room temperature in a hydrogen atmosphere until complete conversion was achieved (TLC control). The vessel was carefully evacuated and flushed with argon. 1.80 mL Triethylamine (1.32 g, 13.0 mmol, 3.0 eq.) and 52.8 mg *N*,*N*-dimethylaminopyridine (0.432 mmol, 0.1 eq.) were added and the mixture was cooled to 0 °C. The carboxylic chloride solution was added dropwise within 10 minutes and the mixture was allowed to warm to room temperature within 16 hours. The suspension was filtered over a short pad of celite, the pad was washed with 70 mL ethyl acetate, washed with 50 mL 1 N HCl solution and with 50 mL saturated $NaHCO_3$ solution. The organic layer was dried over Na_2SO_4, filtered and the solvent was removed *in vacuo*. The residue was purified by column chromatography (P:EE = 1:1) to afford the title compound as slightly yellow oil in 59% yield (493 mg, 2.55 mmol).

TLC: R_f = 0.08 (P:EE = 4:1, [UV], [$KMnO_4$]).

IR (ATR): $\tilde{\nu}$ = 3014 cm^{-1} (w, sp_2-CH), 2956 (w, sp^3-CH_2), 2918 (w, sp^3-CH_2), 2870 (w, sp^3-CH_2), 1689 (m, CH=CH_2), 1662 (s, $CONR_2$), 1591 (s, sp^2-CH), 1293 (s), 1174 (s).

^{1}H-NMR (360 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.65 (d, ^3J = 6.7 Hz, 3H, CH_3), 2.46 (*virt.* q, $^3J \approx$ 7.3 Hz, 2H, $COCH_2CH_2$), 2.50-2.64 (m, 4H, H-2, $COCH_2$), 4.07 (br s, 2H, H-3*), 5.24-5.66 (m, 2H, H-6*, C*H*=C*H*(CH_3)), 7.42-8.30 (m, 1H, H-5*).

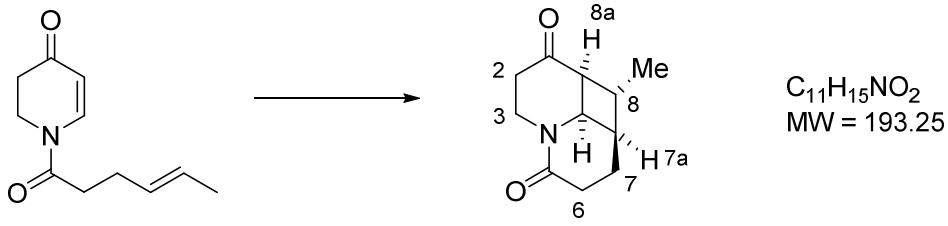
^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 12.7 (q, CH_3), 22.1 (t, $COCH_2CH_2$), 31.3 (t, $COCH_2CH_2$), 35.8 (t, C-2), 50.3 (t, C-3), 107.9 (d, C-6*), 126.0 (d, $CH=CH(CH_3)$), 127.7 (d, $CH=CH(CH_3)$), 142.3 (d, C-5), 171.1 (s, CON), 193.4 (s, C-1).

* signal broadening due to coalescence

MS (EI, 70 eV): *m/z* (%) = 193 (20) $[M]^+$, 178 (38) $[M-CH_3]^+$, 97 (100) $[C_6H_9O]^+$, 69 (89) $[C_5H_9]^+$, 55 (39) $[C_4H_7]^+$, 41 (36) $[C_3H_5]^+$.

HRMS (EI, 70 eV): cal. ($C_{11}H_{15}O_2N$): 193.1097; fnd.: 193.1091

(4^1*R*,7a*R*,8*R*,8a*S*)-8-Methyloctahydro-1*H*,5*H*-cyclobuta[ij]qhinolizin-1,5-dione

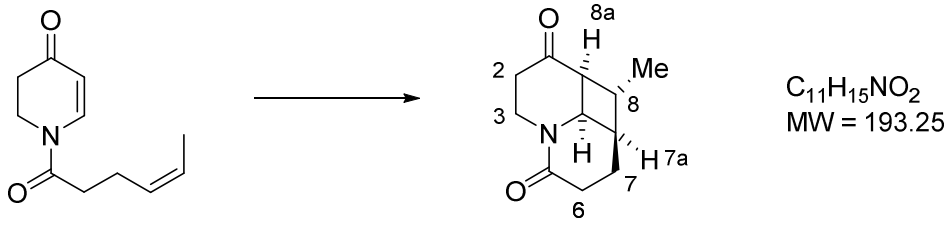


Racemic [2+2] photocycloaddition:

19.3 mg of dihydropyridone **3c** (0.100 mmol, 1.0 eq.) was dissolved in 10 mL dichloromethane and irradiated for 15 minutes at λ = 300 nm at room temperature. The solvent was evaporated and the residue purified by column chromatography to afford the photocycloaddition product **5c** in 71% yield (13.8 mg, 71.3 µmol) as colourless oil.

Enantioselective [2+2] photocycloaddition:

To a solution of 19.3 mg of irradiation precursor **3c** (0.100 mmol, 1.0 eq.) in 1.5 mL dry, degassed dichloromethane was added a solution of the activated oxazaborolidine ### (50.0 µmol, 0.5 eq.) in 1.5 mL dichloromethane and the catalyst vessel was washed twice with 1 mL dichloromethane and this solution added to the irradiation tube. The solution was cooled to −75 °C for 30 minutes and irradiated at λ = 366 nm for 20 hours. The solution was diluted with 15 mL dichloromethane, washed with 20 mL saturated NH_4Cl solution and the aqueous layer is extracted three times with 20 mL dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed in vacuo. The residue was purified by column chromatography (EE) to afford the title compound as colourless oil in 71% yield (13.7 mg, 70.9 µmol, 53% *ee*) and the starting material **5c** as slightly yellow oil in 16% yield (3.2 mg, 16.3 µmol).



$C_{11}H_{15}NO_2$
MW = 193.25

Racemic [2+2] photocycloaddition:

19.3 mg of dihydropyridone **3b** (0.100 mmol, 1.0 eq.) was dissolved in 10 mL dichloromethane and irradiated for 15 minutes at λ = 300 nm at room temperature. The solvent was evaporated and the residue purified by column chromatography to afford the photocycloaddition product **5c** in 62% yield (12.1 mg, 62.4 µmol) as colourless oil.

Enantioselective [2+2] photocycloaddition:

To a solution of 19.3 mg of irradiation precursor **3b** (0.100 mmol, 1.0 eq.) in 1.5 mL dry, degassed dichloromethane was added a solution of the activated oxazaborolidine ### (50.0 µmol, 0.5 eq.) in 1.5 mL dichloromethane and the catalyst vessel was washed twice with 1 mL dichloromethane and this solution added to the irradiation tube. The solution was cooled to −75 °C for 30 minutes and irradiated at λ = 366 nm for 20 hours. The solution was diluted with 15 mL dichloromethane, washed with 20 mL saturated NH_4Cl solution and the aqueous layer is extracted three times with 20 mL dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed in vacuo. The residue was purified by column chromatography (EE) to afford the title compound as colourless oil in 76% yield (14.8 mg, 76.4 µmol, 87% *ee*).

TLC: R_f = 0.17 (EE, [$KMnO_4$]).

IR (ATR): $\tilde{\nu}$ = 3077 cm^{-1} (w, sp^3-CH_2), 3014 (w, sp^3-CH_2), 2925 (w, sp^3-CH_2), 2870 (w, sp^3-CH_2), 1661 (s, CO), 1591 (s, $CONR_2$), 1294, 1175.

^{1}H-NMR (360 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.21 (d, ^3J = 6.5 Hz, 3H, CH_3), 1.66 (ddt, ^2J = 13.7 Hz, ^3J = 10.8 Hz, ^3J ≈ 6.1 Hz, 1H, H-7α*), 2.15 (*virt.* tdd, ^2J ≈ ^3J ≈ 8.4 Hz, ^3J = 6.1 Hz, ^3J = 4.3 Hz, 1H, H-7β*), 2.18-2.28 (m, 1H, H-6α**), 2.35-2.50 (m, 4H, H-2α, H-6β**, H-7a, H-8), 2.56 (dd, ^3J = 8.5 Hz, ^3J = 4.7 Hz, 1H, H-8a), 2.62 (ddd, ^2J = 17.1 Hz, ^3J = 12.7 Hz, ^3J = 6.6 Hz, 1H, H-2β), 2.79 (*virt.* td, ^2J ≈ ^3J ≈ 13.3 Hz, ^3J = 3.4, 1H, H-3β), 4.08 (*virt.* t, ^3J ≈ 6.1 Hz, 1H, H-4[1]), 4.84 (ddd, ^2J = 13.4 Hz, ^3J = 6.6 Hz, ^3J = 1.9 Hz, 1H, H-3α).

* / ** assignment is interconvertible.

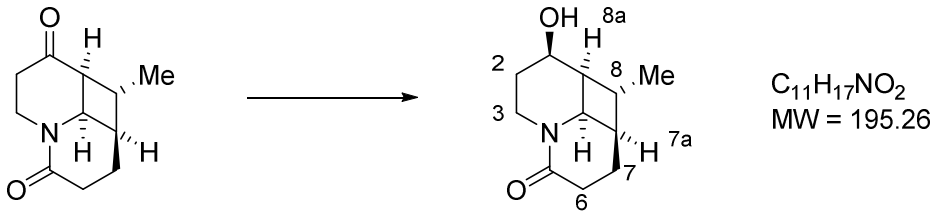
^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 19.8 (q, CH_3), 24.4 (t, C-7), 30.8 (t, C-6), 38.0 (t, C-3), 38.2 (d, C-7a), 38.6 (t, C-3), 42.8 (d, C-8), 49.7 (d, C-8a), 51.8 (d, C-4[1]), 171.1 (s, CON), 207.4 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 193 (42) $[M]^+$, 124 (31) $[M-C_5H_9]^+$, 110 (18) $[M-C_5H_9O]^+$, 98 (65) $[C_5H_8NO]^+$, 97 (100) $[C_5H_7NO]^+$, 82 (31) $[C_5H_8N]^+$, 69 (53) $[C_5H_9]^+$, 55 (18) $[C_4H_7]^+$, 44 (67) $[C_3H_7]^+$.

HRMS (EI, 70 eV): ber. ($C_{11}H_{15}O_2N$): 193.1097; gef.: 193.1095
ber. ($C_{10}{}^{13}CH_{15}O_2N$): 194.1131; gef.: 194.1121.

Specific Rotation: $[\alpha]_D^{20}$ = +128 (*c* = 0.25, CH_2Cl_2) [87% *ee*].

(1*R*,4[1]*R*,7a*R*,8*R*,8a*S*)-1-Hydroxy-8-methyloctahydro-1*H*,5*H*-cyclobuta[ij]quinolizin-5-one



4.35 mg sodium borohydride (0.115 mmol, 1.5 eq.) was cooled to −78 °C and 1 mL dry methanol was added. After stirring for five minutes, a solution of 14.8 mg of cyclobutane **5c** (76.6 µmol, 1.0 eq.) in 1 mL dry methanol was added dropwise and the mixture was allowed to warm to room temperature within 16 hours. The reaction was quenched by addition of 15 mL saturated NH_4Cl solution, stirred for 30 minutes and extracted three times with 20 mL dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed *in vacuo*. Thus, the alcohol was obtained without further purification in quantitative yield (15.0 mg, 76.6 µmol, 87% *ee*) as colourless oil.

TLC: R_f = 0.07 (EE, [$KMnO_4$]).

IR (ATR): $\tilde{\nu}$ = 3278 cm^{-1} (br, OH), 2946 (m, sp^3-CH_2), 2926 (m, sp^3-CH_2), 2865 (w, sp^3-CH_2), 1615 (s, $CONR_2$), 1452 (sp^3-CH_2), 1065 (m, sec-OH).

^{1}H-NMR (360 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.15 (d, ^3J = 6.2 Hz, 3H, CH_3), 1.45-1.60 (m, 2H, H-7α, H-6α*), 1.85-1.93 (m, 1H, H-7β), 2.03 (*virt.* td, $^2J \approx {}^3J \approx$ 14.2 Hz, ^{3}J = 5.1 Hz, 1H, H-2α), 2.08-2.17 (m, 2H, H-6β*, H-7a), 2.17-2.27 (m, 2H, H-8, H-8a), 2.29 (dd, ^2J = 13.4 Hz,

^3J = 1.6 Hz, 1H, H-3β), 2.33 (*virt.* ddt, ^2J = 9.3 Hz, ^3J = 4.4 Hz, $^3J \approx {}^4J \approx$ 2.3 Hz, 1H, H-2β), 3.78 (*virt.* t, $^3J \approx$ 5.5 Hz, 1H, H-4[1]), 3.89 (*virt.* dt, ^3J = 11.6 Hz, $^3J \approx$ 5.6 Hz, 1H, H-1), 4.58 (*virt.* dt, ^2J = 13.4 Hz, $^3J \approx$ 3.5 Hz, 1H, H-3α).

* assignment is interconvertible.

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 20.6 (q, CH3), 25.3 (t, C-6), 30.9 (t, C-7), 31.8 (t, C-2), 37.4 (t, C-3), 37.7 (d, C-7a), 38.0 (t, C-8), 42.9 (d, C-8a), 51.2 (d, C-4[1]), 67.4 (d, C-1), 172.2 (s, CON).

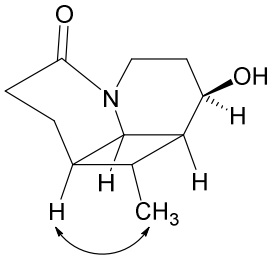
MS (EI, 70 eV): *m/z* (%) = 195 (56) $[M]^+$, 125 (29) $[M-C_5H_{10}]^+$, 110 (65) $[M-C_4H_7O]^+$, 98 (100) $[C_5H_8NO]^+$, 97 (55) $[C_5H_7NO]^+$, 82 (50) $[C_5H_8N]^+$, 69 (28), 55 (19) $[C_4H_7]^+$, 41 (27) $[C_3H_5]^+$.

HRMS (EI, 70 eV): ber. ($C_{11}H_{17}O_2N$): 195.1254; gef.: 195.1253

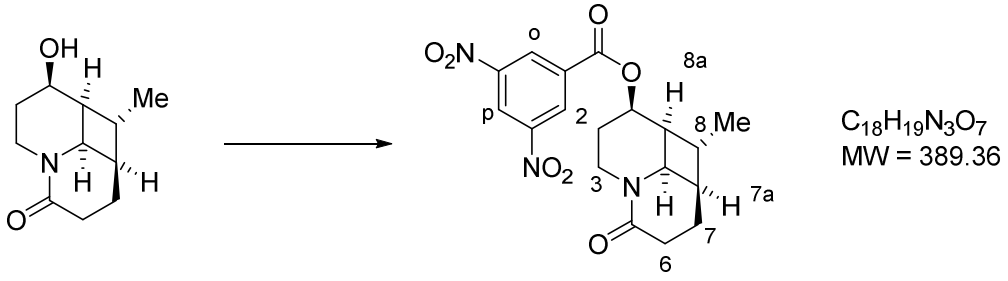
ber. ($C_{10}{}^{13}CH_{17}O_2N$): 196.1287; gef.: 196.1280.

Specific Rotation: $[\alpha]_D{}^{20}$ = +92.4 (*c* = 0.25, CH_2Cl_2) [87% *ee*].

Important NOE contacts:



(1*R*,4[1]*R*,7a*R*,8*R*,8a*S*)-8-Methyl-5-oxooctahydro-1*H*,5*H*-cyclobuta[ij]quinolizin-1-yl-3,5-dinitrobenzoate



A solution of 15.0 mg (1*R*,4[1]*R*,7a*R*,8*R*,8a*S*)-1-hydroxy-8-methyloctahydro-1*H*,5*H*-cyclobuta[ij]quinolizin-5-one (76.6 µmol, 1.0 eq.) was dissolved in 1 mL dry dichloromethane and 9.28 µL pyridine (9.09 mg, 0.115 mmol, 1.5 eq.) and 26.5 mg 3,5-dinitrobenzoyl chloride (0.115 mmol, 1.5 eq.) was added. The mixture was stirred for four hours, the solvent was evaporated and the residue was directly purified by column

chromatography (EE) to afford the title compound as colourless, very viscous oil in 78% yield (23.3 mg, 59.8 μmol, 87% *ee*).

TLC: R_f = 0.38 (EE, [UV]).

IR (ATR): $\tilde{\nu}$ = 3091 cm^{-1} (m, sp^2-CH), 2957 (m, sp^3-CH_2), 2923 (m, sp^3-CH_2), 2868 (m, sp^3-CH_2), 1730 (s, CO_2R), 1652 (s, $CONR_2$), 1636 (m, NO_2), 1541 (s, sp^2-CH), 1457 (m, sp^3-CH_2), 1343 (s, NO_2)

^{1}H-NMR (360 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.11 (d, ^3J = 6.1 Hz, 3H, CH_3), 1.63 (*virt.* tt, $^2J \approx {}^3J \approx$ 12.8 Hz, $^3J \approx$ 4.9 Hz, 1H, H-7α), 1.89 (*virt.* tdd, $^2J \approx {}^3J \approx$ 12.7 Hz, ^3J = 11.4 Hz, ^3J = 3.9 Hz, 1H, H-2α*), 2.05-2.31 (m, 4H, H-2β*, H-6α**, H7β, H-7a), 2.40 (ddd, ^2J = 14.9 Hz, ^3J = 4.6 Hz, ^3J = 2.6 Hz, 1H, H-6β**), 2.42-2.55 (m, 3H, H-3β, H-8, H-8a), 3.94 (*virt.* t, $^3J \approx$ 5.6 Hz, 1H, H-4^1), 4.74 (*virt.* dt, ^2J = 13.8 Hz, $^3J \approx$ 3.6 Hz, 1H, H-3α), 5.29 (*virt.* dt, ^3J = 11.7 Hz, $^3J \approx$ 5.9 Hz, 1H, H-1), 9.11 (d, ^4J = 2.1 Hz, 2H, H-o), 9.23 (t, ^4J = 2.1 Hz, 1H, H-p).

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 20.1 (q, CH3), 25.1 (t, C-7), 27.5 (t, C-2), 31.6 (t, C-6), 36.9 (t, C-3), 38.0 (d, C-7a), 38.1 (d, C-8$^{***)}$, 39.7 (d, C-8a***), 51.3 (d, C-4^1), 72.7 (d, C-1), 122.5 (d, C-p), 129.3 (d, C-o), 133.8 (s, *C*-CO), 148.8 (s, *C*-NO_2), 161.9 (s, C-*C*O), 171.8 (s, CON).

* / **/*** assignment is interconvertible.

MS (EI, 70 eV): *m/z* (%) = 389 (18) $[M]^+$, 329 (16), 194 (55) $[C_7H_2N_2O_5]^+$, 178 (38) $[M–C_7H_3N_2O_6]^+$, 149 (23), 110 (100) $[C_6H_7NO]^+$, 96 (54), 82 (73) $[C_5H_8N]^+$, 81 (65), 57 (60), 55 (50) $[C_4H_7]^+$, 41 (38).

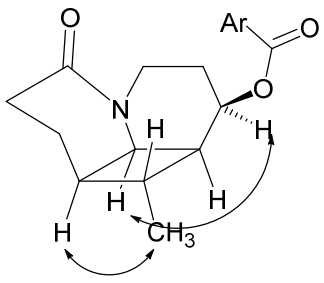
HRMS (EI, 70 eV): ber. ($C_{18}H_{19}O_7N_3$): 389.1218; gef.: 389.1219

ber. ($C_{17}{}^{13}CH_{19}O_7N_3$): 390.1237; gef.: 390.1239.

Chiral HPLC: t_R(1*S*,4^1*S*,7a*S*,8a*R*) = 19.4 min, t_R(1*R*,4^1*R*,7a*R*,8a*S*) = 27.7 min (AD-H, *n*-hexane:*iso*-propanol = 80:20).

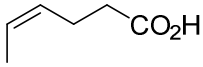
Specific Rotation: $[\alpha]_D^{20}$ = +30.0 (*c* = 0.5, CH_2Cl_2) [87% *ee*].

Important NOE contacts:

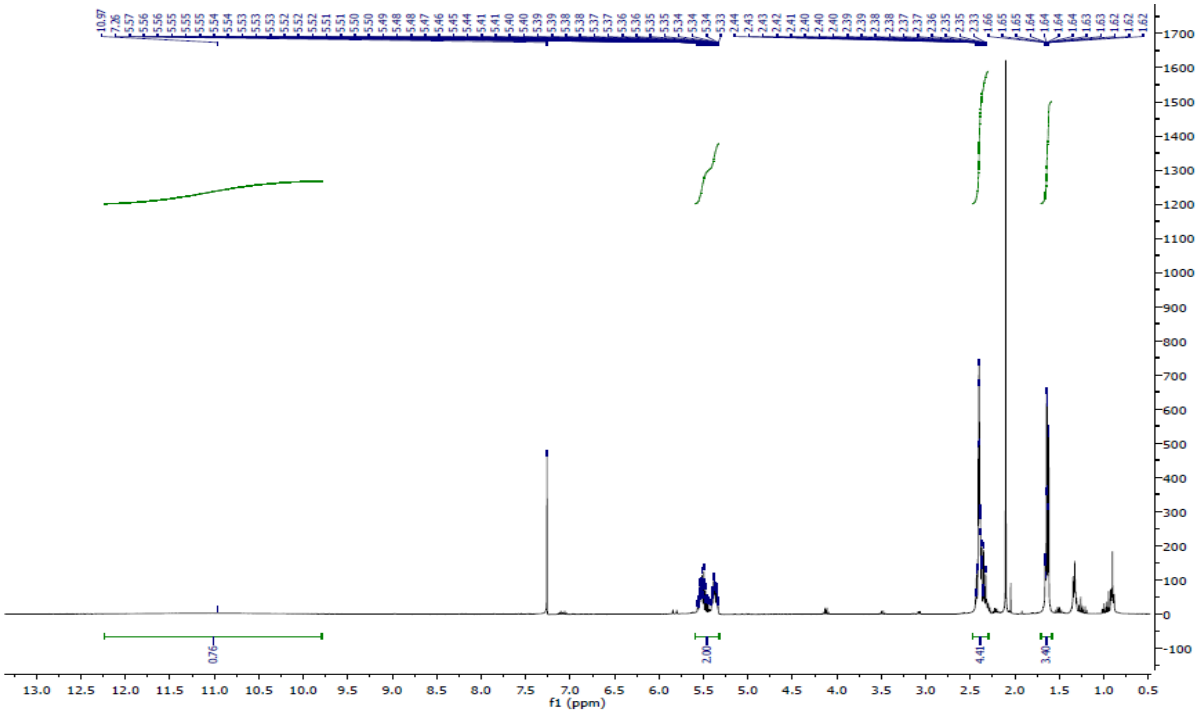


5. NMR Spectra of New Compounds

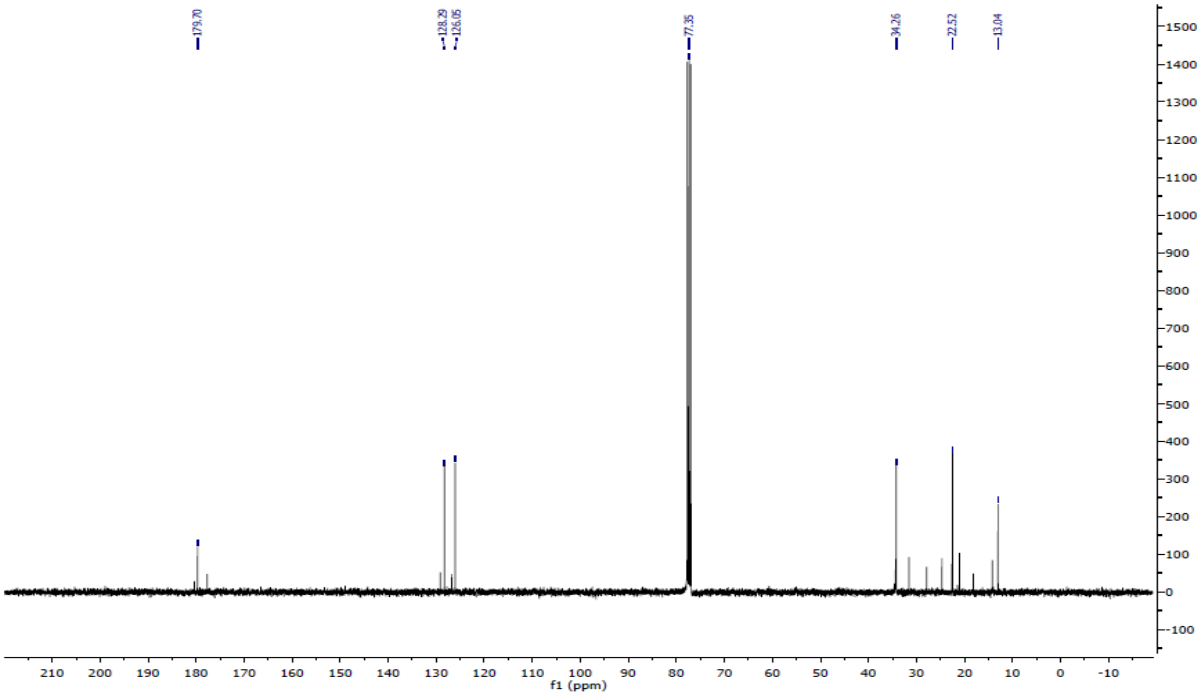
(*Z*)-Hex-4-enoic acid



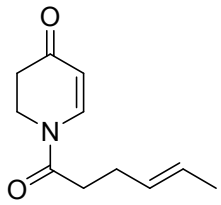
^{1}H-NMR ($CDCl_3$, 500 MHz):



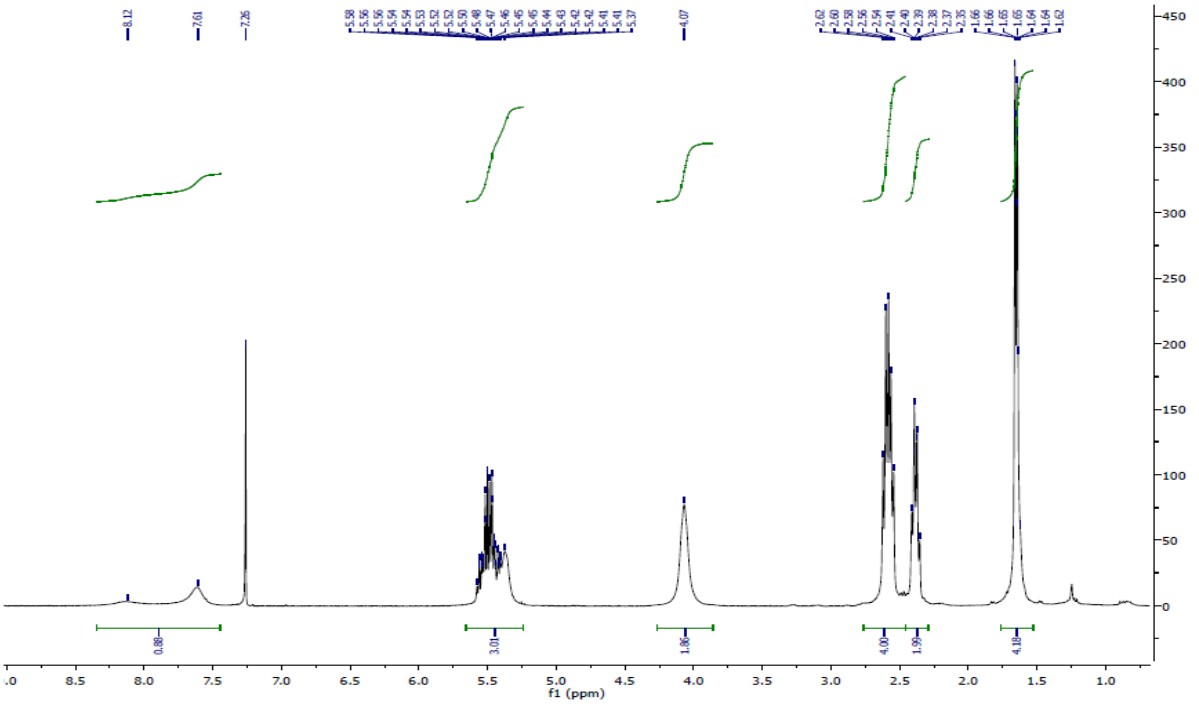
^{13}C-NMR ($CDCl_3$, 128 MHz):



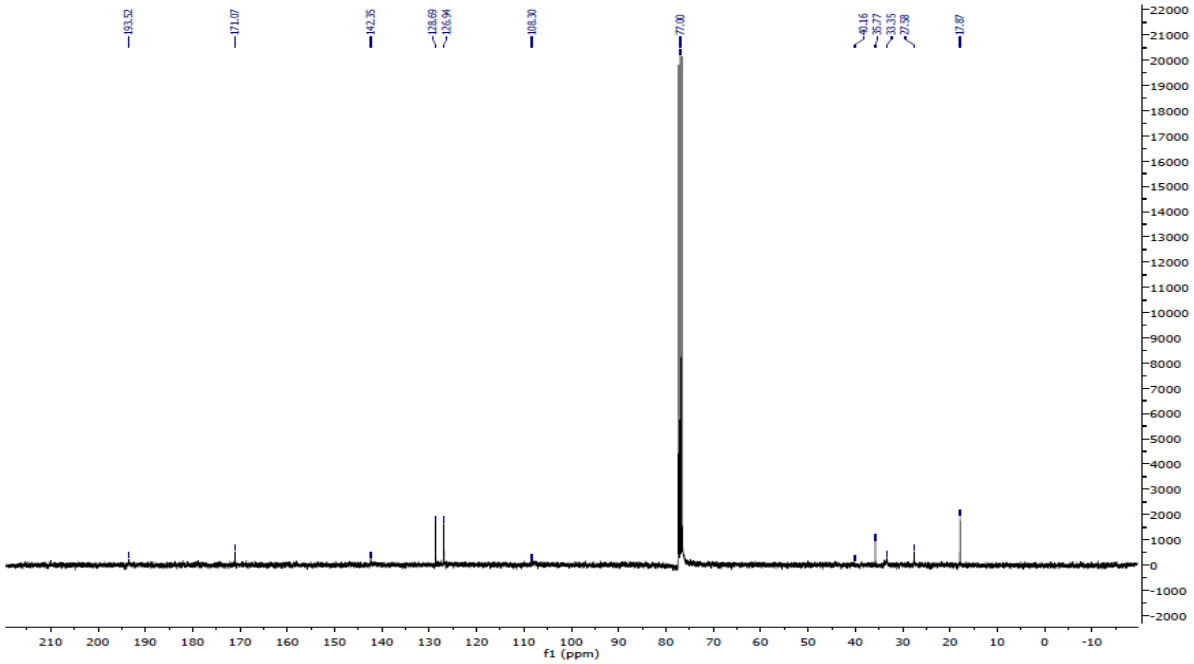
(*E*)-1-(Hex-4-enoyl)-2,3-dihydropyridin-4(1*H*)-one



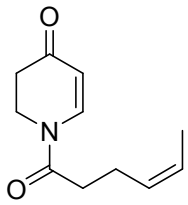
^{1}H-NMR ($CDCl_3$, 500 MHz):



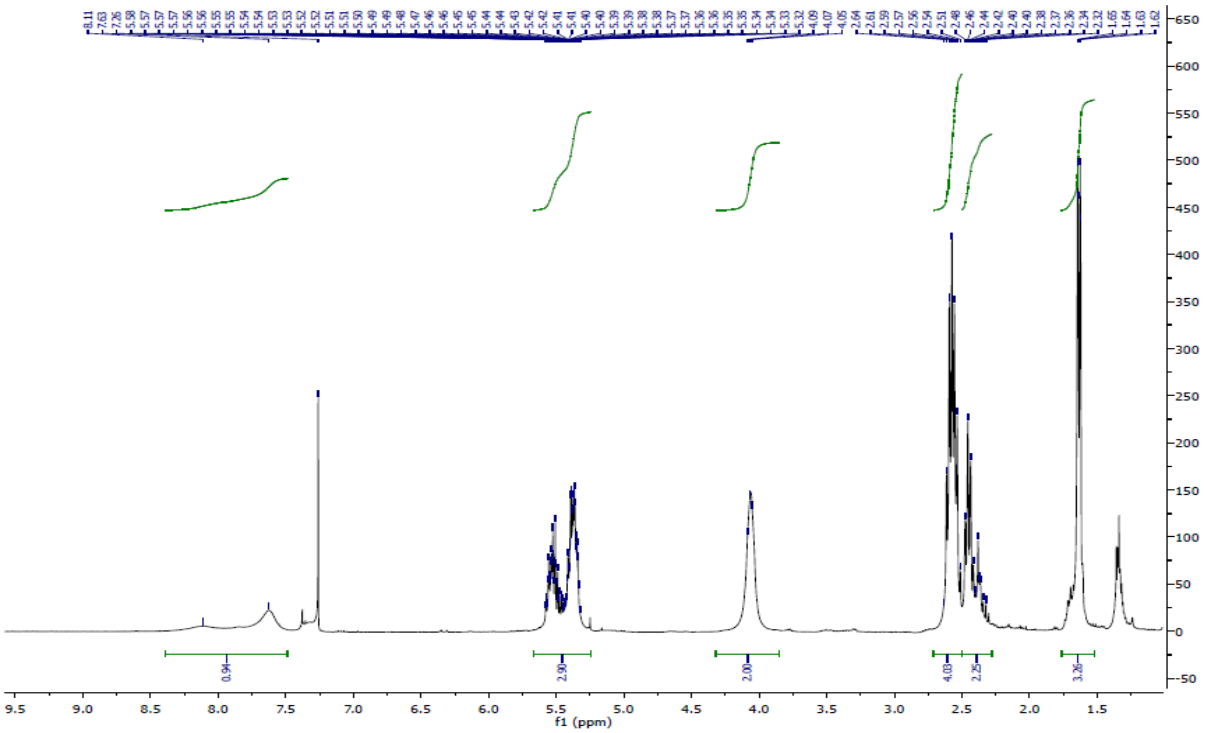
^{13}C-NMR ($CDCl_3$, 128 MHz):



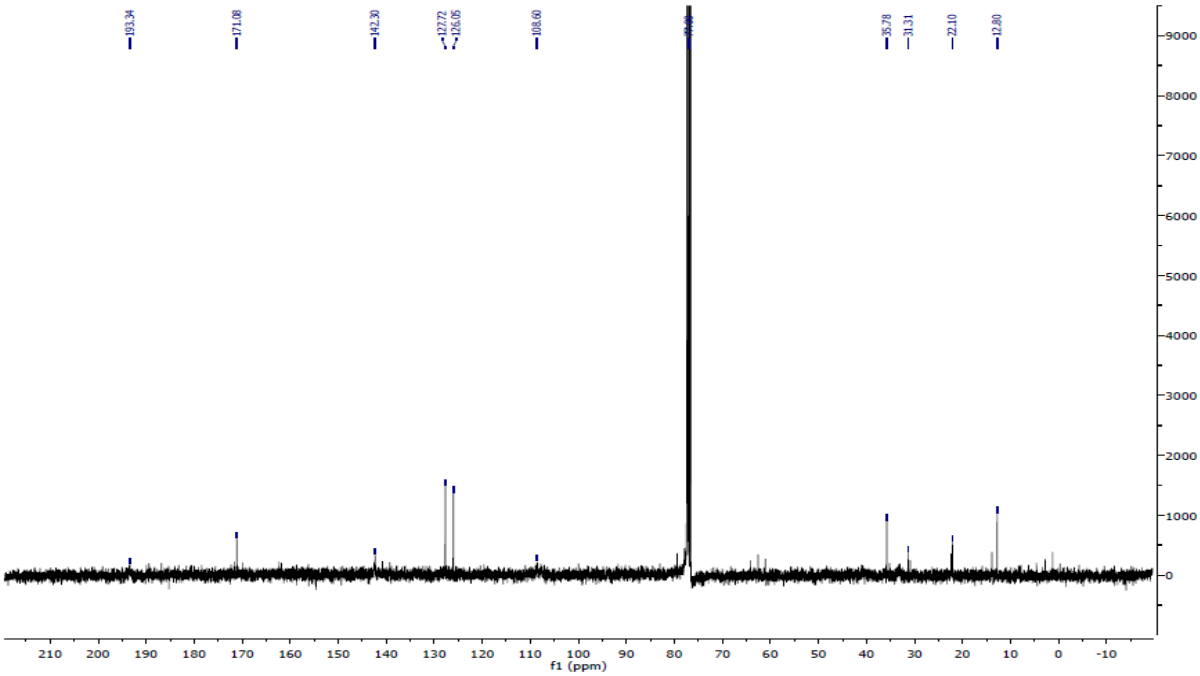
(*Z*)-1-(Hex-4-enoyl)-2,3-dihydropyridin-4(1*H*)-one



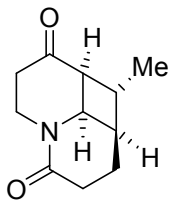
^{1}H-NMR ($CDCl_3$, 500 MHz):



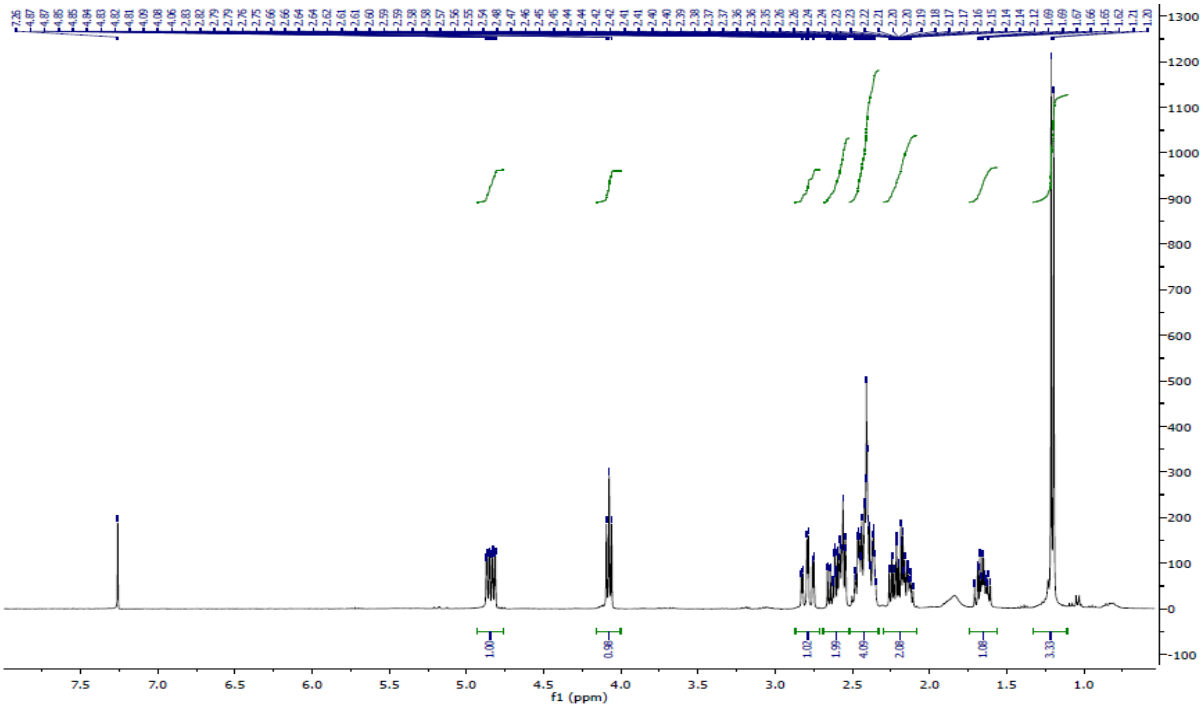
^{13}C-NMR ($CDCl_3$, 128 MHz):



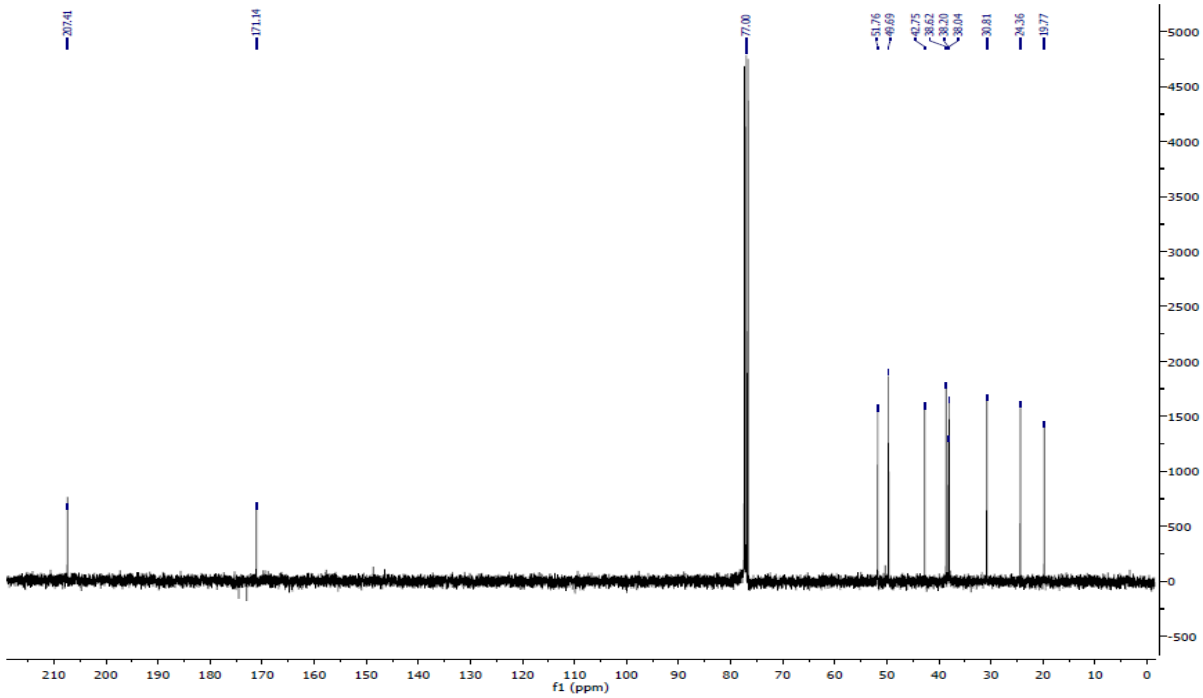
(4[1]*R*,7a*R*,8*R*,8a*S*)-8-Methyloctahydro-1*H*,5*H*-cyclobuta[ij]qhinolizin-1,5-dione



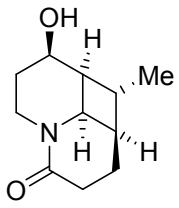
[1]H-NMR ($CDCl_3$, 500 MHz):



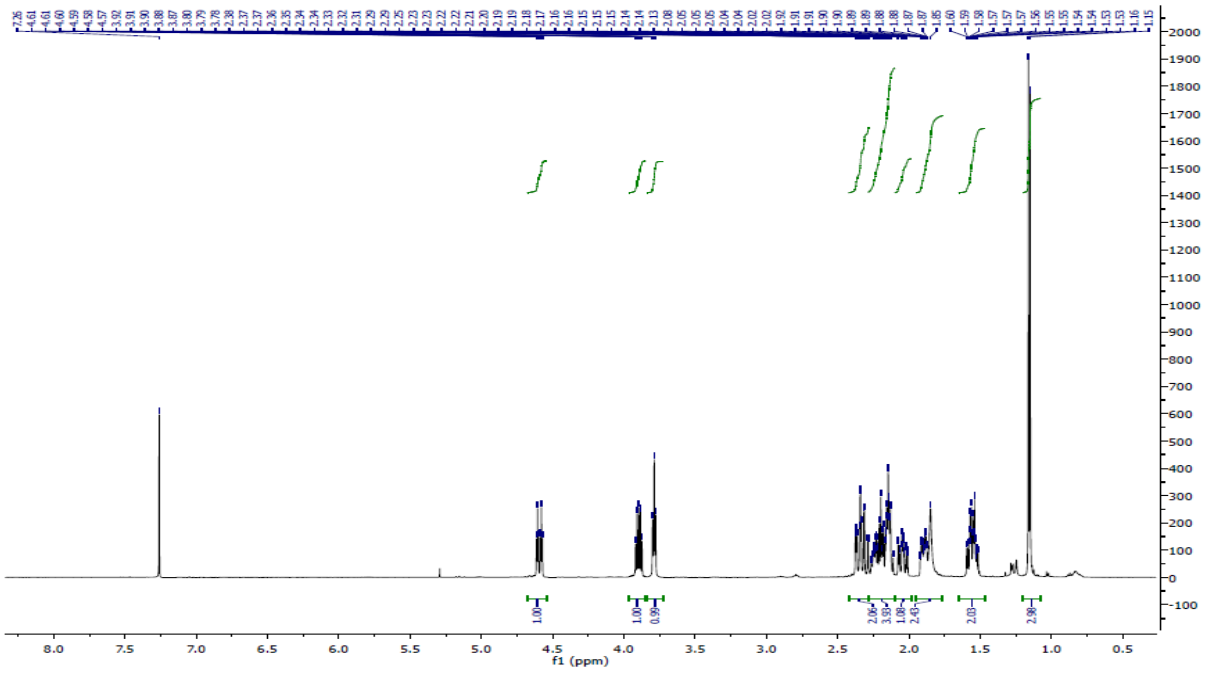
[13]C-NMR ($CDCl_3$, 128 MHz):



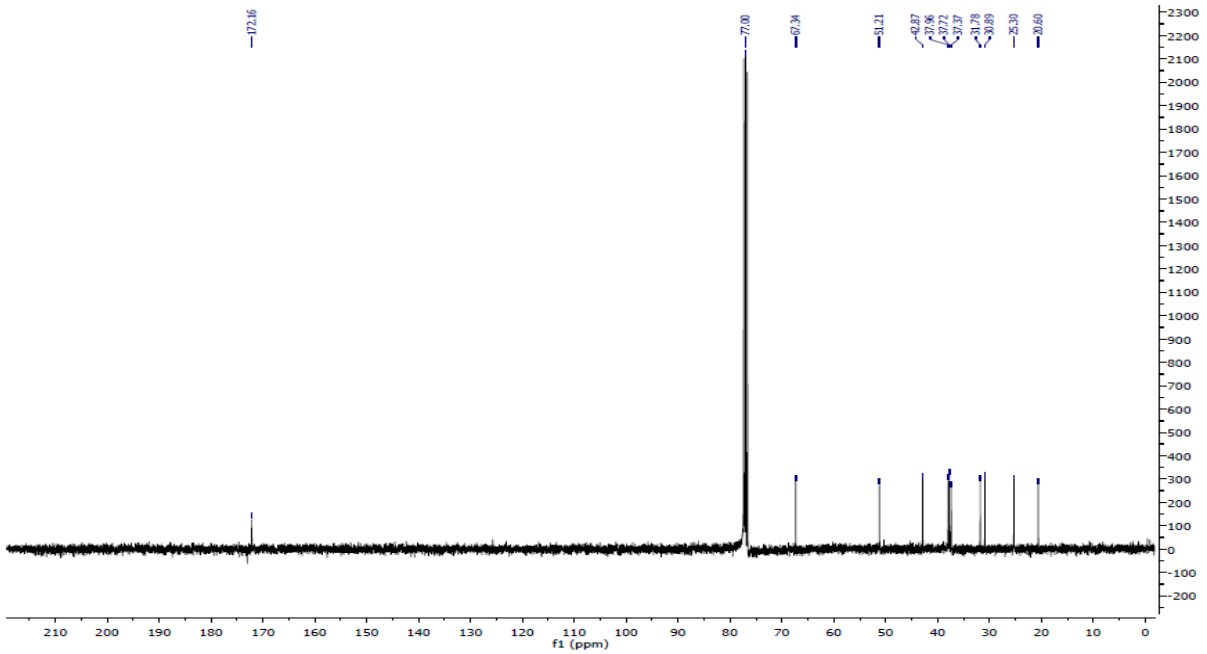
(1*R*,4^1*R*,7a*R*,8*R*,8a*S*)-1-Hydroxy-8-methyloctahydro-1*H*,5*H*-cyclobuta[ij]quinolizin-5-one



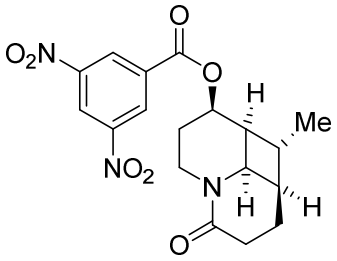
^{1}H-NMR ($CDCl_3$, 500 MHz):



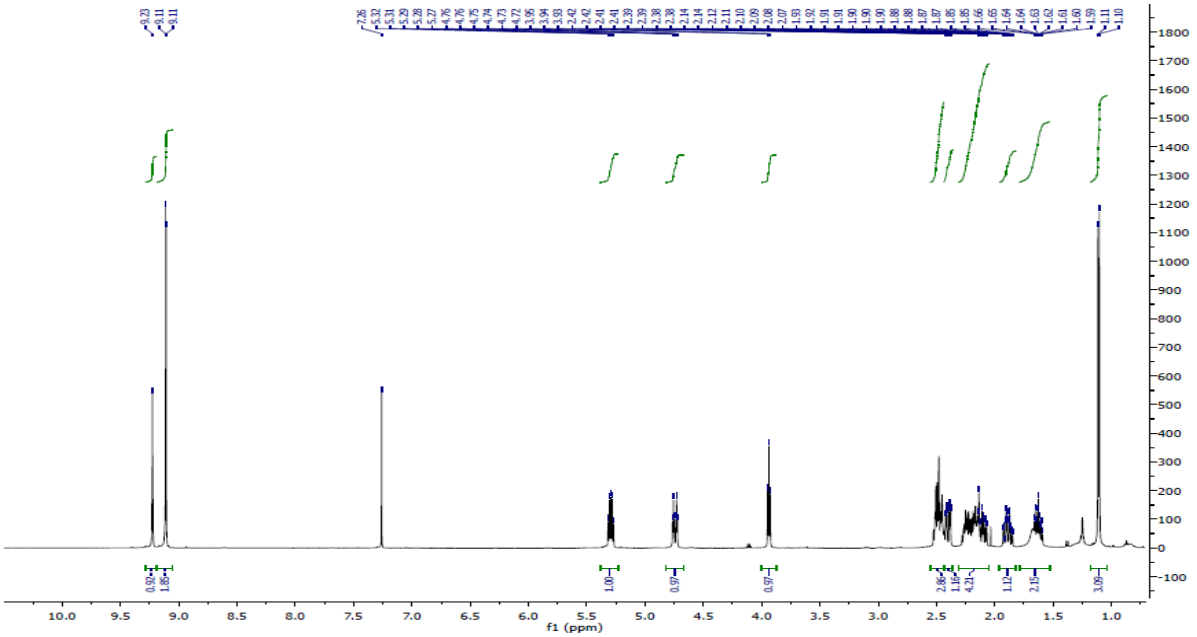
^{13}C-NMR ($CDCl_3$, 128 MHz):



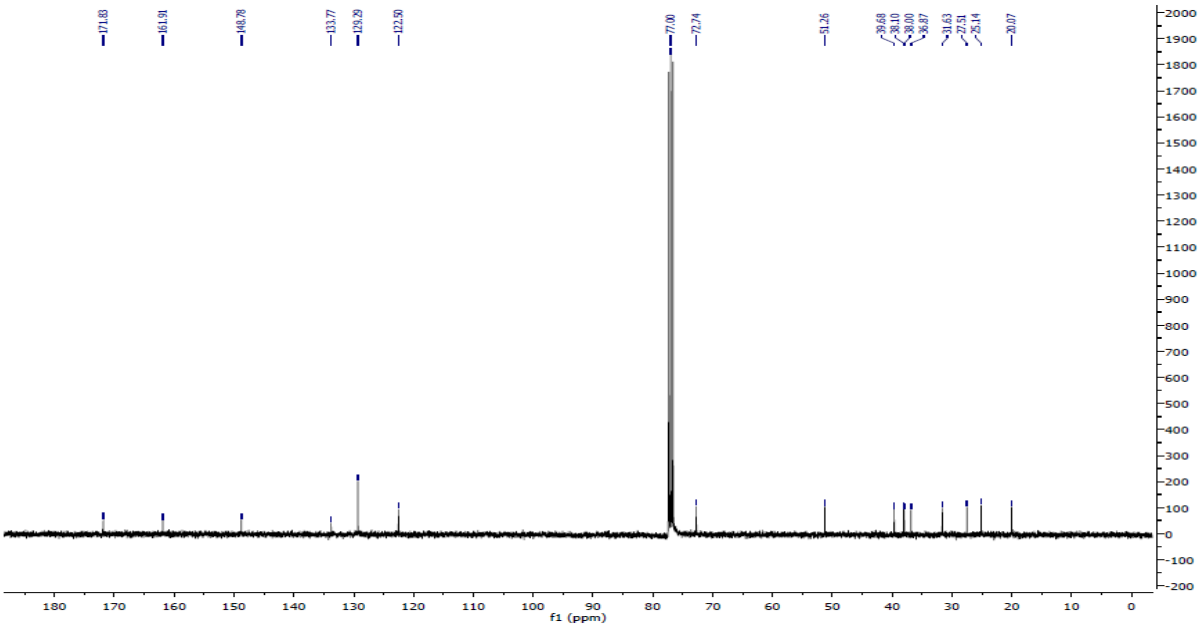
(1*R*,4[1]*R*,7a*R*,8*R*,8a*S*)-8-Methyl-5-oxooctahydro-1*H*,5*H*-cyclobuta[ij]quinolizin-1-yl-3,5-dinitrobenzoate



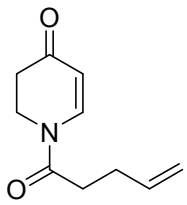
[1]H-NMR ($CDCl_3$, 500 MHz):



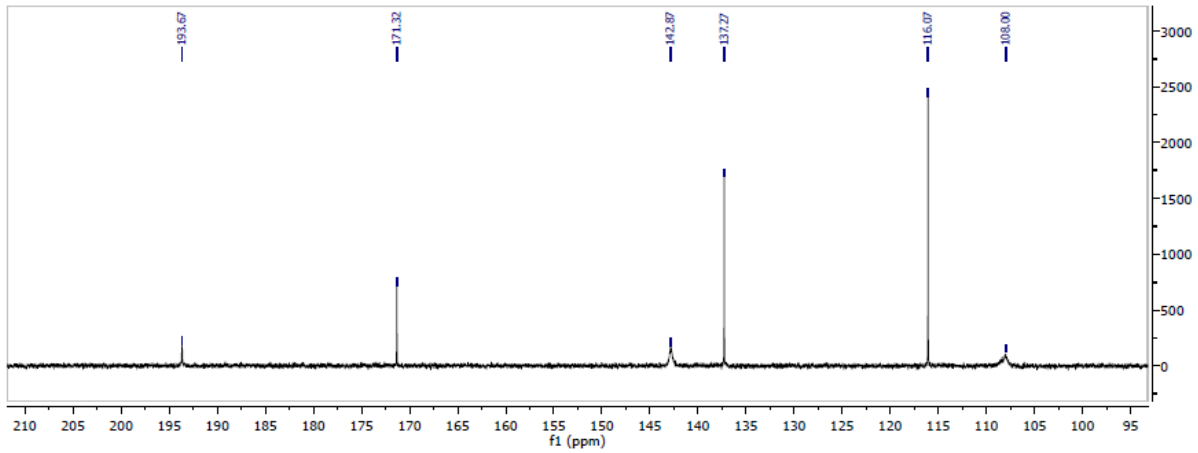
[13]C-NMR ($CDCl_3$, 128 MHz):

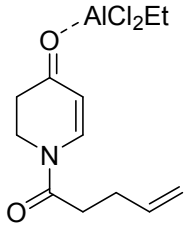


1-(Pent-4-enoyl)-2,3-dihydropyridin-4(1H)-one

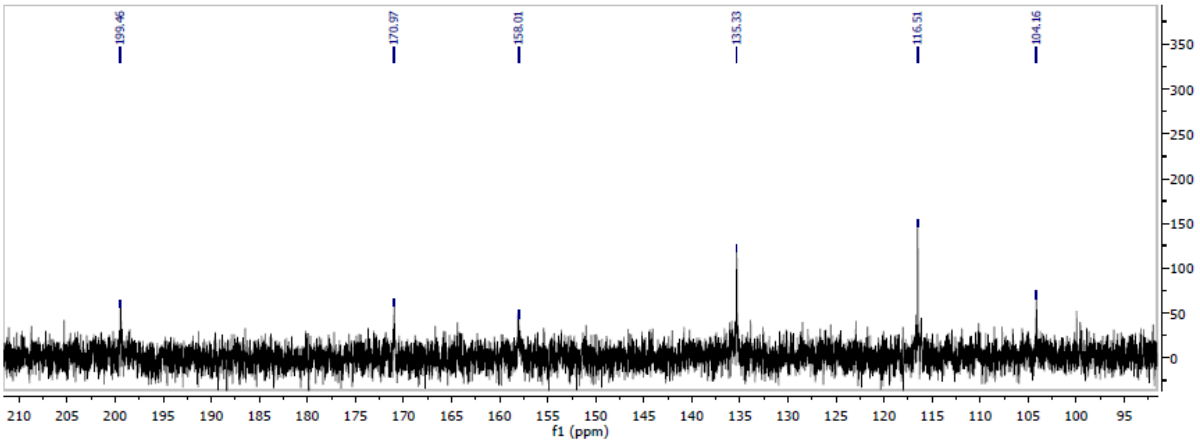


^{13}C-NMR (CD_2Cl_2, 128 MHz):



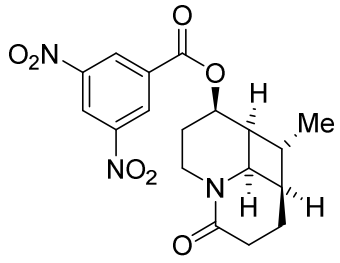


^{13}C-NMR (CD_2Cl_2, 128 MHz):



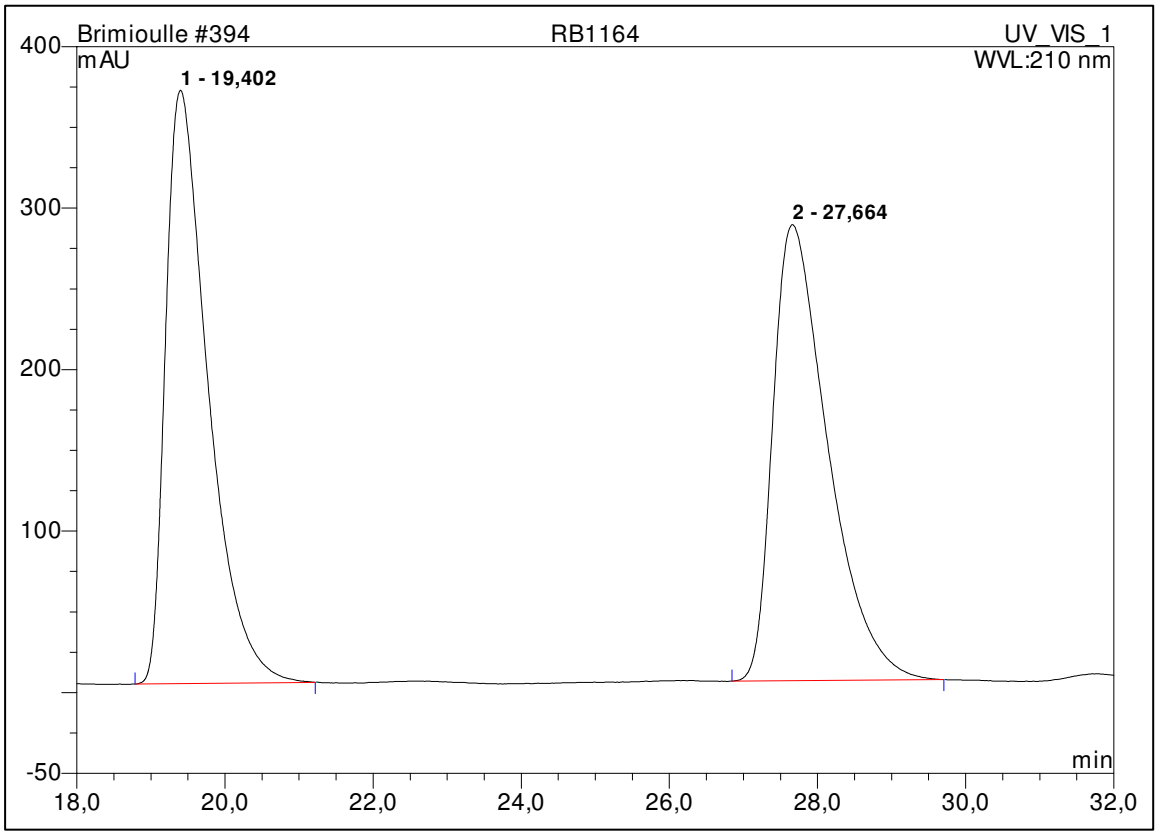
6. HPLC traces of chiral compounds

(1*R*,4^1*R*,7a*R*,8*R*,8a*S*)-8-Methyl-5-oxooctahydro-1*H*,5*H*-cyclobuta[ij]quinolizin-1-yl-3,5-dinitrobenzoate



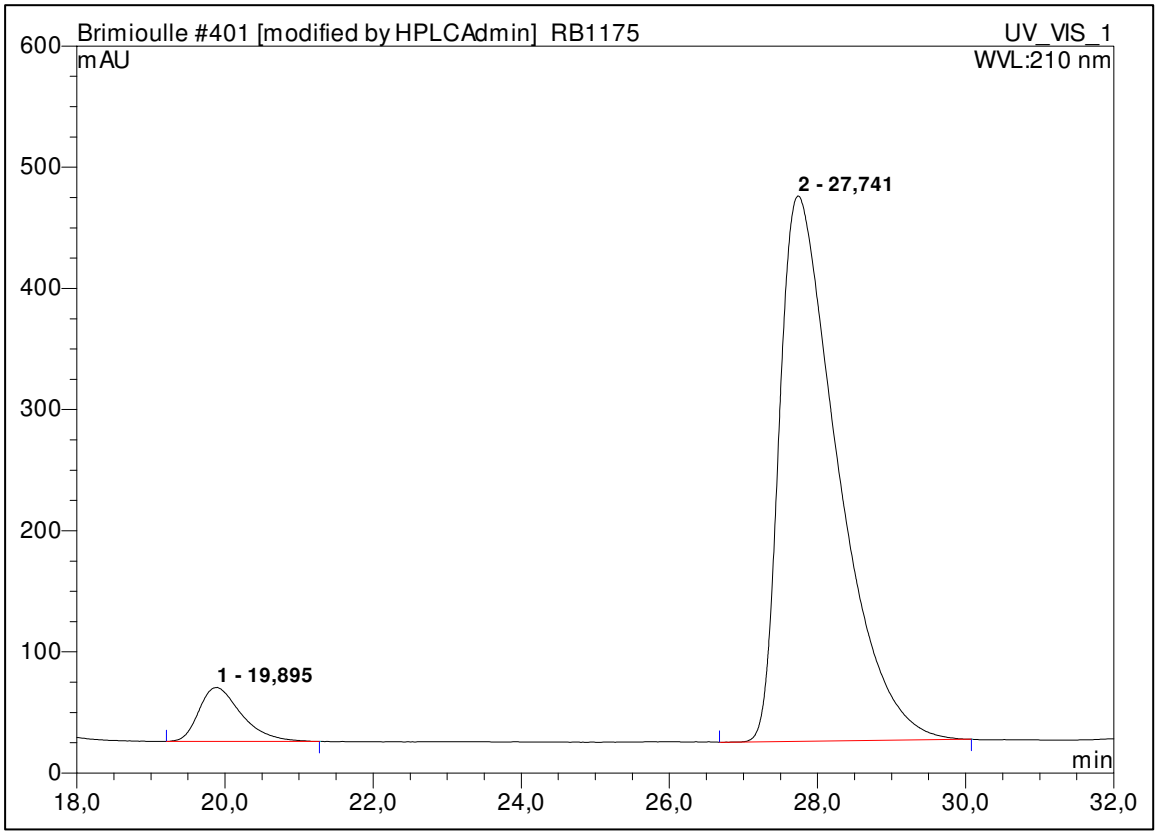
Chiral HPLC: t_R(1*S*,4^1*S*,7a*S*,8a*R*) = 19.4 min, t_R(1*R*,4^1*R*,7a*R*,8a*S*) = 27.7 min (AD-H, *n*-hexane:*iso*-propanol = 80:20).

Racemic product



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	19,40	n.a.	367,520	244,410	50,10	n.a.	BMB
2	27,66	n.a.	282,522	243,422	49,90	n.a.	BMB
Total:			650,042	487,832	100,00	0,000	

Enantiomerically enriched product (87% *ee*)



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	19,90	n.a.	44,567	29,577	6,74	n.a.	BMB
2	27,74	n.a.	450,026	409,240	93,26	n.a.	BMB*
Total:			494,593	438,817	100,00	0,000	

References

[1] M. Noack, R. Göttlich, *Eur. J. Org. Chem.* **2002**, 3171-3178.

[2] W. G. Blenderman, M. M. Joullie, G. Preti, *J. Org. Chem.* **1983**, *48*, 3206-3213.

[3] A. Fürstner, S. Flügge, O. Larionov, Y. Takahashi, T. Kubota, J. Kobayashi, *Chem. Eur. J.* **2009**, *15*, 4011-4029.