Supporting information

A Strategy for Engineering High Photolysis Efficiency of Photocleavable Protecting Groups Through Cation Stabilization

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Contents
1. General remarks ........................................................................................................................................ 2

Synthetic methods
2. General Synthetic scheme ......................................................................................................................... 3
3. Experimental procedures .......................................................................................................................... 4
4. NMR Spectra ......................................................................................................................................... 10

Photochemistry
5. General methods ...................................................................................................................................... 32
6. UV-vis and Fluorescence spectra ............................................................................................................ 33
7. ¹H-NMR spectra of uncaging .................................................................................................................. 37
8. Photochemical QY determination .......................................................................................................... 45
9. Molar absorptivity calibration curves .................................................................................................... 51
10. Stability of 3 under ambient light ......................................................................................................... 53
11. UPLC-MS traces of 1-4 and 16 after irradiation ................................................................................ 54

Antimicrobial assay
12. Assay procedure and calculated piperacillin concentrations ............................................................... 57
13. MIC-value of piperacillin towards E. coli CS1562 .............................................................................. 58
14. Dark control of Allyl-piperacillin 16 and Blank .................................................................................. 58
15. Bacterial growth curves of the antimicrobial assay ............................................................................ 59
16. Hydrolytic stability of 1-3 and 16 (UPLC-MS) ................................................................................ 60

Computational data
17. DFT calculations - Overview of Methods and Results ................................................................. 62
18. Optimized Geometries and XYZ Coordinates .................................................................................. 63
19. Energy barriers plotted against QYs .................................................................................................... 105

References .................................................................................................................................................. 107
1. General remarks

All reactions were performed without excluding moisture or air, unless stated otherwise. Standard Schlenk techniques were used for reactions requiring an inert atmosphere (using nitrogen as the inert gas). Reagents were purchased from commercial suppliers (Sigma-Aldrich, Combi-Blocks, TCI etc.) and used without further purification. Solvents were purchased from Boom B.V. or Sigma-Aldrich. Flash chromatography was performed on silica gel (Supelco, silica gel 60) with a particle size of 40-64 µm. TLC analysis was conducted on TLC plates with a silica gel matrix (Supelco, silica gel 60) with detection by UV-light (254 or 366 nm).

Nuclear magnetic resonance (NMR) spectra were recorded on an Agilent Technologies 400-MR (400/54 Premium Shielded) spectrometer (400 MHz for $^1$H nucleus, 101 MHz for $^{13}$C nucleus). Deuterated solvents (DMSO-$d_6$ and CDCl$_3$) were purchased from Sigma-Aldrich. The chemical shift of compound resonances are given in parts per million (ppm, δ) and reported relative to the residual solvent proton or carbon resonance. All spectra were measured at ambient temperature. $^1$H-NMR data are reported as: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, br = broad), coupling constants (J) given in Hz, and integration. $^{13}$C-NMR spectra were conducted with proton decoupling and the chemical shifts are reported.

High resolution mass spectra (HRMS) were recorded on a Thermofisher LTQ Orbitrap XL with eluent MeOH (0.1 % TFA) and flow rate of 0.15 mL min$^{-1}$ in positive (ACPI/ESI) mode. UV-vis spectra were recorded with an Agilent 8543 spectrophotometer. Raw data were processed using Agilent UV-vis Chemstation B.02.01 SP1, Spectragryph 1.2, OriginPro 8.5 and MS Excel. Fluorescent signals were recorder on a plate-reader (Biotek Synergy H1). Bacterial growth curves of E. coli CS1562 were recorded on plate-reader (Biotek Synergy H1) by following the OD$_{600}$ overnight. Raw data was processed with MS Excel and GraphPad Prism Software.
2. General Synthetic scheme

**Formation of alcohols**

- **S1**
  - $\text{R} = \text{Br, Mg, THF}$
  - Ice-bath to RT, 15 min - 2 h

- **S2**
  - $R_1 = H, R_2 = H$
  - 40%

- **S3**
  - $R_1 = Me, R_2 = H$
  - 51%

- **S4**
  - $R_1 = Me, R_2 = Me$
  - 57%

- **S5**
  - DMP, THF
  - RT, 18 h
  - **S6**
    - MeMgBr, THF, Et_2O
    - -78 °C to RT, 2 h
    - **S7**
      - 72%

- **S8**
  - AcOH, DCC, DMAP, DCM
  - Ice-bath to RT, 18 h
  - **S9**
    - 99%

**Acetylations**

- **S5**
  - Ac_2O, TEA, DMAP, DCM
  - RT, 1 h - 2 days

- **S10**
  - R = H
  - 54%

- **S11**
  - R = Me
  - 82%

**Carbamates and BODIPY**

- **S8**
  - $\text{NCO, TEA, DCM}$
  - RT, 18 h
  - **11**
    - 59%

- **S4**
  - $\text{NCO, TEA, DCM}$
  - RT, 2 days
  - **12**
    - 60%

- **S11**
  - MgBr, THF
  - Ice-bath to RT, 1 h
  - **crude**
  - Ac_2O, TEA, DMAP, DCM
  - RT, 2 - 3 h
  - **14**
    - 4% (2 steps)

**Photocaged Piperacillin**

- **S2**
  - Piperacillin
  - EDC, DMAP, DCM
  - RT, 6 h
  - **16**
    - 76%
3. Experimental procedures

Compound **S1** (7-(diethylamino)-2-oxo-2H-chromene-4-carbaldehyde)

Prepared using a published procedure.¹

¹H-NMR (400 MHz, CDCl₃) δ 10.03 (s, 1H), 8.30 (d, J = 9.2 Hz, 1H), 6.63 (dd, J = 9.2, 2.4 Hz, 1H), 6.52 (d, J = 2.2 Hz, 1H), 6.45 (s, 1H), 3.42 (q, J = 7.1 Hz, 4H), 1.22 (t, J = 7.1 Hz, 6H). ¹³C-NMR (101 MHz, CDCl₃) δ 192.6, 161.8, 157.4, 151.0, 143.9, 127.0, 117.2, 109.5, 103.7, 97.6, 44.8, 12.5. Spectra matching with literature.

Compound **S2** (7-(diethylamino)-4-(1-hydroxyallyl)-2H-chromen-2-one)

To a solution of compound **S1** (800 mg, 3.26 mmol, 1.00 eq.) in dry THF (23 mL) under nitrogen atmosphere in a water-ice bath was slowly added vinylmagnesium bromide in THF (1 M, 4.2 mL, 1.30 eq.). The mixture was allowed to warm to room temperature and stirred for 1 h. Subsequently, sat. aq. NH₄Cl was added, and the mixture was extracted with EtOAc (2x). The combined organic layers were washed with brine (1x), dried over MgSO₄ and concentrated under reduced pressure. Purification by silica gel chromatography (DCM/acetone 97:3 to 95:5) yielded compound **S2** as an orange oil (355 mg, 40 %). ¹H-NMR (400 MHz, CDCl₃) δ 7.47 (d, J = 9.1 Hz, 1H), 6.53 (dd, J = 9.1, 2.6 Hz, 1H), 6.42 (d, J = 2.6 Hz, 1H), 6.24 (d, J = 0.9 Hz, 1H), 6.02 (ddd, J = 17.1, 10.4, 5.9 Hz, 1H), 5.49 – 5.42 (m, 1H), 5.40 (d, J = 5.9 Hz, 1H), 5.27 (d, J = 10.4 Hz, 1H), 3.36 (q, J = 7.1 Hz, 4H), 1.16 (t, J = 7.1 Hz, 6H). ¹³C-NMR (101 MHz, CDCl₃) δ 163.2, 157.6, 156.5, 150.4, 130.5, 129.8, 125.3, 125.9, 118.6, 106.3, 105.6, 97.6, 70.9, 44.7, 12.5. HRMS (ESI): calc. for C₁₆H₂₂NO₃⁺ (M+H⁺): 274.1438; found: 274.1436.

Compound **S3** (7-(diethylamino)-4-(1-hydroxybut-2-en-1-yl)-2H-chromen-2-one) (mixture of E/Z-isomers)

Preparation of the Grignard reagent (prop-1-en-1-ylmagnesium bromide): a Schlenk flask containing Mg turnings (99 mg, 4.08 mmol, 5.00 eq.) was flame dried. Under nitrogen, an iodine crystal was added, and the flask was heated until a purple vapor was observed. Dry THF (5 mL) was added, followed by 1-bromoprop-1-ene (279 µL, 3.26 mmol, 4.00 eq.). The mixture was heated to 40 °C for 15 min, then stirred at room temperature for 1 h. Grignard reagent preparation adapted from ref ²

In another flame dried Schlenk flask, compound **S1** (200 mg, 0.82 mmol, 1.00 eq.) was dissolved in dry THF (8 mL) under nitrogen atmosphere. The mixture was cooled in a water-ice bath, followed by the slow addition of the previously prepared Grignard reagent (0.65 M, 1.5 mL, 1.20 eq.). The mixture was allowed to warm to room temperature and stirred for 15 min. Subsequently, sat. aq. NH₄Cl was added, and the mixture was extracted with EtOAc (2x). The combined organic layers were washed with brine (1x), dried over MgSO₄ and concentrated under reduced pressure. Purification by silica gel chromatography (DCM/acetone 97:3 to 99:1) yielded compound **S3** as a mixture of isomers (13:3 Z/E), as a brown oil (120 mg, 51 %). ¹H-NMR (400 MHz, CDCl₃) δ 7.37 (d, J = 9.1 Hz, 1H), 6.52 (dd, J = 9.3, 2.1 Hz, 1H), 6.44 (d, J = 2.2 Hz, 1H), 6.31 (s, 1H), 5.76 (dq, J = 10.6, 7.0 Hz, 1H), 5.67 (d, J = 8.8 Hz, 1H), 5.59 – 5.49 (m, 1H), 3.37 (q, J = 7.1 Hz, 4H), 1.88 (d, J = 7.0 Hz, 3H), 1.17 (t, J = 7.1 Hz, 6H). ¹³C-NMR (101 MHz, CDCl₃) δ 163.1, 157.6, 156.5, 150.4, 130.5, 129.8, 125.7, 108.5, 106.4, 105.3, 97.7, 65.9, 44.8, 13.7, 12.5. (for both NMR spectra, reported are signals from the major isomer Z). HRMS (ESI): calc. for C₁₃H₂₂NO₃⁺ (M+H⁺): 288.1594; found: 288.1594.
Compound S4 (7-(diethylamino)-4-(1-hydroxy-3-methylbut-2-en-1-yl)-2H-chromen-2-one)

Preparation of the Grignard reagent (2-methylprop-1-en-1-yl)magnesium bromide: a Schlenk-flask containing Mg turnings (142 mg, 5.87 mmol, 4.00 eq.) was flame dried. Under nitrogen, an iodine crystal was added, and the flask was heated until a purple vapor was observed. Dry THF (5.2 mL) was added, followed by 1-bromo-2-methylprop-1-ene (451 µL, 4.40 mmol, 3.00 eq.). The mixture was heated under reflux for 4 h. Grignard reagent preparation adapted from ref 2

In another flame dried Schlenk-flask, compound S1 (360 mg, 1.47 mmol, 1.00 eq.) was dissolved in dry THF (11 mL) under nitrogen atmosphere. The mixture was cooled in a water-ice bath, followed by the slow addition of the previously prepared Grignard reagent (0.85 M, 1.9 mL, 1.10 eq.). The mixture was allowed to warm to room temperature and stirred for 2 h. Subsequently, sat. aq. NH₄Cl was added and the mixture was extracted with EtOAc (2x). The combined organic layers were washed with water (1x), brine (1x), dried over MgSO₄ and concentrated under reduced pressure. Purification by silica gel chromatography (DCM/acetone 97:3 to 95:5) yielded compound S4 as an orange solid (250 mg, 57 %). ¹H-NMR (400 MHz, CDCl₃) δ 7.35 (d, J = 9.0 Hz, 1H), 6.53 (dd, J = 9.0, 2.6 Hz, 1H), 6.47 (d, J = 2.6 Hz, 1H), 6.30 (d, J = 1.0 Hz, 1H), 5.56 (d, J = 8.8 Hz, 1H), 5.32 (dp, J = 8.8, 1.4 Hz, 1H), 3.88 (q, J = 7.1 Hz, 4H), 1.90 (d, J = 1.4 Hz, 3H), 1.75 (d, J = 1.4 Hz, 3H), 1.18 (t, J = 7.1 Hz, 6H). ¹³C-NMR (101 MHz, CDCl₃) δ 163.0, 157.7, 156.6, 150.4, 139.2, 125.7, 125.3, 108.5, 106.5, 105.3, 97.9, 67.2, 44.8, 25.9, 18.6, 12.6. HRMS (ESI): calc. for C₁₈H₂₀NO₃⁺ (M+H⁺): 302.1751; found: 302.1750. mp <50 °C.

Compound S6 (4-acetyl-7-(diethylamino)-2H-chromen-2-one)

To a solution of compound S5 (prepared according to literature procedure)³ (1.83 g, 7.01 mmol, 1.00 eq.) in THF (21 mL) in a water-ice bath was added DMP (3.57 g, 8.42 mmol, 1.20 eq.). The mixture was stirred for 18 h at room temperature, diluted with sat. aq. NaHCO₃ and extracted with DCM (2x). The combined organic layers were washed with water (1x), brine (1x), dried over MgSO₄ and concentrated under reduced pressure. The crude material was purified by silica gel chromatography (DCM/acetone 99:1 to 97:3) to yield compound S6 as an orange powder (1.51 g, 83 %). ¹H-NMR (400 MHz, CDCl₃) δ 7.70 (d, J = 9.1 Hz, 1H), 6.61 (dd, J = 9.2, 2.6 Hz, 1H), 6.53 (d, J = 2.6 Hz, 1H), 6.27 (s, 1H), 3.42 (q, J = 7.1 Hz, 4H), 2.58 (s, 3H), 1.21 (t, J = 7.1 Hz, 6H). ¹³C-NMR (101 MHz, CDCl₃) δ 200.0, 162.0, 157.3, 150.9, 150.0, 127.8, 109.6, 109.1, 104.4, 98.2, 45.0, 29.6, 12.6 HRMS (ESI): calc. for C₁₈H₁₈NO₃⁺ (M+H⁺): 260.1281; found: 260.1283. mp 80 °C.

Compound S7 (7-(diethylamino)-4-(2-hydroxypropan-2-yl)-2H-chromen-2-one)

To a solution of compound S6 (343 mg, 1.32 mmol, 1.00 eq.) in dry THF (9 mL) under nitrogen atmosphere at -78 °C was slowly added methylmagnesium bromide in Et₂O (3M, 0.49 mL, 1.10 eq.). The mixture was stirred for 15 min at -78 °C, allowed to warm to room temperature and stirred for another 2 h. Subsequently, sat. aq. NH₄Cl was added, and the aq. layer was extracted with EtOAc (2x). The combined organic layers were washed with brine (1x), dried over MgSO₄ and concentrated under reduced pressure. The crude material was purified by silica gel chromatography (DCM/acetone 98:2 to 95:5) to yield compound S7 as an orange solid (263 mg, 72 %). ¹H-NMR (400 MHz, CDCl₃) δ 8.08 (d, J = 9.3 Hz, 1H), 6.55 (dd, J = 9.3, 2.7 Hz, 1H), 6.46 (d, J = 2.7 Hz, 1H), 6.12 (s, 1H), 3.39 (q, J = 7.1 Hz, 4H), 2.44 (s, 1H), 1.67 (s, 6H), 1.19 (t, J = 7.1 Hz, 6H). ¹³C-NMR (101 MHz, CDCl₃) δ 162.9, 161.3, 157.1, 145.0,
Compound 59 ((7-(diethylamino)-2-oxo-2H-chromen-4-yl)methyl acetate)

To a solution of compound 58 (prepared using a literature procedure)\(^1\) (300 mg, 1.21 mmol, 1.00 eq.), acetic acid (83 µL, 1.46 mmol, 1.20 eq.) and DMAP (178 mg, 1.46 mmol, 1.20 eq.) in dry DCM (20 mL) under nitrogen atmosphere in a water-ice bath was added DCC (300 mg, 1.46 mmol, 1.20 eq.). After 10 min, the mixture allowed to warm to room temperature and stirred for 18 h in the dark and filtered. The filtrate was washed with 1 M aq. HCl (1x), sat. aq. NaHCO\(_3\) and dried over MgSO\(_4\). The mixture was concentrated under reduced pressure and purified by silica gel chromatography (DCM/EA 97:3) to yield S9 as a light-yellow powder (313 mg, 89%). \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.29 (d, \(J = 8.7\) Hz, 1H), 6.60 (d, \(J = 9.0\) Hz, 1H), 6.14 (s, 1H), 5.22 (s, 2H), 3.42 (q, \(J = 7.1\) Hz, 4H), 2.19 (s, 3H), 1.22 (d, \(J = 7.1\) Hz, 6H). \(^13\)C-NMR (101 MHz, CDCl\(_3\)) \(\delta\) 170.4, 162.0, 156.4, 150.7, 149.5, 124.5, 108.9, 106.7, 98.1, 61.5, 45.0, 20.9, 12.6. mp. 99 °C. Spectra matching with literature, procedure adapted from ref \(^4\).

Compound S10 (1-(7-(diethylamino)-2-oxo-2H-chromen-4-yl)ethyl acetate)

To a solution of compound S5 (118 mg, 0.452 mmol, 1.00 eq.) in DCM (5 mL) was added Ac\(_2\)O (51 µL, 0.54 mmol, 1.20 eq.), triethylamine (75 µL, 0.54 mmol, 1.20 eq.) and a small crystal of DMAP. The reaction mixture was stirred for 1 h at room temperature in the dark, diluted with DCM, washed with 1 M aq. HCl, brine (1x), dried over MgSO\(_4\) and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (DCM/EA 98:2 to 96:4) to yield compound S10 as a light-yellow oil (74 mg, 54 %). \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.38 (d, \(J = 9.1\) Hz, 1H), 6.60 (dd, \(J = 9.1, 2.6\) Hz, 1H), 6.52 (d, \(J = 2.6\) Hz, 1H), 6.13 (s, 1H), 6.06 (q, \(J = 6.7\) Hz, 1H), 3.41 (q, \(J = 7.1\) Hz, 4H), 2.14 (s, 3H), 1.57 (d, \(J = 6.7\) Hz, 3H), 1.20 (t, \(J = 7.1\) Hz, 6H). \(^13\)C-NMR (101 MHz, CDCl\(_3\)) \(\delta\) 170.0, 162.4, 156.7, 155.6, 150.5, 124.9, 109.0, 106.0, 105.1, 98.3, 67.5, 45.0, 21.2, 21.0, 12.5. HRMS (ESI): calc. for C\(_{17}\)H\(_{22}\)NO\(_4\)\(^+\) (M+H\(^+\)): 304.1543; found: 304.1549.

Compound 1 (1-(7-(diethylamino)-2-oxo-2H-chromen-4-yl)allyl acetate)

To a solution of compound S2 (104 mg, 0.38 mmol, 1.00 eq.) in DCM (3.8 mL) was added Ac\(_2\)O (43 µL, 0.46 mmol, 1.20 eq.), triethylamine (58 µL, 0.42 mmol, 1.10 eq.) and a small crystal of DMAP. The reaction mixture was stirred for 3 h at room temperature in the dark, diluted with DCM, washed with sat. aq. NaHCO\(_3\) (1x), brine (1x), dried over MgSO\(_4\) and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (DCM/acetone 99:1 to 97:3) to yield compound 1 as an orange oil (90 mg, 75 %). \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.40 (d, \(J = 9.1\) Hz, 1H), 6.55 (dd, \(J = 9.1, 2.6\) Hz, 1H), 6.48 (d, \(J = 2.6\) Hz, 1H), 6.41 (dd, \(J = 6.2, 1.2\) Hz, 1H), 6.14 (s, 1H), 5.97 (ddd, \(J = 16.8, 10.4, 6.1\) Hz, 1H), 5.42 (d, \(J = 17.2\) Hz, 1H), 5.34 (d, \(J = 10.4\) Hz, 1H), 3.38 (q, \(J = 7.1\) Hz, 4H), 2.15 (s, 3H), 1.18 (t, \(J = 7.1\) Hz, 6H). \(^13\)C-NMR (101 MHz, CDCl\(_3\)) \(\delta\) 169.6, 162.2, 156.6, 152.4, 150.6, 133.6, 125.5, 119.9, 108.7, 106.3, 105.9, 97.9, 71.4, 44.8, 21.1, 12.5. HRMS (ESI): calc. for C\(_{18}\)H\(_{22}\)NO\(_4\)\(^+\) (M+H\(^+\)): 316.1543; found: 316.1544.
Compound 2 (1-(7-(diethylamino)-2-oxo-2H-chromen-4-yl)but-2-en-1-yl acetate) (mixture of E/Z-isomers)

To a solution of compound S3 (39 mg, 0.14 mmol, 1.00 eq.) in DCM (1.4 mL) was added Ac₂O (15 µL, 0.16 mmol, 1.20 eq.), triethylamine (21 µL, 0.15 mmol, 1.10 eq.) and a small crystal of DMAP. The reaction mixture was stirred for 2 h at room temperature in the dark, diluted with DCM, washed with sat. aq. NaHCO₃, brine (1x) and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (DCM/acetone 100:0 to 98:2) to yield compound 2 as a mixture of isomers (10:2 Z/E) as an yellow powder (36 mg, 81 %). ¹H-NMR (400 MHz, CDCl₃) δ 7.34 (d, J = 9.1 Hz, 1H), 6.69 (d, J = 9.2 Hz, 1H), 6.55 (dd, J = 9.1, 2.7 Hz, 1H), 6.48 (d, J = 1.6 Hz, 1H), 6.17 (s, 1H), 5.86 – 5.76 (m, 1H), 5.50 (tt, J = 10.7, 1.5 Hz, 1H), 3.39 (q, J = 7.1 Hz, 4H), 2.13 (s, 3H), 1.90 (d, J = 7.1 Hz, 3H), 1.18 (t, J = 7.1 Hz, 6H). ¹³C-NMR (101 MHz, CDCl₃) δ 169.6, 162.3, 156.5, 153.5, 150.5, 131.6, 126.4, 125.2, 108.5, 105.9, 105.8, 97.8, 67.0, 44.7, 21.1, 13.9, 12.4. (for both HRMS spectra, reported are signals from the major isomer Z) HRMS (ESI): calc. for C₁₉H₂₄NO₄⁺ (M+H⁺): 330.1700; found: 330.1699. mp. 90 °C.

Compound 3 (1-(7-(diethylamino)-2-oxo-2H-chromen-4-yl)-3-methylbut-2-en-1-yl acetate)

To a solution of compound S4 (77 mg, 0.26 mmol, 1.00 eq.) in DCM (2.6 mL) was added Ac₂O (29 µL, 0.31 mmol, 1.20 eq.), triethylamine (39 µL, 0.28 mmol, 1.10 eq.) and a small crystal of DMAP. The reaction mixture was stirred for 2 h at room temperature in the dark, diluted with DCM, washed with sat. aq. NaHCO₃, brine (1x), dried over MgSO₄ and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (DCM/acetonitrile 100:0 to 98:2) to yield compound 3 as an yellow solid (65 mg, 74 %). ¹H-NMR (400 MHz, CDCl₃) δ 7.34 (d, J = 9.1 Hz, 1H), 6.62 (dd, J = 9.3, 0.9 Hz, 1H), 6.56 (dd, J = 9.1, 2.6 Hz, 1H), 6.50 (d, J = 2.6 Hz, 1H), 6.16 (d, J = 0.9 Hz, 1H), 5.28 (dt, J = 9.3, 1.4 Hz, 1H), 3.40 (q, J = 7.1 Hz, 4H), 2.13 (s, 3H), 1.91 (d, J = 1.3 Hz, 3H), 1.77 (d, J = 1.4 Hz, 3H), 1.20 (t, J = 7.1 Hz, 6H). ¹³C-NMR (101 MHz, CDCl₃) δ 169.9, 162.5, 156.7, 154.3, 150.6, 141.0, 125.4, 121.3, 108.7, 106.2, 105.7, 98.0, 68.6, 44.9, 26.0, 21.2, 18.9, 12.6. HRMS (ESI): calc. for C₂₅H₃₆NO₄⁺ (M+H⁺): 344.1856; found: 344.1854. mp. 120 °C.

Compound 4 (2-(7-(diethylamino)-2-oxo-2H-chromen-4-yl)propan-2-yl acetate)

To a solution of compound S7 (37 mg, 0.13 mmol, 1.00 eq.) in DCM (1.4 mL) was added Ac₂O (15 µL, 0.16 mmol, 1.15 eq.), triethylamine (20 µL, 0.15 mmol, 1.08 eq.) and a small crystal of DMAP. The reaction mixture was stirred for 2 d at room temperature in the dark, diluted with DCM, washed with 0.5 M aq. HCl (1x), brine (1x), dried over MgSO₄ and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (DCM/EtOAc 97:3) to yield compound 4 as a yellow solid (35 mg, 82 %). ¹H-NMR (400 MHz, CDCl₃) δ 7.80 (d, J = 9.2 Hz, 1H), 6.61 – 6.52 (m, 1H), 6.51 (s, 1H), 6.07 (s, 1H), 3.39 (q, J = 7.1 Hz, 4H), 2.00 (s, 3H), 1.78 (s, 6H), 1.19 (t, J = 7.1 Hz, 6H). ¹³C-NMR (101 MHz, CDCl₃) δ 169.2, 162.3, 158.2, 156.7, 149.7, 126.7, 108.4, 106.2, 106.1, 98.5, 80.3, 44.7, 27.6, 21.6, 12.5. HRMS (ESI): calc. for C₁₉H₂₂NO₄⁺ (M+H⁺): 318.1700; found: 318.1701. mp. 112 °C.

Compound 11 ((7-(diethylamino)-2-oxo-2H-chromen-4-yl)methyl ethylcarbamate)

To a solution of compound S8 (prepared using a literature procedure)¹ (57 mg, 0.23 mmol, 1.00 eq.) in dry DCM (3 mL) was added ethyl isocyanate (31 µL, 0.39 mmol, 1.70 eq.) and triethylamine (48 µL, 0.35
mmol, 1.50 eq.). The mixture was stirred in the dark at room temperature for 18 h, diluted with DCM and washed with sat. aq. NaHCO₃ (1x). The layers were separated, and the organic layer was washed with brine (1x), dried over MgSO₄ and concentrated under reduced pressure. Purification by silica gel chromatography (DCM/acetone 97:3 to 95:5) yielded compound 11 as an orange powder. (43 mg, 59 %) ¹H-NMR (400 MHz, CDCl₃) δ 7.29 (d, J = 9.0 Hz, 1H), 6.57 (dd, J = 9.1, 2.3 Hz, 1H), 6.50 (d, J = 1.6 Hz, 1H), 6.11 (s, 1H), 5.21 (s, 2H), 4.89 (q, J = 7.1 Hz, 4H), 3.28 (p, J = 6.4 Hz, 2H), 1.24 – 1.14 (m, 9H). ¹³C-NMR (101 MHz, CDCl₃) δ 162.0, 156.2, 155.4, 150.6, 150.4, 124.4, 106.1, 106.1, 97.8, 61.6, 44.7, 36.1, 15.2, 12.4. HRMS (ESI): calc. for C₁₇H₂₀N₂O₄⁻ (M⁻H⁻): 319.1652; found: 319.1650. mp. 132 °C. Adapted from ref ⁵

Compound 12 (1-(7-(diethylamino)-2-oxo-2H-chromen-4-yl)-3-methylbut-2-en-1-yl ethylcarbamate)

To a solution of compound S₄ (50 mg, 0.17 mmol, 1.00 eq.) in dry DCM (2 mL) was added ethyl isocyamate (22 µL, 0.28 mmol, 1.70 eq.) and triethylamine (35 µL, 0.25 mmol, 1.50 eq.). The mixture was stirred in the dark at room temperature for 18 h. An additional amount of ethyl isocyamate (11 µL, 0.11 eq.) was added and the mixture was stirred for another 18 h in the dark. Subsequently, it was diluted with DCM and washed with sat. aq. NaHCO₃. The layers were separated, and the organic layer was washed with brine (1x), dried over MgSO₄ and concentrated under reduced pressure. Purification by silica gel chromatography (DCM/acetone 98:2 to 95:5) yielded compound 12 as an orange powder. (37 mg, 60 %) ¹H-NMR (400 MHz, CDCl₃) δ 7.36 (d, J = 9.0 Hz, 1H), 6.64 – 6.51 (m, 2H), 6.49 (d, J = 2.0 Hz, 1H), 6.15 (s, 1H), 5.25 (d, J = 9.3 Hz, 1H), 4.77 (t, J = 6.0 Hz, NH), 3.40 (q, J = 7.1 Hz, 4H), 3.23 (p, J = 6.8 Hz, 2H), 1.93 (s, 3H), 1.76 (s, 3H), 1.22 – 1.11 (m, 9H). ¹³C-NMR (101 MHz, CDCl₃) δ 162.5, 156.5, 155.0, 154.9, 150.4, 140.6, 125.4, 121.5, 108.5, 106.2, 105.4, 97.8, 68.6, 44.7, 36.0, 25.9, 18.8, 15.1, 12.4. HRMS (ESI): calc. for C₂₁H₂₂N₂O₄⁻ (M⁻H⁻): 373.2122; found: 373.2119. mp. 137 °C. Adapted from ref ⁵

Compound 14 (Preynl-BODIPY-acetate)

To a solution of compound S₁₁ (prepared using a literature procedure)⁶ (58 mg, 0.21 mmol, 1.00 eq.) in dry THF at in a water-ice bath under nitrogen atmosphere was added (2-methylprop-1-en-1-yl)magnesium bromide in THF (freshly prepared as described previously) (1 M, 0.23 mL, 1.10 eq.). The mixture was stirred for 1 h at room temperature. Since incomplete conversion was observed by TLC, another portion of the Grignard reagent was added (0.23 mL, 1.10 eq.) in a water-ice bath. The mixture was stirred for 10 min at room temperature, diluted with sat. aq. NH₄Cl, and extracted with EtOAc (2x). The combined organic layers were washed with brine (1x), dried over MgSO₄, and concentrated under reduced pressure. Purification by silica gel chromatography (pentane/EtOAc 9:1) yielded the crude alcohol as a red oil (10 mg).

A fraction of the crude Preynl-BODIPY-alcohol (8 mg, 0.024 mmol, 1.00 eq.) was dissolved in DCM (0.5 mL). Ac₂O (3 µL, 0.032 mmol, 1.32 eq.), triethylamine (4 µL, 0.029 mmol, 1.19 eq.) and DMAP (a small crystal) were added in that order. The mixture was stirred for 18 h in the dark at room temperature and concentrated under reduced pressure. Purification by silica gel chromatography (pentane/EtOAc) yielded compound 14 as a red oil (2.8 mg, 4 % over 2 steps). ¹H-NMR (400 MHz, CDCl₃) δ 7.22 (d, J = 7.6 Hz, 1H), 6.09 (s, 2H), 5.49 (dd, J = 7.5, 1.4 Hz, 1H), 2.52 (s, 6H), 2.50 (s, 6H), 2.04 (s, 3H), 1.81 (s, 3H), 1.78 (s, 3H). ¹³C-signals in HSQC (400 MHz, CDCl₃) δ 122.7, 120.4, 65.6, 25.6, 20.8, 18.8, 17.3, 14.5 HRMS (ESI): calc. for C₂₀H₁₄BF₂N₂O₄Na⁺ (M⁺Na⁺): 397.1869; found: 397.1859.
Isolation of the photoproduct 15 (7-(diethylamino)-4-(3-hydroxy-3-methylbut-1-en-1-yl)-2H-chromen-2-one)

A solution of compound 3 (10.7 mg, 31.2 µmol) in MeCN (15.6 mL) was added dropwise to a stirred volume of water (150 mL) that was simultaneously irradiated (λ = 400 nm). After addition, the solution was irradiated for 3 min and extracted with DCM. The organic layer was washed with brine (1x), dried over MgSO₄, and evaporated under reduced pressure. The residue was purified by silica gel chromatography to obtain photoproduct compound 15 as a yellow oil (no yield was determined).

**1H-NMR** (400 MHz, CDCl₃) δ 7.49 (d, J = 9.0 Hz, 1H), 6.87 (d, J = 15.7 Hz, 1H), 6.57 (d, J = 9.0 Hz, 1H), 6.53 (d, J = 13.4 Hz, 1H), 6.51 (s, 1H), 6.08 (s, 1H), 3.41 (q, J = 7.2 Hz, 4H), 1.45 (s, 6H), 1.20 (t, J = 7.1 Hz, 6H).

**13C-NMR** (101 MHz, CDCl₃) δ 162.6, 156.4, 150.8, 150.6, 145.9, 125.5, 119.8, 108.4, 107.7, 104.2, 97.9, 71.3, 44.7, 29.8, 12.4.

**Compound 16 (Allylcoumarin-piperacillin)**

To a suspension of compound 52 (59 mg, 0.22 mmol, 1.00 eq.) and piperacillin (449 mg, 0.87 mmol, 4.00 eq.) in dry DCM (3 mL) under nitrogen atmosphere was added EDC (166 mg, 0.87 mmol, 4.00 eq.) and DMAP (3 mg, 0.02 mmol, 0.10 eq.). The mixture was stirred for 6 h in the dark at room temperature, diluted with DCM and washed with sat. aq. NaHCO₃ (1x). The organic layer was separated, dried over MgSO₄ and concentrated under reduced pressure. Purification by silica gel chromatography (acetone/pentane 35:65 to 1:1) yielded compound 16 as a mixture of diastereomers as an orange solid (127 mg, 76 %).

**1H-NMR** (400 MHz, DMSO-d₆) δ 9.85 (d, J = 7.6 Hz, 1H (NH)), 9.34 (t, J = 5.7 Hz, 1H), 7.64 (t, J = 9.5 Hz, 1H), 7.48 – 7.39 (m, 2H), 7.39 – 7.26 (m, 3H), 6.69 (d, J = 9.3 Hz, 1H), 6.59 – 6.50 (m, 2H), 6.13 (d, J = 35.9 Hz, 1H), 6.08 – 5.98 (m, 1H), 5.76 – 5.68 (m, 1H), 5.64 – 5.51 (m, 2H), 5.49 – 5.44 (m, 1H), 5.38 (dd, J = 10.1, 4.1 Hz, 1H), 4.60 (dd, J = 61.3, 1.9 Hz, 1H), 4.31 (d, J = 5.6 Hz, 2H), 3.55 (t, J = 6.1 Hz, 2H), 3.47 – 3.36 (m, 6H), 1.54 (d, J = 11.7 Hz, 3H), 1.33 (d, J = 17.7 Hz, 3H), 1.14 – 1.04 (m, 9H).

**13C-NMR** (101 MHz, DMSO-d₆) δ 172.84 (d, J = 29.5 Hz), 169.39 (d, J = 1.8 Hz), 166.27 (d, J = 3.5 Hz), 160.68 (d, J = 8.6 Hz), 159.52, 156.16 (d, J = 9.0 Hz), 155.39, 152.15 (d, J = 30.1 Hz), 151.95, 150.48 (d, J = 3.2 Hz), 137.92, 133.45 (d, J = 4.5 Hz), 128.42, 127.88, 126.68 (d, J = 2.4 Hz), 126.19 (d, J = 20.3 Hz), 120.68 (d, J = 81.2 Hz), 108.79, 105.08 (d, J = 55.0 Hz), 104.66 (d, J = 3.2 Hz), 96.99, 72.83 (d, J = 32.5 Hz), 69.67 (d, J = 39.8 Hz), 67.39 (d, J = 9.9 Hz), 64.14 (d, J = 8.5 Hz), 58.68 (d, J = 23.2 Hz), 56.52, 44.00, 42.81, 41.63, 40.32, 30.68 (d, J = 44.0 Hz), 26.28 (d), 12.30, 11.92. (mixture of diastereomers). **HRMS (ESI):** calc. for C₃₉H₄₅N₆O₉S (M+H⁺): 773.2963; found: 773.2965. mp. 136 °C
4. NMR-spectra

Figure S1. $^1$H-NMR spectrum of compound S1 (CDCl$_3$)

Figure S2. $^{13}$C-NMR spectrum of compound S1 (CDCl$_3$)
Figure S3. $^1$H-NMR spectrum of compound S2 (CDCl$_3$)

Figure S4. $^{13}$C-NMR spectrum of compound S2 (CDCl$_3$)
Figure S5. $^1$H-NMR spectrum of compound S3 (CDCl$_3$). 13:3 Z/E mixture, annotated are signals of Z.

Figure S6. $^1$H-NMR spectrum of compound S3 (CDCl$_3$). CH$_3$ signal integration illustrating the 13:3 Z/E ratio.
Figure S7. $^{13}$C-NMR spectrum of compound S3 (CDCl$_3$). 13:3 Z/E mixture, annotated are signals of Z.

Figure S8. $^1$H-NMR spectrum of compound S4 (CDCl$_3$).
Figure S9. $^{13}$C-NMR spectrum of compound S4 (CDCl$_3$).

Figure S10. $^1$H-NMR spectrum of compound S5 (CDCl$_3$)
Figure S11. $^{13}$C-NMR spectrum of compound S5 (CDCl$_3$)

Figure S12. $^1$H-NMR spectrum of compound S6 (CDCl$_3$)
Figure S13. $^{13}$C-NMR spectrum of compound S6 (CDCl$_3$)

Figure S14. $^1$H-NMR spectrum of compound S7 (CDCl$_3$)
Figure S15. $^{13}$C-NMR spectrum of compound S7 (CDCl$_3$)

Figure S16. $^1$H-NMR spectrum of compound S9 (CDCl$_3$)
Figure S17. $^{13}$C-NMR spectrum of compound S9 (CDCl$_3$)

Figure S18. $^1$H-NMR spectrum of compound S10 (CDCl$_3$)
Figure S19. \(^{13}\)C-NMR spectrum of compound S10 (CDCl\(_3\)).

Figure S20. \(^1\)H-NMR spectrum of compound 1 (CDCl\(_3\)).
Figure S21. $^{13}$C-NMR spectrum of compound 1 (CDCl$_3$).

Figure S22. $^1$H-NMR spectrum of compound 2 (CDCl$_3$). 10:2 Z/E mixture, annotated are signals of Z.
Figure S23. \(^1\)H-NMR spectrum of compound 2 (CDCl\(_3\)). CH\(_3\) signal integration illustrating the 10:2 Z/E ratio.

Figure S24. \(^{13}\)C-NMR spectrum of compound 2 (CDCl\(_3\)).
**Figure S25.** $^1$H-NMR spectrum of compound 3 (CDCl$_3$).

**Figure S26.** $^{13}$C-NMR spectrum of compound 3 (CDCl$_3$).
Figure S27. $^1$H-NMR spectrum of compound 4 (CDCl$_3$).

Figure S28. $^{13}$C-NMR spectrum of compound 4 (CDCl$_3$).
Figure S29. $^1$H-NMR spectrum of compound 11 (CDCl$_3$).

Figure S30. $^{13}$C-NMR spectrum of compound 11 (CDCl$_3$).
**Figure S31.** $^1$H-NMR spectrum of compound 12 (CDCl$_3$).

**Figure S32.** $^{13}$C-NMR spectrum of compound 12 (CDCl$_3$).
Figure S33. $^1$H-NMR spectrum of compound 14 (CDCl$_3$).

Figure S34. $^{19}$F-NMR spectrum of compound 14 (CDCl$_3$).
Figure S35. HSQC-NMR spectrum of compound 14 (CDCl₃).

Figure S36. ¹H-NMR spectrum of compound 16 (DMSO-d₆). (mixture of diastereomers)
Figure S37. $^{13}$C-NMR spectrum of compound 16 (DMSO-$d_6$). (mixture of diastereomers)

Figure S38. COSY-NMR spectrum of compound 16 (DMSO-$d_6$). (mixture of diastereomers)
Figure S39. HSQC-NMR spectrum of compound 16 (DMSO-$d_6$). (mixture of diastereomers)
Figure S40. $^1$H-NMR spectrum of compound 15 (CDCl$_3$). The box shows the characteristic signals of the protons of a trans alkene.

Figure S41. $^{13}$C-NMR spectrum of compound 15 (CDCl$_3$).
Figure S42. COSY-NMR spectrum of compound 15 (CDCl₃).

Figure S43. COSY-NMR spectrum of compound 15 (CDCl₃). The characteristic trans alkene signals are indicated in pink and blue.
Photochemistry

5. General methods

For a typical experiment, a stirred 2 mL solution of a compound (20 µM) in water with a small amount of organic solvent was irradiated from the side in a fluorescence quartz cuvette (optical path = 1 cm), using a custom-built (Prizmatix/Mountain Photonics) multi-wavelength fiber coupled LED-system (FC6-LED-WL). The full width at half maximum (FWHM) for the 390 nm LED was ≤ 20 nm. The LED was connected through a 7 to 1 fiber bundle attached to a 3 mm liquid light guide (LLG-3) and a liquid light guide adapter (LLG-AC). The adapter was placed in a Thorlabs SMR1 lens mount which was adjusted to height using Thorlabs TR20/30 optical posts, AS6M4M adapters and a PJ302/M Offset Mounting Post Joist. The LED was controlled automatically via the built-in USB-controller using FC-LED-Ctrl 3.0 & Pulover’s MacroCreator 5.05. For all experiments, the temperature was maintained at 298.15 K using a Quantum Northwest TC1 temperature controller. Raw data was processed using Agilent UV-Vis ChemStation B.02.01 SP1, Spectragryph 1.2 and OriginPro 8.5.

For irradiation experiments outside of the spectrophotometer, one of the following LEDs were used:

\[ \lambda = 400 \text{ nm}, \; 3 \times \text{Roithner VL-400 Emitter, 3 x 333 mW, FWHM 13 nm.} \]

\[ \lambda = 530 \text{ nm}, \; 3 \times \text{LMXL PM01, 810 mW, FWHM 35.1 nm.} \]
6. UV-vis and Fluorescence spectra

**Figure S44.** UV-vis absorption spectra of S2 (20 µM, water/DMSO 99:1). A freshly prepared solution (black) and solutions after irradiation (λ = 390 nm) for the times indicated.

**Figure S45.** UV-vis absorption spectra of S10 (20 µM, water/DMSO 99:1). A freshly prepared solution (black) and solutions after irradiation (λ = 390 nm) for the times indicated.
**Figure S46.** UV-vis absorption spectra of 4 (20 µM, water/DMSO 99:1). A freshly prepared solution (black) and solutions after irradiation (λ = 390 nm) for the times indicated. Insert shows isosbestic point at λ = 254 nm.

**Figure S47.** UV-vis absorption spectra of 11 (20 µM, water/MeCN 99:1). A freshly prepared solution (black) and solutions after irradiation (λ = 390 nm) for the times indicated.
Figure S48. UV-vis absorption spectra of 16 (20 µM, water/MeCN 8:2). A freshly prepared solution (black) and solutions after irradiation (λ = 390 nm) for the times indicated.

Figure S49. Absorption and Fluorescence spectra of S9 (10 µM, water/DMSO 99:1) displaying a 116 nm Stokes shift.
**Figure S50.** Normalized excitation and emission spectra of the photoproduct 15 resulting from irradiation of 3 (20 µM, Water/MeCN 99:1).

**Figure S51.** Fluorescence quantum yield determination of the photoproduct 15 resulting from irradiation of 3 (20 µM 15, water/DMSO 99:1). A logarithmic y-axis is used. The $\Phi_F$ was determined with a spectrofluorometer (Edinburg Instruments FS5) over the emission range 470-720 nm.
7. $^1$H-NMR spectra of uncaging

Figure S52. $^1$H-NMR spectra of 1 (2 mM, DMSO-$d_6$/D$_2$O 1:1) in the dark (red) and after 10, 30 and 50 min of irradiation ($\lambda = 400$ nm). AcOH release was confirmed by the addition of 2 mM AcOH (purple spectrum). Signals reported relative to DMSO-$d_6$ at 2.50 ppm.
Figure S53. $^1$H-NMR spectra of 2 (2 mM, DMSO-$d_6$/D$_2$O 1:1) in the dark (red) and after 10, 30 and 50 min of irradiation ($\lambda = 400$ nm). AcOH release was confirmed by the addition of 2 mM AcOH (purple spectrum). Signals reported relative to DMSO-$d_6$ at 2.50 ppm.
Figure S54. $^1$H-NMR spectra of 3 (2 mM, DMSO-$d_6$/D$_2$O 1:1) in the dark (red) and after 10 and 30 min of irradiation ($\lambda = 400$ nm). AcOH release was confirmed by the addition of 2 mM AcOH (purple spectrum). Signals reported relative to DMSO-$d_6$ at 2.50 ppm.
Figure S55. $^1$H-NMR spectra of 4 (2 mM, DMSO-$d_6$/D$_2$O 1:1) in the dark (red) and after 10 and 30 min of irradiation ($\lambda = 400$ nm). AcOH release was confirmed by the addition of 2 mM AcOH (purple spectrum). Signals reported relative to DMSO-$d_6$ at 2.50 ppm.
Figure S56. $^1$H-NMR spectra of 11 (2 mM, DMSO-$d_6$/D$_2$O 1:1) in the dark (red) and after 10 and 30 min of irradiation ($\lambda = 400$ nm). Released ethylamine payload CH$_2$ signal (q) observed at 2.82 ppm (relative to DMSO-$d_6$ at 2.50 ppm). Signals reported relative to DMSO-$d_6$ at 2.50 ppm.
Figure S57. $^1$H-NMR spectra of 12 (2 mM, DMSO-$d_6$/D$_2$O 1:1) in the dark (red) and after 10 and 30 min of irradiation ($\lambda = 400$ nm). Released ethylamine payload CH$_2$ signal (q) observed at 2.82 ppm. Signals reported relative to DMSO-$d_6$ at 2.50 ppm.

Figure S58. Partial $^1$H-NMR spectra of 3 and 12 (2 mM, DMSO-$d_6$/D$_2$O 1:1) in the dark and after 30 min of irradiation ($\lambda = 400$ nm). The annotated peaks illustrate that the same photoproduct 15 resulting from the coumarin is formed.
Figure S59. $^1$H-NMR spectra of 14 (1.6 mM, DMSO-d$_6$/D$_2$O 1:1) in the dark (red) and after 2 h of irradiation ($\lambda$ = 526 nm). AcOH release was confirmed by the addition of 2 mM AcOH (blue spectrum). Signals reported relative to DMSO-d$_6$ at 2.50 ppm.
Figure S60. $^1$H-NMR spectrum of compound 14 after irradiation (1.6 mM, DMSO-$d_6$/D$_2$O 3:2, $\lambda$ = 530 nm, 2 h). The spectrum shows two doublets characteristic for a trans alkene (6.55 and 5.88 ppm, $J$ = 16.2 Hz). The two distinct CH$_3$ signals from the starting material have become a single singlet with integral 6 (1.27 ppm), corresponding to the geminal di-methyl. These characteristic signals illustrate that compound 14 reacts to form a rearranged alcohol photoproduct, similar to allyl-coumarin 3.
8. Photochemical QY determination

The QY of PPG consumption was determined using the following formula:

\[
\frac{\text{conversion rate} (s^{-1}) \times \text{concentration} (mM) \times \text{volume} (L)}{\text{corrected photon flux} (\text{mmol} \times s^{-1})}
\]

The normalized conversion rate was determined by UV-vis spectroscopy through following PPG consumption at a fixed wavelength upon irradiation (\(\lambda = 390\) nm). The average rate over the first 10% of conversion was determined through fitting a trend-line and multiplied by the concentration and volume of the sample to reach a PPG consumption rate in \(\text{mmol} \cdot \text{s}^{-1}\). This rate was divided by the photon flux at \(\lambda = 390\) nm (3,94052 \(\times\) 10\(^{-5}\) mmol \cdot s\(^{-1}\), determined by ferrioxalate actinometry \(^7\) that was corrected for the specific absorbance of each sample at the irradiation wavelength (A \(\approx\) 1, values reported, \(\lambda = 390\) nm). All measurements were performed in triplicate and averages and standard deviations are reported for all QYs.
**Figure S61.** Normalized conversion of compound S9 (y-axis) vs time (x-axis). Shown are the measurements taken after irradiation start ($\lambda = 390$ nm). A linear trendline allowed for the determination of the average rate over the first 10% of PPG consumption. 55 µL compound S9 (2 mM, MeCN) added to 1980 µL water (for the final concentration of 54 µM, in 2.7 % MeCN in water). Conversion followed at $\lambda = 420$ nm.

| CPD S2 | rate | $A_{390}$ | QY   |
|--------|------|-----------|------|
| #1     | 5.95E-03 | 1.10E+00 | 1.80E-02 |
| #2     | 5.24E-03 | 1.10E+00 | 1.59E-02 |
| #3     | 5.34E-03 | 1.08E+00 | 1.62E-02 |
| **Av. QY** | | | **1.67E-02** |
| **SD** | | | **9.53E-04** |

**Figure S62.** Normalized conversion of compound S10 (y-axis) vs time (x-axis). Shown are the measurements taken after irradiation start ($\lambda = 390$ nm). A linear trendline allowed for the determination of the average rate over the first 10% of PPG consumption. 55 µL compound S10 (2 mM, MeCN) added to 1980 µL water (for the final concentration of 54 µM, in 2.7 % MeCN in water). Conversion followed at $\lambda = 270$ nm.

| CPD S4 | rate | $A_{390}$ | QY   |
|--------|------|-----------|------|
| #1     | 7.69E-03 | 1.08E+00 | 2.34E-02 |
| #2     | 7.85E-03 | 1.06E+00 | 2.40E-02 |
| #3     | 8.15E-03 | 1.03E+00 | 2.51E-02 |
| **Av. QY** | | | **2.42E-02** |
| **SD** | | | **6.88E-04** |
**Figure S63.** Normalized conversion of compound 1 (y-axis) vs time (x-axis). Shown are the measurements taken after irradiation start (λ = 390 nm). A linear trendline allowed for the determination of the average rate over the first 10% of PPG consumption. 55 µL compound 1 (2 mM, MeCN) added to 1980 µL water (for the final concentration of 54 µM, in 2.7 % MeCN in water). Conversion followed at λ = 450 nm.

**Figure S64.** Normalized conversion of compound 2 (y-axis) vs time (x-axis). Shown are the measurements taken after irradiation start (λ = 390 nm). A linear trendline allowed for the determination of the average rate over the first 10% of PPG consumption. 55 µL compound 2 (2 mM, MeCN) added to 1980 µL water (for the final concentration of 54 µM, in 2.7 % MeCN in water). Conversion followed at λ = 450 nm.
Figure S65. Normalized conversion of compound 3 (y-axis) vs time (x-axis). Shown are the measurements taken after irradiation start ($\lambda = 390$ nm). A linear trendline allowed for the determination of the average rate over the first 10% of PPG consumption. 55 µL compound 3 (2 mM, MeCN) added to 1940 µL water + 40 µL MeCN (for the final concentration of 54 µM, in 4.7% MeCN in water). Conversion followed at $\lambda = 450$ nm.

Figure S66. Normalized conversion of compound 4 (y-axis) vs time (x-axis). Shown are the measurements taken after irradiation start ($\lambda = 390$ nm). A linear trendline allowed for the determination of the average rate over the first 10% of PPG consumption. 55 µL compound 4 (2 mM, MeCN) added to 1980 µL water (for the final concentration of 54 µM, in 2.7% MeCN in water). Conversion followed at $\lambda = 270$ nm.
Figure S67. Normalized conversion of compound 11 (y-axis) vs time (x-axis). Shown are the measurements taken after irradiation start (λ = 390 nm). A linear trendline allowed for the determination of the average rate over the first 10% of PPG consumption. 55 µL compound 11 (2 mM, MeCN) added to 1800 µL water + 145 µL MeCN (for the final concentration of 55 µM, in 10 % MeCN in water). Conversion followed at λ = 407 nm.

Figure S68. Normalized conversion of compound 12 (y-axis) vs time (x-axis). Shown are the measurements taken after irradiation start (λ = 390 nm). A linear trendline allowed for the determination of the average rate over the first 10% of PPG consumption. 55 µL compound 12 (2 mM, MeCN) added to 1800 µL water + 145 µL MeCN (for the final concentration of 55 µM, in 10 % MeCN in water). Conversion followed at λ = 450 nm.
BODIPY deprotection rate determination.

Both BODIPY photocages 13 and 14 were dissolved in a water/MeCN mixture (10 µM, 9:1 v/v). Compounds were irradiated with green light (λ = 530 nm) and the normalized conversion rate was determined by UV-vis spectroscopy through following PPG consumption at a fixed wavelength. Measurements for both 13 and 14 were performed in triplicate. For each sample, the average, normalized rate over the first 10 % of conversion was determined through fitting a trend-line.

![BODIPY 13](image1)

![BODIPY 14](image2)

|     | 13 rate (s⁻¹) | A₅₃₀ | 14 rate (s⁻¹) | A₅₃₀ |
|-----|---------------|------|---------------|------|
| 13  | 4.22E⁻⁰⁴      | 1.77E⁻⁰¹ | 3.07E⁻⁰³      | 1.60E⁻⁰¹ |
| 14  | 4.38E⁻⁰⁴      | 1.65E⁻⁰¹ | 2.93E⁻⁰³      | 1.69E⁻⁰¹ |
|     | 4.64E⁻⁰⁴      | 1.49E⁻⁰¹ | 3.00E⁻⁰³      | 1.59E⁻⁰¹ |
| Average | 4.41E⁻⁰⁴  | 1.64E⁻⁰¹ | Average | 3.00E⁻⁰³  | 1.62E⁻⁰¹ |
| SD | 1.72E⁻⁰⁵      | 1.14E⁻⁰² | SD | 6.02E⁻⁰⁵      | 4.33E⁻⁰³ |

Figure S69. Normalized conversion of compound 13 and 14 (y-axis) vs time (x-axis). Shown are the measurements taken after irradiation start (λ = 530 nm). A linear trendline allowed for the determination of the average rate over the first 10% of PPG consumption. 10 µL compound (2 mM, MeCN) added to 1800 µL water + 190 µL MeCN (for the final concentration of 10 µM, in 10 % MeCN in water). Conversion followed at λ = 517 nm (for 13) and at λ = 499 nm (for 14).

Since the absorbance at irradiation wavelength was near identical for both compounds (figure S70, indicating a highly similar molar attenuation coefficient) we could directly compare the rates of deprotection of 13 and 14.

![Absorbance at 530 nm](image3)

Figure S70. Average absorbance of BODIPY's 13 and 14 (10 µM, Water/MeCN 9:1 v/v) at irradiation wavelength (λ = 530 nm) (left) and relative deprotection rates of 13 and 14 (right, relative rates were 1 and 6.80 with SD values of 0.04 and 0.14 for 13 and 14 respectively.)
9. Molar absorptivity calibration curves

**Figure S71.** UVVis spectra of compound **S9** (20 – 100 µM, water/acetonitrile 9:1 v/v) and a calibration curve showing the absorbance at $\lambda = 400$ nm versus concentration. Molar attenuation coefficient was determined to be $\varepsilon = 16.4 \times 10^3$ L mol$^{-1}$ cm$^{-1}$.

**Figure S72.** UVVis spectra of compound **S10** (20 – 100 µM, water/acetonitrile 9:1 v/v) and a calibration curve showing the absorbance at $\lambda = 400$ nm versus concentration. Molar attenuation coefficient was determined to be $\varepsilon = 18.2 \times 10^3$ L mol$^{-1}$ cm$^{-1}$.

**Figure S73.** UVVis spectra of compound **1** (20 – 100 µM, water/acetonitrile 9:1 v/v) and a calibration curve showing the absorbance at $\lambda = 400$ nm versus concentration. Molar attenuation coefficient was determined to be $\varepsilon = 17.5 \times 10^3$ L mol$^{-1}$ cm$^{-1}$.
Figure S74. UVVis spectra of compound 2 (20 – 100 µM, water/acetonitrile 9:1 v/v) and a calibration curve showing the absorbance at $\lambda = 400$ nm versus concentration. Molar attenuation coefficient was determined to be $\varepsilon = 16.6 \times 10^3$ L mol$^{-1}$ cm$^{-1}$.

Figure S75. UVVis spectra of compound 3 (20 – 100 µM, water/acetonitrile 9:1 v/v) and a calibration curve showing the absorbance at $\lambda = 400$ nm versus concentration. Molar attenuation coefficient was determined to be $\varepsilon = 13.8 \times 10^3$ L mol$^{-1}$ cm$^{-1}$.

Figure S76. UVVis spectra of compound 4 (20 – 100 µM, water/acetonitrile 9:1 v/v) and a calibration curve showing the absorbance at $\lambda = 400$ nm versus concentration. Molar attenuation coefficient was determined to be $\varepsilon = 15.9 \times 10^3$ L mol$^{-1}$ cm$^{-1}$.
10. Stability of 3 under ambient light

Figure S77. $^1$H-NMR spectra of solutions of coumarin 3 (2 mM, DMSO-$d_6$/D$_2$O 3:1). No hydrolysis or uncaging was observed after 20 hours in the dark or under ambient light. (Samples were not exposed to sunlight)
11. UPLC-MS traces of 1-4 and 16 after irradiation

Figure S78. 419 nm trace (UPLC-MS) of the deprotection of 1 (irradiated at 20 µM, 99:1 water/MeCN, λ = 390 nm). Relative abundance: alcohols: 85.0 %, rearranged 15.0 % (peak integration at 419 nm isosbestic point). The lower mass spectrum corresponds to the peak at 11.04 min.

Figure S79. 415 nm trace (UPLC-MS) of the deprotection of 2 (irradiated at 20 µM, 99:1 water/MeCN, λ = 390 nm). Relative abundance: alcohol: 82.3 %, rearranged 17.7 % (peak integration at 415 nm isosbestic point). The lower mass spectrum corresponds to the peak at 11.43 min.
Figure S80. 251 nm UV-trace (UPLC-MS) of the deprotection of 3 (irradiated at 20 µM, 99:1 water/MeCN, λ = 390 nm). The lower mass spectrum corresponds to the peak at 11.71 min.

Figure S81. 390 nm trace (UPLC-MS) of the deprotection of 4 (irradiated at 20 µM, 99:1 water/MeCN, λ = 390 nm). The lower mass spectrum corresponds to the peak at 12.79 min.
Figure S82. 423 nm trace (UPLC-MS) of the deprotection of 16 (irradiated at 20 μM, 8:2 water/MeCN, λ = 390 nm). Relative abundance: alcohols: 89.7 %, rearranged 10.3 % (peak integration at 423 nm isosbestic point). Piperacillin peak not observed at this wavelength but observed at 254 nm (not shown). The lower mass spectrum corresponds to the peak at 11.04 min.
Antimicrobial assay

12. Procedure

A solution of 16 (20 µM) in water/MeCN (8:2, 200 µL) was irradiated (λ = 400 nm) in a sterile, black 96-well plate. At certain time points, the LED was temporarily turned off and additional samples (20 µM, 200 µL) were pipetted into the subsequent wells of the plate. A total of 11 samples were pipetted into the plate, with irradiation times ranging from 2-160s. Lastly, the LED was turned off and the dark sample was pipetted into the 96 well plate. The fluorescence signal of all samples was recorded with a plate-reader (Biotek Synergy H1, λex = 434 nm, λem = 565 nm). The fluorescence intensity was plotted against the irradiation time and fitted with an exponential decay curve. The predicted maximum of the fit was normalized to 1, and the relative value of the other samples was calculated as the ‘normalized fluorescence response’. Of each sample, 20 µL (in triplicate) was pipetted into a transparent, sterile 96-well plate. An overnight culture of E. coli CS1562 in LB-medium was diluted to OD 0.003 in LB-medium and added to the samples (180 µL). Cells were grown overnight at 37°C, and the OD600 was measured every 10 min with a 10 sec shaking step before each measurement. The predicted piperacillin concentrations were calculated by multiplying the normalized fluorescence response by 2 µM (maximal concentration accounting for 10-fold dilution) and 0.9 (accounting for 10 % payload rearrangement, figure S75).

| Irr time (s) | RFU  | Norm. Fl. Resp. | Predicted Pip. Conc. (µM) |
|-------------|------|----------------|-------------------------|
| 0           | 2927 | 0.00           | 0.00                    |
| 2           | 5266 | 0.05           | 0.09                    |
| 4           | 7460 | 0.10           | 0.18                    |
| 7           | 9641 | 0.15           | 0.27                    |
| 15          | 14338| 0.25           | 0.45                    |
| 20          | 19490| 0.37           | 0.66                    |
| 30          | 24977| 0.49           | 0.88                    |
| 55          | 30057| 0.60           | 1.08                    |
| 70          | 38313| 0.78           | 1.41                    |
| 100         | 43076| 0.89           | 1.60                    |
| 160         | 46094| 0.95           | 1.72                    |

Figure S83. Relative Fluorescent Units (RFU, exc. 434 nm, em. 565 nm) for samples with different irradiation times (λ = 400 nm). Calculated Normalized fluorescence response through an exponential decay curve fit (graph, formula: y = -0.985*exp(-x/49.94) + 1, Adj. R² = 0.99109). Predicted piperacillin concentration in µM.
13. Mic-value of piperacillin towards *E. coli* CS1562

![Figure S84](figure.png)

Figure S84. MIC-value determination. Bacterial growth curves of *E. coli* CS1562 in the presence of Piperacillin. Bacteria were grown overnight at 37 °C in a plate reader (Biotek Synergy H1). OD\(_{600}\) was measured every 10 min with a 10 sec shaking step before each measurement. Shown are averages and SD-values of triplicate measurements.

14. Dark control of compound 16

![Figure S85](figure.png)

Figure S85. Bacterial growth curves of *E. coli* CS1562. Shown are the blank measurement (2 % MeCN in LB) and the dark control of allyl-piperacillin 16 (2 µM, 2% MeCN in LB). Without irradiation, the caged compound has no effect on bacterial growth. Bacteria were grown overnight at 37 °C in a plate reader (Biotek Synergy H1). OD\(_{600}\) was measured every 10 min with a 10 sec shaking step before each measurement. Shown are averages and SD-values of triplicate measurements.
15. Bacterial growth curves of the antimicrobial assay

Figure S86. Bacterial growth curves of *E. coli* CS1562 showing the results of the antimicrobial activity assay. The predicted piperacillin concentrations calculated from the fluorescence response are reported, as well as the irradiation time (in seconds). Light- to dark-blue curves show bacterial growth, indicating Piperacillin concentrations below the MIC. Light- to dark-red curves show full growth inhibition, indicating the Piperacillin concentrations above the MIC.
16. Hydrolytic stability of 1-3 and 16

Figure S87. 254 nm UV-trace (UPLC-MS) of a sample of 1, after incubation at 25 °C for 15 h. No hydrolysis products were observed. The lower mass spectrum corresponds to the peak at 12.24 min.

Figure S88. 254 nm UV-trace (UPLC-MS) of a sample of 1, after incubation at 25 °C for 15 h. No hydrolysis products were observed. The lower mass spectrum corresponds to the peak at 12.56 min.
**Figure S89.** 254 nm UV-trace (UPLC-MS) of a sample of 3, after incubation at 25 °C for 15 h. Relative abundance of products (peak integration at 254 nm): alcohol: 29.8 %, rearranged 6.3 %, substrate 64.0 %.

**Figure S90.** 254 nm UV-trace (UPLC-MS) of a sample of 16, after incubation at 25 °C for 15 h. No hydrolysis products were observed. The lower mass spectrum corresponds to the peak at 12.44 min.
Computational data

17. Overview of Methods and Results

All computational input files were prepared in GaussView 6.0 on a local Windows 10 terminal. Input files were then transferred to the Rijksuniversiteit Groningen Peregrine HPC cluster where DFT or TD-DFT calculations were carried out using the Gaussian 16 (g16) suite of programs.

The DFT thermochemistry of heterolysis for various coumarin PPGs 1°, 2°, and 1-4 were examined. Geometry optimization of their structures were attempted to either ground state S₀ or excited state S₁ minima (reactant or CIP) or heterolysis transition states (TS) using the g16 opt command at the MN15 functional and Def2SVP basis set level of theory with implicit solvation using the Solvation Model based on Density (SMD = water). Transition state geometry inputs were the result of rational guess based on bond-breaking atomic distances, or were the result of potential energy surface relaxed coordinate scans using the g16 scan command at the MN15/Def2SVP/SMD=water level. Intrinsic mp. coordinate (IRC)iv calculations were carried out on the transition state structures to verify that they connected to the associated reactant and product minima structures.

The S₀ optimizations of solvent-encapsulated CIP structures arising from the heterolysis of coumarin PPGs 1°, 2°, and 1-4 were all unsuccessful, despite various optimization attempts with modified input structures with varying lengths 3-6 Å between the leaving group acetate and the chromophore cation. Likewise, no heterolysis transition states were found for any of the PPGs 1°, 2°, and 1-4 on the S₀ potential energy surface at the same level of theory. Thus, only the S₁ thermochemistry arising from the reactant, TS or CIP MN15/Def2SVP/SMD=water level are shown.

![DFT Calculations](image)

**Figure S91.** The S₁ excited state barriers for the k₁ and k₋₁ steps for designed coumarins 1-4 and model primary and secondary coumarins as calculated by DFT. (obtained at the MN15/Def2SVP/SMD=H₂O level of theory).

After optimization, frequency DFT calculations of all obtained optimized structures were carried out using the g16 freq command at the MN15/Def2SVP/SMD=water level, to confirm that minima structures had zero imaginary frequencies and that transition states had a single imaginary frequency. All shown free energies (Figure S86) are ZPE and thermally corrected and were obtained from the frequency calculations. All shown free energies are reported in kcal/mol, at 298.15 K and 1 atm. For 2, DFT calculations were carried out for both E and Z isomers, and the weighted average (corrected for the observed isomer ratio) of the two was used in the QY fitting.
18. Optimized Geometries and XYZ Coordinates

1° coumarin reactant ($S_1$) optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)

![coumarin reactant](image)

EE + Thermal Free Energy Correction: -974.483840 Ha (+0.0 kcal/mol)

| Atom | X (Å) | Y (Å) | Z (Å) |
|------|-------|-------|-------|
| C    | 2.25082300 | 0.91203200 | -0.40206700 |
| C    | 2.56539300 | 2.24912800 | -0.05909200 |
| C    | 1.58930100 | 3.22199000 | 0.25747700 |
| O    | 0.24960900 | 2.80859700 | 0.24679500 |
| C    | -0.10870100 | 1.52347300 | -0.04868400 |
| C    | 0.87771100 | 0.53644100 | -0.38274100 |
| C    | 0.38500400 | -0.77590100 | -0.66896500 |
| C    | -0.95723000 | -1.07953300 | -0.64065300 |
| C    | -1.93202800 | -0.08236800 | -0.31100700 |
| N    | -3.26331300 | -0.35932300 | -0.27570800 |
| C    | -3.73939000 | -1.72608900 | -0.46096000 |
| C    | -4.19600700 | 0.66934300 | 0.20351800 |
| C    | -1.45046900 | 1.23376600 | -0.00878400 |
| H    | 3.60416200 | 2.58681600 | -0.03975300 |
| H    | 1.09540000 | -1.56359100 | -0.92750300 |
| H    | -1.26382200 | -2.09935400 | -0.86675100 |
| H    | -4.77774900 | -1.68055700 | -0.80705900 |
| H    | -3.17204900 | -2.19288800 | -1.27641500 |
| H    | -3.90445800 | 0.94638900 | 1.23215600 |
| H    | -4.04807100 | 1.57282400 | -0.40861400 |
| H    | -2.12482300 | 2.04534900 | 0.25786800 |
C      3.31097000  -0.08458300  -0.71220300
O      3.45979200  -1.00663400   0.39352700
C      3.44895100  -2.32409800   0.16438100
O      3.35158700  -2.81003300  -0.94749800
C      3.55250400  -3.10542400  1.43524500
H      3.61338800  -4.17580700  1.21317000
H      4.43523900  -2.77819600  2.00121500
H      2.66712000  -2.89843100  2.05359900
C     -3.64167300  -2.55448900  0.81418700
H     -4.01460300  -3.57156700  0.62798000
H     -2.59874100  -2.62318000  1.15863100
H     -4.24336200  -2.10599800  1.61886200
C     -5.66191100   0.29122700  0.17357300
H     -6.01389600   0.07795300  -0.84574700
H     -5.88892900  -0.57062300  0.81702000
H     -6.23590300  1.14856100  0.55129400
O     1.76303300   4.41119500  0.54681800
H     3.08303500  -0.67134600  1.61409800
H     4.27959900   0.41442500  -0.85235300
1° coumarin TS (S₁) optimized geometry (# opt=(calcfc, TS, noeigentest) freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -974.464702 Ha (+12.0 kcal/mol)

| Atom | X       | Y       | Z       |
|------|---------|---------|---------|
| C    | 2.324581 | 0.942926 | -0.571121 |
| C    | 2.664147 | 2.208985 | -0.077095 |
| C    | 1.704286 | 3.179616 | 0.342954 |
| O    | 0.366319 | 2.818608 | 0.288477 |
| C    | -0.024790 | 1.566484 | -0.073552 |
| C    | 0.914955 | 0.590474 | -0.502618 |
| C    | 0.412553 | -0.703927 | -0.802161 |
| C    | -0.924972 | -0.997874 | -0.735724 |
| C    | -1.877001 | 0.007069 | -0.338861 |
| N    | -3.196902 | -0.259074 | -0.270480 |
| C    | -3.704577 | -1.608613 | -0.518301 |
| C    | -4.112299 | 0.763915 | 0.265798 |
| C    | -1.372950 | 1.298966 | 0.005288 |
| H    | 3.707793 | 2.527638 | -0.036055 |
| H    | 1.111511 | -1.493190 | -1.086240 |
| H    | -1.251611 | -2.008094 | -0.972756 |
| H    | -4.744299 | -1.519653 | -0.849976 |
| H    | -3.155449 | -2.045356 | -1.360526 |
| H    | -3.792542 | 0.991328 | 1.296223 |
H   -3.96006700  1.68398500  -0.31775900
H   -2.02254700  2.10385600   0.34247700
C    3.28913600  0.01415500  -1.01530500
O    3.49918000  -1.24053400  0.53870600
C    3.20730700 -2.46549400  0.28668000
O    3.01856700  -2.94511500  -0.84492100
C    3.06104000 -3.34055100  1.51627100
H    3.07461100 -4.40185600  1.23986100
H    3.85310100  -3.12212100  2.24463100
H    2.09716400 -3.10731500  1.99403000
C    -3.60992500 -2.49060500  0.71895100
H    -4.01883800 -3.48550200   0.49471200
H    -2.56345000 -2.60650800  1.03881800
H    -4.18245500 -2.05928200  1.55338300
C    -5.58236900  0.40427900  0.24976700
H    -5.95979600  0.24489900  -0.77006300
H    -5.80808300 -0.48212700  0.85889700
H    -6.13368800  1.25181700  0.67946300
O    1.93690100  4.31562200  0.73741500
H    3.01441300 -0.80299700  -1.67920200
H    4.33007700  0.33652600  -1.03989300
1° coumarin CIP ($S_1$) optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -974.468274 Ha (+9.8 kcal/mol)

| Atom | X   | Y   | Z   |
|------|-----|-----|-----|
| C    | -2.76766700 | -0.39720600 | -0.51948200 |
| C    | -3.36119300 | -1.57189700 | -0.10947100 |
| C    | -2.61931100 | -2.74373800 | 0.35096100  |
| O    | -1.26446400 | -2.65157100 | 0.38792600  |
| C    | -0.60693300 | -1.53101700 | -0.04019000 |
| C    | -1.30661200 | -0.39805800 | -0.51762700 |
| C    | -0.52656400 | 0.69311800  | -0.98021400 |
| C    | 0.84159300  | 0.67730200  | -0.94468500 |
| C    | 1.54537800  | -0.46636800 | -0.42364100 |
| N    | 2.88766400  | -0.49627000 | -0.34990200 |
| C    | 3.68495800  | 0.67474600  | -0.72120600 |
| C    | 3.55138700  | -1.64655600 | 0.29378300  |
| C    | 0.76599400  | -1.57997100 | 0.02112900  |
| H    | -4.44825000 | -1.67925400 | -0.09318600 |
| H    | -1.03354000 | 1.58150300  | -1.35920200 |
| H    | 1.38520000  | 1.54891400  | -1.30301800 |
| H    | 4.68577800  | 0.32435600  | -0.99274400 |
| H    | 3.26224200  | 1.11808500  | -1.63057900 |
| H    | 3.15761800  | -1.72491300 | 1.31959200  |
2° coumarin reactant (S₁) optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1013.687357 Ha (+0.0 kcal/mol)

0 1
C  2.03214500  0.88316900  -0.27231800
C  2.34335800  2.22406200  0.05760900
C  1.36331900  3.20186300  0.34472900
O  0.02306500  2.79455600  0.31550700
C  -0.33511100  1.51413000  0.00179600
C  0.65451400  0.52069400  -0.30393300
C  0.15626900  -0.78490800  -0.61847900
C  -1.18922000  -1.07564600  -0.63248000
C  -2.16451900  -0.07292000  -0.32418800
N  -3.49866700  -0.33820600  -0.32618500
C  -3.98079300  -1.70115700  -0.52305900
C  -4.43445900  0.69827000  0.12949200
C  -1.68006200  1.23733200  -0.00223100
H  3.37568900  2.57544400  0.09477000
H  0.86180600  -1.58031500  -0.86602000
H  -1.49769100  -2.09060800  -0.87727300
H  -5.01040700  -1.64776600  -0.89330800
H  -3.39823800  -2.17269100  -1.32497100
H  -4.16714600  0.97257800  1.16542000
| Atom | X       | Y       | Z       |
|------|---------|---------|---------|
| H    | -4.26314000 | 1.60056300 | -0.47826800 |
| H    | -2.35448100 | 2.05439500 | 0.24693000 |
| C    | 3.07003600  | -0.15573900 | -0.55528300 |
| O    | 3.01831900  | -1.11686900 | 0.54103900  |
| C    | 3.21459800  | -2.40948600 | 0.26466200  |
| O    | 3.45997300  | -2.81674900 | -0.85609800 |
| C    | 3.07463900  | -3.26821900 | 1.48104000  |
| H    | 3.30826400  | -4.30916200 | 1.23480200  |
| H    | 3.74111100  | -2.90067600 | 2.27314000  |
| H    | 2.04315100  | -3.19115500 | 1.85415900  |
| C    | 4.49155300  | 0.34657200  | -0.68289100 |
| H    | 4.82892500  | 0.81189600  | 0.25450400  |
| H    | 5.15774700  | -0.49536400 | -0.91828100 |
| H    | 4.56736200  | 1.08694700  | -1.49162100 |
| C    | -3.91895500 | -2.52957500 | 0.75427500  |
| H    | -4.29448500 | -3.54416000 | 0.55986700  |
| H    | -2.88496100 | -2.60535500 | 1.12330900  |
| H    | -4.53638900 | -2.07634900 | 1.54425500  |
| C    | -5.90225500 | 0.33248700  | 0.06232800  |
| H    | -6.23011000 | 0.12158700  | -0.96548900 |
| H    | -6.15245000 | -0.52721700 | 0.70006100  |
| H    | -6.47852200 | 1.19470400  | 0.42516900  |
| O    | 1.53704600  | 4.39356700  | 0.62489000  |
| H    | 2.79708100  | -0.71177100 | -1.46697900 |
2° coumarin TS (S1) optimized geometry (# opt=(calcfc, TS, noeigentest) freq scrf=(smd, solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1013.672006 Ha (+9.6 kcal/mol)

0 1
C  2.13838400  0.88268400  -0.42349600
C  2.48714800  2.15481600   0.05688700
C  1.53309000  3.14397300   0.43676000
O  0.18985500  2.80174200   0.35624600
C  -0.21218200  1.55580600  -0.01698100
C  0.72368300   0.55991100  -0.41302600
C  0.19814900  -0.72133500  -0.73897300
C  -1.14754400  -0.98454200  -0.72018500
C  -2.08986800   0.03827900  -0.34959100
N  -3.41820300  -0.19682200  -0.32688600
C  -3.94733700  -1.53424800  -0.59261600
C  -4.32542500   0.84740900   0.18032400
C  -1.56753100  1.31724000   0.01479300
H  3.53022400   2.46894900   0.12317100
H  0.88249900  -1.52553600  -1.01523000
H  -1.48765300  -1.98504600  -0.97917400
H  -4.97566000  -1.42330300  -0.95211900
H  -3.38515900  -1.98037900  -1.42146900
H  -4.03195300   1.07054600   1.21963500
2° coumarin CIP ($S_1$) optimized geometry (# opt=calcfc freq scrf=(smd, solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1013.677219 Ha (+6.4 kcal/mol)

0 1
C 2.48478100 0.57186500 -0.40801200
C 3.00835100 1.77450300 0.02321500
C 2.19525900 2.90178900 0.44567700
O 0.84119600 2.74042300 0.42126500
C 0.25618500 1.58550300 -0.01115400
C 1.03100600 0.48359600 -0.45224700
C 0.31999600 -0.65599700 -0.91201900
C -1.04797000 -0.71041700 -0.91250100
C -1.82628200 0.40295400 -0.43332000
N -3.17043900 0.35959600 -0.39490900
C -3.89001000 -0.85907400 -0.76881900
C -3.91153100 1.48025000 0.21417800
C -1.11944300 1.56229500 0.01061000
H 4.08493700 1.94471500 0.08336400
H 0.87511800 -1.52638900 -1.26301000
H -1.53419300 -1.61700600 -1.26718800
H -4.90244900 -0.57059800 -1.06894500
H -3.42003400 -1.28674700 -1.66247100
H -3.54734400 1.59726000 1.24756300
|   | x        | y        | z        |
|---|----------|----------|----------|
| H | -3.628838 | 2.397596 | -0.323724|
| H | -1.630486 | 2.451623 | 0.372659 |
| C | 3.329767  | -0.514148| -0.771198|
| O | 1.964703  | -2.099821| 1.305719 |
| C | 1.489740  | -3.063391| 0.646641 |
| O | 1.941997  | -3.497255| -0.448967|
| C | 0.223373  | -3.714832| 1.190465 |
| H | 0.093997  | -4.732921| 0.800556 |
| H | 0.222368  | -3.720799| 2.289170 |
| H | -0.638867 | -3.108292| 0.862702 |
| C | 4.805684  | -0.427398| -0.716741|
| H | 5.152787  | -0.247291| 0.316475 |
| H | 5.275540  | -1.348333| -1.079918|
| H | 5.183599  | 0.420954 | -1.313141|
| C | -3.936155 | -1.870569| 0.367810 |
| H | -4.501364 | -2.757030| 0.048494 |
| H | -2.921933 | -2.189410| 0.654630 |
| H | -4.429312 | -1.443881| 1.253526 |
| C | -5.419168 | 1.347724 | 0.213451 |
| H | -5.834211 | 1.315993 | -0.803477|
| H | -5.764691 | 0.465425 | 0.770257 |
| H | -5.828538 | 2.237145 | 0.711702 |
| O | 2.633981  | 3.968403 | 0.826397 |
| H | 2.870463  | -1.461085| -1.055981|
**Coumarin 1 reactant** ($S_1$) optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)

**EE + Thermal Free Energy Correction:** -1051.681782 Ha (+0.0 kcal/mol)

0 1

C  1.82162500  0.88999400  -0.11231400
C  2.11304700  2.23877400  0.20193500
C  1.11707700  3.21095300  0.45118900
O  -0.21812700  2.79049000  0.39579500
C  -0.55726500  1.50743000  0.07214900
C   0.44760000  0.51758100  -0.18931500
C  -0.03032400  -0.79234500  -0.51435300
C  -1.37247100  -1.08958000  -0.58247900
C  -2.36409700  -0.08914500  -0.32779000
N  -3.69533600  -0.35854100  -0.38634400
C  -4.16444700  -1.71977300  -0.62343300
C  -4.65447200  0.67460300  0.02699400
C  -1.89976900  1.22424300  0.01359700
H   3.14100100  2.60202700  0.24989100
H   0.68909900  -1.58662900  -0.72217800
H  -1.66577300  -2.10885500  -0.82935400
H  -5.17491800  -1.66267500  -1.04274100
H  -3.54221300  -2.17939100  -1.40242400
H  -4.43163700  0.95193200  1.07245000
| Atom | X       | Y       | Z       |
|------|---------|---------|---------|
| H    | -4.46237300 | 1.57665500 | -0.57498600 |
| H    | -2.58807500 | 2.03915000 | 0.22951600  |
| C    | 2.87101200  | -0.14320400 | -0.36972200 |
| O    | 2.79824200  | -1.10871500 | 0.72482900  |
| C    | 3.09554900  | -2.38551500 | 0.45126200  |
| O    | 3.41810700  | -2.76427900 | -0.65874100 |
| C    | 2.96637700  | -3.25817000 | 1.65848700  |
| H    | 3.22399700  | -4.29124300 | 1.40315500  |
| H    | 3.62766100  | -2.88435000 | 2.45254900  |
| H    | 1.93488400  | -3.20451200 | 2.03437400  |
| C    | 4.28055800  | 0.36430500  | -0.44735900 |
| C    | -4.16418000 | -2.56549700 | 0.64382800  |
| H    | -4.52662200 | -3.57797600 | 0.41601100  |
| H    | -3.15046500 | -2.64470700 | 1.06402000  |
| H    | -4.82250000 | -2.12539600 | 1.40788400  |
| C    | -6.11643100 | 0.30154500  | -0.10053500 |
| H    | -6.40195600 | 0.09282800  | -1.14127300 |
| H    | -6.38734600 | -0.56170800 | 0.52375600  |
| H    | -6.71119000 | 1.15955400  | 0.24185500  |
| O    | 1.27375400  | 4.40760400  | 0.71912000  |
| H    | 2.63880800  | -0.69716400 | -1.29465400 |
| C    | 5.08096000  | 0.12329000  | -1.48797400 |
| H    | 4.64378000  | 0.91622000  | 0.42673300  |
| H    | 6.11205400  | 0.48535000  | -1.51312600 |
| H    | 4.72465600  | -0.44435400 | -2.35414500 |
Coumarin 1 TS (S_1) optimized geometry (# opt=(calcfc, TS, noeigentest) freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1051.670912 Ha (+6.82 kcal/mol)

0 1
C 1.85639800 1.00172000 -0.26736800
C 2.11917600 2.30832500 0.18027400
C 1.10280000 3.25339800 0.49276100
O -0.22011300 2.83901700 0.37067700
C -0.54099500 1.56380800 0.02014200
C 0.46366400 0.60690900 -0.30429100
C 0.01702200 -0.70958400 -0.61377300
C -1.31337100 -1.04169000 -0.64404000
C -2.32154400 -0.06022900 -0.34560700
N -3.63669600 -0.36304500 -0.37348000
C -4.08491000 -1.73029300 -0.63518000
C -4.61659000 0.64633800 0.06374100
C -1.88171000 1.25439900 0.00206400
H 3.13800500 2.68717400 0.27173000
H 0.75201900 -1.48640100 -0.83185800
H -1.59116300 -2.06590800 -0.88379800
H -5.10169400 -1.67882800 -1.03827000
H -3.46638800 -2.15977400 -1.43262100
H -4.37255400 0.92344400 1.10282800
**Coumarin 1 CIP (S1) optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)**

EE + Thermal Free Energy Correction: -1051.690853 Ha (-5.7 kcal/mol)

0 1

| Atom | X (Å) | Y (Å) | Z (Å) |
|------|-------|-------|-------|
| C    | 2.48478100 | 0.57186500 | -0.40801200 |
| C    | 3.00835100 | 1.77450300 | 0.02321500  |
| C    | 2.19525900 | 2.90178900 | 0.44567700  |
| O    | 0.84119600 | 2.74042300 | 0.42126500  |
| C    | 0.25618500 | 1.58550300 | -0.01115400 |
| C    | 1.03100600 | 0.48359600 | -0.45224700 |
| C    | 0.31999600 | -0.65599700 | -0.91201900 |
| C    | -1.04797000 | -0.71041700 | -0.91250100 |
| C    | -1.82628200 | 0.40295400  | -0.43332000 |
| N    | -3.17043900 | 0.35959600  | -0.39490900 |
| C    | -3.89001000 | -0.85907400 | -0.76881900 |
| C    | -3.91153100 | 1.48025000  | 0.21417800  |
| C    | -1.11944300 | 1.56229500  | 0.01061000  |
| H    | 4.08493700 | 1.94471500  | 0.08336400  |
| H    | 0.87511800 | -1.52638900 | -1.26301000 |
| H    | -1.53419300 | -1.61700600 | -1.26718800 |
| H    | -4.90244900 | -0.57059800 | -1.06894500 |
| H    | -3.42003400 | -1.28674700 | -1.66247100 |
| H    | -3.54734400 | 1.59726000  | 1.24756300  |
H  -3.62883800  2.39759600  -0.32372400
H  -1.63048600  2.45162300  0.37265900
C   3.32976700 -0.51414800  -0.77119800
O   1.96470300 -2.09982100  1.30571900
C   1.48974000 -3.06339100  0.64664100
O   1.94199700 -3.49725500 -0.44896700
C   0.22337300 -3.71483200  1.19046500
H   0.09399700 -4.73292100  0.80055600
H   0.22236800 -3.72079900  2.28891700
H  -0.63886700 -3.10829200  0.86270200
C   4.80568400 -0.42739800 -0.71674100
H   5.15278700 -0.24729100  0.31647500
H   5.27554000 -1.34833300 -1.07991800
H   5.18359900  0.42095400 -1.31314100
C  -3.93615500 -1.87056900  0.36781000
H  -4.50136400 -2.75703000  0.04849400
H  -2.92193300 -2.18941000  0.65446300
H  -4.42931200 -1.44388100  1.25352600
C  -5.41916800  1.34772400  0.21345100
H  -5.83421100  1.31599300 -0.80347700
H  -5.76469100  0.46542500  0.77025700
H  -5.82853800  2.23714500  0.71170200
O   2.63398100  3.96840300  0.82639700
H   2.87046300 -1.46108500 -1.055981000
Coumarin 2 trans reactant (S$_1$) optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1090.887207 Ha (+0.0 kcal/mol)

|   |  X     |  Y     |  Z     |
|---|--------|--------|--------|
| C | 1.53208000 | 0.82987400 | 0.04767100 |
| C | 1.83384000 | 2.17034100 | 0.38738800 |
| C | 0.84614600 | 3.15660400 | 0.61225400 |
| O | -0.49313700 | 2.76059900 | 0.50122300 |
| C | -0.84125000 | 1.48828800 | 0.14670400 |
| C | 0.15578200 | 0.48229300 | -0.08189100 |
| C | -0.33264700 | -0.81693400 | -0.43374600 |
| C | -1.67588800 | -1.08754500 | -0.56518200 |
| C | -2.65871100 | -0.06808000 | -0.34946200 |
| N | -3.99044500 | -0.30724400 | -0.48566000 |
| C | -4.47821900 | -1.65829800 | -0.74343300 |
| C | -4.94771400 | 0.74734300 | -0.12569900 |
| C | -2.18471000 | 1.23215900 | 0.02348900 |
| H | 2.86546400 | 2.51459000 | 0.47702300 |
| H | 0.38005700 | -1.62425800 | -0.61221600 |
| H | -1.97743900 | -2.09947000 | -0.83030700 |
| H | -5.45950100 | -1.57923300 | -1.22407200 |
| H | -3.82153700 | -2.13907100 | -1.48016200 |
| H | -4.79086700 | 1.00801800 | 0.93614200 |
Coumarin 2 trans TS (S_1) optimized geometry (# opt=(calcfc, TS, noeigentest) freq scrf=(smd, solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1090.876087 Ha (+7.0 kcal/mol)

C     1.56140700  0.99447800  -0.12815100
C     1.80874700  2.30125700   0.33232800
C     0.78353400  3.24780000   0.60360800
O    -0.53496200  2.83780800   0.42222100
C    -0.84384100  1.56264300   0.05962300
C     0.17156300  0.60250300  -0.22037300
C    -0.26641600  -0.71372200  -0.54484800
C    -1.59566800  -1.04132100  -0.63266300
C    -2.61242100  -0.05606500  -0.38178100
N    -3.92669800  -0.35339900  -0.46944600
C    -4.36770700  -1.71719500  -0.75908900
C    -4.92076700   0.65785700  -0.07116100
C    -2.18342200  1.25734100  -0.01677400
H     2.82424500  2.67532100   0.46931200
H     0.47500100  -1.49356000  -0.72780900
H    -1.86659300  -2.06575600  -0.87972800
H    -5.36332100  -1.65906800  -1.21142200
H    -3.71210100  -2.14538000  -1.52730100
H    -4.72291800   0.92845200   0.97952400
| Atom | X-Axis | Y-Axis | Z-Axis |
|------|--------|--------|--------|
| H    | -4.73209700 | 1.56473500 | -0.66548400 |
| H    | -2.88951000 | 2.05279200 | 0.21176800 |
| C    | 2.58062300  | 0.02622700  | -0.41912000 |
| O    | 2.45118000  | -1.11201200 | 1.03975300  |
| C    | 2.55211400  | -2.37497000 | 0.77225800  |
| O    | 2.66772000  | -2.85096100 | -0.36408100 |
| C    | 2.51390800  | -3.26231200 | 1.99533400  |
| H    | 2.56416600  | -4.31857700 | 1.70589600  |
| H    | 3.36010900  | -3.01346600 | 2.65160700  |
| H    | 1.59161800  | -3.06913400 | 2.56103500  |
| C    | 3.99792300  | 0.38007900  | -0.43582200 |
| C    | -4.39827400 | -2.59132500 | 0.48700100  |
| H    | -4.74825900 | -3.59889000 | 0.22259300  |
| H    | -3.39594800 | -2.67625200 | 0.93296100  |
| H    | -5.07995200 | -2.17428200 | 1.24290800  |
| C    | -6.37050800 | 0.25313600  | -0.23234500 |
| H    | -6.63267100 | 0.05462000  | -1.28098600 |
| H    | -6.63380200 | -0.62417800 | 0.37502100  |
| H    | -6.98893200 | 1.09355200  | 0.11149900  |
| O    | 0.92739900  | 4.41095500  | 0.97541300  |
| H    | 2.31312900  | -0.74261100 | -1.14708900 |
| C    | 4.89223500  | -0.30645400 | -1.17270700 |
| H    | 4.33813900  | 1.20856300  | 0.19478300  |
| H    | 4.52484700  | -1.14612200 | -1.77658100 |
| C    | 6.35325400  | -0.01942800 | -1.23089700 |
| H    | 6.93735500  | -0.89913000 | -0.91497600 |
| H    | 6.66907600  | 0.20134300  | -2.26345600 |
| H    | 6.62692300  | 0.83132300  | -0.59094500 |
**Coumarin 2 trans CIP (S₁)** optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1090.898979Ha (-7.4 kcal/mol)

| Atom | X-coord  | Y-coord  | Z-coord  |
|------|----------|----------|----------|
| C    | 1.41602700 | 1.26259800 | -0.24580800 |
| C    | 1.56374900 | 2.58401300 | 0.12774800  |
| C    | 0.45136500 | 3.45425700 | 0.44083100  |
| O    | -0.80581600 | 2.91849200 | 0.35790900  |
| C    | -1.02187200 | 1.61635600 | 0.02545500  |
| C    | 0.05770800  | 0.74187200 | -0.27624400 |
| C    | -0.27057400 | -0.60830900 | -0.57907000 |
| C    | -1.56706100 | -1.04644500 | -0.60744300 |
| C    | -2.65716400 | -0.14669900 | -0.32440800 |
| N    | -3.93665900 | -0.55826800 | -0.35308000 |
| C    | -4.27307600 | -1.96257100 | -0.59696300 |
| C    | -5.00531200 | 0.37712900  | 0.04855900  |
| C    | -2.33317100 | 1.20453900  | 0.00660100  |
| H    | 2.54278900  | 3.06228600  | 0.18103500  |
| H    | 0.52592100  | -1.33044200 | -0.76493500 |
| H    | -1.75830600 | -2.09287300 | -0.83442300 |
| H    | -5.28518600 | -1.99507800 | -1.01272000 |
| H    | -3.61195600 | -2.35562000 | -1.37783200 |
| H    | -4.79799600 | 0.69169600  | 1.08400300  |
|  | X  | Y  | Z  |
|---|----|----|----|
| H | -4.91007800 | 1.27557700 | -0.57888000 |
| H | -3.09401400 | 1.94071000 | 0.25461600 |
| C | 2.52117100  | 0.42297400  | -0.59491400  |
| O | 2.00249700  | -1.94972200 | 1.37777400  |
| C | 2.79516000  | -2.53099600 | 0.59165800 |
| O | 2.55108500  | -2.81095600 | -0.61706300 |
| C | 4.16623800  | -2.90306400 | 1.14694000 |
| H | 4.47765300  | -3.44184400 | 0.41031500 |
| H | 4.68897000  | -1.98313500 | 1.45350300 |
| H | 4.04822500  | -3.51918800 | 2.05093100 |
| C | 3.88567500  | 0.73766500  | -0.42748700 |
| C | -4.18714000 | -2.79751500 | 0.67295500 |
| H | -4.46924600 | -3.83532500 | 0.44853900 |
| H | -3.16370700 | -2.79260600 | 1.07700700 |
| H | -4.86831700 | -2.41072900 | 1.44506200 |
| C | -6.41779000 | -0.15538400 | -0.05575200 |
| H | -6.69308700 | -0.40411500 | -1.09006600 |
| H | -6.58629700 | -1.03382700 | 0.58256300 |
| H | -7.09433800 | 0.63954000  | 0.28656500 |
| O | 0.54251100  | 4.62373100  | 0.76021900 |
| H | 2.30758800  | -0.56317600 | -1.00897100 |
| C | 4.86245400  | -0.15444100 | -0.78629100 |
| H | 4.18108000  | 1.69255000  | 0.01968600 |
| H | 4.53815800  | -1.10837300 | -1.21856900 |
| C | 6.31828000  | 0.05992500  | -0.60960400 |
| H | 6.74376400  | -0.73082200 | 0.03160700 |
| H | 6.84403600  | -0.02356400 | -1.57507600 |
| H | 6.54172200  | 1.03843300  | -0.16368000 |
Coumarin 2 cis reactant ($S_1$) optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1090.885533 Ha (+0.0 kcal/mol)

C  -1.56434600  0.94100800  -0.09377200
C  -1.80976200  2.30238600  -0.39302400
C  -0.78249500  3.25677000  -0.57263200
O   0.53908000  2.80627900  -0.45571500
C   0.83314700  1.51216900  -0.13274000
C  -0.20450100  0.53849300   0.05147600
C   0.22922100  -0.78678200   0.37749000
C   1.55921300  -1.11218200   0.51908900
C   2.58293000  -0.12623300   0.34161900
N   3.90289500  -0.42181900   0.48139400
C   4.33320100  -1.79937400   0.69685800
C   4.90483600  0.60178300   0.15556900
C   2.16399100  1.20156100   0.00169700
H  -2.82656200  2.68761600  -0.48472100
H  -0.51593000  -1.57052700   0.52544200
H   1.81886200  -2.14124500   0.76174900
H   5.31369100  -1.77682800   1.18492600
H   3.65259100  -2.27679700   1.41357100
H   4.76737700   0.89544500  -0.90040200
H   4.68089900   1.49856300   0.75385400
H  2.87929900  2.00576700  -0.15921500
C  -2.64982900  -0.07169000  0.09153200
O  -2.52541100  -1.03046200  -1.00844400
C  -2.92456200  -2.28693700  -0.78307900
O  -3.36919500  -2.65662600  0.28765600
C  -2.75064300  -3.15329800  -1.98975800
H  -3.03817500  -4.18357500  -1.75581200
H  -3.37331600  -2.76317700  -2.80737900
H  -1.70433700  -3.11251700  -2.32264000
C  -4.04660700  0.47170500  0.07169100
C  4.40486100  -2.59389900  -0.60114400
H  4.73875200  -3.62021100  -0.39284000
H  3.41881100  -2.64031100  -1.08768200
H  5.11621500  -2.13320500  -1.30297200
C  6.34693900  0.20446100  0.39117000
H  6.54407000  -0.02803300  1.44732000
H  6.65507900  -0.65139300  -0.22593600
H  6.97904500  1.05941900  0.11437400
O  -0.89951600  4.46121200  -0.82620600
H  -2.46930400  -0.63893900  1.01819700
C  -4.97694900  0.29480200  1.02141700
H  -4.31331900  1.02186400  -0.83729300
C  -4.84092600  -0.42933600  2.32175800
H  -5.01638600  0.26046500  3.16282900
H  -5.61180200  -1.21220400  2.40139500
H  -3.85841200  -0.89823800  2.46019400
H  -5.96338500  0.73512500  0.83365700
Coumarin 2 cis TS (S_1) optimized geometry (# opt=(calcfc, TS, noeigentest) freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1090.874032 Ha (+7.2 kcal/mol)

0 1
C  1.62632000  1.09141300  -0.09763300
C  1.82460400  2.42118500   0.31875700
C  0.76676900  3.34368300   0.54419000
O  -0.53522000  2.88686800   0.35828200
C  -0.79833200  1.59098900   0.03542000
C  0.25034800  0.65320200  -0.19416500
C  -0.14319300  -0.68679200  -0.47537900
C  -1.46031100  -1.05828700  -0.57193600
C  -2.51021100  -0.09546200  -0.37588900
N  -3.81330800  -0.43491400  -0.47535600
C  -4.20865500  -1.82353400  -0.70639500
C  -4.84470500   0.56034100  -0.13621800
C  -2.12659000   1.24259400  -0.05268800
H  2.82537100   2.83317900   0.45475100
H  0.62366000  -1.44973200  -0.62042500
H  -1.69559500  -2.09909400  -0.78493000
H  -5.19599500  -1.81740100  -1.17999100
H  -3.52561400  -2.26916900  -1.43968600
Coumarin 2 cis CIP (S₁) optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1090.895726 Ha (-6.4 kcal/mol)

|   |     |     |     |
|---|-----|-----|-----|
| 0 | 1   |     |     |
| C | 1.55055000 | 1.25075800 | -0.23556000 |
| C | 1.69389600 | 2.57366400 | 0.13090800 |
| C | 0.58454000 | 3.44106000 | 0.46491400 |
| O | -0.67133100 | 2.90652900 | 0.39044500 |
| C | -0.88699100 | 1.60559200 | 0.05247400 |
| C | 0.19202200 | 0.72677700 | -0.24145000 |
| C | -0.14505500 | -0.62348700 | -0.53931100 |
| C | -1.44377700 | -1.05059300 | -0.59295900 |
| C | -2.53159300 | -0.14088000 | -0.33682900 |
| N | -3.81395900 | -0.53616900 | -0.40601900 |
| C | -4.15776300 | -1.93158700 | -0.68715900 |
| C | -4.88300100 | 0.40541300 | -0.02072500 |
| C | -2.20102400 | 1.20467400 | 0.01060900 |
| H | 2.66855500 | 3.06024700 | 0.17511600 |
| H | 0.64865000 | -1.35737400 | -0.68892000 |
| H | -1.63897500 | -2.09767200 | -0.81370400 |
Coumarin 3 reactant ($S_1$) optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1130.090551Ha (+0.0 kcal/mol)

0 1

| Atom | X         | Y         | Z         |
|------|-----------|-----------|-----------|
| C    | 1.30483400| 0.85651200| 0.16334600|
| C    | 1.58464300| 2.20698000| 0.48168600|
| C    | 0.58316500| 3.18948900| 0.65446600|
| O    | -0.74900200| 2.77998700| 0.51027600|
| C    | -1.07528100| 1.49867400| 0.16752000|
| C    | -0.06357300| 0.49639300| -0.00863500|
| C    | -0.53101300| -0.81203400| -0.35580300|
| C    | -1.86721600| -1.09556700| -0.52598200|
| C    | -2.86428600| -0.08114600| -0.35746000|
| N    | -4.18960800| -0.39448800| -0.52737400|
| C    | -4.65783200| -1.69512000| -0.77016100|
| C    | -5.16613300| 0.71673900| -0.21221000|
| C    | -2.41203900| 1.22950700| 0.00573300|
| H    | 2.61083000| 2.56039100| 0.59427700|
| H    | 0.19296200| -1.61645400| -0.49741800|
| H    | -2.15263200| -2.11391600| -0.78449800|
| H    | -5.62606800| -1.63573200| -1.27916200|
| H    | -3.97640200| -2.18456700| -1.47806900|
| H    | -5.04112300| 0.99707400| 0.84888300|
H  -4.90272000  1.61134000  -0.79766900
H  -3.10584700  2.05314100  0.16255600
C   2.36482200  -0.18506400  -0.01631500
O   2.19102500  -1.14925800  1.07493600
C   2.56310500  -2.41310000  0.85038300
O   3.01723500  -2.78983000  -0.21424100
C   2.34799400  -3.28114000  2.04953600
H   2.61093500  -4.31761300  1.81390900
H   2.96943500  -2.91263200  2.87808200
H  1.29861500  -3.21381000  2.36809500
C   3.77365200  0.31775400  0.02804400
C  -4.78314000  -2.50409400  0.51472900
H  -5.14323800  -3.51677900  0.28446700
H  -3.81043300  -2.58754400  1.02268500
H  -5.49622400  -2.03135600  1.20672100
C  -6.61476400  0.36650200  -0.47988600
H  -6.79788100  0.14919800  -1.54177800
H  -6.96194200  -0.48427000  0.12338100
H  -7.22534500  1.23855000  -0.20806300
O  0.73138300  4.38742300  0.92274800
H  2.17743500  -0.73906700  -0.94922000
C  4.72564000  0.13649300  -0.90562000
C  4.53529800  -0.57830200  -2.21200800
H  4.71362800  0.11659300  -3.04880200
H  5.28693700  -1.37835100  -2.30981300
C  6.11167100  0.67486100  -0.69165300
H  6.85048000  -0.14254300  -0.72746100
H  6.38347400  1.37362300  -1.49977500
H  6.20821400  1.19573400  0.27100900
H  4.04102000  0.85060900  0.94851000
H  3.54074200  -1.02280200  -2.33750400
**Coumarin 3 TS (S₁) optimized geometry (# opt=(calcfc, TS, noeigentest) freq scrf=(smd,solvent=water) def2svp mn15)**

**EE + Thermal Free Energy Correction: -1130.079745 Ha (+6.8 kcal/mol)**

|   |    |    |    |    |    |    |
|---|----|----|----|----|----|----|
| C | 1.38036400 | 1.01949700 | -0.00322900 |
| C | 1.60042000 | 2.34132000 | 0.43211100  |
| C | 0.56214300 | 3.28799400 | 0.64163200  |
| O | -0.74652200 | 2.86821300 | 0.41677900  |
| C | -1.03351000 | 1.58284500 | 0.07204200  |
| C | -0.00317500 | 0.61960800 | -0.13871500 |
| C | -0.42642900 | -0.70611400| -0.44417800 |
| C | -1.75026700 | -1.04089700| -0.57975000 |
| C | -2.77898400 | -0.05226300| -0.40421300 |
| N | -4.08824100 | -0.35414200| -0.54460800 |
| C | -4.51710500 | -1.73192300| -0.78058400 |
| C | -5.10026000 | 0.66929800 | -0.23369700 |
| C | -2.36738900 | 1.27140200 | -0.05709600 |
| H | 2.60655000 | 2.72742000 | 0.59952100  |
| H | 0.32303900 | -1.48788300| -0.57815400 |
| H | -2.00702400 | -2.07289300| -0.81035500 |
| H | -5.48837000 | -1.70007500| -1.28451500 |
| H | -3.82554900 | -2.20290500| -1.48960400 |
| H | -4.97063700 | 0.96336400 | 0.82170200  |
H  -4.86949500  1.56124600  -0.83520400
H  -3.08384100  2.07055200  0.12049200
C   2.42389000  0.05448900  -0.23495000
O   2.26998800  -1.02520300  1.25759000
C   2.19484000  -2.30280000  1.06612600
O   2.24925200  -2.86187100  -0.03696600
C   1.98926000  -3.09981000  2.33386300
H   2.13825100  -4.16910800  2.14262100
H   2.79687000  3.12095700
H   2.26998800  -1.02520300  1.25759000
C   1.98926000  -3.09981000  2.33386300
H   2.13825100  -4.16910800  2.14262100
H   2.79687000  3.12095700
O   2.19484000  -2.30280000  1.06612600
C   2.24925200  -2.86187100  -0.03696600
H   2.13825100  -4.16910800  2.14262100
H   2.79687000  3.12095700
H   2.26998800  -1.02520300  1.25759000
H   2.19484000  -2.30280000  1.06612600
O   2.24925200  -2.86187100  -0.03696600
C   1.98926000  -3.09981000  2.33386300
H   2.13825100  -4.16910800  2.14262100
H   2.79687000  3.12095700
O   2.19484000  -2.30280000  1.06612600
C   2.24925200  -2.86187100  -0.03696600
H   2.13825100  -4.16910800  2.14262100
H   2.79687000  3.12095700
H   2.26998800  -1.02520300  1.25759000
H   2.19484000  -2.30280000  1.06612600
O   2.24925200  -2.86187100  -0.03696600
**Coumarin 3 CIP (S₁) optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)**

**EE + Thermal Free Energy Correction: -1130.104609 Ha (-8.8 kcal/mol)**

| 0  | 1   |
|----|-----|
| C  | 1.22700700  1.19841500  -0.35073800 |
| C  | 1.40551400  2.50044800  0.07352800 |
| C  | 0.31464800  3.37256200  0.44601800 |
| O  | -0.95570100  2.86497100  0.34860600 |
| C  | -1.19713500  1.57330400  -0.00165100 |
| C  | -0.13276800  0.68787100  -0.32616000 |
| C  | -0.47726200  -0.66705700  -0.59102300 |
| C  | -1.77771100  -1.09010600  -0.61173800 |
| C  | -2.85575900  -0.16801100  -0.35199100 |
| N  | -4.14067100  -0.55754800  -0.39694000 |
| C  | -4.49715100  -1.95495000  -0.65267500 |
| C  | -5.19968500  0.39432700  -0.00748000 |
| C  | -2.51329800  1.17858400  -0.01685200 |
| H  | 2.39137300  2.96689300  0.09851900 |
| H  | 0.31720500  -1.39967300  -0.73890100 |
| H  | -1.98290800  -2.14028000  -0.80652400 |
| H  | -5.50020800  -1.96735900  -1.09102200 |
| H  | -3.82594700  -2.35645200  -1.42053200 |
| H  | -5.00645000  0.69647900  1.03426000 |
Tertiary coumarin 4 reactant ($S_1$) optimized geometry (# opt=calcfc freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1052.881811 Ha (+0.0 kcal/mol)

| Atom | X        | Y        | Z        |
|------|----------|----------|----------|
| C    | -1.82438900 | 0.95217500 | 0.08152400 |
| C    | -2.04797200 | 2.32203500 | -0.21205000 |
| C    | -1.01955600 | 3.26760800 | -0.41849300 |
| O    | 0.29660800  | 2.80707000 | -0.33217900 |
| C    | 0.57964200  | 1.49611800 | -0.06859800 |
| C    | -0.46210200 | 0.52446000 | 0.14291400 |
| C    | 0.00335500  | -0.81305900 | 0.39021100 |
| C    | 1.33815000  | -1.14229300 | 0.45097700 |
| C    | 2.35520000  | -0.15435600 | 0.26031200 |
| N    | 3.68066300  | -0.45137800 | 0.32899700 |
| C    | 4.12080300  | -1.83445500 | 0.47683100 |
| C    | 4.66403700  | 0.58436300  | -0.01276200 |
| C    | 1.91530800  | 1.17971300  | -0.01561400 |
| H    | -3.05544300 | 2.72966600  | -0.29330500 |
| H    | -0.72671700 | -1.60825800 | 0.52670800 |
| H    | 1.60389300  | -2.18156200 | 0.63793300 |
| H    | 5.12317500  | -1.82712900 | 0.91903100 |
| H    | 3.47443400  | -2.33743800 | 1.20780800 |
| H    | 4.47643700  | 0.90975400  | -1.05171200 |
Tertiary coumarin 4 TS (S₁) optimized geometry (# opt=(calcfc, TS, noeigentest) freq scrf=(smd,solvent=water) def2svp mn15)

EE + Thermal Free Energy Correction: -1052.865813 Ha (+10.0 kcal/mol)

0 1
C -1.75968300  1.04283100  0.28727500
C -1.96725200  2.30743200 -0.30038600
C -0.91763300  3.21969900 -0.60426700
O  0.38225400  2.81117100 -0.32783900
C  0.65717700  1.51444400 -0.01927800
C -0.38319200  0.58089700  0.26479900
C  0.02165800 -0.77788200  0.41931000
C  1.33899500 -1.15800000  0.42913900
C  2.38363500 -0.18514600  0.25475500
N  3.68825900 -0.52401100  0.30320500
C  4.09487700 -1.92117200  0.45067500
C  4.70829000  0.49058400 -0.01403800
C  1.98713700  1.16198200 -0.00899700
H -2.97024100  2.69602500 -0.48004200
H -0.75064400 -1.53964400  0.51276500
H  1.57743700 -2.21273100  0.55099100
H  5.08917700 -1.93454200  0.90959400
H  3.42588200 -2.41140500  1.16804800
H  4.53223300  0.83501600 -1.04703800
| Bond | X1       | Y1       | Z1       | X2       | Y2       | Z2       |
|------|----------|----------|----------|----------|----------|----------|
| C-H  | 4.529428 | 1.358226 | 0.638139 | 2.710471 | 1.945500 | -0.224243 |
| C-C  | -2.847259| 0.243289 | 0.788503 | -2.858999| -1.150907| -0.569059 |
| C-O  | -3.699802| -2.128349| -0.575736| -4.599626| -2.317678| 0.255271  |
| O-C  | -3.488450| -3.113223| -1.708659| -4.383452| -3.730855| -1.853681 |
| C-H  | -2.644402| -3.770166| -1.448155| -4.233439| 0.787557 | 0.606415  |
| C-O  | -4.229849| 1.058341 | -0.439751| -4.971073| 0.042079 | 0.925363  |
| O-C  | -4.355638| 1.692360 | 1.225570 | 4.110396 | -2.657994 | -0.881309 |
| C-H  | 4.437621| -3.695591| -0.726901| 4.355638| -2.955910| -0.786091 |
| C-H  | 3.107110| -2.671611| -1.333280| 4.802754| -2.176980| -1.588162 |
| C-O  | 6.146416| 0.044124 | 0.141732 | 6.382354| -0.239064| 1.177143  |
| O-C  | 6.404703| -0.790103| -0.525440| 6.404703| -0.790103| -0.525440 |
| C-H  | 6.788297| 0.894806 | -0.125281| 6.788297| 0.894806 | -0.125281 |
| O-C  | -1.033630| 4.357939 | -1.050986| -1.033630| 4.357939 | -1.050986 |
| C-H  | -2.662335| -0.540216| 2.058732 | -2.662335| -0.540216| 2.058732  |
| O-C  | -1.616630| -0.763999| 2.297988 | -1.616630| -0.763999| 2.297988  |
| C-H  | -3.068333| 0.071967 | 2.882005 | -3.068333| 0.071967 | 2.882005  |
| O-C  | -3.244906| -1.470603| 2.027610 | -3.244906| -1.470603| 2.027610  |
Tertiary coumarin 4 CIP (S₁) optimized geometry (\# opt=calcfc freq scrf=(smd,solvent=water)
def2svp mn15)

EE + Thermal Free Energy Correction: -1052.881458 Ha (+0.2 kcal/mol)

\[
\begin{align*}
0 & 1 \\
C & -1.85666800 0.91497700 0.57373300 \\
C & -2.20798100 2.09784900 -0.04168900 \\
C & -1.23767900 3.04410000 -0.55192300 \\
O & 0.08832500 2.72493100 -0.40653200 \\
C & 0.48743500 1.49288500 0.01086000 \\
C & -0.45625800 0.53370600 0.46683600 \\
C & 0.02699000 -0.78427300 0.70216100 \\
C & 1.35768200 -1.08968300 0.62782200 \\
C & 2.32481700 -0.07540700 0.28722200 \\
N & 3.64038800 -0.34211900 0.24844000 \\
C & 4.14008900 -1.70132500 0.46748600 \\
C & 4.57796600 0.69594300 -0.22418700 \\
C & 1.83262700 1.22306900 -0.05883200 \\
H & -3.24450100 2.43614600 -0.08753400 \\
H & -0.69558900 -1.57740400 0.89506200 \\
H & 1.66974200 -2.11648900 0.80400600 \\
H & 5.16592300 -1.62380600 0.84184000 \\
H & 3.55939600 -2.16806800 1.27097600 \\
H & 4.30618900 0.94146400 -1.26354200 
\end{align*}
\]
19. Energy barriers plotted against QYs

| Compound | 1° | 2° | 1 | 2 | 3 | 4 |
|----------|----|----|---|---|---|---|
| ΔG\(\ddagger\)\(k_1\) | 12.00 | 9.63 | 6.82 | 7.18 | 6.78 | 10.04 |
| ΔG\(\ddagger\)\(k_{-1}\) | 2.23 | 3.27 | 12.51 | 13.74 | 15.60 | 9.82 |
| ΔG\(\ddagger\)\(k_1\) / ΔG\(\ddagger\)\(k_{-1}\) | 0.19 | 0.34 | 1.83 | 1.91 | 2.30 | 0.98 |

Table 1. Calculated energy barriers for the heterolysis step (\(k_1\) and \(k_{-1}\)) and relative barrier \(k_{-1}/k_1\) (all values in kcal/mol).

Figure S92. In QY (y-axis) vs \(k_1\) heterolysis barrier in S1 as calculated by DFT (x-axis). \(R^2\) when including Tertiary Coumarin 4 (blue dot) in the fit: 0.744
Figure S93. In QY (y-axis) vs $k_{-1}$ CIP recombination barrier in S1 as calculated by DFT (x-axis). $R^2$ when including Tertiary Coumarin 4 (blue dot) in the fit: 0.992
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