Supporting Information

For

Rational Design of a Photoswitchable DNA Glue Enabling High Regulatory Function and Supramolecular Chirality Transfer

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1. Synthesis and Characterization

1.1. General Remarks

**Synthesis and isolation of compounds.** DNA was purchased from Integrated DNA Technologies, Thermo Fisher Scientific, and Eurofins genomics. All chemicals for synthesis were obtained from commercial sources (Sigma-Aldrich, TCI, Alfa Aesar, and Boom) and used as received unless stated otherwise. Solvents used were reagent grade for synthesis and technical grade for isolation if not otherwise stated. Dry solvents were collected from a Pure Solve MD5 solvent dispenser from Demaco or by drying them for 48 h over fresh 3 Å molecular sieves. For thin-layer chromatography (TLC) aluminum foils with a silica gel matrix (Supelco, silica gel 60, 56524) were used, and components were visualized with a UV lamp at 254 nm or through staining with NH₄CeSO₄ x H₂O (10 g/L) or ninhydrin if necessary. Flash chromatography was performed on a Büchi ReveVeris® X2 flash chromatography system on Büchi EcoFlex silica columns (4 - 40 g, 40–63 μM, 60 Å). HPLC purifications were conducted with a JASCO HPLC system consisting of PU-4086 Binary semi-preparative pump and UV-4070 UV-vis detector. Compounds were purified with a reversed phase column (COSMOSIL 5C₁₈-MS-II, 20ID*150 mm) using a linear gradient (from 5% to 40% for 45 min) of acetonitrile in 0.1% aqueous AcOH at a flow rate of 10 mL/min. The effluent was monitored at 254 nm.

**Compound characterization.** Nuclear magnetic resonance spectroscopy (NMR) was carried out using an Agilent Technologies 400-MR (400/54 Premium Shielded) spectrometer (400 MHz), JEOL JNM-LA400 (400 MHz), and Bruker BioSpin AVANCEIII700 (700 MHz) and recorded at room temperature (22–24 °C). Chemical shifts are reported in δ[ppm] relative to an internal standard (solvent residual peak). The solvents used are indicated for each spectrum. Coupling constants are reported in Hertz [Hz]. Characterization of the signals: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad singlet, dd = doublet of doublet, dt = doublet of triplet. Integration is directly proportional to the number of the protons. Characterization of the ¹³C-NMR signals: (+) for CH₃ or CH, (-) for CH₂ and (q) for quaternary C-atoms. The latter assignment resulted from DEPT135. Infrared (IR) spectra were recorded on a PerkinElmer UATR (Single Reflection Diamond) Spectrum Two device (4000–700 cm⁻¹; resolution 4 cm⁻¹). Melting point ranges were determined on a Stuart analogue capillary melting point SMP11 apparatus. High Resolution Mass Spectra were recorded on a Thermofisher LTQ Orbitrap XL with eluent MeOH (0.1% FA) and flow rate of 0.15 mL/min⁻¹ in positive (ACPI/ESI) mode. For analytical RP-HPLC, a JASCO HPLC system consisting of PU-2084 Quaternary gradient pump and MD-2010 Multiwavelength detector was used. Compounds were analyzed with a reversed phase column (COSMOSIL 5C₁₈-MS-II, 4.6ID*150 mm) using a linear gradient (from 0% to 30% for 30 min) of acetonitrile in 0.1% aqueous AcOH at a flow rate of 1 mL/min. The effluent was monitored at 251 nm.
1.2. Synthetic Procedures

Route 1: Alkylation as Key Step

\[
\begin{align*}
\text{HO-} & \quad 5 \\
\text{HCl, MeOH} & \quad \text{water} \\
\text{0°C to r.t.} & \quad 6 \quad 59\% \\
\text{Br-} & \quad 7 \quad 59\% \\
\end{align*}
\]

Scheme S1. Synthesis of target compounds 2 and 3 via N-alkylation as the key step.

\((E)-4,4'-(\text{Diazene-1,2-diyl})\text{diphenol (6)}\)\(^1\)

A solution of 4-aminophenol (5.00 g, 45.82 mmol) in HCl (1M, aq, 100 mL) was cooled to 0 °C and NaNO\(_2\) (4.67 g, 67.70 mmol) in water (75 mL) was added through a dropping funnel. The reaction mixture was stirred for 1h, diluted with cold MeOH (100 mL) and stirred for an additional 40 min. Then, phenol (4.31 g, 45.80 mmol) in NaOH (3M, aq, 32.5 mL) was added to the reaction mixture at 0 °C through a dropping funnel. Stirring was continued for 30 min at 0 °C and additional 2 h at ambient temperature. The dark solution was acidified with HCl (36% aq.). The formed precipitated was filtered off, washed with water, and dried under vacuum to give the title compound as dark solid (5.79 g, 27.02 mmol, 59%). The compound was converted without further purification. An analytical sample was purified by column chromatography on silica gel (pentane / EtOAc = 1:1) to result in a yellow powder. \(^1\)H NMR (400 MHz, Chloroform-\(d\): Methanol-\(d_4\) 1:1) \(\delta = 7.73\) (d, \(J = 8.8\) Hz, 4H), 6.86 (d, \(J = 2.1\) Hz, 4H). The analytical data was in agreement with published data.\(^1\)

\((E)-1,2\text{-bis}(4-(2\text{-bromoethoxy})\text{phenyl})\text{diazene (7)}\)

To a solution of anhydrous potassium carbonate (485 mg, 3.51 mmol) in dry acetone (5 mL) was added 4,4'-dihydroxyazobenzene 6 (107 mg, 0.50 mmol) and dibromomethane (1.02 g, 5.43 mmol). The solution was stirred at 70 °C for 24 h before the reaction mixture was poured...
into water. The solution was extracted with EtOAc. The yellow phase was washed with water several times, dried over anhydrous MgSO<sub>4</sub> and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (CHCl<sub>3</sub> / MeOH = 10:1) to give 7 (127 mg, 0.30 mmol, 59%) as a yellow powder. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ = 7.88 (d, 4H), 7.01 (d, 4H), 4.38 (t, 4H), 3.68 (t, 4H).

(E)-3-((N-(2-((4-((4-((3-(((7-methyl-1,8-naphthyridin-2-yl)carbamoyloxy)propyl)-2-nitrophenyl)sulfonamido)ethoxy)phenyl)diazene)phenox)ethyl)-2-nitrophenyl)sulfonamido)propyl (7-methyl-1,8-naphthyridin-2-yl)carbamate (10)

To a solution of 7 (32.0 mg, 0.075 mmol) in anhydrous N,N-dimethylformamide (DMF, 1 mL) were successively added 9 (112.0 mg, 0.25 mmol)<sup>2</sup> and K<sub>2</sub>CO<sub>3</sub> (107.2 mg, 0.78 mmol), and the mixture was stirred at ambient temperature for 3 d. The reaction mixture was diluted with NaHCO<sub>3</sub> (sat., aq.) and extracted with EtOAc. The organic layer was successively dried over MgSO<sub>4</sub>, filtered, and evaporated in vacuo. The crude product was purified by column chromatography on silica gel (CHCl<sub>3</sub> / MeOH = 10:1) to give 10 (52.4 mg, 0.045 mmol, 61%) as a yellow solid. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ = 8.18 (d, J = 8.8 Hz, 2H), 8.11 - 8.03 (4H), 7.95 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 9.2 Hz, 4H), 7.71 (br, 2H), 7.68 - 7.59 (6H), 7.23 (t, J = 5.1 Hz, 4H), 3.59 (t, J = 7.0 Hz, 4H), 2.73 (s, 6H), 2.14-2.07 (m, 4H);

13C NMR (CDCl<sub>3</sub>, 100 MHz) δ = 163.3, 160.0, 154.7, 153.2, 152.9, 148.2, 147.3, 139.2, 136.5, 133.8, 133.1, 131.9, 131.0, 124.5, 124.4, 121.5, 118.1, 114.6, 112.6, 67.2, 63.0, 47.1, 46.2, 27.7, 25.7; ESI-MS m/z: calcd. For [C<sub>54</sub>H<sub>52</sub>N<sub>12</sub>O<sub>14</sub>S<sub>2</sub> + Na]<sup>+</sup> 1179.31; found 1179.05.

(E)-(((diazene-1,2-diylbis(4,1-phenylene))bis(oxy))bis(ethane-2,1-diyl))bis(azanediyl))bis(propane-3,1-diyl) bis((7-methyl-1,8-naphthyridin-2-yl)carbamate) (2)

To a solution of 10 (6.4 mg, 5.5 µmol) in anhydrous N,N-dimethylformamide (DMF, 0.5 mL) were successively added benzenethiol (2.40 mg, 0.02 mmol) and K<sub>2</sub>CO<sub>3</sub> (12.2 mg, 0.09 mmol), and the mixture was stirred at ambient temperature for 1 h. The reaction mixture was diluted with saturated NaHCO<sub>3</sub> and extracted with EtOAc. The organic layer was successively dried over MgSO<sub>4</sub>, filtered, and the solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel (CHCl<sub>3</sub> / MeOH = 100:1 to 4:1) to give 2 (2.7 mg, 3.4 µmol, 62%) as a yellow powder. Compound 2 in CD<sub>3</sub>OD exists as a 91 : 9 mixture of E : Z isomer and the following NMR spectrum was reported for the E isomer unless noted. <sup>1</sup>H NMR
To a solution of anhydrous potassium carbonate (516 mg, 3.73 mmol) in dry DMF (2 mL) was added 4,4'-dihydroxyazobenzene 6 (77.4 mg, 0.37 mmol). After stirred for 30 min, dibromopropane (739 mg, 3.73 mmol) was added, and the solution was then stirred for 24 h before the reaction mixture was poured into water. The mixture was extracted with EtOAc. The yellow organic phase was washed with water several times, dried over by anhydrous Na₂SO₄ and the solvent was removed under reduced pressure. Then the solid residue was recrystallized from CHCl₃ / MeOH to give 8 (92.8 mg, 0.20 mmol, 56%) as a yellow powder.

(E)-3-((N-(3-((4-((4-(3-((((7-methyl-1,8-naphthyridin-2-yl)carbamoyl)oxy)propyl)-2-nitrophenyl)sulfonamido)propoxy)phenyl)diazenyl)phenoxy)propyl)-2-nitrophenyl)sulfonamido)propyl (7-methyl-1,8-naphthyridin-2-yl)carbamate (11)
To a solution of 11 (22.1 mg, 0.019 mmol) in anhydrous \( N, N \)-dimethylformamide (DMF, 1 mL) were successively added benzenethiol (8.30 mg, 0.075 mmol) and \( \text{K}_2\text{CO}_3 \) (36.0 mg, 0.26 mmol), and the mixture was stirred at ambient temperature for 1 h. The reaction mixture was diluted with \( \text{NaHCO}_3 \) (sat., aq.) and extracted with EtOAc. The organic layer was successively dried over \( \text{MgSO}_4 \), filtered, and the solvent was evaporated \textit{in vacuo}. The residue was added \( \text{HCl} \) (4M, aq.) and the reaction mixture was extracted with EtOAc. The water layer was diluted with \( \text{NaHCO}_3 \) (sat., aq.) and extracted with EtOAc. The crude product was purified by HPLC to give 3 (12.0 mg, 0.015 mmol, 79%) as a yellow solid. Compound 3 in CD\textsubscript{3}OD exists as a 85 : 15 mixture of \( E \) : \( Z \) isomer and the following NMR spectrum is reported for \( E \) isomer unless noted. \(^1\text{H} \text{NMR (CD}_3\text{OD, 700 MHz)} \delta = 8.86 (d, \text{ } J = 8.2 \text{ Hz}, 2\text{H}), 8.58 (d, \text{ } J = 9.0 \text{ Hz}, 2\text{H}), 8.52 (d, \text{ } J = 9.0 \text{ Hz}, 2\text{H}), 7.78 (d, \text{ } J = 8.6 \text{ Hz}, 2\text{H}), 7.09 (d, \text{ } J = 9.0 \text{ Hz}, 4\text{H}), 6.90 (8\text{H for } Z \text{ isomer}), 4.40 (t, \text{ } J = 6.0 \text{ Hz}, 4\text{H}), 4.25 (t, \text{ } J = 5.6 \text{ Hz}, 4\text{H}), 3.33 (t, \text{ } J = 7.3 \text{ Hz}, 4\text{H}), 3.27 (t, \text{ } J = 7.5 \text{ Hz}, 4\text{H}), 2.94 (s, 6\text{H}), 2.30-2.26 (m, 4\text{H}), 2.22-2.18 (m, 4\text{H}); \(^{13}\text{C} \text{NMR (CD}_3\text{OD, 176 MHz)} \delta = 160.7, 159.4, 157.8, 153.1, 147.4, 147.0, 146.1, 139.8, 124.0, 121.8, 119.6, 116.1, 114.5, 65.2, 62.8, 45.5, 45.0, 25.8, 25.5, 19.3; \text{ESI-MS } m/z: \text{calcd. For } [\text{C}_{44}\text{H}_{50}\text{N}_{10}\text{O}_6+\text{H}]^+ 815.3988; \text{found 815.3951.}

**Route 2: Reductive Amination as Key Step**

**Scheme S2.** Synthesis of target compound 4 \textit{via} reductive amination as key step.

Alkylation of 6 with 12 was facilitated using \( \text{Cs}_2\text{CO}_3 \) in DMF to give compound 13. Deprotection of the aldehyde functionalities was achieved quantitatively with pyridinium \( p\)-toluenesulfonate (PPTS). Target compound 4 could be successfully synthesized \textit{via} reductive amination treating 14 with \( \text{NaBH(OAc)}_3 \) and the corresponding amine 15 (Scheme S2).
(E)-1,2-bis(4-(4,4-dimethoxybutoxy)phenyl)diazene (13)

Acetal 12 was synthesized following a published protocol employing 4-bromo butanol (15, 800 mg, 5.23 mmol) and was isolated in 95% yield and used in the next step without further purification.\(^1\) H NMR (400 MHz, Chloroform-\(d\)) \(\delta = 4.39 (t, J = 5.6 \text{ Hz}, 1\text{H}), 3.43 (t, J = 6.7 \text{ Hz}, 2\text{H}), 3.32 (s, 6\text{H}), 2.00 – 1.85 (m, 2\text{H}), 1.79 – 1.71 (m, 2\text{H}).\) The analytical data were in agreement with published data.\(^3\)

Compound 6 (150 mg, 0.70 mmol), Cs\(_2\)CO\(_3\) (913 mg, 2.8 mmol), and KI (12 mg, 0.07 mmol) were added to a Schlenk flask under nitrogen and dissolved in dry DMSO (5 mL). The reaction mixture was heated at 80 °C for 15 min and cooled to ambient temperature. Then, acetal 12 (275 mg, 1.40 mmol) was added and the resulting mixture was stirred at 80 °C for 16 h. The solution was cooled to ambient temperature and diluted with water (150 mL) and EtOAc (60 mL). The phases were separated, and the organic phase was washed with water (100 mL) and brine (80 mL) and dried over Na\(_2\)SO\(_4\). The volatiles were removed in vacuo to give the title compound as an orange solid (285 mg, 0.64 mmol, 91%).\(^1\) H NMR (400 MHz, Acetone-\(d_6\)) \(\delta = 7.87 (d, J = 8.9 \text{ Hz}, 4\text{H}), 7.09 (d, J = 8.8 \text{ Hz}, 4\text{H}), 4.45 (t, J = 5.4 \text{ Hz}, 2\text{H}), 4.13 (t, J = 6.3 \text{ Hz}, 4\text{H}), 3.29 (s, 12\text{H}), 1.96 – 1.81 (m, 4\text{H}), 1.77 (dt, J = 10.8, 5.7 \text{ Hz}, 4\text{H}).\) \(^{13}\)C NMR (101 MHz, Acetone-\(d_6\)) \(\delta = 161.3 (q), 146.8 (q), 124.2 (+), 114.7 (+), 104.1 (+), 67.8 (-), 52.0 (+), 28.9 (-), 24.3 (-).\) IR [cm\(^{-1}\)] (neat) = 2956 (m), 1595 (s), 1500 (s), 1467 (m), 1393 (m), 1251 (s), 1128 (s), 842 (s), 735 (m), 553 (m). The compound could not be ionized in MS spectroscopy. Mp: 82-85 °C. \(R_f: 0.8\) (pentane : EtOAc = 1:1 (v/v).)

(E)-4,4’-((diazene-1,2-diylbis(4,1-phenylene))bis(oxy)) dibutanal (14)

Acetal 7 (10.0 mg, 22.4 µmol) was dissolved in acetone (300 µL) and pyridinium p-toluene sulfonate (PTSA, 1.7 mg, 6.7 µmol) was added. The solution was warmed to 40 °C for 18h and then cooled to ambient temperature. The reaction mixture was filtered over a plug of celite using acetone as an eluent to remove PTSA. The volatiles were removed in vacuo to give a dark yellow solid (7.9 mg, 22.3 µmol, quant.). The identity of the compound was confirmed by \(^1\)H spectroscopy, and the title compound was converted without further purification. \(^1\)H NMR (400 MHz, Acetone-\(d_6\)) \(\delta = 9.82 (t, J = 1.3 \text{ Hz}, 2\text{H}), 7.98 – 7.77 (m, 4\text{H}), 7.14 – 7.05 (m, 4\text{H}), 4.15 (t, J = 6.3 \text{ Hz}, 4\text{H}), 2.69 (td, J = 7.1, 1.3 \text{ Hz}, 4\text{H}), 2.17 – 2.11 (m, 4\text{H}).\) \(R_f: 0.3\) (pentane : EtOAc = 1:1 (v/v).)

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(E)-3-((4-(4-((3-(((7-methyl-1,8-naphthyridin-2-yl)carbamoyl)oxy)propyl)amino)propoxy)phenyl)diazenyl)phenoxy)butyl)amino)propyl (7-methyl-1,8-naphthyridin-2-yl)carbamate (4)

To a mixture of 14 (30.0 mg, 0.085 mmol) and 15 (43.7 mg, 0.17 mmol) in CHCl₃ (7 mL) was added acetic acid (25 μL, 0.43 × 10⁻³ mmol) and the reaction mixture was stirred at ambient temperature for 30 min. Sodium triacetoxyborohydride (189 mg, 0.90 mmol) in methanol (3 mL) was added to the reaction mixture. After 16 h stirring, the solvent was removed in vacuo and the residue was diluted with saturated aqueous NaHCO₃ solution and extracted with EtOAc. The organic phase was washed with brine, dried over anhydrous MgSO₄, filtered, and concentrated in vacuo. Then, 4M hydrochloric acid was added to the residue. The reaction mixture was extracted with EtOAc. The water layer was diluted with NaHCO₃ (sat, aq.) and extracted with EtOAc. The crude product was purified by HPLC to give 4 (4.3 mg, 0.005 mmol, 6%) as a yellow solid. Compound 4 in CD₃OD exists as a 84 : 16 mixture of E : Z isomer and the following NMR spectrum was reported for E isomer unless noted. ^1H NMR (CD₃OD, 700 MHz) δ = 8.77 (br, 2H), 8.54 (d, J = 9.3 Hz, 2H), 8.49 (d, J = 9.0 Hz, 2H), 7.81 (d, J = 9.0 Hz, 4H), 7.72 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 9.0 Hz, 4H), 6.87 (d, J = 9.0 Hz, 4H for Z isomer), 6.84 (d, J = 9.3 Hz, 4H for Z isomer), 4.39 (t, J = 6.1 Hz, 4H), 4.14 (m, 4H), 3.23 (t, J = 7.7 Hz, 4H), 3.18-16 (m, 4H), 2.90 (s, 6H), 2.19-2.15 (m, 4H), 1.97-1.94 (m, 8H); ^13C NMR (CD₂OD, 176 MHz) δ = 161.0, 159.9, 158.4, 157.2, 153.2, 146.8, 146.5, 139.7, 123.9, 122.4, 121.7, 119.3, 115.5, 114.4, 67.1, 62.5, 44.7, 44.7, 25.9, 25.5, 22.9, 19.9; ESI-MS m/z: calcd. For [C₄₆H₅₄N₁₀O₆ + Na]^+ 865.4120; found 865.1820.
2. Photochemical and Thermal Isomerization by UV-Vis and NMR Spectroscopy

UV/Vis absorption spectra were recorded on an Agilent 8453 UV-Visible Spectrophotometer. Photochemical isomerization was achieved by irradiation from the side in a fluorescence quartz cuvette (width = 1.0 cm) using a custom-built (Prizmatix/Mountain Photonics) multi-wavelength fiber coupled LED-system (FC6-LED-WL) including the following LEDs: 365A, 390B, 420Z, 445B, 535R, 630CA. A detailed description of the setup was published in reference 5. A Quantum Northwest TC1 temperature controller was used to maintain the temperature at 25 °C during photochemical studies. Thermal isomerization kinetics were recorded using a JASCO V750 at 25 °C using a PTC 424S/15 temperature controller. Raw data were processed using Agilent UV-Vis ChemStation B.02.01 SP1, Spectra Manager, Spectragryph 1.2, and OriginPro 2016.

For photostationary distribution (PSD) determination by $^1$H NMR 0.6 mL of a 1 mM solution of the respective compound in D$_2$O was thermally equilibrated in the dark at 60 °C for 1h, or irradiated in a glass NMR tube using a 365 nm hand-held lamp (Spectroline ENB-280C) or a Sahlmann cooled 3 x Roithner SMB-1N 430h (426 nm, FWHM = 16 nm, power output = 600 mW), respectively.

2.1. UV-Vis spectra at Different Concentration for $\varepsilon$ Determination

Figure S1. NCDA3 in Tris buffer (aq., 50 mM, 150 mM NaCl, pH = 7.5).

Figure S2. Compound 2 in Tris buffer (aq., 50 mM, 150 mM NaCl, pH = 7.5).
Figure S3. Compound 3 in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0).

Figure S4. Compound 4 in water.

2.2. Spectra of Photoisomerization

Figure S5. NCDA3 in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0) and dsDNA (5 μM). NCDA3 without DNA see main text.
Figure S6. **Left.** Compound 2 in Tris buffer (aq., 50 mM, 150 mM NaCl, pH = 7.5). **Right.** Compound 2 in phosphate buffer (0.01 M, 100 mM NaCl, pH = 7.0) and dsDNA (5µM).

Figure S7. Compound 3 in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0) and dsDNA (5µM). Compound 3 without DNA see main text.

Figure S8. **Left.** Compound 4 in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0). **Right.** Compound 3 in phosphate buffer (aq., 5 mM, 50 mM NaCl, pH = 7.0) and dsDNA (5µM).
2.3. QY Determination

**Chemical actinometry.** A modification of a standard protocol was applied for the determination of the photon flux. An aqueous H$_2$SO$_4$ solution (0.05 M) containing freshly recrystallized K$_3$[Fe(C$_2$O$_4$)$_3$] (41 mM, 2 mL, 1 cm quartz cuvette) was irradiated at 20 °C for a given period of time in the dark with a 365 nm LED. The solution was then diluted with 1.0 mL of an aqueous H$_2$SO$_4$ solution (0.5 M) containing phenanthroline (1 g/L) and NaOAc (122.5 g/L) and left to react for 10 min. The absorption at $\lambda = 510$ nm was measured and compared to an identically prepared non-irradiated sample. The concentration of [Fe(phenanthroline)$_3$]$^{2+}$ complex was calculated using its molar absorptivity ($\varepsilon = 11100$ M$^{-1}$ cm$^{-1}$) and considering the dilution. The quantity of Fe$^{2+}$ ions expressed in mol was plotted versus time (expressed in seconds) and the slope, obtained by linear fitting the data points to the equation $y = ax +b$ using Origin software, equals the rate of formation of the Fe$^{2+}$ ions at the given wavelength under standardized conditions. This rate can be converted into the photon flux (I) by dividing it by the quantum yield of [Fe(phenanthroline)$_3$]$^{2+}$ complex ($\Phi_{365\text{nm}} = 1.29$) at 365 nm and by the probability of photon absorption at 365 nm of the Fe$^{3+}$ complex (approximated to 1 as the experiment was performed in the total absorption regime). The obtained photon flux was $I = 3.70588 \times 10^{-5}$ E s$^{-1}$.

**Quantum yield measurement.** The quantum yields of the compounds were determined by monitoring the decrease of the $\pi\pi^*$ transition band at the wavelength of irradiation by UV-Vis spectroscopy (Agilent 8453) following published procedures. Irradiation was performed in quartz fluorescence cuvettes (pathlength = 1 cm) with defined volumes (vide infra) using the 365 nm LED of our multi-wavelength fiber coupled LED-system with a defined photon flux (vide supra) under stirring at 25 °C.

2.3.1. Without DNA

**Table S1.** NCDA3, 25 µM in Tris buffer (aq., 50 mM, 150 mM NaCl, pH = 7.5)

| NCDA3 | Lambda(nm) | 320 |
|-------|------------|-----|
|       | Conc       | 0.000025 |
|       | Photon flux | 3.7059E-05 |
|       | A          | 0.8007 |
|       | Slope      | -0.00226 |
|       | Volume(ml) | 2 |
|       | rate       | -5.65E-08 |
|       | QY         | 0.00362239 |
Table S2. Compound 2, 25 µM in Tris buffer (aq., 50 mM, 150 mM NaCl, pH = 7.5)

| Compound | Lambda(nm) | Conc   | Photon flux | A     | Slope   | Volume(ml) | rate  | QY     |
|----------|------------|--------|-------------|-------|---------|------------|-------|--------|
|          | 365        | 0.000025 | 3.7059E-05  | 0.335 | -0.1675 | 2          | -4.1875E-06 | 0.42035707 |

Table S3. Compound 3, 50 µM in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0)

| Compound | Lambda(nm) | Conc   | Photon flux | A     | Slope   | Volume(ml) | rate  | QY     |
|----------|------------|--------|-------------|-------|---------|------------|-------|--------|
|          | 365        | 0.000005 | 3.7059E-05  | 0.567 | -0.14339 | 2          | -7.1695E-06 | 0.53077552 |

Table S4. Compound 4, 25 µM in water

| Lambda(nm) | Conc   | Photon flux | A     | Slope   | Volume(ml) | rate  | QY     |
|------------|--------|-------------|-------|---------|------------|-------|--------|
| 365        | 2.50E-05 | 3.71E-05    | 0.30127 | -0.0985 | 2          | -2.4625E-06 | 0.26564674 |

2.3.2. With dsDNA

Table S5. NCDA3, 10 µM in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0, with 5 µM dsDNA)

| NCDA3     | Lambda(nm) | Conc   | Photon flux | A     | Slope   | Volume(ml) | rate  | QY     |
|-----------|------------|--------|-------------|-------|---------|------------|-------|--------|
|           | 321        | 0.000001 | 3.7059E-05  | 0.2872 | -0.00933 | 2          | -9.33E-08 | 0.01040722 |
Table S6. Compound 2, 10 µM in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0, with 5 µM dsDNA)

| Compound2 | Lambda(nm) | 365 |
|-----------|------------|-----|
| Conc      | 0.00001    |     |
| Photon flux | 3.7059E-05 |     |
| A         | 0.1792     |     |
| Slope     | -0.0934    |     |
| Volume(ml) | 2          |     |
| rate      | -9.34E-07  |     |
| QY        | 0.14909214 |     |

Table S7. Compound 3, 20 µM in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0, with 10 µM dsDNA)

| Compound3 | Lambda(nm) | 367 |
|-----------|------------|-----|
| Conc      | 0.00002    |     |
| Photon flux | 3.7059E-05 |     |
| A         | 0.3444     |     |
| Slope     | -0.05701   |     |
| Volume(ml) | 2          |     |
| rate      | -1.1402E-06|     |
| QY        | 0.11238793 |     |

Table S8. Compound 4, 24µM in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0, with 5 µM dsDNA)

| Compound4 | Lambda(nm) | 367 |
|-----------|------------|-----|
| Conc      | 2.40E-05   |     |
| Photon flux | 3.71E-05  |     |
| A         | 0.17419    |     |
| Slope     | -0.03592   |     |
| Volume(ml) | 1.9        |     |
| rate      | -8.6208E-07|     |
| QY        | 0.13376985 |     |

2.4. Switching Cycles for Fatigue (with and without DNA)

To analyze the fatigue resistance of compounds 2-4, we performed repeated irradiation cycles using alternating 365 nm and 445 nm light. The decrease and increase of the ππ* transition band was followed by UV-Vis spectroscopy (Agilent 8453) at 25 °C. The obtained data is depicted below.
2.4.1. Compound 2, $\lambda^{\text{obs}} = 365$ nm

*Figure S9.* Left: 25 µM in Tris buffer (aq., 50 mM, 150 mM NaCl, pH = 7.5); Right: 10 µM in phosphate buffer (0.01 M, 100 mM NaCl, pH = 7.0, with 5 µM dsDNA).

2.4.2. Compound 3

Data for compound 3 see main text

2.4.3. Compound 4, $\lambda^{\text{obs}} = 367$ nm

*Figure S10.* Left: 25 µM in Tris buffer (aq., 50 mM, 150 mM NaCl, pH = 7.5); Right: 10 µM in phosphate buffer (0.01 M, 100 mM NaCl, pH = 7.0, with 5 µM dsDNA).
2.5. Thermal Lifetime $\tau$ of Z Isomer (with and without DNA)

Samples were prepared and irradiated with a 365 nm hand-held lamp (Spectroline ENB-280C) at the final concentration until PSS was reached. Then, the cuvettes were placed in a JASCO V750 spectrophotometer and the appearance of the $\pi\pi^*$ transition (or $\lambda_{\text{max}}$ for NCDA3) was followed while stirring at 25 °C. The data were fitted using a first-order exponential function in OriginPro 2016.

2.5.1. Without DNA

**Figure S11.** NCDA3, 10 µM in Tris buffer (aq., 50 mM, 150 mM NaCl, pH = 7.5). The scattering in the measurement is cause by the very small difference in absorbance between PSS$^{365}$ and the thermal equilibrium.

**Figure S12.** Compound 2, 10 µM in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0).
Figure S13. Compound 3, 10 µM in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0).

Figure S14. Compound 4, 10 µM in water.

2.5.2. With dsDNA

Figure S15. NCDA3, 10 µM in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0), 5µM dsDNA.
Figure S16. Compound 2, 10 µM in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0), 5µM dsDNA.

Figure S17. Compound 3, 10 µM in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0), 5µM dsDNA.

Figure S18. Compound 4, 10 µM in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0) and water (1:1), 5µM dsDNA.
2.6. PSD Determination by NMR

Figure S19. NCDA3, D$_2$O, 1 mM.

Figure S20. Compound 2, D$_2$O, 1 mM.
Figure S21. Compound 3, D$_2$O, 1 mM.

Figure S22. Compound 4, D$_2$O, 1 mM.
2.7. PSD Determination by HPLC

2.7.1. Without DNA

A solution containing 2, 3, 4 (20 μM) in a phosphate buffer (aq., 10 mM, pH 7.0) containing NaCl (100 mM) was prepared for HPLC analyses. Samples at the photostationary state at 365 nm (PSS_{365nm}) and 460 nm (PSS_{460nm}) light were prepared by photoirradiation with a light source, ZUV-C20H (365 nm, for 20 sec) and UHP-Black-LED-460 (460 nm, for 10 min) at a distance of 10 cm, respectively. Thermally adapted samples were prepared by incubation at 60 °C for 1 h under dark condition. The sample solutions were analyzed by reversed phase HPLC (JASCO HPLC system consisting of PU-2084 Quaternary gradient pump and MD-2010 Multiwavelength detector) equipped with COSMOSIL packed column (4.6 × 150 mm) detected at 251 nm (the wavelength of the isosbestic point); elution with a solvent mixture of 0.1% acetic acid and 0–30% acetonitrile in water (linear gradient for 30 min) at a flow rate 1.0 mL/min.

![HPLC profiles of compounds at the PSS_{365nm}](image1)

![HPLC profiles of compounds at the PSS_{460nm}](image2)

**Figure S23.** E-Z ratio of compounds 2 (A–C), 3 (D–F), and 4 (G–I) at the photostationary state determined by HPLC analyses. A, D, and G. HPLC profiles of compounds at the PSS_{365nm}. B, E, and H. HPLC profiles of compounds at the PSS_{460nm}. C, F, and I. HPLC profiles of the thermally adapted samples.

2.7.2. With DNA

A solution containing 2, 3, 4 (20 μM) in phosphate buffer (0.01 M, 100 mM NaCl, pH = 7.0), 5μM dsDNA was prepared for HPLC analyses. Samples at the photostationary state at 365 nm (PSS_{365nm}), 430 nm (PSS_{430nm}) and 470 nm (PSS_{470nm}) light were prepared by photoirradiation with a light source, 365 nm hand-held lamp (Spectroline ENB-280C), or a Sahlmann cooled 3 x Roithner SMB-1N 430h (426 nm, FWHM = 16 nm, power output = 600 mW), or a Sahlmann cooled 3 x Nichia NCSB219B-V1 (464 nm, FWHM = 28 nm, power output = 1000 mW), respectively, at 1 cm distance for 3 min each. Thermally adapted samples were prepared by incubation at 60 °C for 1 h under dark conditions. The sample solutions were analyzed by reversed phase HPLC (Shimadzu UFLC system with a SPD-M20A photodiode array detector)
equipped with XTerra®MS C18 3.5 µm packed column (3.0 × 150 mm) detected at 251 nm (the wavelength of the isosbestic point); elution with a solvent mixture of 0.1% formic acid and 20% acetonitrile (isocratic for 8 min (MBL 2 and 3) or 18 min (MBL 4), respectively) at a flow rate 0.5 mL/min. The isomers were identified via the UV-Vis spectrum. The additional signal present in a part of the traces is a result of the injection containing residual DNA.

**Figure S24.** $E$-$Z$ ratio of compounds 2, 3, and 4 (top to bottom): HPLC traced at 251 nm at the thermal equilibrium 3 (A), the PSS $^{365\text{nm}}$ (B), the PSS $^{430\text{nm}}$ (C), and the PSS $^{470\text{nm}}$ (D).
3. DNA-Melting Experiments

Sample solutions were prepared by mixing DNA duplex (5 μM) and compounds 2, 3, 4 (20 μM) in 10 mM sodium phosphate buffer (aq., pH 7.0) and 100 mM NaCl. Thermal denaturation profiles were recorded on a SHIMADZU UV-2700 UV–vis spectrometer equipped with a SHIMADZU TMSPC-8 temperature controller. The absorbance of the samples was monitored at 260 nm from 2 °C to 80 °C with heating rate of 1 °C/min. Melting profiles ranged between 2 °C to 60 °C are given in Figure 5 in main text. Samples at the photostationary state at 365 nm (PSS\textsuperscript{365nm}) and 460 nm (PSS\textsuperscript{460nm}) light were prepared by photoirradiation with a light source, ZUV-C20H (365 nm, for 20 sec) and UHP-Black-LED-460 (460 nm, for 10 min) at a distance of 10 cm, respectively. Non-irradiated control samples contain compounds under thermally adapted states that were prepared by incubation at 60 °C for 1 h under dark condition. In the repeated irradiation experiments (Figure 5D in main text), the samples were not subjected to the thermal treatment. The $T_m$ values were determined as the temperature crossing the melting curve and the median of two straight lines drawn for the single and duplex region in the melting curve.
4. SPR Analysis

Surface plasmon resonance (SPR) assay was performed using Biacore T200 platform (GE Healthcare, Life Science). Immobilization of oligonucleotides on Series S sensor chip SA surface was carried out using streptavidine-biotin coupling in HBS-EP+ buffer (10 mM pH 7.4 HEPES, 150 mM NaCl, 3 mM EDTA, 0.005% surfactant P20). 5’-Biotinylated oligonucleotides (5’-biotin-CTAAC\textsubscript{N1}GAATGTTTTCATT\textsubscript{N2}GTTAG-3’; for GG mismatch \(N_1 = N_2 = G\), for CC mismatch \(N_1 = N_2 = C\), and for full match sequence \(N_1 = C\) and \(N_2 = G\)) were purchased from Eurofins genomics. Concentration of the 5’-biotinylated oligonucleotides were adjusted to be 0.6 µM in 10 mM HEPES-500 mM NaCl, which were injected onto the chip. The amounts of immobilization were 912.1, 924.6, and 922.8 response unit (RU) for GG mismatch, CC mismatch, fullmatch DNA, respectively. Blank immobilization was performed in the flow cell 1 to permit reference subtraction. Each compound was dissolved in HBS-EP+ buffer 5% DMSO and was irradiated with 365 nm light for 20 sec. The samples were injected onto the chip for 60 sec (contact time) at a flow rate of 30 µL/min, followed by injection of running buffer (180 s) as a dissociation phase. All sensorgrams were corrected by reference subtraction of blank flow cell response.

![Figure S25](image)

**Figure S25.** SPR analysis of the binding of ligands 2 (A, D), 3 (B, E), and 4 (C, F) to hairpin dsDNA containing a CCG/CCG site. Either ligands at thermal equilibrium (A, B, C) or ligands after irradiation at 365 nm (D, E, F) were injected to surface immobilized with the dsDNA containing a CC mismatch. Ligands at a series of concentrations (0.031, 0.063, 0.13, 0.25, 0.5 µM) were injected during association steps (from 57 to 117 s) followed by dissociation step where running buffer was injected.
Figure S26. SPR analysis of the binding of ligands 2 (A, D), 3 (B, E), and 4 (C, F) to hairpin dsDNA containing a CCG/CGG site. Either ligands at thermal equilibrium (A, B, C) or ligands after irradiation at 365 nm (D, E, F) were injected to surface immobilized with the fullmatch dsDNA. Ligands at a series of concentrations (0.031, 0.063, 0.13, 0.25, 0.5 µM) were injected during association steps (from 57 to 117 s) followed by dissociation step where running buffer was injected.
5. CD Spectroscopy

Circular dichroism (CD) spectra were recorded on JASCO J815 CD spectrometer (scan-rate 20 nm/min). For a standard experiment, a fluorescence quartz cuvette (width = 1.0 cm) was equipped with 2 mL sample volume and studied at 25 °C. Irradiation was performed outside of the spectrometer with a suitable light source in a distance of ca. 1 cm. For irradiation, a 365 nm hand-held lamp (Spectroline ENB-280C), or a Sahlmann cooled 3 x Roithner SMB-1N 430h (426 nm, FWHM = 16 nm, power output = 600 mW), or a Sahlmann cooled 3 x Nichia NCSB219B-V1 (464 nm, FWHM = 28 nm, power output = 1000 mW), respectively, were used.

For binding studies, increasing amounts of MBL (1 mM stock solutions in water) were added to a fixed amount of an 11-mer dsDNA (5 µM in phosphate buffer) containing a d(CGG)/d(CGG) mismatch. The MBL stock solutions were thermally adapted and stored and handled in the dark. Cuvettes containing samples were handled in the dark or covered with aluminum foil until the measurement. To study the Z isomers, the respective cuvettes were irradiated after every ligand addition for 1 min in the case of NCDA3 or 10 s in the case of compound 2 to 4, respectively, with 365 nm light. Blue-light irradiation was conducted for 5 min for all samples.

Reversibility was investigated by irradiation of the same sample altering between UV and blue light to toggle between both PSSs using compound 3 an illustrative example.

5.1. NCDA3

![Figure S27. Titration of increasing amounts of MBL NCDA3 in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0). A. CD spectra at the PSS\textsuperscript{365nm}. B. UV-Vis spectra at the PSS\textsuperscript{365nm}. C. CD spectra of the thermally adapted sample. D. UV-Vis spectra of the thermally adapted sample.](image-url)
5.2. Compound 2

**Figure S28.** Titration of increasing amounts of MBL 2 in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0). **A.** CD spectra at the PSS\(^{365\text{nm}}\). **B.** UV-Vis spectra at the PSS\(^{365\text{nm}}\). **C.** CD spectra of the thermally adapted sample. **D.** UV-Vis spectra of the thermally adapted sample.
Figure S29. Titration of increasing amounts of MBL 3 in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0). A. CD spectra at the PSS$^{365\text{nm}}$. B. UV-Vis spectra at the PSS$^{365\text{nm}}$. C. CD spectra of the thermally adapted sample. D. UV-Vis spectra of the thermally adapted sample.
Figure S30. CD spectra of MBL 3 in phosphate buffer (aq., 0.01 M, 100 mM NaCl, pH = 7.0) at the thermal equilibrium (black), the PSS$^{365\text{nm}}$ (red), the PSS$^{430\text{nm}}$ (grey), and the PSS$^{470\text{nm}}$ (cyan) containing varying amounts of $Z$ isomer.
5.4. Compound 4

**Figure S31.** Titration of increasing amounts of MBL 4. **A.** CD spectra at the PSS $365\text{nm}$. **B.** UV-Vis spectra at the PSS $365\text{nm}$. **C.** CD spectra of the thermally adapted sample. **D.** UV-Vis spectra of the thermally adapted sample.

5.5. Apparent $K_D$ values

Apparent dissociation constant ($K_D$) was estimated by single set of identical binding sites model.\textsuperscript{7} This is simplified binding model for the MBL–DNA interaction and only provide a rough estimation of $K_D$ of each compound. CD titration data were fitted to following equation

$$\theta = \frac{\theta_{\text{max}}}{2 \cdot n \cdot M_t} \left( \frac{1}{K_A + x + n \cdot M_t} - \sqrt{\left( \frac{1}{K_A + x + n \cdot M_t} \right)^2 - 4 n \cdot M_t \cdot x} \right)$$

, where $n$ is number of binding sites, $K_A$ is binding constant, $M_t$ is bulk concentration of DNA, $x$ is bulk concentration of ligand, and $\theta_{max}$ is saturated value of CD. $n$ is fixed to 2 according to reported binding stoichiometry of NCDA derivatives to CGG/CGG sequence.\textsuperscript{4} Intensities at 341 nm in the induced CD band (Figures S28-31) are plotted against total ($Z$ and $E$) concentration of each compound (Figure S32). Fitting to the equation provided qualitative KD values, 15.2, 0.7, and 23.6 $\mu$M for compound 2, 3, and 4, respectively.
Figure S32. Qualitative fit of the titration studies to determine the apparent $K_D$ value using a single set of identical sites model. Black filled circle, compound 2; Red filled diamond, 3; Blue filled circle, 4.
6. Computational Data

6.1. Cartesian Coordinates of the optimized structures

The structures of both $E$ and $Z$ isomers of the model compounds as well as of the naphthyridine carbamate core were optimized at the oB97X-D/def2-SVP level of theory in vacuum using the Gaussian 16, Version B.01 software package. The cartesian coordinates, the energies and the thermochemical parameters of the structures are provided in the following section. All the compounds reported were confirmed to be minima after checking the absence of imaginary frequencies.

$E$-$\text{CH}_2\text{NHCH}_3$

|   |   |   |
|---|---|---|
| C | -3.75247293 | -0.81118506 | 0.20516196 |
| C | -4.56475076 | 0.33288953 | 0.2021894 |
| C | -3.95704066 | 1.58930682 | 0.12713083 |
| C | -2.57122325 | 1.70453697 | 0.06629909 |
| C | -1.77072898 | 0.56017908 | 0.07114569 |
| C | -2.37032908 | -0.7052024 | 0.1393267 |
| N | -0.37253603 | 0.77857412 | 0.00099492 |
| N | 0.32726422 | -0.24707671 | -0.00418046 |
| C | 1.72549113 | -0.02931276 | -0.0733499 |
| C | 2.52680269 | -1.17352219 | -0.07786576 |
| C | 3.91249923 | -1.06220401 | -0.14323548 |
| C | 4.51967545 | 0.19584373 | -0.20247665 |
| C | 3.70714208 | 1.33898597 | -0.1910698 |
| C | 2.32432713 | 1.23655601 | -0.13108643 |
| C | -6.06724418 | 0.20749535 | 0.3111752 |
| C | 6.02218585 | 0.3237824 | -0.31018685 |
| N | -6.57208356 | -0.97881189 | -0.34143105 |
| C | -7.9967954 | -1.1706319 | -0.20198325 |
| N | 6.71988938 | -0.75558723 | 0.34977001 |
| C | 8.15608956 | -0.7097104 | 0.2030017 |
| H | -4.23377301 | -1.79001815 | 0.25261554 |
| H | -4.57641413 | 2.49019493 | 0.11309646 |
| H | -2.08276704 | 2.67900741 | 0.00678978 |
| H | -1.73073212 | -1.58847763 | 0.1403802 |
| H | 2.03680686 | -2.14807787 | -0.0301028 |
Energy = -839.8180282
Zero-point correction = 0.341198 (Hartree/Particle)
Thermal correction to Gibbs Free Energy = 0.290754
Sum of electronic and zero-point Energies = -839.476830
Sum of electronic and thermal Energies = -839.457693
Sum of electronic and thermal Enthalpies = -839.456749
Sum of electronic and thermal Free Energies = -839.527274

**Z-CH₂NHCH₃**

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|   | C     |         |         |
|---|-------|---------|---------|
|   | -2.34186416 | 0.13351592 | -0.93151132 |
|   | -3.34458839 | 0.15931815 | 0.04483123 |
|   | -3.44884197 | -0.92320358 | 0.92394708 |
|   | -2.58420673 | -2.0092244 | 0.82737636 |
|   | -1.5576134 | -1.99958371 | -0.11906316 |
|   | -1.44883043 | -0.92856139 | -1.01283306 |
|   | -0.73826723 | -3.16652724 | -0.20982183 |
|   | 0.49696352 | -3.1208472 | -0.25789697 |
|   | 1.23878295 | -1.91355523 | -0.07445672 |
|   | 2.25476437 | -1.63607854 | -0.99230019 |
|   | 3.051818 | -0.50796077 | -0.830154 |
|   | 2.88721581 | 0.33169031 | 0.27727325 |
| C   | 1.90439671 | 0.00980202 | 1.21889021 |
|-----|------------|------------|------------|
| C   | 1.07607085 | -1.09428591| 1.04700725 |
| C   | -4.3212797 | 1.31121544 | 0.11384387 |
| C   | 3.74293132 | 1.56730348 | 0.44142508 |
| N   | 5.0753412  | 1.38970498 | -0.08895457|
| C   | 5.90313425 | 2.5713676  | -0.02160407|
| N   | -3.71711366| 2.56773702 | -0.26678178|
| C   | -4.63157422| 3.68563496 | -0.27955786|
| H   | -2.26432408| 0.97507126 | -1.62255218|
| H   | -4.2291368 | -0.92432643| 1.69001382 |
| H   | -2.68234849| -2.8693776 | 1.49266474 |
| H   | -0.6655143 | -0.93054593| -1.77263963|
| H   | 2.40113516 | -2.31176036| -1.83749899|
| H   | 3.83625203 | -0.27242619| -1.55196946|
| H   | 1.78079666 | 0.6367068  | 2.10625213 |
| H   | 0.3086126  | -1.3272323 | 1.78684198 |
| H   | -5.1542609 | 1.11327512 | -0.58641131|
| H   | -4.78380345| 1.33311877 | 1.12586945 |
| H   | 3.27034838 | 2.4008897  | -0.11124683|
| H   | 3.73128348 | 1.87645349 | 1.51047117 |
| H   | 5.52846633 | 0.60555554 | 0.37442397 |
| H   | 6.90811196 | 2.34800184 | -0.40776148|
| H   | 5.47548479 | 3.36318555 | -0.65787621|
| H   | 6.01428904 | 2.99500072 | 0.99979735 |
| H   | -2.91938769| 2.76169262 | 0.33394343 |
| H   | -4.09352248| 4.60781088 | -0.54256575|
| H   | -5.40486238| 3.52614762 | -1.04841272|
| H   | -5.15759425| 3.85796089 | 0.68416802 |

Energy = -839.79752
Zero-point correction = 0.341123 (Hartree/Particle)
Thermal correction to Gibbs Free Energy = 0.291393
Sum of electronic and zero-point Energies = -839.456397
Sum of electronic and thermal Energies = -839.437457
Sum of electronic and thermal Enthalpies = -839.436513
Sum of electronic and thermal Free Energies = -839.506127
$E\text{-OCH}_3$

![Image of E-OCH3 molecule]

|   | C   | C   | C   | C   | N   | N   | C   | C   | C   | C   | C   | O   | O   | C   | C   | H   | H   | H   | H   | H   | H   | H   | H   | H   | H   | H   | H   | H   | H   | H   | H   |
|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|   | 3.697662 | 1.293092 | 0.000087 | 4.525044 | 0.154485 | 0.00007 | 3.948188 | -1.120399 | -0.000037 | 2.55921 | -1.242931 | -0.000124 | 1.736693 | -0.117741 | -0.000109 | 2.322726 | 1.160786 | 0 | 0.34473 | -0.357496 | -0.000215 | -0.373516 | 0.657129 | -0.000203 | -1.766449 | 0.419088 | -0.000115 | -2.591408 | 1.551725 | -0.000063 | -3.970328 | 1.422059 | 0.000015 | -4.555409 | 0.146975 | 0.000044 | -3.735401 | -0.992363 | -0.000011 | -2.352062 | -0.850941 | -0.000088 | 5.850764 | 0.389739 | 0.000159 | -5.901733 | 0.111447 | 0.000115 | 6.738266 | -0.69545 | 0.000129 | -6.556604 | -1.128158 | 0.000196 | 4.174588 | 2.274752 | 0.000169 | 4.563942 | -2.019563 | -0.000053 | 2.087041 | -2.227292 | -0.000209 | 1.670768 | 2.034883 | 0.000008 | -2.118519 | 2.535694 | -0.000088 | -4.626179 | 2.293885 | 0.000056 | -4.166553 | -1.993602 | 0.000002 | -1.700978 | -1.725882 | -0.000135 | 7.750475 | -0.27352 | 0.000195 | 6.61407 | -1.325401 | 0.898093 | 6.614141 | -1.325292 | -0.897921 | -7.632248 | -0.914502 | 0.000287 | -6.311104 | -1.721235 | -0.897843 | -6.310945 | -1.721203 | 0.898212 |

Energy $= -800.9583381$

Zero-point correction $= 0.259059$ (Hartree/Particle)

Thermal correction to Gibbs Free Energy $= 0.214186$

Sum of electronic and zero-point Energies $= -800.699279$

Sum of electronic and thermal Energies $= -800.683501$

Sum of electronic and thermal Enthalpies $= -800.682557$

Sum of electronic and thermal Free Energies $= -800.744152$
Z-OCH₃

|   |          |          |          |
|---|----------|----------|----------|
| C | -2.01135269 | 0.42180974 | -1.24787692 |
| C | -3.06853079 | 0.67639996 | -0.35938967 |
| C | -3.27362749 | -0.18074152 | 0.72715745 |
| C | -2.42700755 | -1.27371139 | 0.91329934 |
| C | -1.34497456 | -1.4948093 | 0.06460794 |
| C | -1.15508278 | -0.6445914 | -1.03642717 |
| N | -0.57071246 | -2.67376746 | 0.29007323 |
| N | 0.66677255  | -2.69491232 | 0.24666677 |
| C | 1.46864067  | -1.51929902 | 0.13157137 |
| C | 2.54177807  | -1.56115648 | -0.76774502 |
| C | 3.40126698  | -0.48149268 | -0.88713594 |
| C | 3.0908852   | 0.64591401  | -0.06764331 |
| C | 2.20165898  | 0.66805368  | 0.87229003  |
| C | 1.31985334  | -0.40752739 | 0.96169939  |
| O | -3.83396913 | 1.7506371   | -0.63942914 |
| O | 4.1294636   | 1.64306643  | -0.24390219 |
| C | -4.91923725 | 2.05022442  | 0.19484695  |
| C | 4.02691512  | 2.79703519  | 0.54440836  |
| H | -1.88296196 | 1.08663892  | -2.10347417 |
| H | -4.09747643 | -0.02362763 | 1.42322433  |
| H | -2.59761374 | -1.96972705 | 1.73748788  |
| H | -0.33407039 | -0.82617153 | -1.73170423 |
| H | 2.69073605  | -2.45491703 | -1.37922787 |
| H | 4.22779101  | -0.49034218 | -1.59937468 |
| H | 2.06456587  | 1.51806372  | 1.54050479  |
| H | 0.50940049  | -0.37679943 | 1.69166654  |
| H | -5.39274263 | 2.95026557  | -0.21554537 |
| H | -5.66141619 | 1.23302225  | 0.2113636   |
| H | -4.59558155 | 2.25830582  | 1.22985188  |
| H | 4.83582901  | 3.46673872  | 0.22835104  |
| H | 3.06064887  | 3.3102113   | 0.39599728  |
| H | 4.15008289  | 2.57236683  | 1.61837289  |
Energy= -800.9355395
Zero-point correction= 0.258698 (Hartree/Particle)
Thermal correction to Gibbs Free Energy= 0.214176
Sum of electronic and zero-point Energies= -800.676841
Sum of electronic and thermal Energies= -800.661195
Sum of electronic and thermal Enthalpies= -800.660251
Sum of electronic and thermal Free Energies= -800.721364

Naphthyridine Carbamate Core

|    |    |    |    |
|----|----|----|----|
| C  | 5.27217528 | -1.01452077 | -0.00018759 |
| O  | 4.30949858 | 0.02313602 | -0.00002403 |
| C  | 3.0195378 | -0.38030549 | 0.00016057 |
| N  | 2.23631189 | 0.76039081 | 0.00010496 |
| O  | 2.66866746 | -1.52250984 | 0.00006732 |
| C  | 0.84849262 | 0.87293522 | 0.00007722 |
| N  | 0.10332997 | -0.19538204 | 0.0000552 |
| C  | -1.24454315 | -0.05632013 | 0.00003143 |
| C  | -1.86953601 | 1.22220477 | 0.00003777 |
| C  | -1.03121365 | 2.36789435 | 0.0002722 |
| C  | 0.32386409 | 2.20717795 | 0.0001883 |
| N  | -1.96863009 | -1.20116871 | 0.0002114 |
| C  | -3.27979169 | -1.13628392 | 0.0001082 |
| C  | -3.99082887 | 0.10018396 | 0.00005923 |
| C  | -3.28403178 | 1.27300414 | 0.0006754 |
| C  | -4.04550283 | -2.43124569 | 0.0000438 |
| H  | 6.25159826 | -0.52280984 | 0.0004101 |
| H  | 5.16835686 | -1.64897161 | 0.8920973 |
| H  | 5.16798439 | -1.64904373 | -0.89237674 |
| H  | 2.76330761 | 1.62350951 | 0.0008555 |
| H  | -1.47641127 | 3.36607794 | -0.0005124 |
| H  | 0.99605403 | 3.06776172 | 0.0000216 |
| H  | -5.08267027 | 0.09766368 | -0.0009655 |
| H  | -3.79137369 | 2.24159055 | -0.0009732 |
| H  | -3.34299337 | -3.2728714 | -0.00016167 |
| H  | -4.69385433 | -2.50164102 | 0.88728211 |
| H  | -4.69413977 | -2.50150211 | -0.88707476 |
Energy = -739.7516139 
Zero-point correction = 0.213184 (Hartree/Particle) 
Thermal correction to Gibbs Free Energy = 0.169885 
Sum of electronic and zero-point Energies = -739.538430 
Sum of electronic and thermal Energies = -739.524249 
Sum of electronic and thermal Enthalpies = -739.523305 
Sum of electronic and thermal Free Energies = -739.581729

6.2. TD-DFT Spectra

Using the optimized geometries, we simulated the UV-Vis spectra of the different components using TD-DFT at the PBE0/6-311+G(2d,p) level of theory using a conductor-like polarizable continuum model (C-PCM, ε = 78.4 for water). Single point calculations up to the first 25 singlet states were performed to describe the UV-Vis absorption spectra. The five lowest transitions are reported including the energy (in eV), the associated wavelength (in nm), and its oscillator strength. The numbers of the orbitals involved in the transition (with general formula occupied → unoccupied) and the associated (largest) coefficient in the CI expansion is depicted.

The spectra were processed using GaussView 6.0.16 and OriginPro 2016.

**E-CH$_2$NHCH$_3$**

| Excited State | Singlet-A | Energy (eV) | Wavelength (nm) | Oscillator Strength |
|---------------|-----------|-------------|-----------------|-------------------|
| 1: 69 → 73    | 2.6805    | 462.55      | 0.67532         | 0.0001            |
| 71 → 73       | -0.15880  |
| 2: 72 → 73    | 3.2908    | 376.76      | 0.70115         | 0.5364            |
| 3: 69 → 73    | 3.4106    | 363.52      | 0.15827         | 0.0002            |
| 71 → 73       | 0.68468   |
| 4: 70 → 73    | 3.6290    | 341.65      | 0.69703         | 0.6110            |
| 5: 68 → 73    | 4.1720    | 297.18      | 0.67891         | 0.0475            |
| 70 → 74       | -0.11821  |
| 72 → 74       | -0.12284  |

**Z-CH$_2$NHCH$_3$**

| Excited State | Singlet-A | Energy (eV) | Wavelength (nm) | Oscillator Strength |
|---------------|-----------|-------------|-----------------|-------------------|
| 1: 66 → 73    | 2.7042    | 458.48      | 0.19131         | 0.0662            |
| 68 → 73       | 0.12373   |
| 70 → 73       | 0.30682   |
| Transition   | Energy (eV) | Wavelength (nm) | f |
|--------------|-------------|-----------------|---|
| 72 → 73      | 0.58662     |                 |   |
| Excited State 2: Singlet-A | 3.6784 eV 337.06 nm | f=0.0434 |
| 66 → 73      | 0.11137     |                 |   |
| 70 → 73      | 0.36357     |                 |   |
| 71 → 73      | 0.50956     |                 |   |
| 72 → 73      | -0.28215    |                 |   |
| Excited State 3: Singlet-A | 3.7229 eV 333.03 nm | f=0.0152 |
| 70 → 73      | -0.44090    |                 |   |
| 71 → 73      | 0.47626     |                 |   |
| 72 → 73      | 0.24229     |                 |   |
| Excited State 4: Singlet-A | 4.0897 eV 303.16 nm | f=0.0994 |
| 66 → 73      | 0.25702     |                 |   |
| 68 → 73      | 0.58056     |                 |   |
| 70 → 73      | -0.24659    |                 |   |
| Excited State 5: Singlet-A | 4.1749 eV 296.97 nm | f=0.0313 |
| 69 → 73      | 0.67619     |                 |   |
| **E-OCH₃**   |             |                 |   |
| Excited State 1: Singlet-A | 2.8024 eV 442.42 nm | f=0.0000 |
| 63 → 65      | 0.70180     |                 |   |
| Excited State 2: Singlet-A | 3.2433 eV 382.27 nm | f=1.1184 |
| 64 → 65      | 0.70524     |                 |   |
| Excited State 3: Singlet-A | 4.2703 eV 290.34 nm | f=0.0073 |
| 60 → 65      | -0.22969    |                 |   |
| 61 → 65      | -0.10470    |                 |   |
| 62 → 65      | 0.63658     |                 |   |
| 64 → 66      | 0.10882     |                 |   |
| Excited State 4: Singlet-A | 4.3671 eV 283.91 nm | f=0.0005 |
| 60 → 65      | -0.13800    |                 |   |
| 61 → 65      | 0.60058     |                 |   |
| 64 → 66      | -0.28536    |                 |   |
| 64 → 67      | 0.13028     |                 |   |
| Excited State 5: Singlet-A | 4.4040 eV 281.52 nm | f=0.0001 |
| 60 → 65      | 0.55876     |                 |   |
| 62 → 65      | 0.25828     |                 |   |
| 64 → 66      | -0.11745    |                 |   |
| 64 → 67      | -0.27078    |                 |   |
| **Z-OCH₃**   |             |                 |   |
| Excited State 1: Singlet-A | 2.6491 eV 468.02 nm | f=0.0971 |
| 62 → 65      | 0.25273     |                 |   |
| 64 → 65      | 0.64890     |                 |   |
Excited State 2: Singlet-A
61 → 65: 0.11326
62 → 65: 0.62454
63 → 65: 0.10680
64 → 65: -0.26746

Excited State 3: Singlet-A
63 → 65: 0.67553

Excited State 4: Singlet-A
61 → 65: -0.36036
64 → 66: 0.59123

Excited State 5: Singlet-A
60 → 65: 0.46952
63 → 66: 0.13681
64 → 67: 0.49260

Naphthyridine Carbamate Core

Excited State 1: Singlet-A
55 → 59: -0.19310
57 → 58: 0.67665

Excited State 2: Singlet-A
56 → 58: 0.69848

Excited State 3: Singlet-A
55 → 58: 0.58229
57 → 59: 0.38622

Excited State 4: Singlet-A
54 → 58: 0.64164
56 → 59: -0.23675
56 → 60: 0.13738

Excited State 5: Singlet-A
54 → 58: 0.21497
56 → 59: 0.65542
56 → 60: 0.12474

Excited State 2: Singlet
3.8493 eV 322.10 nm  f=0.1955
Excited State 3: Singlet
3.9322 eV 315.30 nm  f=0.0860
Excited State 4: Singlet
4.2783 eV 289.80 nm  f=0.0207
Excited State 5: Singlet
4.5252 eV 273.99 nm  f=0.0039

Excited State 1: Singlet-A
4.2078 eV 294.65 nm  f=0.3939
Excited State 2: Singlet-A
4.3471 eV 285.21 nm  f=0.0001
Excited State 3: Singlet-A
4.8696 eV 254.61 nm  f=0.0038
Excited State 4: Singlet-A
5.0049 eV 247.73 nm  f=0.0023
Excited State 5: Singlet-A
5.2127 eV 237.85 nm  f=0.0007
6.3. Conformational Search and Molecular Dynamic Simulations

The calculations and analysis were performed either on a HP EliteDesk, with an Intel Core i7-6700 processor with four cores and an NVIDIA GeForce GTX 1060 3GB graphics card (System preparation and Conformational search), or on the Peregrine cluster at the University of Groningen (Molecular Dynamics). The system preparation and the conformational search were carried out with Maestro (ver 12.4, Schrödinger Release 2020-2: Maestro, Schrödinger, LLC, New York, NY, 2020), using the OPLS3e force field. Molecular Dynamics (MD) simulations were performed using GROMACS 2018.4. The dihedral measurements were performed with KNIME (ver 4.1.1, KNIME AG, Zurich, Switzerland), using Schrödinger nodes and a custom Python script (based on the measure_by_smarts.py script) provided by Schrödinger. All the plots were generated with OriginPro 2019.

6.3.1. Preparation of the models

The model of the glue-DNA complex was built by modifying a similar structure that was previously released (PDB ID: 1X26). Five structures were chosen out of the 30 NMR conformers using Clustering of conformers in Maestro (Hierarchical sampling, on atomic RMSD for heavy atoms, RMSD in place, linkage method: Ward, output: 5 clusters). The structure which was the closest to the centroid of each cluster was selected, i.e. conformers 3, 11, 13, 23 and 28. The molecular glues of these five complexes were manually modified to compound Z-2, Z-3, and Z-4, then prepared with the Protein Preparation Wizard (restrained minimization to 0.8 Å RMSD) and finally minimized with MacroModel (method: TNCG, 50000 max iterations). Concurrently, the molecular glues of the 5 selected complexes (conformers 3, 11, 13, 23 and 28) were deleted to produce 5 complexes without any photoswitchable glue. In total, this workflow generated 15 complexes with photoswitchable glues (Z-2, Z-3 and Z-4) and 5 complexes with no photoswitchable glue.

6.3.2. Conformational search

The conformational search on the 15 complexes with photoswitchable glues (Z-2, Z-3 and Z-4) was carried out with MacroModel (OPLS3e force field). The DNA atoms were kept frozen and a distance constraint (1000 kJ/mol) was applied between the DNA and the glue atoms involved in a hydrogen bond (enhanced sampling, method: TNCG, 50000 max iterations, convergence threshold 0.05, 62.8 kJ/mol window, redundant conformers with max atom deviation of 0.5 Å are eliminated). Finally, the complexes were minimized with MacroModel with no constraints. The potential energies calculated in this last step were visualized through violin plots (Figure S33). The complexes with Z-4 consistently resulted in higher energies, thus suggesting that complexes with Z-2 and Z-3 would be energetically more favorable.
Figure S33. Violin plots of the potential energy calculated with the conformational search of the photoswitchable glue-DNA 2:1 complexes with Z-2 (2C), Z-3 (3C), and Z-4 (4C). From left to right: conformer 3, 11, 13, 23 and 28.

6.3.3. Molecular dynamics (MD) simulations

All the models prepared in the first subsection (15 complexes with and 5 complexes without photoswitchable glue) were further studied with MD. The parameter files for the MD simulations were prepared using the tLeap module of Ambertools and the DNA.bsc1 force field for DNA. Glue parameters were obtained using the Antechamber module\textsuperscript{13} and AM1-BCC charge methods. The dihedral parameters for the azobenzene moiety were adapted from a previous study.\textsuperscript{14} The general outlook of the dihedral section of the .top files is as follows:

\begin{verbatim}
ai aj ak al funct c0 c1 c2
 c N N c 9 0.0 31.5 1
 c N N c 9 180.0 60.0 2
 N N c c 1 180.0 16.0 2
 N N c c 1 180.0 0.0 2
 c c N N 1 180.0 16.0 2
\end{verbatim}
The starting structures were immersed in a pre-equilibrated cubic box of around 10000 TIP3P water molecules with 0.1 M NaCl, and sodium ions were added to maintain the electrical neutrality. The systems were minimized over 50000 steps of the steepest descent algorithm before MD simulations were performed. The minimized structures were used as a starting point for the MD simulations at increasing temperatures (300, 325, 350, 400 and 500 K). During the equilibration steps, the heavy atoms of the DNA-glue complex were kept fixed with a constraint of 1000 kcal/mol. In the first step, a constant volume simulation (NVT) was performed, during which the system was heated from 0 K to the target temperature over 100 ps. In the second step, an isothermal and isobaric simulation (NPT) was performed using the Berendsen algorithm for 100 ps. After the equilibration steps, the systems were further relaxed with 1 ns of unrestrained MD, using the Parrinello-Rahman algorithm for pressure coupling. Finally, 300 ns MD production trajectories were run without restraint, collecting frames at 100 ps intervals and using a 2 fs time step. Particle mesh Ewald (PME)\textsuperscript{15} was used to treat the long-range electrostatic interactions. All bonds were constrained using the LINCS algorithm. Gmx rms was used to calculate the RMSD of the DNA heavy atoms after least square fitting to the DNA heavy atoms. The complexes with Z-3 consistently showed a higher stability (RMSD < 1.5 Å) than the other complexes throughout 300 ns MD simulations at increasing temperatures (Figure S34-S38).

**Figure S34.** RMSD of DNA throughout the 300 ns MD simulation at increasing temperatures for conformer 3. From left to right: complexes with Z-2, Z-3, Z-4, and with no glue.
Figure S35. RMSD of DNA throughout the 300 ns MD simulation at increasing temperatures for conformer 11. From left to right: complexes with Z-2, Z-3, Z-4, and with no glue.

Figure S36. RMSD of DNA throughout the 300 ns MD simulation at increasing temperatures for conformer 13. From left to right: complexes with Z-2, Z-3, Z-4, and with no glue.
Figure S37. RMSD of DNA throughout the 300 ns MD simulation at increasing temperatures for conformer 23. From left to right: complexes with Z-2, Z-3, Z-4, and with no glue.

Figure S38. RMSD of DNA throughout the 300 ns MD simulation at increasing temperatures for conformer 28. From left to right: complexes with Z-2, Z-3, Z-4, and with no glue.
6.3.4. Analysis of (M)Z and (P)Z helical configurations

Gmx trjconv was used to extract 301 snapshots (every 1 ns) from the 300 ns MD runs at 300K. The structures without the explicit solvent shell were then optimized at the GFN-FF level, using the Born implicit solvent model for water. All the optimization were carried out with the xTB software package.16

The output structures were analyzed through KNIME to measure the ccNN dihedral angles with the measure_by_smarts.py script by Schrödinger. The helicity around the cis-azo double bond for each photoswitchable glue molecule was defined based on the ccNN/NNcc dihedral angle $\phi$, as follows:

| Helicity | $\Phi$ (°)                        |
|----------|----------------------------------|
| M        | -90 < $x$ < -10 v                 |
| P        | 10 < $x$ < 90 v -170 < $x$ < -90 |

![Diagram of helicity definition](image1)

**Figure S39.** The dihedral angle used for the definition of the helicity. A. (M)Z-azobenzene. B. (P)Z-azobenzene.

The systems could adopt three different configurations: (PP)Z, a mixed (PM/MP)Z, and (MM)Z. Based on these three configurations, the energies obtained at the GFN-FF level were visualized through violin plots (Figure S40-44). The complexes showed a preference for (PP)Z, especially compared to the (MM)Z configuration.

![Violin plots of energy distribution](image2)

**Figure S40.** Conformer 3. Violin plots of the energy and distribution of two molecules of Z-2 (left), Z-3 (center) and Z-4 (right) in a 2:1 complex to mismatched DNA adopting (PP)Z, (PM/MP)Z, and (MM)Z.
Figure S41. Conformer 11. Violin plots of the energy and distribution of two molecules of Z-2 (left), Z-3 (center) and Z-4 (right) in a 2:1 complex to mismatched DNA adopting (PP)Z, (PM/MP)Z, and (MM)Z.

Figure S42. Conformer 13. Violin plots of the energy and distribution of two molecules of Z-2 (left), Z-3 (center) and Z-4 (right) in a 2:1 complex to mismatched DNA adopting (PP)Z, (PM/MP)Z, and (MM)Z.

Figure S43. Conformer 23. Violin plots of the energy and distribution of two molecules of Z-2 (left), Z-3 (center) and Z-4 (right) in a 2:1 complex to mismatched DNA adopting (PP)Z, (PM/MP)Z, and (MM)Z.

Figure S44. Conformer 28. Violin plots of the energy and distribution of two molecules of Z-2 (left), Z-3 (center) and Z-4 (right) in a 2:1 complex to mismatched DNA adopting (PP)Z, (PM/MP)Z, and (MM)Z.
7. NMR-Data

**Compound 6** ($^1$H NMR; 400 MHz, Chloroform-$d$ : Methanol-$d_4$ 1:1)
**Compound 10** $^{1}H$ NMR, 400 MHz, CDCl$_3$)

![NMR spectrum of Compound 10 (H NMR)](image)

**Compound 10** $^{13}C$ NMR, 100 MHz, CDCl$_3$)

![NMR spectrum of Compound 10 (C NMR)](image)
**Compound 2** ($^1$H NMR, 700 MHz, CD$_3$OD)

![NMR spectrum of Compound 2](image)

**Compound 2** ($^{13}$C NMR, CD$_3$OD, 176 MHz)

![NMR spectrum of Compound 2](image)
Compound 11 (\(^1\)H NMR, 400 MHz, CDCl\(_3\))

\[
\text{\includegraphics[width=0.8\textwidth]{Compound11_HNMR.png}}
\]

Compound 11 (\(^{13}\)C NMR, 100 MHz, CDCl\(_3\))

\[
\text{\includegraphics[width=0.8\textwidth]{Compound11_CNMR.png}}
\]
**Compound 3** ($^1$H NMR, 700 MHz, CD$_2$OD)

![Compound 3 ($^1$H NMR, 700 MHz, CD$_2$OD)](image)

**Compound 3** ($^{13}$C NMR, CD$_2$OD, 176 MHz)

![Compound 3 ($^{13}$C NMR, CD$_2$OD, 176 MHz)](image)
**Compound 13** ($^1$H NMR; 400 MHz, Acetone-$d_6$)

![Compound 13 ($^1$H NMR; 400 MHz, Acetone-$d_6$)](image)

**Compound 13** ($^{13}$C NMR; 101 MHz, Acetone-$d_6$)

![Compound 13 ($^{13}$C NMR; 101 MHz, Acetone-$d_6$)](image)
**Compound 14** \(^{1}H \text{NMR, 400 MHz, Acetone-}d_{6}\)
Compound 4 ($^1$H NMR, 700 MHz, CD$_3$OD)

![NMR spectrum of Compound 4 (1H)](image)

Compound 4 ($^{13}$C NMR, CD$_3$OD, 176 MHz)

![NMR spectrum of Compound 4 (13C)](image)
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