Supporting Information

All-Red-Light Photoswitching of Indirubin

Controlled by Supramolecular Interactions

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Table of contents

1 Materials and General Methods .................................................................4
  1.1 General experimental ..................................................................................4
  1.2 Synthesis .....................................................................................................6
    1.2.1 General procedure for the synthesis of $N$-unsubstituted indirubins .......... 7
    1.2.2 General procedure for the synthesis of $N$-monoalkylated $N,N'$-dialkylated indirubins ................................................................. 7
    1.2.3 (Z)-1,1'-dipropyl-[2,3'-biindolylidene]-2',3-dione (1a) ......................... 7
    1.2.4 (Z)-[2,3'-biindolylidene]-2',3-dione (Indirubin1b) ............................ 8
    1.2.5 (Z)-1'-propyl-[2,3'-biindolylidene]-2',3-dione (1c) ............................. 8
    1.2.6 (Z)-1'-(pentan-3-yl)-1-propyl-[2,3'-biindolylidene]-2',3-dione (2a) ......... 9
    1.2.7 (Z)-1'-(pentan-3-yl)-[2,3'-biindolylidene]-2',3-dione (2c) .................. 10
    1.2.8 (Z)-5',6'-difluoro-1,1'-dipropyl-[2,3'-biindolylidene]-2',3-dione (3a) .... 10
    1.2.9 (Z)-5',6'-difluoro-[2,3'-biindolylidene]-2',3-dione (3b) ....................... 11
    1.2.10 (Z)-5'-fluoro-6'-morpholino-1,1'-dipropyl-[2,3'-biindolylidene]-2',3-dione (4a) ................................................................. 12
    1.2.11 (Z)-5'-fluoro-6'-(methylthio)-[2,3'-biindolylidene]-2',3-dione (4b) ....... 12
    1.2.12 (Z)-5'-fluoro-6'-[(methylthio)-1,1'-dipropyl-[2,3'-biindolylidene]-2',3-dione (5a) ................................................................. 13
    1.2.13 (Z)-5'-fluoro-6'-morpholino-[2,3'-biindolylidene]-2',3-dione (5b) ....... 14
    1.2.14 5-fluoro-6-(methylthio)indoline-2,3-dione (9) ................................. 14
    1.2.15 5-fluoro-6-morpholinooindoline-2,3-dione (10) ............................... 15
  2 Photophysical and photochemical properties .............................................16
    2.1 Molar absorption coefficients .................................................................16
    2.2 Photoisomerization experiments ............................................................20
      2.2.1 General procedures ...........................................................................20
      2.2.2 Photoisomerization of indirubins 1a to 5a at NMR concentrations in toluene-$d_8$ solution 22
      2.2.3 Photoisomerization of indirubins 1a to 5a in the presence of STC at NMR concentrations in toluene-$d_8$ solution ................................................................. 25
      2.2.4 Photoisomerization of indirubins 1a to 5a at NMR concentrations in CD$_2$Cl$_2$ solution 28
      2.2.5 Photoisomerization of indirubins 1a to 5a in the presence of STC at NMR concentrations in CD$_2$Cl$_2$ solution ................................................................. 31
      2.2.6 Photoisomerization of indirubins 1a to 5a at UV/vis concentrations in toluene solution 39
2.2.7 Photoisomerization of indirubins 1a to 5a at UV/vis concentrations in CH$_2$Cl$_2$ solution 41
2.2.8 Photoisomerization of indirubins 1a to 5a in the presence of STC at UV/vis concentrations in toluene solution ................................................................. 43
2.2.9 Photoisomerization of indirubins 1a to 5a in the presence of STC at UV/vis concentrations in CH$_2$Cl$_2$ solution ................................................................. 45
2.2.10 Photoisomerization of indirubins 1b and 1c at UV/vis concentrations 47
2.3 Quantum yield determination ........................................................................ 48
2.4 Photochemical stabilities of indirubins 1a and 2a with and without the addition of STC 52

3 Thermal stabilities of E isomeric states .................................................. 53
  3.1 First order kinetics without entering equilibria ........................................ 53
  3.1.1 Measurement procedure ................................................................... 53
  3.1.2 Thermal E to Z isomerization in toluene solution ............................... 56
  3.1.3 Thermal E to Z isomerization in CH$_2$Cl$_2$/CD$_2$Cl$_2$ solution .............. 64

4 Theoretical Description ............................................................................ 73
  4.1 General calculation procedure ............................................................. 73
  4.2 Optimized molecular structures of indirubins 1a to 5a ....................... 74
  4.3 Molecular orbitals involved in the electronic excitation of indirubin 1a .... 76
  4.4 Theoretical UV/vis absorption spectra of indirubins 1a to 5a ............... 77

5 NMR spectra of 1a – 5a ........................................................................ 82

6 Crystallographic Data ........................................................................... 87

7 References ......................................................................................... 91
1 Materials and General Methods

1.1 General experimental

Reagents and solvents were obtained from Acros, Aldrich, Fluka, Merck, or Sigma-Aldrich in the qualities puriss., p.a., or purum and used as received. Technical solvents were distilled before use for column chromatography and extraction on a rotary evaporator (vacuubrand CVC 3000). Reactions were monitored on Merck Silica 60 F254 or Aluminium oxide 60 F254 neutral TLC plates. Detection was done by irradiation with UV light (254 nm or 366 nm).

Column chromatography was performed with silica gel 60 (Merck, particle size 0.063 - 0.200 mm) and distilled technical solvents.

$^1$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra were measured on a Varian Mercury 200 VX, Varian 300, Inova 400, Varian 600 NMR, Bruker Avance Neo HD 400 MHz, Bruker Avance Neo HDX 500 MHz, Bruker Avance Neo HDX 600 MHz with cryo probe DCH-Z$^{13}$C/$^1$H, or Bruker Avance III HD 800 MHz spectrometer. Chemical shifts (\(\delta\)) are given relative to tetramethylsilane as external standard. Deuterated solvents were obtained from Cambridge Isotope Laboratories and used without further purification. Residual solvent signals in the $^1$H and $^{13}$C NMR spectra were used as internal reference: For $^1$H NMR: CD$_2$Cl$_2$ = 5.32 ppm and toluene-$d_8$ = 2.08 ppm. For $^{13}$C NMR: CD$_2$Cl$_2$ = 53.84 ppm and toluene-$d_8$ = 20.43 ppm. The resonance multiplicity is indicated as s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sext (sextet) and m (multiplet) and br (broad signal). The chemical shifts are given in parts per million (ppm) on the delta scale (\(\delta\)) and the coupling constant values (\(J\)) are given in hertz (Hz). Signal assignments are given in the experimental part using the arbitrary numbering indicated.

Electron Impact (EI) mass spectra were measured on a Finnigan MAT95Q or on a Finnigan MAT90mass spectrometer.

Electrospray ionization (ESI) mass spectra were measured on a Thermo Finnigan LTQ-FT. The most important signals are reported in m/z units with M as the molecular ion.

Infrared spectra were recorded on a Perkin Elmer Spectrum BX-FT-IR instrument equipped with a Smith DuraSampIR II ATR-device. Transmittance values are qualitatively described by wavenumber (cm$^{-1}$) as very strong (vs) strong (s), medium (m) and weak (w).

UV/vis spectra were measured on a Varian Cary 5000 spectrophotometer. The spectra were recorded in a quartz cuvette (1 or 10 mm path length). Solvents for spectroscopy were obtained from VWR and Merck. Absorption wavelength ($\lambda$) are reported in nm and the extinction coefficients (\(\varepsilon\)) L·mol$^{-1}$cm$^{-1}$ are given in brackets. Shoulders are declared as sh.

Melting points (m.p.) were measured on a Büchi B-540 melting point apparatus in open capillaries.

High performance liquid chromatography (HPLC) was performed on a Merck-Hitachi LaChromSeries HPLC system consisting of a D-7000 interface, a L-7150 solvent delivery module, a L-7350 column oven, a L-7420 UV/vis detector and a L-7455 diode array detector.
using a preparative Machery-Nagel VP 250/21 NUCLEODUR Sphinx RP 5 μm column (acetonitrile/water 65:35 v/v, 13-15 mL/min, 35 °C column temperature).

**Photoisomerization experiments:** Irradiations at ambient temperatures were conducted using LEDs from Roithner Lasertechnik GmbH (H2A3-H625, 625 nm) and Thorlabs (M660D2, 660 nm) For in situ irradiation studies a Prizmatix ultra high power LED 625 nm (UHP-T-625-DI) was used as light source and the light beam was guided by a fiber-optic cable from Thorlabs (FT1500UMT, 0.39 NA, 1500 μm, one SMA, one blank end) and pointed directly into the NMR tube during NMR measurements.
1.2 Synthesis

Commercially available isatins 7 and 8 as well as indoxyl acetate 6 were used as initial starting materials for the syntheses of respective indirubins 1 to 5.

Scheme S1: Synthesis of isatins 9 and 10 starting from commercially available isatin 8.

For synthesis of indirubins 1b and 2b isatin 7 was used for the condensation reaction with indoxyl acetate 6. Isatins 9 and 10 were prepared from commercially available 5,6-difluoroisatin (8) via nucleophilic substitution reactions. Subsequently isatins 8, 9, and 10 were each condensed with indoxyl acetate 6 to give indirubins 3b, 4b, and 5b, respectively. A final alkylation with 1-iodopropane or 3-bromopentane gave either mono-alkylated products 1c and 2c or dialkylated indirubins 1a to 5a.

Scheme S2 General synthesis of indirubins 1b to 5b and di-n-propylated indirubins 1a, 3a, 4a, and 5a starting by a condensation reaction of commercially available 7 and 8 or previously synthesized isatins 9 and 10 with indoxyl acetate 6. Conditions: i) Na₂CO₃, MeOH, 24 °C; ii) NaH, 1-iodopropane, DMF, 90 °C.
1.2.1 General procedure for the synthesis of \(N\)-unsubstituted indirubins

The respective isatin (1 equiv.) and indoxyl acetate (1 equiv.) starting materials were dissolved in methanol (26 mL/mmol). Argon was bubbled through the solution for one hour in order to remove dioxygen from the solvent. Then solid \(\text{Na}_2\text{CO}_3\) (2.2 equiv.) was added to the solution. The resulting suspension was stirred for 2 h at 22 °C and was then filtered. The solid residue was first washed with cold ethyl acetate and then with water until the filtrate showed no basic reaction. The respective indirubin could be obtained as purple solid in high purity and was used in the next synthetic step without further purification.

1.2.2 General procedure for the synthesis of \(N\)-monoalkylated \(N,N'\)-dialkylated indirubins

In a nitrogen-flushed Schlenk flask equipped with a magnetic stirring bar and a rubber septum the respective unsubstituted indirubin (1b, 3b, 4b, and 5b; 1 equiv. in each case) was dissolved in dry DMF (3.5 mL/mmol). To the solution NaH (60% dispersion in mineral oil; 4 equiv.) was added slowly. The mixture was stirred for 10 minutes at 22 °C before 1-iodopropane (4 equiv. for synthesis of indirubins 1a, 3a, 4a, 5a, and 1c) or 3-bromopentane (4 equiv. for synthesis of indirubin 2c) was added slowly. The suspension was then either kept stirring at 22 °C (for the synthesis of \(N\)-monoalkylated indirubins 1c and 2c) or heated to 90 °C (for the synthesis of dialkylated indirubins 1a, 3a, 4a, and 5a) and stirred at that temperature for 16 h. For the synthesis of indirubin 2a monosubstituted 2c (1 equiv.) was dissolved in dry DMF (3.5 mL/mmol) and after addition of NaH (60% dispersion in mineral oil; 4 equiv.) and stirring for 10 min at 22 °C 1-iodopropane (3 equiv.) was added and the mixture was heated to 90 °C for 16 h. Subsequently the respective mixture was allowed to cool down and was then neutralized with a saturated aq. ammonium chloride solution and extracted with ethyl acetate (3x). The combined organic phases were dried over solid water-free \(\text{Na}_2\text{SO}_4\) and the volatiles were removed \textit{in vacuo}. Subsequent purification by flash column chromatography (SiO\(_2\); 9:1 to 4:1 iHex:EtOAc) and further purification by reverse phase HPLC (NUCLEODUR Sphinx RP 5 μm; acetonitrile/water 65:35 v/v) gave the respective dipropylated indirubin.

1.2.3 \((Z)-1,1'\text{-dipropyl-[2,3'\text{-biindolylidene}]-2',3\text{-dione}}\) (1a)

Blue solidified oil, yield: 150 mg (0.572 mmol, 19%),

\[R_f = \text{SiO}_2, \text{iHex/EtOAc} 9:1 = 0.21; \text{\textsuperscript{1}H NMR} (600 MHz, toluene-\text{d}_8) \delta = 9.07 (dd, J = 7.9, 0.6 Hz, 1H, H-C(11)), 7.52 (d, J = 6.5 Hz, 1H, H-C(6)), 7.04 (td, J = 7.6, 1.0 Hz, 1H, H-C(13)),\]
7.00 – 6.93 (m, 2H, H-C(2/12)), 6.59 (t, J = 7.4 Hz, 1H, H-C(1)), 6.46 (d, J = 8.2 Hz, 1H, H-C(3)), 6.43 (d, J = 7.6 Hz, 1H, H-C(14)), 4.12 – 4.06 (m, 2H, H-C(20)), 3.51 (t, J = 7.2 Hz, 1H, H-C(17)), 1.57 – 1.45 (m, 4H, H-C(18/21)), 0.77 (t, J = 7.4 Hz, 3H, H-C(19)), 0.67 (t, J = 7.4 Hz, 3H, H-C(22)) ppm; 13C NMR (151 MHz, toluene-d8) δ = 188.2 (C(8)), 166.7 (C(16)), 154.2 (C(4)), 142.5 (C(15)), 141.9 (C(7)), 135.7 (C(2)), 129.4 (C(13)), 126.3 (C(11)), 124.8 (C(6)), 123.0 (C(10)), 122.0 (C(5)), 121.8 (C(1)), 121.5 (C(12)), 111.5 (C(3)), 110.9 (C(9)), 107.7 (C(14)), 50.4 (C(20)), 41.4 (C(17)), 21.4 (C(18)), 20.8 (C(21)), 11.4 (C(19)), 11.4 (C(22)) ppm;

IR: ν = 3054w, 2963m, 2932w, 2874w, 1737m, 1699m, 1667 s, 1602vs, 1550m, 1465vs, 1379m, 1346s, 1323s, 1300s, 1265m, 1190s, 1158m, 11 29s, 1090vs, 1079vs, 1057m, 1030s, 1015s, 993m, 964s, 916m, 817m, 796m, 789m, 744vs, 709s, 700m, 684m, 674m, 664m, 652m cm−1; HR-EI-MS calc. [C22H22N2O2]: 346.1676, found: 346.1678.

1.2.4 (Z)-[2,3'-biindolinylidene]-2',3-dione (1b)

Purple solid, yield: 3.02 g (11.4 mmol, quantitative).

m.p. 170.8 °C; 1H NMR (400 MHz, DMSO-d6) δ = 11.02 (s, 1H, H-C(17)), 10.89 (s, 1H, H-C(7)), 8.77 (d, J = 7.4 Hz, 1H, H-C(12)), 7.65 (d, J = 7.4 Hz, 1H, H-C(6)), 7.58 (ddd, J = 8.4, 7.4, 1.2 Hz, 1H, H-C(2)), 7.42 (d, J = 8.1 Hz, 1H, H-C(3)), 7.25 (td, J = 7.6, 1.1 Hz, 1H, H-C(14)), 7.02 (t, J = 7.6 Hz, 2H, H-C(1/13)), 6.90 (d, J = 7.7 Hz, 1H, H-C(15)) ppm; 13C NMR (101 MHz, DMSO-d6) δ = 188.7 (C(7)), 171.0 (C(18)), 152.5 (C(4)), 140.9 (C(16)), 138.4 (C(8)), 137.1 (C(2)), 129.3 (C(14)), 124.7 (C(12)), 124.4 (C(6)), 121.5 (C(11)), 121.3 (C(1/13)), 119.0 (C(5)), 113.5 (C(3)), 109.6 (C(15)), 106.6 (C(10)) ppm; HR-EI-MS calc. [C16H10N2O2]: 262.0737, found: 262.0738.

1.2.5 (Z)-1'-propyl-[2,3'-biindolinylidene]-2',3-dione (1c)

Red crystals, yield: 106 mg (0.348 mmol, 92%).

m.p. 170.8 °C; 1H NMR (400 MHz, CD2Cl2) δ = 10.61 (s, 1H, H-N(20)), 8.86 (d, J = 7.1 Hz, 1H, H-C(11)), 7.72 (d, J = 7.5 Hz, 1H, H-C(6)), 7.52 (ddd, J = 8.4, 7.6, 1.3 Hz, 1H, H-C(2)), 7.31 (td, J = 7.7, 1.2 Hz, 1H, H-C(13)), 7.11 (td, J = 7.7, 1.0 Hz, 1H, H-C(12)), 7.04 (d, J = 8.1 Hz, 1H, H-C(3)), 7.02 (t, J = 7.5 Hz, 2H, H-C(1)), 6.92 (d, J = 7.8 Hz, 1H, H-C(14)), 3.79 (t, J = 7.2 Hz, 2H, H-C(17)), 1.75 (h, J = 7.4 Hz, 2H, H-C(18)), 0.97 (t, J = 7.5 Hz, 3H, H-C(19))
ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta = 189.0$ (C(8)), 171.1 (C(16)), 152.4 (C(4)), 142.3 (C(15)), 139.8 (C(7)), 137.4 (C(2)), 129.7 (C(13)), 125.8 (C(11)), 125.5 (C(6)), 122.7 (C(12)), 122.0 (C(1)), 121.8 (C(10)), 120.6 (C(5)), 112.6 (C(3)), 108.8 (C(14)), 107.1 (C(9)), 42.0 (C(17)), 21.7 (C(18)), 11.8 (C(19)) ppm; IR $\nu = 3309w$, 3058w, 2963w, 2932w, 2874w, 1704m, 1662s, 1651s, 1626m, 1607vs, 1481s, 1465vs, 1382m, 1360s, 1321s, 1295m, 1265w, 1212m, 1192m, 1178m, 1158w, 1145m, 1134s, 1102s, 1095s, 1082m, 1031m, 1000w, 971w, 937w, 915w, 889w, 872w, 855w, 802w, 794w, 780w, 746s, 711m, 693w, 664w cm$^{-1}$; HR-EI-MS calc. $[C_{19}H_{16}N_2O_2]$: 304.1206, found: 304.1205.

1.2.6 (Z)-1’-(pentan-3-yl)-1-propyl-[2,3’-biindolinylidene]-2’,3-dione (2a)

Blue solidified oil, yield: 25.6 mg (68.4 mmol, 15%).

$R_t = (\text{SiO}_2, i\text{Hex/EtOAc} 9:1) = 0.33$; $^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta = 8.61$ (dd, $J = 8.4$, 1.1 Hz, 1H, H-C(11)), 7.69 (ddd, $J = 7.5$, 1.3, 0.6 Hz, 1H, H-C(6)), 7.57 (ddd, $J = 8.2$, 7.4, 1.4 Hz, 1H, H-C(2)), 7.22 (td, $J = 7.8$, 1.2 Hz, 1H, H-C(13)), 7.14 (d, $J = 8.1$ Hz, 1H, H-C(3)), 7.07 (td, $J = 7.4$, 0.7 Hz, 1H, H-C(1)), 7.02 – 6.93 (m, 2H, H-C(12/14)), 4.29 – 4.21 (m, 2H, H-C(20)), 2.13 – 1.99 (m, 1H, H-C(18)), 1.81 (qd, $J = 14.8$, 7.4, 5.4 Hz, 2H, H-C(18’)), 1.63 (h, $J = 7.4$ Hz, 2H, H-C(21)), 0.85 (t, $J = 7.4$ Hz, 6H, H-C(19)), 0.79 (t, $J = 7.4$ Hz, 3H, H-C(22)) ppm; $^{13}$C NMR (101 MHz, CD$_2$Cl$_2$) $\delta = 189.1$ (C(8)), 167.6 (C(16)), 154.6 (C(4)), 142.3 (C(7)), 136.9 (C(2)), 129.7 (C(13)), 125.6 (C(11)), 125.2 (C(6)), 122.9 (C(10)), 122.6 (C(1)), 122.2 (C(5)), 121.3 (C(12/14)), 112.4 (C(3)), 111.2 (C(15)), 109.8 (C(9)), 50.4 (C(20)), 25.6 (C(18)), 20.7 (C(21)), 11.7 (C(22)), 11.6 (C(19)) ppm; IR: $\nu = 3053w$, 2963m, 2930w, 2892w, 2873w, 1728w, 1698w, 1669s, 1612m, 1600s, 1550m, 1464vs, 1398w, 1378w, 1349m, 1311s, 1265w, 1236w, 1189vs, 1161m, 1131m, 1094vs, 1069m, 1051w, 1035w, 1014m, 1000w, 982w, 967m, 929w, 908w, 879w, 875w, 855w, 825w, 821w, 804w, 794w, 778w, 745s, 708w, 693w, 674w, 669w, 658w cm$^{-1}$; HR-EI-MS calc. $[C_{24}H_{26}N_2O_2]$: 374.1989, found: 374.1995.

Proton and Carbon 17 could not be observed at ambient conditions. Variable temperature experiments evidenced the signal positions of these nuclei.
1.2.7 (Z)-1'-(pentan-3-yl)-[2,3'-biindolinylidene]-2',3-dione (2c)

Red crystals, yield: 106 mg (0.348 mmol, 91%).

$^1$H NMR (600 MHz, CDCl$_3$) $\delta = 10.69$ (s, 1H, H-N(20)), 8.96 (d, J = 7.6 Hz, 1H, H-C(11)), 7.74 (d, J = 7.6 Hz, 1H, H-C(6)), 7.49 (td, J = 8.0, 1.2 Hz, 1H, H-C(2)), 7.30 – 7.24 (m, 1H, H-C(13)), 7.12 (t, J = 7.6 Hz, 1H, H-C(12)), 7.02 (d, J = 7.0 Hz, 1H, H-C(14)), 7.03 – 6.98 (m, 1H, H-C(1)), 6.95 (d, J = 8.1 Hz, 1H, H-C(3)), 4.30 (bs, 0H, H-C(17)), 2.09 (s, 2H, H-C(18)), 1.85 (dqd, J = 14.7, 7.5, 5.9 Hz, 2H, H-C(18')), 0.88 (t, J = 7.4 Hz, 6H, H-C(19)) ppm; $^{13}$C NMR (151 MHz, CDCl$_3$) $\delta = 188.6$ (C(8)), 171.5 (C(16)), 151.8 (C(4)), 139.4 (C(7)), 137.0 (C(2)), 129.1 (C(13)), 125.7 (C(11)), 125.4 (C(6)), 122.3 (C(12)), 121.6 (C(1)), 121.5 (C(10)), 120.2 (C(5)), 112.0 (C(3)), 106.9 (C(15)), 25.4 (C(18)) ppm; IR $\nu = 3342$w, 3277w, 3183w, 3047w, 2960m, 2924m, 2865m, 2853m, 1734w, 1698m, 1656s, 1624m, 1598s, 1589s, 1519w, 1480m, 1457s, 1310s, 1292s, 1259m, 1206s, 1188s, 1177s, 1162m, 1151m, 1141s, 1128s, 1109m, 1104m, 1094s, 1061m, 1029m, 1020m, 1002m, 980m, 962m, 940w, 929w, 907m, 857w, 837w, 817w, 802w, 783w, 748vs, 715m, 709m, 681m, 670w cm$^{-1}$; HR-EI-MS calc. [C$_{21}$H$_{20}$N$_2$O$_2$]: 332.1519 found: 332.1521.

1.2.8 (Z)-5',6'-difluoro-1,1'-dipropyl-[2,3'-biindolinylidene]-2',3-dione (3a)

Red crystals, yield: 236 mg (0.617 mmol, 31%).

$^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta = 8.56$ (dd, $J = 12.2, 8.6$ Hz, 1H, H-C(11)), 7.73 – 7.67 (m, 1H, H-C(6)), 7.59 (ddd, $J = 8.6, 7.5, 1.3$ Hz, 1H, H-C(2)), 7.14 (d, $J = 8.2$ Hz, 1H, H-C(3)), 7.09 (t, $J = 7.5$ Hz, 1H, H-C(1)), 6.67 (dd, $J = 10.4, 6.7$ Hz, 1H, H-C(14)), 4.25 (t, $J = 7.4$ Hz, 2H, H-C(22)), 3.71 (t, $J = 7.2$ Hz, 2H, H-C(19)), 1.76 – 1.61 (m, 4H, H-C(20/23)), 0.95 (t, $J = 7.4$ Hz, 3H, H-C(21)), 0.82 (t, $J = 7.4$ Hz, 3H, H-C(24)) ppm; $^{13}$C NMR (101 MHz, CD$_2$Cl$_2$) $\delta = 189.3$ (C(8)), 167.0 (C(16)), 154.6 (C(4)), 151.23 (dd, $J = 249.4, 14.8$ Hz, C(12/13)), 145.69 (dd, $J = 236.6, 13.3$ Hz, C(12/13)), 142.5 (C(7)), 139.49 (dd, $J = 9.1, 1.7$ Hz, C(15)), 137.2 (C(2)), 125.3 (C(6)), 123.0 (C(1)), 121.9 (C(5)), 118.37 (dd, $J = 8.2, 4.0$ Hz, C(10)), 114.69 (d, $J = 22.8$ Hz, C(11)), 112.5 (C(3)), 109.3 (C(9)), 97.73 (d, $J$
= 23.2 Hz, C(14)), 50.5 (C(22)), 42.3 (C(19)), 21.5 (C(20)), 20.9 (C(23)), 11.7 (C(21)), 11.6 (C(24)) ppm; $^{19}$F NMR (377 MHz, CD$_2$Cl$_2$) $\delta$ = -135.12 (dt, J = 19.8, 9.6 Hz), -148.48 (ddd, J = 19.8, 12.2, 6.7 Hz) ppm; IR: $\bar{\nu}$ = 3372w, 3224w, 3052w, 2999w, 2967w, 2953w, 2934w, 2873w, 2361w, 2327w, 1951w, 1809vw, 1781w, 1738w, 1725w, 1707w, 1686m, 1651w, 1633w, 1607m, 1548m, 1490m, 1470m, 1462s, 1444m, 1401m, 1397m, 1347m, 1328s, 1315m, 1306m, 1296m, 1284m, 1272m, 1225w, 1215m, 1189m, 1158m, 1136w, 1105s, 1090s, 1054m, 1031m, 1012m, 983m, 948m, 912m, 898m, 880s, 861m, 838m, 829w, 816m, 791s, 773m, 765m, 748vs, 734m, 715m, 703s, 667w, 659m cm$^{-1}$; HR-EI-MS calc. [C$_{22}$H$_{20}$F$_2$N$_2$O$_2$]: 382.1487, found: 382.1489.

1.2.9 (Z)-5',6'-difluoro-[2,3'-biindolinyldene]-2',3-dione (3b)

Purple solid, yield: 738 mg (2.47 mmol, 91%).

m.p. degradation at 324 °C; $^1$H NMR (800 MHz, DMSO-$d_6$) $\delta$ = 8.71 – 8.66 (m, 1H, H-C(15)), 7.62 (d, J = 7.3 Hz, 1H, H-C(6)), 7.56 (t, J = 7.4 Hz, 1H, H-C(2)), 7.38 (d, J = 7.8 Hz, 1H, H-C(3)), 7.00 (t, J = 7.2 Hz, 1H, H-C(1)), 6.89 – 6.85 (m, 1H, H-C(12)) ppm; $^{13}$C NMR (201 MHz, DMSO-$d_6$) $\delta$ = 189.0 (C(9)), 171.8 (C(18)), 152.8 (C(4)), 149.70 (dd, J = 247.1, 14.2 Hz C(13/14)), 144.17 (dd, J = 234.5, 13.1 Hz, C(13/14)), 139.36 (d, J = 4.5 Hz, C(10)), 138.4 (C(8)), 137.2 (C(2)), 124.4 (C(6)), 121.4 (C(1)), 119.0 (C(5)), 117.71 (d, J = 7.8 Hz, C(16)), 113.6 (C(3)), 112.94 (d, J = 22.4 Hz, C(15)), 105.7 (C(11)), 99.08 (d, J = 22.3 Hz, C(12)) ppm; $^{19}$F NMR (377 MHz, DMSO-$d_6$) $\delta$ = -135.79, -148.53 (dq, J = 18.9, 10.4, 9.1 Hz) ppm; IR: $\bar{\nu}$ = 3333w, 3167w, 3103w, 3053w, 2999w, 2958w, 2949w, 2893w, 2879w, 2817w, 2765w, 2699w, 2358w, 1713w, 1676s, 1623m, 1615m, 1598s, 1550w, 1503m, 1480m, 1465vs, 1411w, 1392w, 1358w, 1334m, 1308s, 1295s, 1239s, 1210m, 1184s, 1164s, 1150m, 1145m, 1096m, 1078w, 1018m, 1015m, 1006s, 961w, 952w, 948w, 888m, 860w, 834s, 820s, 799w, 795w, 776s, 754s, 746vs, 709s, 686s, 656m cm$^{-1}$; HR-EI-MS calc. [C$_{16}$H$_{8}$F$_2$N$_2$O$_2$]: 298.0548, found: 298.0552.
12.10 (Z)-5'-fluoro-6'-morpholino-1,1'-dipropyl-[2,3'-biindolinylidene]-2',3-dione (4a)

Blue crystals, yield: 144 mg (0.320 mmol, 37%).

Rf (SiO2, iHex/EtOAc 2:1) = 0.33; m.p. 207 °C; 1H NMR (400 MHz, CD2Cl2) δ = 8.40 (d, J = 14.7 Hz, 1H, H-C(11)), 7.68 (d, J = 6.8 Hz, 1H, H-C(6)), 7.60 – 7.51 (m, 1H, H-C(2)), 7.13 (d, J = 8.2 Hz, 1H, H-C(3)), 7.05 (td, J = 8.0, 7.4, 0.5 Hz, 1H, H-C(1)), 6.35 (d, J = 7.3 Hz, 1H, H-C(14)), 4.27 – 4.19 (m, 2H, H-C(23)), 3.89 – 3.82 (m, 6H, H-C(19)), 3.72 (t, J = 7.2 Hz, 2H, H-C(20)), 3.21 – 3.14 (m, 6H, 29, H-C(18)), 1.71 (dq, J = 15.0, 7.5 Hz, 2H, H-C(21)), 1.63 (dq, J = 14.6, 7.4 Hz, 2H, H-C(24)), 0.96 (t, J = 7.4 Hz, 3H, H-C(22)), 0.79 (t, J = 7.4 Hz, 3H, H-C(25)) ppm; 13C NMR (101 MHz, CD2Cl2) δ = 189.0 (C(8)), 167.5 (C(16)), 154.5 (C(4)), 150.48 (d, J = 235.3 Hz, C(12)), 142.01 (d, J = 10.5 Hz, C(13)), 140.80 (d, J = 0.5 Hz, C(7)), 140.33 (d, J = 1.0 Hz, C(15)), 136.7 (C(2)), 125.0 (C(6)), 122.4 (C(1)), 122.1 (C(5)), 115.79 (d, J = 10.4 Hz, C(10)), 113.97 (d, J = 27.1 Hz, C(11)), 112.4 (C(3)), 111.50 (d, J = 3.2 Hz, C(9)), 98.20 (d, J = 3.0 Hz, C(14)), 67.4 (C(19)), 51.33 (d, J = 4.1 Hz, C(18)), 50.3 (C(23)), 42.0 (C(20)), 21.7 (C(21)), 20.9 (C(24)), 11.8 (C(22)), 11.6 (C(25)) ppm; 19F NMR (377 MHz, CD2Cl2) δ -129.84 (dd, J = 14.8, 7.3 Hz, 27 ppm; IR: δ = 2957w, 2928w, 2890w, 2873w, 2856w, 1698w, 1665s, 1636w, 1607s, 1559w, 1544w, 1522w, 1489m, 1468s, 1456s, 1432m, 1398m, 1374m, 1366m, 1356m, 1330s, 1320m, 1299m, 1289m, 1266s, 1236m, 1222m, 1194s, 1164m, 1137m, 1115s, 1093s, 1077s, 1068s, 1042m, 1029m, 1016m, 987s, 969m, 952m, 917m, 902m, 886m, 870s, 839s, 802m, 791m, 770m, 754vs, 733s, 722m, 711s, 690m, 666m cm⁻¹; HR-EI-MS calc. [C26H28FN3O3]: 449.2109, found: 449.2107.

12.11 (Z)-5'-fluoro-6'-(methylthio)-[2,3'-biindolinylidene]-2',3-dione (4b)

Purple solid, yield: 472 mg (1.31 mmol, 92%).

m.p. 300 °C; 1H NMR (400 MHz, DMSO-d6) δ = 10.98 (s, 1H, H-N(7)), 10.87 (s, 1H, H-N(17)), 8.54 (d, J = 11.7 Hz, 1H, H-C(12)), 7.64 (d, J = 7.6 Hz, 1H, H-C(6)), 7.57 (t, J = 7.7
Hz, 1H, H-C(2)), 7.41 (d, J = 8.0 Hz, 1H, H-C(3)), 7.02 (t, J = 7.4 Hz, 1H, H-C(1)), 6.74 (d, J = 6.6 Hz, 1H, H-C(15)) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ = 188.7 (C(9)), 171.0 (C(18)), 153.60 (d, J = 231.2 Hz, C(13)), 152.4 (C(4)), 138.04 (d, J = 1.6 Hz, C(10)), 138.03 (d, J = 0.9 Hz, C(8)), 137.1 (C(2)), 126.82 (d, J = 19.7 Hz, C(14)), 124.4 (C(6)), 121.4 (C(1)), 119.0 (C(5)), 118.55 (d, J = 10.2 Hz, C(11)), 113.5 (C(3)), 110.65 (d, J = 27.5 Hz, C(12)), 106.57 (d, J = 2.7 Hz, C(16)), 106.19 (d, J = 3.2 Hz, C(15)), 13.78 (d, J = 1.9 Hz, C(20)) ppm; $^{19}$F NMR (376 MHz, DMSO-$d_6$) $\delta$ = -122.43 (dd, J = 11.6, 6.8 Hz, 21) ppm; IR: $\bar{\nu}$ = 3333w, 3310w, 3262w, 3181m, 3145m, 3113w, 3063w, 3028w, 2986w, 2922w, 2830w, 2362w, 2340w, 1691m, 1659vs, 1624s, 1612s, 1592m, 1582m, 1483s, 1462s, 1435m, 1425m, 1398s, 1330w, 1323w, 1304vs, 1288m, 1279s, 1228s, 1224s, 1195m, 1179s, 1152s, 1140vs, 1099m, 1077m, 1069m, 1045m, 1016s, 1005vs, 979m, 949m, 938m, 885s, 851m, 817s, 792m, 777m, 749vs, 731m, 724m, 672s cm$^{-1}$; HR-EI-MS calc. [C$_{17}$H$_{11}$FN$_2$O$_2$S]: 326.0520, found: 326.0524.

1.2.12 (Z)-5'-fluoro-6'-(methylthio)-1,1'-dipropyl-[2,3'-biindolinylidene]-2',3-dione (5a)

Blue crystals, yield: 25.2 mg (61.3 µmol, 10%).

m.p. 117 °C; $^1$H NMR (600 MHz, toluene-$d_8$) $\delta$ = 8.89 (d, J = 11.7 Hz, 1H, H-C(11)), 7.48 (d, J = 7.5 Hz, 1H, H-C(6)), 6.96 (d, J = 1.3 Hz, 1H, H-C(2)), 6.59 (t, J = 7.4 Hz, 1H, H-C(1)), 4.10 – 4.05 (m, 2H, H-C(22)), 3.47 (t, J = 7.1 Hz, 2H, H-C(19)), 2.06 (s, 3H, H-C(18)), 1.56 (h, J = 7.4 Hz, 2H, H-C(23)), 1.46 (h, J = 7.3 Hz, 2H, H-C(20)), 0.75 (t, J = 7.4 Hz, 3H, H-C(21)), 0.70 (t, J = 7.3 Hz, 3H, H-C(24)) ppm; $^{13}$C NMR (151 MHz, toluene-$d_8$) $\delta$ = 188.2 (C(8)), 166.8 (C(16)), 156.2 (d, J = 234.6 Hz, C(12)), 154.0 (C(4)), 141.7 (d, J = 0.8 Hz, C(7)), 139.1 (d, J = 1.6 Hz, C(15)), 135.9 (C(2)), 127.2 (d, J = 20.3 Hz, C(13)), 124.9 (C(6)), 122.0 (C(1)), 121.7 (C(5)), 121.2 (d, J = 9.8 Hz, C(10)), 113.1 (d, J = 28.4 Hz, C(11)), 111.4 (C(3)), 109.9 (d, J = 3.3 Hz, C(9)), 106.7 (d, J = 2.5 Hz, C(14)), 50.3 (C(22)), 41.5 (C(19)), 21.4 (C(20)), 15.4 (d, J = 3.6 Hz, C(18)), 11.5 (C(21)), 11.4 (C(24)) ppm; $^{19}$F NMR (377 MHz, toluene-$d_8$) $\delta$ = -120.23 (dd, J = 11.7, 6.2 Hz, 27) ppm; IR: $\bar{\nu}$ = 2962m, 2926m, 2872w, 2853w, 2359w, 2333w, 1733m, 1717m, 1704m, 1700m, 1674s, 1653w, 1647w, 1635w, 1608s, 1576w, 1569w, 1564w, 1558w, 1549w, 1533w, 1525w, 1517w, 1506w, 1469vs, 1433m, 1404w, 1378w, 1355m, 1346m, 1324s, 1299m, 1243w, 1211m, 1193m, 1171m, 1156w, 1138w, 1121s, 1090s, 1082s, 1059w, 1047w, 1029w, 1014w, 987m, 943w, 875w, 841w, 790w, 774w, 752m, 721w, 706w, 699w, 695w, 668w, 659w, 653w cm$^{-1}$; HR-EI-MS calc. [C$_{23}$H$_{23}$FN$_2$O$_2$S]: 410.1459, found: 410.1457.
1.2.13 (Z)-5'-fluoro-6'-morpholino-[2,3'-biindolinylidene]-2',3-dione (5b)

Purple solid, yield: 372 mg (1.02 mmol, 76%).

**m.p.** 286 °C; **1H NMR** (800 MHz, DMSO-\(\text{d}_6\)) \(\delta = 8.55\) (d, \(J = 14.5\) Hz, 1H, H-C(12)), 7.63 (d, \(J = 7.2\) Hz, 1H, H-C(6)), 7.56 (ddd, \(J = 8.3,\ 7.3,\ 1.2\) Hz, 1H, H-C(2)), 7.40 (d, \(J = 8.1\) Hz, 1H, H-C(3)), 7.04 – 6.98 (m, 1H, H-C(1)), 6.49 (d, \(J = 7.6\) Hz, 1H, H-C(15)), 3.77 – 3.73 (m, 4H, H-C(21)), 3.10 – 3.07 (m, 4H, H-C(20)) ppm; **13C NMR** (201 MHz, DMSO-\(\text{d}_6\)) \(\delta = 188.5\) (C(9)), 171.4 (C(18)), 152.5 (C(4)) 149.35 (d, \(J = 234.4\) Hz, C(13)), 140.97 (d, \(J = 10.2\) Hz, C(14)), 138.8 (C(16)), 136.9 (C(2)), 136.6 (8), 124.2 (C(6)), 121.0 (C(1)), 119.0 (C(5)), 114.19 (d, \(J = 10.7\) Hz, C(11)), 113.5 (C(3)), 112.53 (d, \(J = 26.9\) Hz, C(12)), 107.2 (C(10)), 99.74 (d, \(J = 2.4\) Hz, C(15)), 66.1 (C(21)), 50.2 (C(20)) ppm; **19F NMR** (377 MHz, DMSO-\(\text{d}_6\)) \(\delta = -130.92\) (dd, \(J = 14.6,\ 7.5\) Hz) ppm; **IR:** \(\tilde{\nu}_\text{max} = 3334\)w, 3243w, 3163w, 3131w, 3109w, 3079w, 3006w, 2992w, 2974w, 2951w, 2920w, 2894w, 2857w, 2805w, 1731w, 1703w, 1663s, 1621s, 1592m, 1480s, 1463s, 1447m, 1397m, 1380m, 1359m, 1334m, 1298s, 1273m, 1265s, 1236s, 1228m, 1216s, 1193m, 1174s, 1166s, 1143s, 1128m, 1113vs, 1094s, 1077m, 1066s, 1043m, 1031m, 1017vs, 1006vs, 972s, 953m, 926m, 919m, 901m, 890s, 882m, 868m, 855s, 849s, 843s, 823s, 803m, 793s, 780m, 746s, 710s, 698s, 672s, 654s cm\(^{-1}\); **HR-EI-MS** calc. [C\(_{20}\)H\(_{16}\)FN\(_3\)O\(_3\)$]$ : 365.1170, found: 365.1188.

1.2.14 5-fluoro-6-(methylthio)indoline-2,3-dione (9)

Commercially available 5,6-difluoroindoline-2,3-dione (5,6-difluoroisatin 8; 1.00 g; 5.46 mmol; 1 equiv.) was dissolved in DMF (10 mL). Under vigorous stirring sodium thiomethoxide (21% in H\(_2\)O, 2 mL, 6.6 mmol; 1.2 equiv.) was added slowly to the solution, which instantly turned dark orange. After stirring the reaction mixture for 10 minutes at 22 °C a suspension resulted and the solid was filtered and washed with H\(_2\)O until the filtrate showed no alkaline reaction. After drying in vacuo isatin 9 could be obtained as orange solid (0.964 g, 4.56 mmol 84%).
m.p. degradation at 299 °C; \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6) \delta = 11.00 (s, 1H, H\text{-}N(1)), 7.36 (d, J = 8.8 Hz, 1H, H\text{-}C(5)), 6.71 (d, J = 5.9 Hz, 1H, H\text{-}C(8)), 2.58 (s, 3H, H\text{-}C(11)) ppm; \textsuperscript{13}C NMR (101 MHz, DMSO-\textit{d}_6) \delta = 182.53 (d, J = 2.2 Hz, C(3)), 160.15 (d, J = 1.6 Hz, C(2)), 153.97 (d, J = 1.2 Hz, C(9)), 140.05 (d, J = 1.8 Hz, C(7)), 113.65 (d, J = 7.0 Hz, C(4)), 108.05 (d, J = 1.6 Hz, C(8)), 13.22 (d, J = 1.7 Hz, C(11)) ppm; \textsuperscript{19}F NMR (377 MHz, DMSO-\textit{d}_6) \delta = -122.06 (dd, J = 8.7, 6.0 Hz, F(10)) ppm; IR: \nu = 3286\textit{m}, 3223\textit{w}, 3210\textit{w}, 3118\textit{w}, 2927\textit{w}, 2361\textit{w}, 2337\textit{w}, 1825\textit{w}, 1760\textit{s}, 1736\textit{s}, 1714\textit{s}, 1692\textit{w}, 1675\textit{w}, 1608\textit{w}, 1526\textit{w}, 1464\textit{s}, 1427\textit{m}, 1416\textit{m}, 1347\textit{m}, 1299\textit{m}, 1289\textit{m}, 1271\textit{m}, 1227\textit{m}, 1220\textit{m}, 1184\textit{m}, 1172\textit{m}, 1131\textit{m}, 1104\textit{w}, 1070\textit{w}, 1035\textit{s}, 973\textit{w}, 949\textit{w}, 940\textit{w}, 882\textit{w}, 865\textit{m}, 808\textit{w}, 792\textit{s}, 761\textit{w}, 783\textit{m}, 724\textit{m}, 692\textit{w}, 676\textit{cm}^{-1}; HR-EI-MS calc. [C\textsubscript{9}H\textsubscript{6}FNO\textsubscript{2}S]: 211.0098, found: 211.0097.

1.2.15 5-fluoro-6-morpholinoindoline-2,3-dione (10)

![Chemical Structure](image)

Commercially available 5,6-difluoroindoline-2,3-dione (5,6-difluoroisatin 8; 500 mg; 2.73 mmol; 1 equiv.) and 1,4-oxazinane (morpholine; 0.3 mL; 3.44 mmol; 1.25 equiv.) were suspended in ethanol (5 mL). The solution was stirred at 80 °C under reflux for 60 minutes. After letting the solution cool down, the resulting solid was filtered and washed with hexanes and EtOAc. After drying in vacuo isatin 10 was obtained as dark orange solid (641 mg, 2.56 mmol, 94%).

m.p. 251 °C; \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6) \delta = 10.82 (s, 1H, H\text{-}C(1)), 7.29 (d, J = 12.4 Hz, 1H, H\text{-}C(5)), 6.35 (d, J = 6.9 Hz, 1H, H\text{-}C(8)), 3.77 – 3.70 (m, 4H, H\text{-}C(12)), 3.33 – 3.26 (m, 4H, H\text{-}C(11z)) ppm; \textsuperscript{13}C NMR (101 MHz, DMSO-\textit{d}_6) \delta = 180.8 (d, J = 2.4 Hz, C(3)), 161.0 (d, J = 1.5 Hz, C(2)), 149.5 (C(9)) 149.4 (d, J = 240.3 Hz, C(6)), 148.2 (d, J = 8.7 Hz, C(7)), 112.4 (d, J = 23.5 Hz, C(5)), 108.4 (d, J = 7.7 Hz, C(4)), 100.5 (d, J = 2.4 Hz, C(8)), 65.8 (C(12)), 49.5 (d, J = 5.8 Hz, C(11)) ppm; \textsuperscript{19}F NMR (377 MHz, DMSO-\textit{d}_6) \delta = -129.77 (dd, J = 12.4, 6.8 Hz, F(10)) ppm; IR: \nu = 3336\textit{w}, 3244\textit{w}, 3164\textit{w}, 3138\textit{w}, 3109\textit{w}, 3083\textit{w}, 3049\textit{w}, 3029\textit{w}, 3008\textit{w}, 2994\textit{w}, 2976\textit{w}, 2952\textit{w}, 2923\textit{w}, 2897\textit{w}, 2879\textit{w}, 2867\textit{w}, 2858\textit{w}, 2806\textit{w}, 2752\textit{w}, 2692\textit{w}, 1704\textit{w}, 1663\textit{vs}, 1621\textit{s}, 1593\textit{m}, 1480\textit{w}, 1463\textit{s}, 1448\textit{m}, 1399\textit{m}, 1382\textit{m}, 1359\textit{m}, 1334\textit{w}, 1299\textit{s}, 1266\textit{s}, 1237\textit{s}, 1228\textit{m}, 1216\textit{s}, 1193\textit{m}, 1173\textit{s}, 1167\textit{s}, 1143\textit{m}, 1126\textit{m}, 1114\textit{vs}, 1094\textit{s}, 1076\textit{m}, 1067\textit{s}, 1043\textit{m}, 1016\textit{s}, 1006\textit{w}, 972\textit{m}, 954\textit{w}, 927\textit{w}, 919\textit{w}, 900\textit{m}, 890\textit{m}, 882\textit{m}, 868\textit{m}, 856\textit{m}, 848\textit{m}, 844\textit{m}, 824\textit{s}, 803\textit{m}, 793\textit{m}, 780\textit{m}, 746\textit{s}, 711\textit{vs}, 698\textit{s}, 673\textit{m} cm\textsuperscript{-1}; HR-EI-MS calc. [C\textsubscript{12}H\textsubscript{11}F\textsubscript{2}N\textsubscript{2}O\textsubscript{3}]: 250.0748, found: 250.0744.
2 Photophysical and photochemical properties

2.1 Molar absorption coefficients

Figure S1: Molar absorption coefficients of indirubins in the Z isomeric state (blue) and in the E isomeric state (red). a) Indirubin 1a in toluene, b) indirubin 1a in CH₂Cl₂, c) indirubin 2a in toluene, d) indirubin 2a in CH₂Cl₂, e) indirubin 3a in toluene, f) indirubin 3a in CH₂Cl₂. Molar absorptions of the respective E isomers are obtained from measuring the absorption of an E enriched solution and subtracting the spectral components of remaining Z isomer.
Figure S2: Molar absorption coefficients of indirubins in the $Z$ conformeric state (blue) and in the $E$ conformeric state (red). a) Indirubin 4a in toluene, b) indirubin 4a in CH$_2$Cl$_2$, c) indirubin 5a in toluene, d) indirubin 5a in CH$_2$Cl$_2$. Molar absorptions of the respective $E$ isomers are obtained from measuring the absorption of an $E$ enriched solution and subtracting the spectral components of remaining $Z$ isomer.
Figure S3: Molar absorption coefficients of indirubins in the Z isomeric state (blue) and in the E isomeric state (red) in the absence (solid lines) and in the presence of 4 equivalents of STC (dashed lines) in toluene solution. Error borders of ±5% for the determination of the molar absorption coefficients of the E isomers in the presence of STC are also shown (red, dotted lines). a) Indirubin 1a, b) indirubin 2a, c) indirubin 3a, d) indirubin 4a. Molar absorptions of the respective E isomers are obtained from measuring the absorption of an E enriched solution and subtracting the spectral components of remaining Z isomer.
Figure S4: Molar absorption coefficients of indirubins in the Z isomeric state (blue) and in the E isomeric state (red) in the absence (solid lines) and in the presence of 20 equivalents of STC (dashed lines) in CH$_2$Cl$_2$ solution. Error borders of ±5% for the determination of the molar absorption coefficients of the E isomers in the presence of STC are also shown (red, dotted lines). a) Indirubin 1a, b) indirubin 2a, c) indirubin 3a, d) indirubin 4a. Molar absorptions of the respective E isomers are obtained from measuring the absorption of an E enriched solution and subtracting the spectral components of remaining Z isomer.
2.2 Photoisomerization experiments

2.2.1 General procedures

Molar absorption coefficients were determined by charging a 5 or 10 mL volumetric flask with 0.3000 - 0.6000 mg (weighted on a Sartorius Cubis® MSE2.7S balance) of the respective indirubin and the desired solvent (spectroscopic grade) to obtain defined $2 \times 10^{-5}$ - $4 \times 10^{-5}$ M solutions. Molar absorption coefficients of pure $Z$ isomers could then be determined directly using the Lambert-Beer law. Taking into account the previously determined positions of isosbestic points and molar absorption coefficients of pure $Z$ isomers, the corresponding molar absorption coefficients of the $E$ isomers could be determined from isomeric mixtures with defined $E/Z$ isomeric ratios, which were independently determined by $^1$H NMR spectroscopy.

Solution photoisomerization experiments were conducted in NMR tubes at concentrations of $\sim 1 \times 10^{-3}$ to $5 \times 10^{-3}$ mol $\text{L}^{-1}$ in deuterated solvents (toluene-$d_8$, CD$_2$Cl$_2$) or in 10 mm Hellma quartz cuvettes at concentrations of $\sim 2.5 \times 10^{-5}$ mol·L$^{-1}$ with regular undeuterated solvents. LEDs from Roithner Lasertechnik GmbH and Thorlabs GmbH (340 nm, 53 mW; 365 nm, 1150 mW; 385 nm, 1650 mW; 395 nm, 400 mW; 405 nm, 1500 mW; 420 nm, 174 mW; 430 nm, 490 mW; 450 nm, 1850 mW; 470 nm, 760 mW; 490 nm, 205 mW; 515 nm, 150 mW; 530 nm, 370 mW; 565 nm, 880 mW; 590 nm 230 mW, 595 nm, 820 mW; 625 nm, 700 mW; 660 nm, 1050 mW; 680 nm, 210 mW, 730 nm, 680 mW) were used for irradiation of UV/vis samples. LEDs from Mountain Photonics GmbH (625 nm, UHP-T-625-DI and 450 nm, UHP-T-LED-450) were used for irradiation of NMR samples.

The $E/Z$ isomeric ratios obtained in the photostationary state (pss) at different irradiation wavelengths were determined either by irradiation of solutions in NMR tubes at 20 °C with frequent dipping of the sample tubes into an -80 °C cooling bath to eliminate possible photoheating effects. After irradiation was finished the samples were cooled to -80 °C and transferred to the NMR spectrometer, which was precooled to 0 °C. Subsequent analysis of the isomer composition was done at 0 °C by $^1$H NMR spectroscopy (Table S1 and Figures S5 - S24).

Alternatively irradiation was conducted using solutions in UV/vis cuvettes and subsequently analysis proceeded by UV/vis spectroscopy at 20 °C taking into account the previously measured molar absorption coefficients (Table S2 and Figures S25 – S32). For UV/vis measurements concentrations of indirubins were significantly lower than for the NMR experiments. The lower concentrations lead to less complex formation with STC and for this reason more equiv. of STC were added for UV/vis photoisomerization experiments. Nevertheless the achieved isomer conversions are typically decreased in comparison to the NMR experiments because of concentration effects on the supramolecular interaction.
**Table S1**  \( E/Z \) isomeric ratios of dialkylated indirubins 1a – 5a obtained in the pss after irradiation with light of different wavelengths. All values given were determined in deuterated solvents using \(^1\)H NMR spectroscopy.

| Indirubin | Solvent | without *Schreiner’s* thiourea catalyst (STC) | in presence of 1 equiv. of *Schreiner’s* thiourea catalyst (STC) |
|-----------|---------|-----------------------------------------------|---------------------------------------------------------------|
|           |         | 625 nm | 450 nm | 625 nm | 450 nm | 625 nm | 450 nm | 625 nm | 450 nm | 625 nm | 450 nm | 625 nm | 450 nm | 625 nm | 450 nm | 625 nm | 450 nm |
| 1a        | toluene-\( d_8 \) | 46 % \( E \) | 83 % \( Z \) | 84 % \( E \) | 61 % \( Z \) |
| 2a        | toluene-\( d_8 \) | 40 % \( E \) | 87 % \( Z \) | 84 % \( E \) | 72 % \( Z \) |
| 3a        | toluene-\( d_8 \) | 46 % \( E \) | 86 % \( Z \) | 69 % \( E \) | 86 % \( Z \) |
| 4a        | toluene-\( d_8 \) | 40 % \( E \) | 85 % \( Z \) | 75 % \( E \) | 88 % \( Z \) |
| 5a        | toluene-\( d_8 \) | 24 % \( E \) | 90 % \( Z \) | 64 % \( E \) | 89 % \( Z \) |
| 1a        | CD\(_2\)Cl\(_2\) | 62 % \( E \) | 72 % \( Z \) | 82 % \( E \) | 59 % \( Z \) |
| 2a        | CD\(_2\)Cl\(_2\) | 59 % \( E \) | 75 % \( Z \) | 76 % \( E \) | 56 % \( Z \) |
| 3a        | CD\(_2\)Cl\(_2\) | 59 % \( E \) | 72 % \( Z \) | 67 % \( E \) | 79 % \( Z \) |
| 4a        | CD\(_2\)Cl\(_2\) | 51 % \( E \) | 75 % \( Z \) | 67 % \( E \) | 82 % \( Z \) |
| 5a        | CD\(_2\)Cl\(_2\) | 27 % \( E \) | 85 % \( Z \) | 32 % \( E \) | 88 % \( Z \) |
2.2.2 Photoisomerization of indirubins 1a to 5a at NMR concentrations in toluene-$d_8$ solution

Figure S5: Partial $^1$H NMR spectra (0 °C, toluene-$d_8$) of pure Z-1a (top), 1a in the pss after irradiation with 625 nm (56% Z/44% E; middle), and 1a in the pss after irradiation with 450 nm (83% Z/17% E; bottom).
Figure S6: Partial $^1$H NMR spectra (0 °C, toluene-$d_8$) of pure Z-2a (top), 2a in the pss after irradiation with 625 nm (60% Z/40% E; middle), and 2a in the pss after irradiation with 450 nm (87% Z/13% E; bottom).

Figure S7: Partial $^1$H NMR spectra (0 °C, toluene-$d_8$) of pure Z-3a (top), 3a in the pss after irradiation with 625 nm (54% Z/46% E; middle), and 3a in the pss after irradiation with 450 nm (86% Z/14% E; bottom).
Figure S8: Partial $^1$H NMR spectra (0 °C, toluene-$d_8$) of pure Z-4a (top), 4a in the pss after irradiation with 625 nm (60% Z/40% E; middle), and 4a in the pss after irradiation with 450 nm (85% Z/15% E; bottom).

Figure S9: Partial $^1$H NMR spectra (0 °C, toluene-$d_8$) of pure Z-5a (top), 5a in the pss after irradiation with 625 nm (76% Z/24% E; middle), and 5a in the pss after irradiation with 450 nm (90% Z/10% E; bottom).
2.2.3 Photoisomerization of indirubins 1a to 5a in the presence of STC at NMR concentrations in toluene-$d_8$ solution

Figure S10: Partial $^1$H NMR spectra (0 °C, toluene-$d_8$) of 1a in the presence of 1 equiv. STC. Pure Z-1a + STC (top), 1a + STC in the pss after irradiation with 625 nm (16% Z/84% E; second spectrum), 1a + STC in the pss after irradiation with 450 nm (61% Z/39% E; third spectrum), and 1a + STC in the pss after another irradiation with 625 nm (17% Z/83% E; bottom).
Figure S11: Partial $^1$H NMR spectra (0 °C, toluene-$d_8$) of 2a in the presence of 1 equiv. STC. Pure Z-2a + STC (top), 2a + STC in the pss after irradiation with 625 nm (18% Z/82% E; second spectrum), and 2a + STC in the pss after irradiation with 450 nm (72% Z/28% E; third spectrum), and 2a + STC in the pss after another irradiation with 625 nm (16% Z/84% E; bottom).

Figure S12: Partial $^1$H NMR spectra (0 °C, toluene-$d_8$) of 3a in the presence of 1 equiv. STC. Pure Z-3a + STC (top), 3a + STC in the pss after irradiation with 625 nm (31% Z/69% E; second spectrum), and 3a + STC in the pss after irradiation with 450 nm (86% Z/14% E; third spectrum), and 3a + STC in the pss after another irradiation with 625 nm (32% Z/68% E; bottom).
Figure S13: Partial $^1$H NMR spectra (0 °C, toluene-$d_8$) of 4a in the presence of 1 equiv. STC. Pure Z-$4a$ + STC (top), 4a + STC in the pss after irradiation with 625 nm (35% Z/65% E; second spectrum), and 4a + STC in the pss after irradiation with 450 nm (88% Z/12% E; third spectrum), and 4a + STC in the pss after another irradiation with 625 nm (25% Z/75% E; bottom).

Figure S14: Partial $^1$H NMR spectra (0 °C, toluene-$d_8$) of 5a in the presence of 1 equiv. STC. Pure Z-$5a$ + STC (top), 5a + STC in the pss after irradiation with 625 nm (36% Z/64% E; middle), and 5a + STC in the pss after irradiation with 450 nm (89% Z/11% E; bottom), and 5a + STC in the pss after another irradiation with 625 nm (37% Z/63% E; bottom).
2.2.4 Photoisomerization of indirubins 1a to 5a at NMR concentrations in CD$_2$Cl$_2$ solution

Figure S15: Partial $^1$H NMR spectra (0 °C, CD$_2$Cl$_2$) of pure Z-1a (top), 1a in the pss after irradiation with 625 nm (38% Z/62% E; middle), and 1a in the pss after irradiation with 450 nm (72% Z/28% E; bottom).
Figure S16: Partial $^1$H NMR spectra (0 °C, CD$_2$Cl$_2$) of pure Z-2a (top), 2a in the pss after irradiation with 625 nm (41% Z/59% E; middle), and 2a in the pss after irradiation with 450 nm (75% Z/25% E; bottom).

Figure S17: Partial $^1$H NMR spectra (0 °C, CD$_2$Cl$_2$) of pure Z-3a (top), 3a in the pss after irradiation with 625 nm (41% Z/59% E; middle), and 3a in the pss after irradiation with 450 nm (72% Z/28% E; bottom).
Figure S18: Partial $^1$H NMR spectra (0 °C, CD$_2$Cl$_2$) of pure Z-4a (top), 4a in the pss after irradiation with 625 nm (49% Z/51% E; middle), and 4a in the pss after irradiation with 450 nm (75% Z/25% E; bottom).

Figure S19: Partial $^1$H NMR spectra (0 °C, CD$_2$Cl$_2$) of pure Z-5a (top), 5a in the pss after irradiation with 625 nm (73% Z/27% E; middle), and 5a in the pss after irradiation with 450 nm (85% Z/15% E; bottom).
2.2.5 Photoisomerization of indirubins 1a to 5a in the presence of STC at NMR concentrations in CD$_2$Cl$_2$ solution

Figure S20: Partial $^1$H NMR spectra (0 °C, CD$_2$Cl$_2$) of 1a in the presence of 1 equiv. STC. Pure Z-1a + STC (top), 1a + STC in the pss after irradiation with 625 nm (18% Z/82% E; middle), and 1a + STC in the pss after irradiation with 450 nm (59% Z/41% E; bottom).
Figure S21: Partial $^1$H NMR spectra (0 °C, CD$_2$Cl$_2$) of 2a in the presence of 1 equiv. STC. Pure Z-2a + STC (top), 2a + STC in the pss after irradiation with 625 nm (24% Z/76% E; middle), and 2a + STC in the pss after irradiation with 450 nm (56% Z/44% E; bottom).

Figure S22: Partial $^1$H NMR spectra (0 °C, CD$_2$Cl$_2$) of 3a in the presence of 1 equiv. STC. Pure Z-3a + STC (top), 3a + STC in the pss after irradiation with 625 nm (33% Z/67% E; middle), and 3a + STC in the pss after irradiation with 450 nm (79% Z/21% E; bottom).
Figure S23: Partial $^1$H NMR spectra (0 °C, CD$_2$Cl$_2$) of 4a in the presence of 1 equiv. STC. Pure Z-4a + STC (top), 4a + STC in the pss after irradiation with 625 nm (30% Z/70% E; middle), and 4a + STC in the pss after irradiation with 450 nm (82% Z/18% E; bottom).

Figure S24: Partial $^1$H NMR spectra (0 °C, CD$_2$Cl$_2$) of 5a in the presence of 1 equiv. STC. Pure Z-5a + STC (top), 5a + STC in the pss after irradiation with 625 nm (68% Z/32% E; middle), and 5a + STC in the pss after irradiation with 450 nm (88% Z/12% E; bottom).
Table S2: Photoisomerization measurements at UV/vis concentrations in the UV/vis spectrometer. Percentage of each isomer of the respective dialkylated indirubins 1a to 5a obtained in the pss at different wavelengths of irradiation. Photoisomerizations were measured in the absence and in the presence of STC (4 equiv. in toluene and 20 equiv. in CH$_2$Cl$_2$ solution). The respective values of each isomer have been obtained by taking into account the previously measured molar absorption coefficients.

| Indirubin | Solvent     | Irr. wavelength [nm] | % E isomer | % Z isomer |
|-----------|-------------|----------------------|------------|------------|
| 1a        | toluene     | 730                  | 36         | 64         |
|           |             | 680                  | 36         | 64         |
|           |             | 660                  | 41         | 59         |
|           |             | **625**              | **48**     | **52**     |
|           |             | 595                  | 47         | 53         |
|           |             | 565                  | 43         | 57         |
|           |             | 530                  | 37         | 63         |
|           |             | 515                  | 36         | 64         |
|           |             | 505                  | 34         | 66         |
|           |             | 490                  | 32         | 68         |
|           |             | 470                  | 21         | 79         |
|           |             | **450**              | **15**     | **85**     |
|           |             | 430                  | 18         | 82         |
|           |             | 420                  | 25         | 75         |
|           |             | 405                  | 32         | 68         |
| 1a        | toluene + STC | **730 + 3c7** Filter | **54**     | **46**     |
|           |             | 730                  | 62         | 38         |
|           |             | 680                  | 69         | 31         |
|           |             | 660                  | 72         | 28         |
|           |             | **625**              | **75**     | **25**     |
| 2a        | toluene     | 730                  | 33         | 67         |
|           |             | 680                  | 34         | 66         |
|           |             | 660                  | 37         | 63         |
|           |             | **625**              | **47**     | **53**     |
|           |             | 595                  | 45         | 55         |
|           |             | 565                  | 41         | 59         |
|           |             | 530                  | 36         | 64         |
|           |             | 515                  | 36         | 64         |
|           |             | 505                  | 32         | 68         |
|           |             | 490                  | 31         | 69         |
|           |             | 470                  | 20         | 80         |
|           |             | **450**              | **17**     | **83**     |
|           |             | 430                  | 21         | 79         |
|           |             | 420                  | 26         | 74         |
|           |             | 405                  | 33         | 67         |
| 2a        | toluene + STC | **730 + 3c7** Filter | **50**     | **50**     |
|           |             | 730                  | 60         | 40         |
|           |             | 680                  | 68         | 32         |
|           |             | **660**              | **74**     | **26**     |
|           |             | 625                  | 71         | 29         |
|   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **3a** | toluene | 730 | 33 | 67 |
|   |   | 680 | 33 | 67 |
|   |   | 660 | 37 | 63 |
|   |   | **625** | **46** | **54** |
|   |   | 595 | 44 | 56 |
|   |   | 565 | 42 | 58 |
|   |   | 530 | 39 | 61 |
|   |   | 515 | 37 | 63 |
|   |   | 505 | 33 | 67 |
|   |   | 490 | 32 | 68 |
|   |   | 470 | 22 | 78 |
|   |   | **450** | **17** | **83** |
|   |   | 430 | 18 | 82 |
|   |   | 420 | 21 | 79 |
|   |   | 405 | 26 | 74 |
|   |   | 395 | 40 | 60 |
|   |   | 385 | 41 | 59 |
|   |   | **3a** | toluene + STC | **730 + 3c7** | Filter | 63 | 37 |
|   |   | 730 | 70 | 30 |
|   |   | 680 | 76 | 24 |
|   |   | **660** | **82** | **18** |
|   |   | 625 | 69 | 31 |
|   |   | **4a** | toluene | 730 | -- | -- |
|   |   | 680 | 39 | 61 |
|   |   | **660** | **40** | **60** |
|   |   | 625 | 38 | 62 |
|   |   | 595 | 39 | 61 |
|   |   | 565 | 38 | 62 |
|   |   | 530 | 32 | 68 |
|   |   | 515 | 30 | 70 |
|   |   | 505 | 24 | 76 |
|   |   | 490 | 25 | 75 |
|   |   | 470 | -- | -- |
|   |   | **450** | **17** | **83** |
|   |   | 430 | 25 | 75 |
|   |   | 420 | 33 | 67 |
|   |   | 395 | 36 | 64 |
|   |   | 385 | 37 | 63 |
|   |   | 340 | 28 | 72 |
|   |   | **4a** | toluene + STC | **730 + 3c7** | Filter | 64 | 36 |
|   |   | 730 | 65 | 35 |
|   |   | 680 | 71 | 29 |
|   |   | **660** | **87** | **13** |
|   |   | **625** | **55** | **45** |
|   |   | **5a** | toluene | **730** | **46** | **54** |
|   |   | 680 | 32 | 68 |
|   |   | 660 | 34 | 66 |
|   |   | 625 | 36 | 64 |
|   |   | 595 | 32 | 68 |
|   |   | 565 | 30 | 70 |
|   |   | 35 |
|      |      |      |
|------|------|------|
| 530  | 22   | 78   |
| 515  | 19   | 81   |
| 505  | 16   | 84   |
| 490  | 17   | 83   |
| **470** | **13** | **87** |
| 450  | 15   | 85   |
| 430  | 22   | 78   |
| 420  | 24   | 76   |
| 405  | 26   | 74   |
|      |      |      |
| 1a   | CH₂Cl₂ |      |
|      |      |      |
| 730  | 43   | 57   |
| 680  | 43   | 57   |
| 660  | 55   | 45   |
| **625** | **56** | **44** |
| 595  | 54   | 46   |
| 565  | 50   | 50   |
| 530  | 45   | 55   |
| 515  | 44   | 56   |
| 505  | 40   | 60   |
| 490  | 41   | 59   |
| 470  | 28   | 72   |
| 450  | 25   | 75   |
| 430  | 28   | 72   |
| 420  | 34   | 66   |
| 405  | 38   | 62   |
| 395  | 35   | 65   |
| **385** | **1** | **99** |
| 1a   | CH₂Cl₂ + STC |      |
|      |      |      |
| 730  | 52   | 48   |
| 680  | 54   | 46   |
| 660  | 63   | 37   |
| **625** | **66** | **34** |
| **595** | **66** | **34** |
| 565  | 61   | 39   |
| 530  | 53   | 47   |
| 515  | 55   | 45   |
| 505  | 49   | 51   |
| 490  | 51   | 49   |
| 470  | 38   | 62   |
| 450  | 34   | 66   |
| 430  | 37   | 63   |
| 420  | 41   | 59   |
| 405  | 46   | 54   |
| 395  | 41   | 59   |
| **385** | **4** | **96** |
| 365  | 5    | 95   |
|      |      |      |
| 2a   | CH₂Cl₂ |      |
|      |      |      |
| 730  | 37   | 63   |
| 680  | 39   | 61   |
| **660** | **51** | **49** |
| 625  | 47   | 53   |
| 595  | 50   | 50   |
| 530  | 42   | 58   |
| 515  | 35   | 65   |
| 36   |      |      |
| Temperature | 2a CH₂Cl₂ + STC | 3a CH₂Cl₂ | 3a CH₂Cl₂ + STC |
|-------------|-----------------|------------|-----------------|
| 505         | 34              | 66         |                 |
| 490         | 43              | 57         |                 |
| 470         | 34              | 66         |                 |
| 450         | **22**          | **78**     |                 |
| 430         | 24              | 76         |                 |
| 420         | 32              | 68         |                 |
| 405         | 34              | 66         |                 |
| 395         | 36              | 64         |                 |
| 385         | 41              | 59         |                 |
| 565         | **71**          | **29**     |                 |
| 530         | 69              | 31         |                 |
| 515         | 70              | 30         |                 |
| 505         | 68              | 32         |                 |
| 490         | 67              | 33         |                 |
| 470         | 59              | 41         |                 |
| 450         | **22**          | **78**     |                 |
| 660         | **52**          | **48**     |                 |
| 625         | **52**          | **48**     |                 |
| 595         | 50              | 50         |                 |
| 565         | 46              | 54         |                 |
| 530         | 44              | 56         |                 |
| 515         | 43              | 57         |                 |
| 505         | 39              | 61         |                 |
| 490         | 39              | 61         |                 |
| 470         | 29              | 71         |                 |
| 450         | **23**          | **77**     |                 |
| 430         | 25              | 75         |                 |
| 420         | 28              | 72         |                 |
| 405         | 33              | 67         |                 |
| 395         | 41              | 59         |                 |
| 385         | 43              | 57         |                 |
| 565         | **85**          | **15**     |                 |
| 530         | 81              | 19         |                 |
| 515         | 80              | 20         |                 |
| 505         | 79              | 21         |                 |
| 490         | 76              | 24         |                 |
| 470         | 66              | 34         |                 |
| 450         | 48              | 52         |                 |
| 430         | 40              | 60         |                 |

37
|    |    |    |    |
|----|----|----|----|
| 4a | CH₂Cl₂ |    |    |
| 780 | 24 | 76 |
| 730 | 48 | 52 |
| 680 | 45 | 55 |
| 660 | 58 | 42 |
| 625 | 53 | 47 |
| 595 | 50 | 50 |
| 565 | 49 | 51 |
| 530 | 41 | 59 |
| 515 | 40 | 60 |
| 505 | 39 | 61 |
| 490 | 38 | 62 |
| 470 | 31 | 69 |
| 450 | 29 | 71 |
| 430 | 35 | 65 |
| 420 | 36 | 64 |
| 405 | 39 | 61 |
| 4a  | CH₂Cl₂ + STC |    |    |
| 730 | 59 | 41 |
| 680 | 61 | 39 |
| 660 | 70 | 30 |
| 625 | 39 | 61 |
| 595 | 59 | 41 |
| 565 | 63 | 37 |
| 530 | 55 | 45 |
| 515 | 49 | 51 |
| 505 | 44 | 56 |
| 490 | 40 | 60 |
| 470 | 28 | 72 |
| 450 | 22 | 78 |
| 430 | 20 | 80 |
| 420 | 25 | 75 |
| 405 | 24 | 76 |
| 5a  | CH₂Cl₂ |    |    |
| 780 | 9  | 91 |
| 730 | 52 | 48 |
| 680 | 21 | 79 |
| 660 | 68 | 32 |
| 625 | 44 | 56 |
| 595 | 34 | 66 |
| 565 | 36 | 64 |
| 530 | 12 | 88 |
| 515 | 14 | 86 |
| 505 | 11 | 89 |
| 490 | 12 | 88 |
| 470 | 11 | 89 |
| 450 | 14 | 86 |
| 430 | 24 | 76 |
| 420 | 27 | 73 |
| 405 | 30 | 70 |
| 395 | 26 | 74 |
| 385 | 28 | 72 |
2.2.6  Photoisomerization of indirubins 1a to 5a at UV/vis concentrations in toluene solution

Figure S25: UV/vis absorptions of indirubin solutions (toluene, 20 °C) measured after the pss was reached at different irradiation wavelengths. a) Indirubin 1a, b) enlarged spectral regions of 1a absorption, c) indirubin 2a, d) enlarged spectral regions of 2a absorption, e) indirubin 3a, f) enlarged spectral regions of 3a absorption.
Figure S26: UV/vis absorptions of indirubin solutions (toluene, 20 °C) measured after the pss was reached at different irradiation wavelengths. a) Indirubin 4a, b) enlarged spectral regions of 4a absorption, c) indirubin 5a, d) enlarged spectral regions of 5a absorption.
2.2.7 Photoisomerization of indirubins 1a to 5a at UV/vis concentrations in CH$_2$Cl$_2$ solution

Figure S27: UV/vis absorptions of indirubin solutions (CH$_2$Cl$_2$, 20 °C) measured after the pss was reached at different irradiation wavelengths. a) Indirubin 1a, b) enlarged spectral regions of 1a absorption, c) indirubin 2a, d) enlarged spectral regions of 2a absorption, e) indirubin 3a, f) enlarged spectral regions of 3a absorption.
Figure S28: UV/vis absorptions of indirubin solutions (CH$_2$Cl$_2$, 20 °C) measured after the pss was reached at different irradiation wavelengths. a) Indirubin 4a, b) enlarged spectral regions of 4a absorption, c) indirubin 5a, d) enlarged spectral regions of 5a absorption.
2.2.8 Photoisomerization of indirubins 1a to 5a in the presence of STC at UV/vis concentrations in toluene solution

Figure S29: UV/vis absorptions of indirubin solutions in the presence of STC (4 equiv., toluene, 20 °C) measured after the pss was reached at different irradiation wavelengths. a) Indirubin 1a + STC, b) enlarged spectral regions of 1a + STC absorption, c) indirubin 2a + STC, d) enlarged spectral regions of 2a + STC absorption, e) indirubin 3a + STC, f) enlarged spectral regions of 3a + STC absorption.
Figure S30: UV/vis absorptions of indirubin solutions in the presence of STC (4 equiv., toluene, 20 °C) measured after the pss was reached at different irradiation wavelengths. a) Indirubin 4a + STC, b) enlarged spectral regions of 4a + STC absorption, c) indirubin 5a + STC, d) enlarged spectral regions of 5a + STC absorption.
2.2.9 Photoisomerization of indirubins 1a to 5a in the presence of STC at UV/vis concentrations in CH$_2$Cl$_2$ solution

Figure S31: UV/vis absorptions of indirubin solutions in the presence of STC (20 equiv., CH$_2$Cl$_2$, 20 °C) measured after the pss was reached at different irradiation wavelengths. a) Indirubin 1a + STC, b) enlarged spectral regions of 1a + STC absorption, c) indirubin 2a + STC, d) enlarged spectral regions of 2a + STC absorption, e) indirubin 3a + STC, f) enlarged spectral regions of 3a + STC absorption.
Figure S32: UV/vis absorptions of indirubin solutions in the presence of STC (20 equiv., CH₂Cl₂, 20 °C) measured after the pss was reached at different irradiation wavelengths. a) Indirubin 4a + STC, b) enlarged spectral regions of 4a + STC absorption, c) indirubin 5a + STC, d) enlarged spectral regions of 5a + STC absorption.
2.2.10 Photoisomerization of indirubins 1b and 1c at UV/vis concentrations

Figure S33: UV/vis absorptions of indirubin 1b (DMSO, 20 °C) measured after different periods of irradiation with 565 nm light. No spectral changes are seen upon irradiation indicating the absence of productive photoisomerization.

Figure S34: UV/vis absorptions of indirubin 1c (toluene, 20 °C) measured after different periods of irradiation at different wavelengths. No spectral changes are seen upon irradiation indicating the absence of productive photoisomerization.
2.3 Quantum yield determination

For determination of photoisomerization quantum yields a previously published approach was used including a nonlinear comprehensive analysis.¹

The photoisomerization quantum yield $\phi$ is defined as the ratio of the number of isomerized molecules $n$ (molecules isomerized) and the number of absorbed photons of the respective system. $n(h\nu)$ according to eq. 1:

$$\phi = \frac{n(\text{molecules isomerized})}{n(h\nu)} \quad \text{eq. 1}$$

For determination of the quantum yield $\phi$, a sample with known concentration of either pure 1a or a mixture of 1a with 4 equiv. of STC was irradiated in toluene with a focused light beam of a 625 nm high power LED within the instrumental setup from the group of E. Riedle.² The number of absorbed photons $n(h\nu)$ were obtained from the directly measured change of Power $\Delta P$ at the thermal photometer:

$$n(h\nu) = \frac{\Delta P \cdot \lambda_{\text{exc}} \cdot t}{c \cdot h} \quad \text{eq. 2}$$

with:

- $c =$ speed of light (2.99792 $\cdot 10^8$ m·s⁻¹)$h =$ Planck’s constant (6.62607 $\cdot 10^{-34}$ J·s)
- $\lambda_{\text{exc}} =$ excitation Wavelenght (625 $\cdot 10^9$ m)
- $t =$ time of irradiation intervals
- $\Delta P =$ difference of the photometers power readout of a toluene filled cuvette ($P_0$) and the cuvette containing a solution of the respective components in toluene ($P_t$) during the irradiation intervals in Watt.

For indirubin 1a the rate of the photoisomerization from $Z$ to the $E$ isomeric state depends on the concentration of $E$ isomers present during irradiation and can be expressed by:

$$r_{Z \rightarrow E} = \phi_{Z \rightarrow E} \cdot I_0 \cdot \varepsilon_Z \cdot d \cdot [Z] \cdot \left( \frac{1 - e^{-d \cdot \varepsilon_E[E]}}{d \cdot \varepsilon_E[E]} \right) \quad \text{eq. 3}$$

with:

- $\phi_{E \rightarrow Z} =$ photoisomerization quantum yield for the phototransition from the $Z$ to the $E$ isomeric state
- $I_0 =$ photon flux (Einstein L⁻¹ s⁻¹)
- $\varepsilon_Z =$ molar absorption coefficient of the $Z$ isomer at the wavelength of irradiation (625 nm)
- $\varepsilon_E =$ molar absorption coefficient of the $E$ isomer at the wavelength of irradiation (625 nm)
- $d =$ pathlength of the cuvette

This relation (eq. 3) is also applicable to the reverse phototransition from $E \rightarrow Z$ isomeric 1a simply by changing the indices leading to the following matrix relation:
\[ M_1 \begin{pmatrix} r_{Z \rightarrow Z} & r_{Z \rightarrow E} \\ r_{E \rightarrow Z} & r_{E \rightarrow E} \end{pmatrix} \quad \text{eq. 4} \]

The Matrix \( M_1 \) (eq. 4) accounts for each of the respective phototransitions (including the nonreactive channels to the isomeric state itself). Each element represents a nonlinear differential equation, which makes an analytical solution not feasible.

In order to simulate the quantum yield measurements the rate elements \( (r_{x \rightarrow y}) \) have to be fitted manually. For an incremental irradiation time step \( (\Delta t) \) expressions eq. 5 and eq. 6 were used to describe the concentrations of each isomer in \( t + \Delta t \):

\[
[Z]_{t + \Delta t} = [Z]_t - r_{Z \rightarrow E} \cdot \Delta t + r_{E \rightarrow Z} \cdot \Delta t \quad \text{eq. 5}
\]

\[
[E]_{t + \Delta t} = [E]_t - r_{E \rightarrow Z} \cdot \Delta t + r_{Z \rightarrow E} \cdot \Delta t \quad \text{eq. 6}
\]

Since each component of each rate \( (r_{x \rightarrow y}) \) is available from the measurements the quantum yield of each phototransformation step \( \phi_{x \rightarrow y} \) can be derived within the means of the best manually acquired fit. The determined photoisomerization quantum yields fits can be seen in Figure S35 derived values for the respective quantum yields are summarized in Table S3.
Figure S35: Concentration changes observed during photoisomerization quantum yield measurements. A solution of Z-1a in toluene was irradiated with 625 nm (fiber focused high power LED by Mountain Photonics GmbH) light while photons were counted. Measured (dots) and fitted (lines) concentration changes are shown as measured by UV/vis spectroscopy. a) Indirubin 1a and b) indirubin 1a in the presence of 4 equiv. of STC.
Table S3: Determined photoisomerization quantum yields of 1a in the absence and in the presence of 4 equiv. STC. Values are measured in toluene solution at 20 °C at 625 nm irradiation.

|                    | in the absence of STC | in the presence of 4 equiv. STC |
|--------------------|------------------------|-------------------------------|
| $\phi_{Z \to E}$   | 0.8%                   | 0.72%                         |
| $\phi_{E \to Z}$   | 1.75%                  | 0.34%                         |
2.4 Photochemical stabilities of indirubins 1a and 2a with and without the addition of STC

In order to assess the photochemical stabilities of indirubins photoswitches 1a and 2a were subjected to up to ten switching cycles. To this end Z isomers of the respective indirubins were dissolved in spectroscopic grade toluene. The samples were alternately irradiated with 625 nm (accumulation of E isomer) and 450 nm (accumulation of Z isomer). After each irradiation step an UV/vis spectrum was recorded from which the isomeric distribution of the respective isomers was calculated taking into account the known molar absorption coefficients (Figure S36 a and c).

In order to investigate the influence of STC on the switching stabilities on indirubins 1a and 2a the respective Z isomers were dissolved in spectroscopic grade toluene and an excess of STC was added. The samples were alternately irradiated with 660 nm (accumulation of E isomer) and 730 nm (3c7 filtered, accumulation of Z isomer). After each irradiation step an UV/vis spectrum was recorded from which the isomeric distribution of the respective isomers was calculated taking into account the known molar absorption coefficients (Figure S36 b and d).

Figure S36: Photochemical stability measurements of a) indirubin 1a, b) 1a with the addition of an excess of STC, c) 2a and d) 2a with the addition of an excess of STC. Blue dots represent the percentage of the Z isomer after irradiation of the samples with the respective wavenlengths given in the subfigures. Green dots represent the absorption intensity of the isosbestic points at a) 536 nm, b) 495 nm, c) 536 nm and d) 499 nm as measured throughout the cycling experiment (right y-axis). Only slight changes of the isosbestic point absorptions can be seen, which indicates no decay of the absolute absorption and thus full photostability of the respective indirubins during 10 cycles.
3 Thermal stabilities of $E$ isomeric states

3.1 First order kinetics without entering equilibria

3.1.1 Measurement procedure

UV/vis cuvettes were charged with the respective indirubin and 3.0 to 3.5 mL of toluene or CH$_2$Cl$_2$ solvent. The cuvettes were then irradiated with 625 nm light to reach a high percentage of the metastable $E$ isomer. Then thermal $E$ to $Z$ isomerizations were monitored via the absorption spectral changes occurring in the dark after irradiation stopped. The ideal observation wavelength was determined by a maximization of the $R^2$ value for the linearized first order kinetics. The rate constants $k$ of thermal $E$ to $Z$ isomerizations were calculated from the increase of the respective $Z$ isomer absorption along with the corresponding decrease of the $E$ isomer absorption. Since the kinetics conform to first order without entering equilibria (quantitative conversions to the $Z$ isomers take place) relative absorption changes can be used to obtain the rate constant $k$ without the necessity to use molar absorptions. The relative isomer concentration changes were calculated by applying eq. 7:

$$\text{relative change} = \frac{(\text{absorption at } t_x - \text{absorption at } t_{\text{start}})}{(\text{absorption at } t_{\text{end}} - \text{absorption at } t_{\text{start}})}$$  \hspace{1cm} \text{eq. 7}

With $t_x$ being the temporal point, $t_{\text{start}}$ being the temporal starting point and $t_{\text{end}}$ being the temporal end point of the respective measurements.

For plotting purposes a relative percentage of the $E$ isomer $\%(\text{rel})$ was then calculated by applying eq. 8, arbitrarily assuming that at the start of the thermal reaction a relative 100\% (corresponding simply to the maximum amount of $E$ isomer at the start) of $E$ isomer is present:

$$\%(\text{rel}) \text{ of } E \text{ isomer} = (1 - \text{relative change}) \cdot 100$$  \hspace{1cm} \text{eq. 8}

The first order kinetics analysis was performed by plotting the time $t$ against the relative isomer changes according to:

$$\ln \left( \frac{\%(\text{rel})E_0}{\%(\text{rel})E_t} \right) = kt$$  \hspace{1cm} \text{eq. 9}

Linear regression of the plot delivers $k$ directly as the slope.

By using the Eyring equation (eq. 10) the Gibbs energy of activation $\Delta G^\ddagger$ can be calculated from the rate constant $k$ of the reaction:

$$k = \frac{k_B T}{h} e^{-\Delta G^\ddagger}$$  \hspace{1cm} \text{eq. 10}

$k_B$ = Boltzmann constant ($1.381 \cdot 10^{-23}$ J·K$^{-1}$)
\[ T = \text{temperature in K} \]

\[ h = \text{Planck constant (6.626} \cdot 10^{-34} \text{J} \cdot \text{s)} \]

\[ k = \text{rate constant of the reaction} \]

Eq. 10 can be rearranged and the numerical value of the rate constant \( k \) obtained from plotting eq. 9 can then be inserted into eq. 11 to obtain the Gibbs energy of activation \( \Delta G^\ddagger \) (in J mol\(^{-1}\)):

\[
\Delta G^\ddagger = R \cdot T \cdot \ln \frac{h}{k_B T}
\]

The thermal \( E \) to \( Z \) isomerizations of indirubin photoswitches 1a – 3a could not be measured in CH\(_2\)Cl\(_2\) solution with the above mentioned approach within the UV/vis spectrophotometer due to significant evaporation of the solvent over the extended time periods needed for these processes at ambient temperatures. Therefore, a different approach employing \(^1\)H NMR spectroscopy was conducted. Here, the isomeric ratios in each timestep could directly be measured via integration of the respective separated \(^1\)H NMR signals of the \( E \) and the \( Z \) isomers. Plotting according to eq. 9 and extraction of \( k \) as well as applying eq. 11 were then used again to yield the corresponding Gibbs energies of activation \( \Delta G^\ddagger \). Similar procedures were used for both, solutions of pure indirubins and mixtures of indirubins and STC. All obtained Gibbs energies of activation \( \Delta G^\ddagger \) for the thermal \( E \) to \( Z \) isomerization of indirubins 1a-5a at 20 °C and corresponding half-lives of the metastable \( E \) isomers are summarized in Table 1 in the manuscript and in Table S3.
Table S4: Gibbs energies of activation $\Delta G^\ddagger$ of the thermal $E$ to $Z$ isomerization of indirubins 1a – 5a at 20 °C and corresponding half-lives of the $E$ isomers.

| Indirubin  | In toluene $\Delta G^\ddagger$ [kcal/mol] | $t_{1/2}$ | In CH$_2$Cl$_2$/CD$_2$Cl$_2$ $\Delta G^\ddagger$ [kcal/mol] | $t_{1/2}$ |
|------------|------------------------------------------|-----------|----------------------------------------------------------|-----------|
| 1a (2.6 mM)| 21.3 ± 0.1                               | 14.7 min  | 22.5 ± 0.1*                                              | 1.9 h*    |
| 1a (0.028 mM)| 22.7 ± 0.1                                | 2.7 h     | 22.3 ± 0.1*                                              | 1.4 h*    |
| 2a (2.5 mM)| 22.1 ± 0.1                               | 58.1 min  | 22.3 ± 0.1*                                              | 2.3 h*    |
| 2a (0.025 mM)| 22.4 ± 0.1                                | 1.6 h     | 22.3 ± 0.1*                                              | 17.5 min  |
| 3a         | 21.9 ± 0.1                               | 41.2 min  | 22.6 ± 0.1*                                              | 2.3 h*    |
| 4a         | 21.6 ± 0.1                               | 24.6 min  | 21.4 ± 0.1                                               | 20.7 min* |
| 5a         | 20.5 ± 0.1                               | 3.7 min   | 20.5 ± 0.1                                               | 3.7 min   |

| Indirubin  | In toluene $\Delta G^\ddagger$ [kcal/mol] | $t_{1/2}$ | In CH$_2$Cl$_2$/CD$_2$Cl$_2$ $\Delta G^\ddagger$ [kcal/mol] | $t_{1/2}$ |
|------------|------------------------------------------|-----------|----------------------------------------------------------|-----------|
| 1a         | 22.4 ± 0.1                               | 1.6 h     | 22.7 ± 0.1*                                              | 2.7 h*    |
| 2a         | 22.5 ± 0.1                               | 1.9 h     | 22.3 ± 0.1*                                              | 1.4 h*    |
| 3a         | 22.2 ± 0.1                               | 1.1 h     | 21.5 ± 0.1*                                              | 20.7 min* |
| 4a         | 21.5 ± 0.1                               | 20.7 min  | 21.7 ± 0.1*                                              | 29.2 min* |
| 5a         | 20.3 ± 0.1                               | 2.6 min   | 20.4 ± 0.1                                               | 3.1 min   |
3.1.2 Thermal E to Z isomerization in toluene solution

Figure S37: Thermal recovery of the thermodynamically more stable Z isomer of indirubins 1a and 2a at 20 °C in toluene solution. The respective Z isomeric indirubins were first irradiated to the pss with 625 nm light to obtain E isomer enriched solutions (red spectrum). Spectra were subsequently recorded in different time intervals in the dark. a) Indirubin 1a (2.6 mol L⁻¹, plotted 10 min intervals), b) indirubin 1a (0.0028 mol L⁻¹, plotted 50 min intervals), c) indirubin 2a (2.5mol L⁻¹, plotted 15 min intervals), d) indirubin 2a (0.0025 mol L⁻¹, plotted 50 min intervals).
Figure S38: Thermal decay of $E$ isomeric indirubin $1a$ at 20 °C in toluene solution (left) and corresponding linearized kinetic plot according to eq. 9 (right). Kinetics were monitored with UV/vis absorption spectroscopy. a) Kinetics at high concentration (2.6 mM) of $1a$, b) kinetics at low concentration (0.028 mM) of $1a$. 
Figure S39: Thermal decay of \(E\) isomeric indirubin 2a at 20 °C in toluene solution (left) and corresponding linearized kinetic plot according to eq. 9 (right). Kinetics were monitored with UV/vis absorption spectroscopy. a) Kinetics at high concentration (2.5 mM) of 2a, b) kinetics at low concentration (0.025 mM) of 2a.
Figure S40: Thermal recovery of the thermodynamically more stable Z isomer of indirubins 3a to 5a at 20 °C in toluene solution. The respective Z isomeric indirubins were first irradiated to the pss with 625 nm light to obtain E isomer enriched solutions (red spectrum). Spectra were subsequently recorded in different time intervals in the dark. a) Indirubin 3a (plotted 40 min intervals), b) indirubin 4a (plotted 20 min intervals), c) indirubin 5a (plotted 90 s intervals).
Figure S41: Thermal decay of $E$ isomeric indirubins 3a to 5a at 20 °C in toluene solution (left) and corresponding linearized kinetic plots according to eq. 9 (right). Kinetics were monitored with UV/vis absorption spectroscopy. a) Kinetics for indirubin 3a, b) kinetics for indirubin 4a, c) kinetics for indirubin 5a.
Figure S42: Thermal recovery of the thermodynamically more stable Z isomer of indirubins 1a to 5a in the presence of 4 equiv. STC at 20 °C in toluene solution. The respective mixtures containing only Z isomeric indirubins were first irradiated to the ps with 625 nm light to obtain E isomer enriched solutions (red spectrum). Spectra were subsequently recorded in different time intervals in the dark. a) Indirubin 1a + STC (plotted 100 min intervals), b) indirubin 2a + STC (plotted in 50 min intervals), c) indirubin 3a + STC (plotted in 50 min intervals), d) indirubin 4a + STC (plotted 15 min intervals), e) indirubin 5a + STC (plotted 150 s intervals).
Figure S43: Thermal decay of $E$ isomeric indirubins $1a$ and $2a$ in the presence of 4 equiv. STC at 20 °C in toluene solution (left) and corresponding linearized kinetic plots according to eq. 9 (right). Kinetics were monitored with UV/vis absorption spectroscopy. a) Kinetics for indirubin $1a + STC$, b) kinetics for indirubin $2a + STC$. 
Figure S44: Thermal decay of $E$ isomeric indirubins 3a to 5a in the presence of 4 equiv. STC at 20 °C in toluene solution (left) and corresponding linearized kinetic plots according to eq. 9 (right). Kinetics were monitored with UV/vis absorption spectroscopy. a) Kinetics for indirubin 3a + STC, b) kinetics for indirubin 4a + STC, c) kinetics for indirubin 5a + STC.
3.1.3 Thermal $E$ to $Z$ isomerization in CH$_2$Cl$_2$/CD$_2$Cl$_2$ solution

Figure S45: Thermal recovery of the thermodynamically more stable $Z$ isomer of indirubins 1a and 2a at 20 °C in CD$_2$Cl$_2$ solution. The respective $Z$ isomeric indirubins were first irradiated to the pss with 625 nm light to obtain $E$ isomer enriched solutions (top spectrum). Spectra were subsequently recorded in different time intervals in the dark. a) Indirubin 1a (plotted in 48 min intervals, last spectrum recorded after 24 h in the dark), b) indirubin 2a (plotted in 37 min intervals, last spectrum recorded after 5.7 h).
Figure S46: Thermal decay of $E$ isomeric indirubin 1a and 2a at 20 °C in CD$_2$Cl$_2$ solution (left) and corresponding linearized kinetic plot according to eq. 9 (right). Kinetics were monitored with $^1$H NMR spectroscopy. a) Kinetics of 1a, b) kinetics of 2a.
Figure S47: Thermal recovery of the thermodynamically more stable Z isomer of indirubins 3a to 5a 20 °C in CD$_2$Cl$_2$ (a) and CH$_2$Cl$_2$ (b, c) solution. The respective Z isomeric indirubins were first irradiated to the pss with 625 nm light to obtain E isomer enriched solutions (a): top spectrum, b) and c): red spectrum). Spectra were subsequently recorded in different time intervals in the dark. a) Indirubin 3a (plotted 48 min intervals, last spectrum recorded after 20.5 h in the dark), b) indirubin 4a (plotted 10 min intervals), c) indirubin 5a (plotted 3 min intervals).
Figure S48: Thermal decay of $E$ isomeric indirubin 3a to 5a at 20 °C in CD$_2$Cl$_2$ (a) and CH$_2$Cl$_2$ (b, c) solution (left) and corresponding linearized kinetic plot according to eq. 9 (right). Kinetics were monitored with $^1$H NMR (a) and UV/vis (b and c) spectroscopy. a) Kinetics of 3a, b) kinetics of 4a, c) kinetics of 5a.
Figure S49: Thermal recovery of the thermodynamically more stable Z isomer of indirubins 1a and 2a in the presence of 1 equiv. STC 20 °C in CD$_2$Cl$_2$ solution. The respective mixtures containing only Z isomeric indirubins were first irradiated to the pss with 625 nm light to obtain $E$ isomer enriched solutions (top spectrum). Spectra were subsequently recorded in different time intervals in the dark. a) Indirubin 1a + STC (plotted in 100 min intervals, last spectrum recorded after 15.7 h), b) indirubin 2a + STC (plotted in 40 min intervals, last spectrum recorded after 7.5 h).
Figure S50: Thermal decay of $E$ isomeric indirubins 1a and 2a in the presence of 1 equiv. STC at 20 °C in CD$_2$Cl$_2$ solution (left) and corresponding linearized kinetic plots according to eq. 9 (right). Kinetics were monitored with $^1$H NMR spectroscopy. a) Kinetics for indirubin 1a + STC, b) kinetics for indirubin 2a + STC.
Figure S51: Thermal recovery of the thermodynamically more stable $Z$ isomer of indirubins 3a and 4a in the presence of 1 equiv. STC at 20 °C in CD$_2$Cl$_2$ solution. The respective mixtures containing only $Z$ isomeric indirubins were first irradiated to the $E$ isomer enriched solutions (top spectrum). Spectra were subsequently recorded in different time intervals in the dark. a) Indirubin 3a + STC (plotted in 30 min intervals, last spectrum recorded after 3 h), b) indirubin 4a + STC (plotted in 20 min intervals, last spectrum recorded after 18.8 h).
Figure S52: Thermal recovery of the thermodynamically more stable \( Z \) isomer of indirubin 5a in the presence of 1 equiv. STC 20 °C in \( \text{CH}_2\text{Cl}_2 \) solution. The mixture containing only \( Z \) isomeric indirubin 5a was first irradiated to the pss with 625 nm light to obtain an \( E \) isomer enriched solution (red spectrum). Spectra were subsequently recorded in 60 s intervals in the dark.
Figure S53: Thermal decay of \( E \) isomeric indirubins 3a to 5a in the presence of 1 equiv. STC at 20 °C in CD\(_2\)Cl\(_2\) (a and c) or CH\(_2\)Cl\(_2\) (b) solution (left) and corresponding linearized kinetic plots according to eq. 9 (right). Kinetics were monitored with \(^1\text{H} \) NMR (a and b) or UV/vis absorption (b) spectroscopy. a) Kinetics for indirubin 3a + STC, b) kinetics for indirubin 4a + STC, c) kinetics for indirubin 5a + STC.
4 Theoretical Description

4.1 General calculation procedure

To benchmark the theoretical description of respective indirubins each indirubin 1a to 5a was optimized on either the B3LYP, MPW1K, or ω-B97X level of theory. From earlier experience the addition of the PCM solvent model is obligatory to obtain good starting geometries although the MPW1K functional does not profit from this addition. Hence the PCM solvent model with either toluene or CH$_2$Cl$_2$ parameters as implemented in Gaussian16$^3$ were used for the optimization on either the B3LYP or ω-B97X level of theory. For the optimizations the pople triple ζ basis 6-311G(d,p) basis along with an ultrafine integration grid and tight optimization thresholds were employed. Obtained geometries were proven to be minima by subsequent frequency analysis yielding only positive modes of vibration.

For calculation of absorption spectra the B3LYP or PBE0 functionals along with a slightly greater 6-311+G(d,p)-PCM(tol) basis were employed based on the obtained minima structures for each of the abovementioned methods. Only singlet states (10 states in total) were taken into account.

For calculation of the interactions of indirubin 1a with STC the conformational space was scanned for potential minima with the MCMM method implemented in the Macromodel program of the Schrödinger Suite.$^4$ For this scan the MMFFs force field without the addition of a solvent was employed. The energetic space was set within 5 kcal/mol. Other parameters were left default. The obtained structures were scrutinized for conformational redundancies via the redundant conformer analysis tool implemented in Macromodel.$^4$ Each unique structure was first preoptimized on the B3LYP-D3BJ/6-31G(d)-PCM(tol) level of theory. Converged structures were again examined for structural and energetic redundancies. The preoptimized unique structures were further optimized on the B3LYP-D3BJ/6-311++G(d,p)-PCM(tol) level of theory. The obtained structures were one last time scrutinized for conformational and energetic redundancies. Unique geometries were taken as basis for a single point calculation on the PW6B95D3/MG3S PCM(tol) level of theory. Structures that were found within 2.5 kcal/mol from the global minimum (on either of the last two calculations) were taken into consideration for a TDDFT analysis, which was carried out as described above. Structures are available upon request from the authors.
4.2 Optimized molecular structures of indirubins 1a to 5a

Figure S54: Depiction of the theoretically obtained optimized molecular structures of indirubins 1a–5a. Structures were optimized on the B3LYP/6-311G(d,p)-PCM(tol) level of theory.
Figure S55: Depiction of the theoretically obtained optimized molecular structure of the supramolecular complex \textit{E-1a–STC} shown from different viewpoints. The structure was optimized on the B3LYP-D3BJ/6-311++G(d,p)-PCM(tol) level of theory. The NH-protons of STC involved in hydrogen bonding are colored green for emphasis.
4.3 Molecular orbitals involved in the electronic excitation of indirubin 1a

Figure S56: Orbitals involved in the electronic excitation of indirubin 1a. HOMO and LUMO are depicted together with the most important orbitals involved in the transition and the resulting sum-excitation energies (purple numbers). a) Z-1a, b) E-1a. Structures were optimized on the B3LYP/6-311G(d,p)-PCM(tol) level of theory and spectra were calculated on the PBE0/6-311+G(d,p)-PCM(tol) level of theory.
4.4 Theoretical UV/vis absorption spectra of indirubins 1a to 5a

Figure S57: Comparison of theoretical (colored) and experimental (black solid line) UV/vis absorption spectra of indirubins 1a to 3a in toluene solution. Spectra are color coded based on the optimization method (red: B3LYP-PCM(tol); green: MPW1K-gp; blue: ω-B97X-PCM(tol)). Solid lines (except black) correspond to TDDFT calculations on the B3LYP-PCM(tol) level of theory, broken lines to the PBE0-PCM(tol) level of theory. a) Z-1a, b) E-1a, c) Z-2a, d) E-2a, e) Z-3a, f) E-3a.
Figure S58: Comparison of theoretical (colored) and experimental (black solid line) UV/vis absorption spectra of indirubins 4a and 5a in toluene solution. Spectra are color coded based on the optimization method (red: B3LYP-PCM(tol); green: MPW1K-gp; blue: ω-B97X-PCM(tol)). Solid lines (except black) correspond to TDDFT calculations on the B3LYP-PCM(tol) level of theory, broken lines to the PBE0-PCM(tol) level of theory. a) Z-4a, b) E-4a, c) Z-5a, d) E-5a.
Figure S59: Comparison of theoretical (colored) and experimental (black solid line) UV/vis absorption spectra of indirubins 1a to 3a in CH$_2$Cl$_2$ solution. Spectra are color coded based on the optimization method (red: B3LYP-PCM(CH$_2$Cl$_2$); green: MPW1K-gp; blue: ω-B97X-PCM(CH$_2$Cl$_2$)). Solid lines (except black) correspond to TDDFT calculations on the B3LYP-PCM(CH$_2$Cl$_2$) level of theory, broken lines to the PBE0-PCM(CH$_2$Cl$_2$) level of theory. a) Z-1a, b) E-1a, c) Z-2a, d) E-2a, e) Z-3a, f) E-3a.
Figure S60: Comparison of theoretical (colored) and experimental (black solid line) UV/vis absorption spectra of indirubins 4a and 5a in CH$_2$Cl$_2$ solution. Spectra are color coded based on the optimization method (red: B3LYP-PCM(CH$_2$Cl$_2$); green: MPW1K-gp; blue: o-B97X-PCM(CH$_2$Cl$_2$)). Solid lines (except black) correspond to TDDFT calculations on the B3LYP-PCM(CH$_2$Cl$_2$) level of theory, broken lines to the PBE0-PCM(CH$_2$Cl$_2$) level of theory. a) Z-4a, b) E-4a, c) Z-5a, d) E-5a.
Figure S61: Calculated (PBE0/6-311+G(d,p)-PCM(tol)/B3LYP-D3BJ/6-311G(d,p)-PCM(tol) level of theory) UV/vis absorption of E-1a (solid black line) and of the complex between E-1a and STC (solid red line, the Boltzmann-averaged spectrum of different complex structures is shown) and comparison to the corresponding experimental spectra in toluene solution (dashed black line for E-1a and dashed red line for the complex between E-1a and STC). Theoretical UV/vis absorptions taking into account two different binding constants $K_a = 1000$ (solid pink line) or $K_a = 100$ (solid blue line) are also shown. (A reference concentration of 1 mmol L$^{-1}$ was assumed for the calculation of E-1a/E-1a-STC equilibrium ratios).
5 NMR spectra of 1a – 5a

Figure S62: $^1$H NMR spectrum (600 MHz, toluene-$d_8$, 27 °C) of 1a.

Figure S63: $^{13}$C NMR spectrum (151 MHz, toluene-$d_8$, 27 °C) of 1a.
Figure S64: $^1$H NMR spectrum (400 MHz, CD$_2$Cl$_2$, 27 °C) of 2a.

Figure S65: $^{13}$C NMR spectrum (101 MHz, CD$_2$Cl$_2$, 27 °C) of 2a.
Figure S66: $^1$H NMR spectrum (400 MHz, CD$_2$Cl$_2$, 27 °C) of 3a.

Figure S67: $^{13}$C NMR spectrum (101 MHz, CD$_2$Cl$_2$, 27 °C) of 3a.
Figure S68: $^1$H NMR spectrum (600 MHz, toluene-$d_8$, 27 °C) of 4a.

Figure S69: $^{13}$C NMR spectrum (151 MHz, toluene-$d_8$, 27 °C) of 4a.
Figure S70: $^1$H NMR spectrum (400 MHz, CD$_2$Cl$_2$, 25 °C) of 5a.

Figure S71: $^{13}$C NMR spectrum (101 MHz, CD$_2$Cl$_2$, 25 °C) of 5a.
6 Crystallographic Data

The X-ray intensity data of 1c, 2c, 3a, 4a, 5a, and 5b were measured on a Bruker D8 Venture TXS system equipped with a multilayer mirror monochromator and a Mo Kα rotating anode X-ray tube (\(\lambda = 0.71073\ \text{Å}\)). The frames were integrated with the Bruker SAINT software package.\(^5\) Data were corrected for absorption effects using the Multi-Scan method (SADABS).\(^6\) The structure was solved and refined using the Bruker SHELXTL Software Package.\(^7\)

1c: refined as perfect inversion-twin

2c: All hydrogen atoms have been calculated in ideal geometry riding on their parent atoms. The disorder of an ethyl group has been described by a split model. The ratio of site occupation factors of the two parts refined to 0.77/0.23. The less-occupied moieties of disordered parts have been omitted for the depictions.

3a and 5a: All hydrogen atoms have been calculated in ideal geometry riding on their parent atoms.

4a: ISOR applied for O2 in order to improve the anisotropic displacement parameters. DELU applied for the atoms of the bond N2-C24. Measurement at room temperature necessary due to instability of the crystals at low temperature (likely a phase transition, crystals crack after a while).

5c: All C-bound hydrogen atoms have been calculated in ideal geometry riding on their parent atoms while the N-bound hydrogen atoms have been refined freely. In the figure shown, one out of three molecules in the asymmetric unit has been depicted.
|                  | 1e (xv587)                      | 2e (yv553)                      |
|------------------|---------------------------------|---------------------------------|
|                  | CCDC 2100391                    | CCDC 2100392                    |
| net formula      | C₁₉H₁₈N₂O₃                     | C₂₁H₂₀N₂O₂                     |
| Mᵣ/g mol⁻¹       | 322.35                          | 332.39                          |
| crystal size/mm   | 0.100 × 0.030 × 0.010            | 0.110 × 0.080 × 0.050           |
| T/K              | 109.(2)                         | 298.(2)                         |
| radiation        | MoKα                            | MoKα                            |
| diffractometer   | 'Bruker D8 Venture TXS'          | 'Bruker D8 Venture TXS'         |
| crystal system    | orthorhombic                    | monoclinic                      |
| space group       | 'P 2₁ 2₁ 2₁'                    | 'P 1 2₁/n 1'                    |
| a/Å              | 5.4290(4)                       | 15.7270(7)                      |
| b/Å              | 16.1269(10)                     | 11.3010(5)                      |
| c/Å              | 17.5328(15)                     | 20.1846(8)                      |
| α/°              | 90                              | 90                              |
| β/°              | 90                              | 98.3350(10)                     |
| γ/°              | 90                              | 90                              |
| V/Å³             | 1535.0(2)                       | 3549.5(3)                       |
| Z                | 4                               | 8                               |
| calc. density/g cm⁻³ | 1.395                         | 1.244                          |
| μ/mm⁻¹           | 0.095                           | 0.081                           |
| absorption correction | Multi-Scan                 | Multi-Scan                     |
| transmission factor range | 0.93–1.00                    | 0.96–1.00                      |
| refls. measured  | 9191                            | 56100                           |
| Rᵣ int           | 0.0508                          | 0.0606                          |
| mean σ(I)/I      | 0.0607                          | 0.0317                          |
| 0 range          | 2.645–26.019                    | 2.890–25.350                    |
| observed refls.  | 2305                            | 4504                            |
| x, y (weighting scheme) | 0.0270, 0.9594                 | 0.0676, 2.1484                  |
| hydrogen refinement | H(C) constr, H(N,O) refallconstr |                                 |
| Flack parameter  | 0.5                             | -                               |
| refls in refinement | 2908                         | 6494                            |
| parameters       | 230                             | 466                             |
| restraints       | 0                               | 2                               |
| R(Fₙₒₛ)         | 0.0496                          | 0.0651                          |
| Rₚ(F²)          | 0.1004                          | 0.1797                          |
| S                | 1.069                           | 1.073                           |
| shift/errormax   | 0.001                           | 0.001                           |
| max electron density/e Å⁻³ | 0.213                        | 0.297                           |
| min electron density/e Å⁻³ | −0.263                       | −0.334                          |
|   | 3a (yv344) | 4a (yv601) |
|---|---|---|
|   | CCDC 2100393 | CCDC 2100394 |
| net formula | C$_{22}$H$_{20}$F$_2$N$_2$O$_2$ | C$_{23}$H$_{23}$FN$_2$O$_2$S |
| $M_r$/g mol$^{-1}$ | 382.40 | 410.49 |
| crystal size/mm | 0.100 × 0.060 × 0.020 | 0.100 × 0.080 × 0.020 |
| $T$/K | 102.(2) | 101.(2) |
| radiation | MoKα | MoKα |
| diffractometer | 'Bruker D8 Venture TXS' | 'Bruker D8 Venture TXS' |
| crystal system | triclinic | monoclinic |
| space group | 'P -1' | 'P 1 21/c 1' |
| $a$/Å | 8.1957(2) | 16.3828(18) |
| $b$/Å | 8.4934(2) | 13.0824(15) |
| $c$/Å | 13.0168(4) | 9.2298(10) |
| $α$/° | 92.3740(10) | 90 |
| $β$/° | 98.9790(10) | 91.526(4) |
| $γ$/° | 91.6990(10) | 90 |
| $V$/Å$^3$ | 893.62(4) | 1977.5(4) |
| $Z$ | 2 | 4 |
| calc. density/g cm$^{-3}$ | 1.421 | 1.379 |
| μ/mm$^{-1}$ | 0.106 | 0.196 |
| absorption correction | Multi-Scan | Multi-Scan |
| transmission factor range | 0.95–1.00 | 0.94–1.00 |
| refls. measured | 15743 | 32511 |
| $R_{int}$ | 0.0283 | 0.0368 |
| mean $σ(I)/I$ | 0.0276 | 0.0225 |
| 0 range | 2.939–27.103 | 2.935–27.095 |
| observed refls. | 3322 | 3812 |
| $x$, $y$ (weighting scheme) | 0.0350, 0.4290 | 0.0284, 1.3868 |
| hydrogen refinement | constr | constr |
| Flack parameter | - | - |
| refls in refinement | 3939 | 4354 |
| parameters | 255 | 265 |
| restraints | 0 | 0 |
| $R(F_{obs})$ | 0.0383 | 0.0358 |
| $R_a(F^2)$ | 0.0920 | 0.0845 |
| $S$ | 1.036 | 1.067 |
| shift/error$_{max}$ | 0.001 | 0.001 |
| max electron density/e Å$^{-3}$ | 0.276 | 0.315 |
| min electron density/e Å$^{-3}$ | −0.230 | −0.288 |
|                  | 5a (yv169)                | 5b (zv006)                |
|------------------|---------------------------|---------------------------|
| net formula      | $\text{C}_{26}\text{H}_{28}\text{FN}_3\text{O}_3$ | $\text{C}_{29}\text{H}_{16}\text{FN}_3\text{O}_3$ |
| $M_r$/g mol$^{-1}$ | 449.51                   | 365.36                    |
| crystal size/mm  | $0.070 \times 0.050 \times 0.020$ | $0.120 \times 0.040 \times 0.030$ |
| $T$/K            | 298.(2)                   | 173.(2)                   |
| radiation        | MoKα                      | MoKα                      |
| diffractometer   | 'Bruker D8 Venture TXS'    | 'Bruker D8 Venture TXS'    |
| crystal system   | triclinic                 | triclinic                 |
| space group      | 'P -1'                    | 'P -1'                    |
| $a$/Å            | 8.9128(6)                 | 10.0411(11)               |
| $b$/Å            | 10.0910(7)                | 13.8754(15)               |
| $c$/Å            | 14.4537(9)                | 17.712(2)                 |
| $\alpha$/°       | 71.075(2)                 | 81.437(4)                 |
| $\beta$/°        | 74.067(2)                 | 88.041(4)                 |
| $\gamma$/°       | 85.605(2)                 | 88.288(4)                 |
| $V$/Å$^3$        | 1182.33(14)               | 2438.0(5)                 |
| $Z$              | 2                         | 6                         |
| calc. density/g cm$^{-3}$ | 1.263                   | 1.493                     |
| $\mu$/mm$^{-1}$  | 0.089                     | 0.110                     |
| absorption correction | Multi-Scan              | Multi-Scan               |
| transmission factor range | 0.95–1.00              | 0.96–1.00                |
| refls. measured  | 12911                     | 43498                     |
| $R_{int}$        | 0.0568                    | 0.0586                    |
| mean $\sigma(I)/I$ | 0.0624                  | 0.0527                    |
| 0 range          | 2.950–25.026              | 2.861–27.484              |
| observed refls.  | 2377                      | 8762                      |
| $x$, $y$ (weighting scheme) | 0.1115, 0.6139         | 0.0452, 1.0755            |
| hydrogen refinement | constr                  | mixed                     |
| Flack parameter  | -                         |                           |
| refls in refinement | 4155                    | 11109                     |
| parameters       | 300                       | 754                       |
| restraints       | 7                         | 0                         |
| $R(F_{\text{obs}})$ | 0.0749                   | 0.0459                    |
| $R_{\text{w}}(F^2)$ | 0.2297                   | 0.1212                    |
| $S$              | 1.027                     | 1.052                      |
| shift/error$_{\text{max}}$ | 0.001                   | 0.001                      |
| max electron density/e Å$^{-3}$ | 0.543                   | 0.291                      |
| min electron density/e Å$^{-3}$ | $-0.290$              | $-0.260$                  |
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