Redshifted and Thermally Bistable One-Way Quantitative Hemithioindigo-derived Photoswitches Enabled by Isomer-Specific Excited State Intramolecular Proton Transfer

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Supporting experimental figures and schemes

**Scheme S1.** Synthesis of hemithioindigo derived photoswitches. Substitution of arylthiols SI 1-2 with 2-bromoacetic acid afforded the corresponding arylthioacetic acids SI 3-4. Subsequently, intramolecular Friedel-Crafts type acylation catalysed by triflic acid to initiate ring-closure, allowed access to thioindigo building blocks SI 5-6 in good yields. Coupling with various aldehydes via aldol condensations catalysed by piperidine resulted in the corresponding HTI photoswitches 1-9 in varying yields. Bipyrole aldehyde SI 9 was the only non-commercially available aldehyde that had to be prepared. This was accomplished in two synthetic steps via PIFA-mediated oxidative homo coupling of pyrrole SI 7 to give bipyrole SI 8 following a Vilsmeier-Haack formylation under stoichiometric control to afford aldehyde SI 9.

**Figure S1.** Normalized UV-Vis spectra (33 µM in CH₂Cl₂) displaying the redshifted trend in π-extended hemithioindigo photoswitches visible to the naked eye. Solid lines (Z-isomers). Dashed lines (E-isomers).
1 Supplementary computational details and figures

1.1 Computational details of DFT and TDDFT calculations

The B3LYP hybrid DFT functional\textsuperscript{1-3} has previously been successfully employed in a computational study of hemiindigo, a class of photoswitches closely related to the hemithioindigo photoswitch in the present work.\textsuperscript{4} Before performing TDDFT vertical excitation energy calculations, we optimized the ground-state geometries of the first and second series of HTI using B3LYP. For the third series, the DLPNO-MP2 method is chosen as the computation benefits from the local correlation scheme especially when more pyrrole rings are connected covalently to the photoswitch. The Dunning’s cc-pVTZ basis set\textsuperscript{5} is employed for both DFT and DLPNO-MP2 geometry optimizations which are performed until the root mean square of the force is less than 10\textsuperscript{-5} a.u. We then conduct frequency calculations to determine the nature of the resulting stationary points and ensure that optimized geometries without imaginary vibrational frequencies are obtained. The solvation model based on density (SMD) scheme\textsuperscript{6} was first tested (see next section) and subsequently used to model the solvent implicitly. The considered solvents of increasing polarity are toluene, DCM, and DMSO.

DFT and TDDFT calculations are performed using Gaussian16. For the TDDFT calculations, we used the maug-cc-pVTZ basis set.\textsuperscript{7} DLPNO-MP2 calculations are performed using ORCA version 4.2.1.\textsuperscript{8,9} Unless otherwise stated, the default settings of the software are used.

The oscillator strength for excited state \(i\) (\(f_i\)), is computed as

\[
 f_i = \frac{8 \pi^2 \tilde{v}_i m_e c}{3 \hbar e^2 D_i,}
\]

where \(\tilde{v}_i\) is the excitation energy corresponding to the electronic excitation of interest \(i\), \(m_e\) is the electron mass, \(c\) is the speed of light, \(\hbar\) is the Planck’s constant, \(e\) is the electronic charge, and \(D_i\) or sometimes refer to as \(\mu_{fi}\) is the dipole strength. The employed formulation allows the value of \(f_i\) to be greater than unity. Moreover, \(f_i\) is proportional to the dipole strength \(D_i\), which means that larger values of \(f_i\) indicate bright excited states whereas lower values of \(f_i\) point to dark excited states.

1.2 Effect of the choice of implicit solvent models

Implicit solvent models can affect the relative energy of the ground state isomers of a photoswitch. For example, a previous study on the DASA photoswitch showed that the reactant isomer in one solvent model was the most stable, whereas for another solvent model, the product was the most stable.\textsuperscript{10} Therefore, we examined two of the most commonly used solvent models: SMD and IEFPCM.\textsuperscript{11}

We have examined the effect of two implicit solvent models (SMD and IEFPCM) on the geometry, relative energy, and vertical excitation energy of four isomers of HTI pyrrole (see Figure below) at the level of B3LYP/cc-pVTZ. The four isomers are the stereoisomers of the two carbon-carbon bonds connecting the hemithioindigo and pyrrole moieties. They are labeled as \(A_x\): the first letter indicates the stereoisomer of the formal double bond (C\(_3\)=C\(_4\)), and the second letter in subscript designated the stereoisomers of the formal single bond (C\(_4\)=C\(_5\)). The “E” isomer in the main text is the “E\(_Z\)” while the main text “Z” isomer refers
either $Z_z$ or $Z_e$ as they are experimentally indiscernible. Six atoms are numbered in red to indicate bonds, the lengths of which are compared.

Table S1 shows the relative ground-state electronic energy of four stereoisomers of HTI pyrrole in different implicit solvent models against isomer $Z_z$. The application of the SMD solvent model results in the same trend of the relative energies (within the chemical accuracy of 1 kcal/mol) as that of the IEFPCM method across three studied solvents of increasing polarity: toluene (nonpolar), DCM (semipolar), and DMSO (polar). The SMD- and IEFPCM-optimized bond-length patterns for an individual isomer on a particular solvent are similar, as shown in Table S2 for five bond lengths connecting atoms O and N. Furthermore, using the same B3LYP/cc-pVTZ/SMD geometry, computation of the wavelength of maximum absorbance ($\lambda_{\text{max}}$) of the first bright excited state using the SMD and IEFPCM methods separately yielded similar results within 1 nm (see Table S3). Altogether, our findings reveal that the quantities of interest are independent of the choice of the two investigated solvent model. Thus, we chose to continue with the SMD method.

**Table S1.** B3LYP/cc-pVTZ relative ground-state electronic energy of HTI pyrrole (6) in kcal/mol

<table>
<thead>
<tr>
<th>Solvent model</th>
<th>Solvent</th>
<th>$Z_z$</th>
<th>$Z_e$</th>
<th>$E_z$</th>
<th>$E_e$</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMD</td>
<td>toluene</td>
<td>0.0</td>
<td>-0.1</td>
<td>-3.5</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>0.0</td>
<td>-0.8</td>
<td>-2.4</td>
<td>3.1</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>0.0</td>
<td>-1.0</td>
<td>-1.9</td>
<td>2.9</td>
</tr>
<tr>
<td>IEFPCM</td>
<td>toluene</td>
<td>0.0</td>
<td>0.0</td>
<td>-3.6</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>0.0</td>
<td>-0.4</td>
<td>-2.6</td>
<td>3.6</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>0.0</td>
<td>-0.5</td>
<td>-2.3</td>
<td>3.5</td>
</tr>
</tbody>
</table>
Table S2. B3LYP/cc-pVTZ ground-state bond lengths of isomers Z\(_2\) and E\(_2\) of HTI pyrrole (6) in Å

<table>
<thead>
<tr>
<th>Isomer</th>
<th>Solvent model</th>
<th>Solvent</th>
<th>O(_1)=C(_2)</th>
<th>C(_2)=C(_3)</th>
<th>C(_3)=C(_4)</th>
<th>C(_4)=C(_5)</th>
<th>C(_5)-N(_6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z(_2)</td>
<td>SMD</td>
<td>toluene</td>
<td>1.222</td>
<td>1.487</td>
<td>1.353</td>
<td>1.421</td>
<td>1.383</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DCM</td>
<td>1.225</td>
<td>1.484</td>
<td>1.355</td>
<td>1.419</td>
<td>1.384</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DMSO</td>
<td>1.225</td>
<td>1.484</td>
<td>1.355</td>
<td>1.419</td>
<td>1.384</td>
</tr>
<tr>
<td></td>
<td>IEFPCM</td>
<td>toluene</td>
<td>1.222</td>
<td>1.486</td>
<td>1.354</td>
<td>1.420</td>
<td>1.384</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DCM</td>
<td>1.226</td>
<td>1.483</td>
<td>1.355</td>
<td>1.419</td>
<td>1.384</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DMSO</td>
<td>1.227</td>
<td>1.482</td>
<td>1.356</td>
<td>1.418</td>
<td>1.384</td>
</tr>
<tr>
<td>E(_2)</td>
<td>SMD</td>
<td>toluene</td>
<td>1.239</td>
<td>1.469</td>
<td>1.367</td>
<td>1.414</td>
<td>1.379</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DCM</td>
<td>1.241</td>
<td>1.468</td>
<td>1.368</td>
<td>1.414</td>
<td>1.379</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DMSO</td>
<td>1.240</td>
<td>1.468</td>
<td>1.368</td>
<td>1.414</td>
<td>1.380</td>
</tr>
<tr>
<td></td>
<td>IEFPCM</td>
<td>toluene</td>
<td>1.240</td>
<td>1.469</td>
<td>1.367</td>
<td>1.414</td>
<td>1.379</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DCM</td>
<td>1.241</td>
<td>1.468</td>
<td>1.368</td>
<td>1.414</td>
<td>1.380</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DMSO</td>
<td>1.242</td>
<td>1.467</td>
<td>1.369</td>
<td>1.413</td>
<td>1.380</td>
</tr>
</tbody>
</table>

Table S3. TDDFT/B3LYP/maug-cc-pVTZ wavelength of maximum absorbance (λ\(_{max}\)) in nm and the corresponding oscillator strength in parenthesis of four isomers of HTI pyrrole (6).

<table>
<thead>
<tr>
<th>Solvent model</th>
<th>Solvent</th>
<th>Z(_2)</th>
<th>Z(_2)</th>
<th>E(_2)</th>
<th>E(_2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMD</td>
<td>toluene</td>
<td>443 (0.50)</td>
<td>449 (0.48)</td>
<td>479 (0.34)</td>
<td>465 (0.36)</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>446 (0.49)</td>
<td>449 (0.48)</td>
<td>476 (0.32)</td>
<td>464 (0.35)</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>446 (0.49)</td>
<td>448 (0.49)</td>
<td>474 (0.33)</td>
<td>463 (0.35)</td>
</tr>
<tr>
<td>IEFPCM</td>
<td>toluene</td>
<td>443 (0.48)</td>
<td>449 (0.45)</td>
<td>478 (0.31)</td>
<td>465 (0.34)</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>446 (0.46)</td>
<td>450 (0.45)</td>
<td>477 (0.30)</td>
<td>466 (0.33)</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>448 (0.46)</td>
<td>450 (0.46)</td>
<td>476 (0.30)</td>
<td>466 (0.33)</td>
</tr>
</tbody>
</table>
1.3 Comparison of MP2 and B3LYP ground-state calculations

Having established the choice of the implicit solvent model, we then investigated the performance of the B3LYP functional and MP2 method in computing the relative energy of four isomers of compounds 6-9 at the corresponding optimized geometries in vacuum and in toluene, DCM and DMSO solutions. As shown in Tables S4 and S5, both B3LYP and MP2 produced similar trend of relative electronic energy, ΔE, It is interesting to note that the (Z - E) decreases as the solvent polarity increases. To directly compare computational and experimental results with respect to the most stable isomer, we computed the Gibbs free energy of each isomer and put a comparison of their relative Gibbs free energies, ΔG, in Table S6. The numbers in Table S6 and S5 are very similar to each other, indicating that comparing the electronic energy of the isomers is already representative of a full Gibbs free energy comparison. The calculations predict that the most stable configuration is isomer E, whereas in experiments, we observed that the most stable is either isomer Z or Z.E. It appears the chosen computational method in this work overstabilizes the E isomer, which has an intramolecular hydrogen bond. However, this discrepancy will not affect vertical excitation energies on the Franck-Condon (FC) geometries of each individual isomer. Thus, we proceed with the B3LYP geometry for the computation of TDDFT vertical excitation energy using the B3LYP functional, as this procedure has been demonstrated to obtain a very good agreement of the computed vertical excitation energy to the measured maximum absorption for a closely related hemiindigo photoswitches.

Table S4. MP2/cc-pVTZ relative ground-state electronic energy in kcal/mol of four isomers of four HTI photoswitches in different media. The last column indicates the (Z - E) energy difference.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Environment</th>
<th>Z</th>
<th>Z</th>
<th>E</th>
<th>E</th>
<th>(Z - E)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>vacuum</td>
<td>0.0</td>
<td>0.2</td>
<td>-4.2</td>
<td>5.0</td>
<td>4.4</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>0.0</td>
<td>-0.6</td>
<td>-3.0</td>
<td>4.1</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>0.0</td>
<td>-1.3</td>
<td>-2.2</td>
<td>3.1</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>0.0</td>
<td>-1.6</td>
<td>-1.8</td>
<td>3.0</td>
<td>0.2</td>
</tr>
<tr>
<td>7</td>
<td>vacuum</td>
<td>0.0</td>
<td>0.4</td>
<td>-2.9</td>
<td>5.4</td>
<td>3.3</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>0.0</td>
<td>-0.4</td>
<td>-1.9</td>
<td>4.6</td>
<td>1.5</td>
</tr>
<tr>
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<td>DCM</td>
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<td>-1.0</td>
<td>-1.2</td>
<td>3.7</td>
<td>0.2</td>
</tr>
<tr>
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<td>DMSO</td>
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<td>-1.2</td>
<td>-0.8</td>
<td>3.7</td>
<td>0.4</td>
</tr>
<tr>
<td>8</td>
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<td>0.3</td>
<td>-4.4</td>
<td>4.9</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>0.0</td>
<td>-0.6</td>
<td>-3.2</td>
<td>4.0</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>0.0</td>
<td>-1.2</td>
<td>-2.4</td>
<td>3.1</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>0.0</td>
<td>-1.5</td>
<td>-2.0</td>
<td>3.0</td>
<td>0.5</td>
</tr>
<tr>
<td>9</td>
<td>vacuum</td>
<td>0.0</td>
<td>0.3</td>
<td>-3.2</td>
<td>5.2</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>0.0</td>
<td>-0.4</td>
<td>-2.1</td>
<td>4.5</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
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<td>-1.5</td>
<td>3.6</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
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<td>-1.3</td>
<td>-1.1</td>
<td>3.5</td>
<td>0.2</td>
</tr>
</tbody>
</table>
Table S5. B3LYP/cc-pVTZ relative ground-state electronic energy in kcal/mol of four isomers of four HTI photoswitches in different media. The last column indicates the (Z<sub>E</sub> – E<sub>Z</sub>) energy difference.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Environment</th>
<th>Z&lt;sub&gt;E&lt;/sub&gt;</th>
<th>Z&lt;sub&gt;E&lt;/sub&gt;</th>
<th>E&lt;sub&gt;Z&lt;/sub&gt;</th>
<th>E&lt;sub&gt;E&lt;/sub&gt;</th>
<th>(Z&lt;sub&gt;E&lt;/sub&gt; – E&lt;sub&gt;Z&lt;/sub&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>vacuum</td>
<td>0.0</td>
<td>0.4</td>
<td>−4.7</td>
<td>4.3</td>
<td>5.1</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>0.0</td>
<td>−0.1</td>
<td>−3.5</td>
<td>4.0</td>
<td>3.4</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
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<td>−0.8</td>
<td>−2.4</td>
<td>3.1</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
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<td>−1.0</td>
<td>−1.9</td>
<td>2.9</td>
<td>0.9</td>
</tr>
<tr>
<td>7</td>
<td>vacuum</td>
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<td>0.5</td>
<td>−3.5</td>
<td>4.6</td>
<td>4.0</td>
</tr>
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<td>toluene</td>
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<tr>
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<td>1.8</td>
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</tr>
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<td>3.9</td>
</tr>
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<td></td>
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<td>2.7</td>
</tr>
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<td>DCM</td>
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<td>−1.8</td>
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<td>1.3</td>
</tr>
<tr>
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<td>DMSO</td>
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<td>−0.7</td>
<td>−1.3</td>
<td>3.4</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Table S6. B3LYP/cc-pVTZ relative ground-state Gibbs free energy in kcal/mol of four isomers of four HTI photoswitches in different media. The last column indicates the (Z<sub>E</sub> – E<sub>Z</sub>) energy difference.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Environment</th>
<th>Z&lt;sub&gt;E&lt;/sub&gt;</th>
<th>Z&lt;sub&gt;E&lt;/sub&gt;</th>
<th>E&lt;sub&gt;Z&lt;/sub&gt;</th>
<th>E&lt;sub&gt;E&lt;/sub&gt;</th>
<th>(Z&lt;sub&gt;E&lt;/sub&gt; – E&lt;sub&gt;Z&lt;/sub&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>vacuum</td>
<td>0.0</td>
<td>0.9</td>
<td>−3.4</td>
<td>4.9</td>
<td>4.3</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
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<td>−0.3</td>
<td>−3.1</td>
<td>3.8</td>
<td>2.8</td>
</tr>
<tr>
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<td>DCM</td>
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<td>3.0</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>0.0</td>
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<td>−1.3</td>
<td>3.0</td>
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</tr>
<tr>
<td>7</td>
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</tr>
<tr>
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<td>toluene</td>
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<td>−0.4</td>
<td>−2.3</td>
<td>4.4</td>
<td>1.9</td>
</tr>
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<td></td>
<td>DCM</td>
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<td>−1.6</td>
<td>3.8</td>
<td>0.6</td>
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<tr>
<td></td>
<td>DMSO</td>
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<td>−1.0</td>
<td>−0.7</td>
<td>2.9</td>
<td>0.3</td>
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<tr>
<td>8</td>
<td>vacuum</td>
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<td>−3.5</td>
<td>4.9</td>
<td>4.3</td>
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<tr>
<td></td>
<td>toluene</td>
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<td>−0.2</td>
<td>−2.5</td>
<td>4.1</td>
<td>2.3</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
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<td>−1.0</td>
<td>−1.7</td>
<td>3.0</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>0.0</td>
<td>−1.2</td>
<td>−1.6</td>
<td>2.8</td>
<td>0.4</td>
</tr>
<tr>
<td>9</td>
<td>vacuum</td>
<td>0.0</td>
<td>0.8</td>
<td>−2.3</td>
<td>5.1</td>
<td>3.1</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>0.0</td>
<td>0.1</td>
<td>−1.7</td>
<td>4.2</td>
<td>1.8</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>0.0</td>
<td>−0.6</td>
<td>−1.1</td>
<td>3.4</td>
<td>0.5</td>
</tr>
<tr>
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<td>−1.0</td>
<td>3.1</td>
<td>0.0</td>
</tr>
</tbody>
</table>
1.4 Vertical excitation energy of the second series of HTI photoswitches

In Table S7, we list the computed vertical excitation energy of four HTI photoswitches belonging to the second series in different media to complement data in Table 1 of the manuscript. Note (i) the redshifting of the $\lambda_{\text{max}}$ and the increasing of oscillator strength when the molecule is embedded in a solution phase and (ii) that the solvent polarity only slightly alters the absorption profile.

Table S7. TDDFT/B3LYP/maug-cc-pVTZ wavelength of maximum absorbance ($\lambda_{\text{max}}$) in nm and the corresponding oscillator strength in parenthesis of four HTI photoswitches different in the location and the number of fused aromatic rings.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Environment</th>
<th>$Z_2$</th>
<th>$Z_4$</th>
<th>$E_2$</th>
<th>$E_4$</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>vacuum</td>
<td>422 (0.33)</td>
<td>431 (0.30)</td>
<td>464 (0.20)</td>
<td>450 (0.22)</td>
</tr>
</tbody>
</table>
<pre><code>| toluene    | 443 (0.50) | 449 (0.48) | 475 (0.32) | 464 (0.35) |
| DCM        | 446 (0.49) | 449 (0.48) | 476 (0.32) | 464 (0.35) |
| DMSO       | 446 (0.49) | 448 (0.49) | 474 (0.33) | 463 (0.35) |
</code></pre>
<p>| 7        | vacuum      | 447 (0.51) | 450 (0.49) | 490 (0.34) | 476 (0.37) |
| toluene    | 471 (0.71) | 471 (0.70) | 509 (0.51) | 495 (0.53) |
| DCM        | 473 (0.68) | 471 (0.68) | 506 (0.48) | 494 (0.50) |
| DMSO       | 473 (0.67) | 469 (0.68) | 504 (0.48) | 492 (0.50) |
| 8        | vacuum      | 443 (0.27) | 452 (0.23) | 472 (0.18) | 464 (0.17) |
| toluene    | 459 (0.52) | 465 (0.48) | 483 (0.37) | 474 (0.35) |
| DCM        | 460 (0.52) | 464 (0.51) | 479 (0.37) | 471 (0.36) |
| DMSO       | 460 (0.53) | 462 (0.53) | 478 (0.37) | 470 (0.37) |
| 9        | vacuum      | 465 (0.45) | 468 (0.40) | 499 (0.31) | 487 (0.30) |
| toluene    | 484 (0.74) | 486 (0.72) | 515 (0.54) | 501 (0.52) |
| DCM        | 485 (0.72) | 487 (0.72) | 510 (0.51) | 499 (0.51) |
| DMSO       | 484 (0.72) | 482 (0.73) | 508 (0.51) | 497 (0.50) |</p>
1.5 Computational details of multireference wavefunction calculations

Multireference wavefunction calculations are performed mainly to investigate the possibility of ESIPT on isomer E. We employ state-averaged complete active-space self-consistent-field (SAn-CASSCF) wave function involving n singlet states with equal weights over the states. For HTI indole (7), three (n=3) states are considered (S₀, S₁, and S₂), and the active space consists of four electrons in three orbitals (see Figure S3), i.e. CAS(4,3). This active space is adequate to model the three states because, from a comparison with SA3-CASSCF calculations using larger active space, i.e. CAS(12,12), the main configuration state function of the three states involves three orbitals (Figure S4) that resemble the CAS(4,3) orbitals. The most important determinant in S₀ is the doubly occupied RHF configuration, i.e., orbitals Aₓ–H and Bₓ–H are doubly occupied, whereas orbital Cₓ–H is empty (X=O,N). S₁ is dominated by an excitation from orbital Bₓ–H to Cₓ–H. The main excitation in S₂ is an excitation from orbital Aₓ–H to Cₓ–H. Note that, the proton-transfer geometry used to compute the SA3-CASSCF wavefunction and plot the active orbitals (depicted in Figures S3b and S4b) is the optimized excited-state (S₁) geometry.

![Figure S2](image)

*Figure S2.* Three active orbitals in a CAS(4,3) active space utilized in SA3-CASSCF and MS3-CASPT2 calculations on the ground-state geometry (a) and proton-transfer S1 geometry (b) of 7.
Figure S3. Three most important SA3-CASSCF and MS3-CASPT2 active orbitals in a CAS(12,12) active space on the ground-state geometry (a) and proton-transfer S1 geometry (b) of 7.

For HTI pyrrole (6), the active space (Figure S5) is slightly larger than that of HTI indole in order to cover all \( \pi\pi^* \) state involved in the ESIPT process. As shown in Table S10, the order of the \( \pi\pi^* \) state is different in both geometries. For instance, the \( A_{N-H} \rightarrow D_{N-H} \) excitation characterizes \( S_3 \) in the ground-state geometry whereas it is the dominant excitation for \( S_1 \) in the proton-transfer geometry.

Figure S4. Four active orbitals in a CAS(6,4) active space utilized in SA4-CASSCF and MS4-CASPT2 calculations on the ground-state geometry (a) and proton-transfer S1 geometry (b) of 6.
Table S8. The most important excitation of three singlet excited states of two $E_2$ tautomers of HTI pyrrole (6) different in the relative position of the polar hydrogen atom

<table>
<thead>
<tr>
<th>State</th>
<th>Ground-state geometry</th>
<th>Proton-transfer geometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S_1$</td>
<td>$C_{N-H} \rightarrow D_{N-H}$</td>
<td>$A_{O-H} \rightarrow D_{O-H}$</td>
</tr>
<tr>
<td>$S_2$</td>
<td>$B_{N-H} \rightarrow D_{N-H}$</td>
<td>$C_{O-H} \rightarrow D_{O-H}$</td>
</tr>
<tr>
<td>$S_3$</td>
<td>$A_{N-H} \rightarrow D_{N-H}$</td>
<td>$B_{O-H} \rightarrow D_{O-H}$</td>
</tr>
</tbody>
</table>

To account for the missing dynamical electron correlation, the energy is refined using multi-state complete-active-space second-order perturbation theory (MS-CASPT2) method$^{13-15}$ using the same active space, basis set, and the same number of states. The gradients of the electronic energy with respect to nuclear coordinates are computed analytically for the CASSCF wave functions$^{16}$ and numerically for the CASPT2 method. In the CASPT2 calculations, we employ the default zero-order Hamiltonian$^{17}$ with an IPEA shift of 0.25 a.u. and, to eliminate intruder-state problems, an imaginary level shift$^{18}$ of 0.2 a.u. is employed. Furthermore, to speed up the CASPT2 calculations, the Cholesky decomposition of the two-electron integrals$^{19}$ with a default threshold of $10^{-4}$ is used. All multireference excited-state calculations use ANO-S-VDZP basis set without polarization functions on hydrogen atoms (denoted as ANO-S-VDZP') and are performed with OpenMolcas package.$^{20}$
1.6 CASCF and CASPT2 results on compound 6

Exploration of the potential energy surface of $S_1$ begins with geometry optimization starting from the ground-state MP2 geometry at the level of SA3-CASSCF(4,3). Our computation found an in-plane minimum (min$_1$) where the hydrogen is covalently bonded to the nitrogen atom as in the FC geometry case. For the investigation of the possibility of ESIPT, we moved the hydrogen atom covalently bonded to the nitrogen atom in the ground-state optimized geometry closer to the oxygen atom by 1.0 Å, and started the $S_1$ geometry optimization. The computation yields another in-plane stationary point in which the proton is covalently bonded to the oxygen atom. Interestingly, this proton-transfer $S_1$ geometry (min$_2$) is more stable by 12.3 kcal/mol (SA3-CASSCF) or 11.1 kcal/mol (MS3-CASPT2) than the previously located $S_1$ minimum (min$_1$).

Table S9. Optimized bond lengths in Å of tautomers of the E$_2$ isomer of HTI indole (7) in different states.

<table>
<thead>
<tr>
<th>Geometry</th>
<th>O$_1$=C$_2$</th>
<th>C$_2$=C$_3$</th>
<th>C$_3$=C$_4$</th>
<th>C$_4$=C$_5$</th>
<th>C$_5$=N$_6$</th>
</tr>
</thead>
<tbody>
<tr>
<td>S0 MP2</td>
<td>1.250</td>
<td>1.489</td>
<td>1.387</td>
<td>1.430</td>
<td>1.385</td>
</tr>
<tr>
<td>S1 SA3-CASSCF(4,3), min$_1$</td>
<td>1.246</td>
<td>1.472</td>
<td>1.361</td>
<td>1.474</td>
<td>1.313</td>
</tr>
<tr>
<td>S1 SA3-CASSCF(4,3), min$_2$</td>
<td>1.321</td>
<td>1.409</td>
<td>1.372</td>
<td>1.473</td>
<td>1.362</td>
</tr>
</tbody>
</table>

The fact that there are two in-plane minima indicates the presence of a barrier connecting them. We therefore scan the $S_1$ potential energy surface along the O—H bond coordinate at the level of SA3-CASSCF(4,3) and show the energy profiles of $S_0$, $S_1$ and $S_2$ in Figure S6. There is a small barrier of 1.4 kcal/mol to overcome from min$_1$ to min$_2$ and this barrier is unrelated to the crossing with higher $S_2$ state. However, the refined MS3-CASPT2(4,3)/SA3-CASSCF(4,3) excited-state ($S_1$) potential energy profile (Figure 1 in main text) reveals that the ESIPT pathway is barrier-less, and has no well-defined crossing points to either the upper ($S_2$) and lower ($S_0$) states. We thus note the significant contribution of dynamic correlation to the pathways.

![Figure S5. SA3-CASSCF(4,3) relative electronic energy of $S_0$, $S_1$ and $S_2$ on the geometries obtained by scanning the $S_1$ potential energy surface along the O—H bond.](image)

S-14
1.7 CASSCF and CASPT2 results on compound 6

In Table S10, we show the relative energy of two in-plane excited-state (S1) E2 tautomers of HTI pyrrole (6) obtained from three different calculations. The effect of the missing electron correlation in SA4-CASSCF(6,4) energy is very apparent in this case: MS4-CASPT2(6,4)/SA4-CASSCF(6,4) calculation reverses the order of the SA4-CASSCF(6,4) relative energy such that the min1 geometry is more stable than the min2 (proton-transfer) geometry. As the size of the HTI pyrrole (5) is smaller than that of HTI indole (6), excited-state (S1) CASPT2 geometry optimization is computationally affordable for 5. In Table S12, we show that the MS4-CASPT2(6,4) energy ordering of the two minima is the same as that of MS4-CASPT2(6,4)/SA4-CASSCF(6,4).

Table S10. Relative energy of two excited-state (S1) E2 tautomers of HTI pyrrole (6) in kcal/mol

<table>
<thead>
<tr>
<th>Method</th>
<th>E(min2) − E(min1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA4-CASSCF(6,4)</td>
<td>−6.6</td>
</tr>
<tr>
<td>MS4-CASPT2(6,4)/SA4-CASSCF(6,4)</td>
<td>6.2</td>
</tr>
<tr>
<td>MS4-CASPT2(6,4)</td>
<td>7.5</td>
</tr>
</tbody>
</table>

In Table S11, we list the bond lengths of tautomers of the E/Z isomer of HTI indole (6) in different states. It is interesting to note that the CASSCF and CASPT2 bond-length pattern of the min1 geometry is different considerably, while those of the min2 are in quite good agreement with each other. As the E/Z photoisomerization occur experimentally, the elongation of the formal C3=C4 double bond from the FC geometry to the MS4-CASPT2(6,4) S1 min1 geometry indicates the weakening of such bond easing the rotation around it. Therefore, the MS4-CASPT2(6,4) method yield more representative picture in the excited states. It is important to note that, while the SA4-CASSCF(6,4) and MS4-CASPT2(6,4) excited-state geometries are quite different especially for the min1 geometry, performing MS4-CASPT2(6,4) single-point calculations on top the SA4-CASSCF(6,4) geometries still results in the correct energy ordering of min1 and min2 as benchmarked against the full MS4-CASPT2(6,4) method (Table S11).

Table S11. Optimized bond lengths in Å of tautomers of the E2 isomer of HTI indole (7) in different states using different methods.

<table>
<thead>
<tr>
<th>Geometry</th>
<th>O1=C2</th>
<th>C2=C3</th>
<th>C3=C4</th>
<th>C4=C5</th>
<th>C5=N6</th>
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</thead>
<tbody>
<tr>
<td>S0 MP2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1 SA4-CASSCF(6,4), min1</td>
<td>1.239</td>
<td>1.523</td>
<td>1.340</td>
<td>1.477</td>
<td>1.337</td>
</tr>
<tr>
<td>S1 SA4-CASSCF(6,4), min2</td>
<td>1.326</td>
<td>1.398</td>
<td>1.384</td>
<td>1.479</td>
<td>1.349</td>
</tr>
<tr>
<td>S2 MS4-CASPT2(6,4), min1</td>
<td>1.294</td>
<td>1.474</td>
<td>1.429</td>
<td>1.403</td>
<td>1.417</td>
</tr>
<tr>
<td>S2 MS4-CASPT2(6,4), min2</td>
<td>1.348</td>
<td>1.440</td>
<td>1.394</td>
<td>1.465</td>
<td>1.384</td>
</tr>
</tbody>
</table>
1.8 Ground-state relative energies and vertical excitation energies of the extended third series of HTI photoswitches

In Table S12, we show the DLPNO-MP2/cc-pVTZ relative ground-state electronic energy of four isomers in different environment. The findings and analysis are similar to those of the second series of HTI photoswitches (Table S4).

Table S12. DLPNO-MP2/cc-pVTZ relative ground-state electronic energy in kcal/mol of four isomers of four HTI oligopyrrole in different media. The last column indicates the \((ZE - EZ)\) energy difference.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Environment</th>
<th>(Z_E)</th>
<th>(Z_Z)</th>
<th>(E_Z)</th>
<th>(E_E)</th>
<th>((Z_E - E_Z))</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTI pyrrole (6)</td>
<td>vacuum</td>
<td>0.0</td>
<td>0.2</td>
<td>-4.2</td>
<td>5.0</td>
<td>4.4</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>0.0</td>
<td>-0.6</td>
<td>-3.0</td>
<td>4.1</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>0.0</td>
<td>-1.3</td>
<td>-2.2</td>
<td>3.1</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>0.0</td>
<td>-1.6</td>
<td>-1.8</td>
<td>3.0</td>
<td>0.2</td>
</tr>
<tr>
<td>HTI bipyrrole  (10)</td>
<td>vacuum</td>
<td>0.0</td>
<td>0.9</td>
<td>-4.4</td>
<td>5.2</td>
<td>5.3</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
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<td>-0.2</td>
<td>-3.6</td>
<td>4.2</td>
<td>3.4</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
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<td>-1.0</td>
<td>-3.2</td>
<td>3.3</td>
<td>2.2</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>0.0</td>
<td>-1.2</td>
<td>-2.9</td>
<td>3.2</td>
<td>1.7</td>
</tr>
<tr>
<td>HTI tripyrrole</td>
<td>vacuum</td>
<td>0.0</td>
<td>0.9</td>
<td>-4.7</td>
<td>5.3</td>
<td>5.6</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>0.0</td>
<td>-0.1</td>
<td>-3.7</td>
<td>4.2</td>
<td>3.6</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>0.0</td>
<td>-0.9</td>
<td>-3.2</td>
<td>3.2</td>
<td>2.3</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>0.0</td>
<td>-1.2</td>
<td>-2.9</td>
<td>3.2</td>
<td>1.7</td>
</tr>
</tbody>
</table>

In Table S13, we show the computed vertical excitation energy of three HTI photoswitches belonging to the third series of HTI photoswitches in different media, extended to include compounds which have not yet been synthesized. Adding more pyrrole rings covalently seem to increase both the maximum absorbance and the oscillator strength. We note that extending the conjugation of the molecule any further, would likely separate the location of HOMO and LUMO orbitals further (as illustrated in Figure S2), increasing the charge-transfer character of the \(S_1\). Therefore, TDDFT results using B3LYP functional, which is known to perform poorly for charge-transfer excited state,\(^{21-23}\) will become inaccurate for larger molecules.
**Table S13.** TDDFT/B3LYP/cc-pVTZ//DLPNO/cc-pVTZ wavelength of maximum absorbance ($\lambda_{\text{max}}$) in nm and the corresponding oscillator strength in parenthesis of four HTI photoswitches different in the number of pyrrole moieties.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Environment</th>
<th>$Z_2$</th>
<th>$Z_4$</th>
<th>$E_2$</th>
<th>$E_4$</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTI pyrrole (6)</td>
<td>vacuum</td>
<td>419 (0.34)</td>
<td>427 (0.30)</td>
<td>463 (0.21)</td>
<td>449 (0.23)</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>440 (0.52)</td>
<td>445 (0.49)</td>
<td>478 (0.34)</td>
<td>464 (0.37)</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>442 (0.50)</td>
<td>444 (0.49)</td>
<td>475 (0.33)</td>
<td>463 (0.36)</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>441 (0.50)</td>
<td>442 (0.50)</td>
<td>474 (0.33)</td>
<td>461 (0.36)</td>
</tr>
<tr>
<td>HTI bipyrrrole (10)</td>
<td>vacuum</td>
<td>466 (0.65)</td>
<td>464 (0.75)</td>
<td>511 (0.47)</td>
<td>482 (0.65)</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>503 (0.85)</td>
<td>502 (1.00)</td>
<td>543 (0.65)</td>
<td>516 (0.92)</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>509 (0.86)</td>
<td>509 (1.02)</td>
<td>541 (0.64)</td>
<td>519 (0.94)</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>510 (0.86)</td>
<td>510 (1.02)</td>
<td>539 (0.64)</td>
<td>520 (0.95)</td>
</tr>
<tr>
<td>HTI tripyrrrole</td>
<td>vacuum</td>
<td>515 (0.78)</td>
<td>512 (0.87)</td>
<td>559 (0.67)</td>
<td>520 (0.91)</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>564 (0.98)</td>
<td>561 (1.10)</td>
<td>604 (0.85)</td>
<td>568 (1.14)</td>
</tr>
<tr>
<td></td>
<td>DCM</td>
<td>578 (0.98)</td>
<td>578 (1.09)</td>
<td>609 (0.85)</td>
<td>581 (1.14)</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>582 (0.98)</td>
<td>581 (1.08)</td>
<td>610 (0.85)</td>
<td>584 (1.14)</td>
</tr>
</tbody>
</table>

**Figure S6.** B3LYP/cc-pVTZ HOMO (left) and LUMO (right) of HTI pyrrole (top) and tripyrrole (bottom) Z-isomers.
2 General directions

**Chemical reactions** were carried out under an inert atmosphere of nitrogen or argon using solvents of HPLC grade or anhydrous solvents (MeCN, DCM, DMF, DMSO, Et₂O, THF and PhMe) obtained from a PureSolv system (Innovative Technology, Tronyx). Synthesis was performed in the dark or reaction equipment was wrapped with aluminium foil to shield it from light. Commercially available reagents were used as received from Sigma Aldrich, Combi-Blocks, Fisher Scientific, Strem or Merck without further purification. Reactions were monitored by thin layer chromatography (TLC) and/or reversed-phase ultra-performance liquid chromatography mass spectrometry (RP-UPLC-MS).

**Analytical TLC** was performed on Merck aluminum sheets covered with silica gel (60 F₂₅₄). The plates were visualized using UV-light or stained by dipping in a developing agent followed by gentle heating. KMnO₄ stain was used as developing agent [3 g in H₂O (300 mL), K₂CO₃ (20 g) and 5% aqueous NaOH (5 mL)].

**Column chromatography** was performed using Merck Si 60A (40-63 μm) silica gel for flash column chromatography (FCC) and Merck Si 60A (15-40 μm) silica gel for dry column vacuum chromatography (DCVC).

**Characterization of new compounds** were done by TLC, NMR, MS (ESI), HRMS (ESI), melting point, UV-Vis spectroscopy, fluorescence spectroscopy and/or HPLC retention time (byproducts were not fully characterized).

**Structural assignments** were made for new compounds using a combination of 2D NMR techniques when relevant (gCOSY, DQF-COSY, HSQC, HMBC, H2BC, 2D NOESY). For the recording of ¹H NMR and ¹³C NMR either a 400 MHz Bruker Ascend with a Prodigy CryoProbe and Avance IIIHD NanoBay console, 400 MHz Bruker UltraShield Plus with a Room Temperature Broadband ¹³F Observe (RT BBFO) SmartProbe and Avance III console, 800 MHz Bruker Ascend refitted with a TCI (Triple Resonance NMR ‘Inverse’) CryoProbe and Avance IIIHD console, or 800 MHz Oxford instruments refitted with a TCI CryoProbe and Avance III console was used. Measurements were performed with a sample temperature of 25°C unless otherwise stated. The chemical shifts (δ) are reported in parts per million (ppm) and the coupling constants (J) in Hz. Spectra were referenced using the residual solvent peaks of the respective solvents; DMSO (δ 2.50 ppm for ¹H NMR DMSO-d₆ and δ 39.52 ppm for ¹³C NMR DMSO-d₆), CDCl₃ (δ 7.26 ppm for ¹H NMR CHCl₃ and δ 77.16 ppm for ¹³C NMR CDCl₃), MeOD (δ 3.31 ppm for ¹H NMR CHD₃OD and δ 49.00 ppm for ¹³C NMR CD₂OD), DCM (δ 5.32 ppm for ¹H NMR CHDCl₂ and δ 54.00 ppm for ¹³C NMR CD₂Cl₂). When THF-H₈ was used as NMR solvent, a double solvent suppression of the proton signals was performed. The following abbreviations were used to report peak multiplicities: s = singlet, bs = broad singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublets of doublets, dt = doublet of triplets, t = triplet, td = triplet of doublets, tt = triplet of triplets, q = quartet, dq = doublet of quartets, m = multiplet. CDCl₃ was treated with K₂CO₃ and filtered before use.

**Analytical RP-UPLC-MS (ESI)** was performed on an S2 Waters AQUITY RP-UPLC system equipped with a diode array detector using a Thermo Accucore C18 column (d 2.6 μm, 2.1 x 50 mm; column temp: 50°C; flow: 1.0 mL/min). Eluents A (0.1% HCO₃H in H₂O) and B (0.1% HCO₃H in MeCN) were used with a linear gradient (5% B to 100% B) in 2.4 min or 4.8 min and then held for 0.1 min at 100% B (total run time: 2.6 min or 5.0 min). Injection volume was 2 µL. The LC system was coupled to a Single Quadrupole Detector (S/QD) 1 or SQD2 mass spectrometer.

**UHPLC-HRMS** analyses were measured on an Agilent Infinity 1290 UHPLC system (Agilent Technologies, Santa Clara, CA, USA) equipped with a diode array detector. Separation was obtained on an Agilent Poroshell 120 phenyl-hexyl column (d 2.7 μm, 2.1 x 250 mm; column temp: 60°C; flow: 0.35 mL/min).
An injection volume of 0.1 μL was used. MS detection was performed in positive detection on an Agilent 6545 Quadrupole Time-Of-Flight (QTOF) MS equipped with Agilent Dual Jet Stream electrospray ion source with a drying gas temperature of 250°C, gas flow of 8 L/min, sheath gas temperature of 300°C and flow of 12 L/min. Capillary voltage was set to 4000 V and nozzle voltage to 500 V. Mass spectra were recorded as centroid data for m/z 50–1000, with an acquisition rate of 10 spectra/s. Lock mass solution in 70:30 MeOH:H₂O was infused in the second sprayer using an extra LC pump at a flow of 15 μL/min using a 1:100 splitter. The solution contained 1 μM tributylamine (Sigma-Aldrich) and 10 μM Hexakis(2,2,3,3-tetrafluoropropoxy)phosphazene (Apollo Scientific Ltd., Cheshire, UK) as lock masses. The [M + H]+ ions (m/z 186.2216 and 922.0098 respectively) of both compounds were used.

**Melting points** were obtained using a Stuart SMP30 melting point apparatus.

**UV-Vis spectroscopy** was measured on an Analytik Jena Specord® 210 PLUS double beam spectrophotometer using precision cells 1088-QS made of quartz Suprasil with a 10 mm light path from Hellma® Analytics. Measurements were calibrated against air and pure dry solvent used to dissolve the respective samples to give a final concentration of 33 μM. Absorption wavelengths (λ) are reported in nm and the extinction coefficients (ε) in L·mol⁻¹·cm⁻¹. Unless otherwise stated, all included spectra were obtained after irradiation with the respective wavelength and photostationary state at 25°C. Spectra of (Z)-isomers are generally reported for non-irradiated samples (dark state) as these mostly gave exclusively the (Z)-isomer.

**UV-Vis thermal relaxation spectroscopy** was obtained similarly to UV-Vis spectroscopy. The relaxation of the metastable (E)-isomer to its stable (Z)-isomer was determined by measuring the absorption every 5 minutes for 10 hours at 28°C in the respective dry solvent unless otherwise stated. The sample was kept dark inside in the instrument. Lambda max (λmax) or representative wavelengths (λ) with a significant change between isomers were used to calculate thermal relaxation. Half-life was calculated similar to the literature²⁴-²⁶ by plotting the absorbance at a specific wavelength relevant for one isomer over time and fitting the data to an exponential using Graphpad Prism.

**Kinetic analysis of thermal E-to-Z isomerisation** was performed by looking at the initial rate of the thermal relaxation from the E-isomer to the Z-isomer assuming first order kinetics as described in V. Josef et al.²⁴

**Fluorescence spectroscopy** were recorded on a Perkin Elmer LS-55 fluorescence spectrophotometer using precision cells 101-QS made of quartz Suprasil with a 10 mm light path from Hellma® Analytics. Measurements were calibrated against air and pure dry solvent used to dissolve the respective samples to give a final concentration of 33 μM. Emission wavelengths (λ) are reported in nm. Unless otherwise stated, all included spectra were obtained after irradiation with the respective wavelength and photostationary state at 25°C.

**Photoirradiation** was carried out with LEDs purchased from Thorlabs (M340L4 (340 nm), M365L2 (365 nm), M415L4 (415 nm), M470L4 (470 nm), M530L3 (530 nm), M590L4 (590 nm), M625L4 (625 nm) and M660L4 (660 nm)) with collimator (SM2F32-A) and power supply/driver (LEDD18) to focus the light beam and control the current, respectively.

**HPLC quantification of photostationary state (PSS) composition** was performed with samples prepared in DCM (2 mg/mL) and irradiated (1 Amp) with respective LEDs in borosilicate glass HPLC vials purchased from Fischer Scientific (fischerbrand 11525884), unless otherwise stated. An Aliquot (0.25 mL) of the...
sample was transferred to a new HPLC vial and the DCM removed with a flow of nitrogen while the sample was kept dark. A solvent mixture of n-hexane/iPrOH (1:1) was added to give the final concentration (0.5 mg/mL). The samples were measured using a Waters 2695 Alliance Separations module HPLC with a ChiralPak AD-H column (5 µm, 250 x 4.6 mm) and a Waters 2996 PhotoDiode Array (PDA) detector. For details regarding the eluent system (n-hexane/iPrOH), see the results for each measured photoswitch. The same eluent system used for HPLC quantification of the respective photoswitch was also used in determining the isosbestic point of that photoswitch by UV-Vis spectroscopy. The composition was determined as area under the curve. Chromatograms are representatives.

**NMR photoisomerization** was achieved by irradiating an NMR sample of the respective compound in the respective deuterated solvent (unless otherwise stated) for 30 min in a 3 mm NMR standard tube using LEDs with wavelengths as described for the UV-Vis spectroscopy data of that compound. The Z/E ratio was determined by $^1$H NMR integration of the singlet enone β-proton or the pyrrole/indole-NH.

**$^1$H NMR thermal relaxation spectroscopy** was obtained similarly to the NMR photoisomerization. The relaxation of the metastable (E)-isomer to its stable (Z)-isomer was monitored by $^1$H NMR with spectra recorded every one hour for 24 hours (y-axes) and the integral of the pyrrole/indole-NH of the (E)-isomer plotted vs. time. The sample was kept dark inside the instrument at a constant temperature of 24°C. Occasionally, a low change in observed relaxation resulted in weak exponential fit. For these instances, half-lives $T_{1/2}$ were reported as worst case (lowest value) and not necessarily for the total 24 hours as indicated by the respective graphs.
3 General procedures

**General procedure A: Coupling of HTI (or derivatives) with mono-aldehydes**

To a heat gun-dried reaction vessel evacuated with inert atmosphere was added hemithioindigo (or derivative) (1 eq.) dissolved in benzene (0.10-0.30 M). Aldehyde (0.9-1 eq.) and piperidine (1-2 drops) were added and the reaction vessel transferred to a pre-warmed oil bath (40 or 100°C) and stirred for the indicated time before cooling to room temperature. A saturated aqueous NH₄Cl solution (10 mL) was added and the aqueous phase extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure by rotary evaporation. Purification by flash column or dry column vacuum chromatography on silica gel afforded the corresponding mono-substituted photoswitch.

**General procedure B: Coupling of HTI (or derivatives) with mono-aldehydes**

To a heat gun-dried reaction vessel evacuated with inert atmosphere was added hemithioindigo (or derivative) (1 eq.) dissolved in PhMe (0.14-0.25 M). Aldehyde (0.8-1 eq.) and piperidine (1-2 drops) were added and the reaction vessel transferred to a pre-warmed oil bath (40 or 100°C) and stirred for the indicated time before cooling to room temperature. n-Hexane (5 mL) was added and the reaction vessel transferred to an ice bath (0°C) for 30-45 min. The precipitate was filtered, washed with cold n-hexane until the filtrate ran clear and dried under high vacuum to afford the corresponding mono-substituted photoswitch.
4 Specific reaction procedures for intermediates and building blocks

Thiophenoxy acetic acid (SI 4)

To a 100 mL round-bottomed flask were added deionized H₂O (30 mL), 2-bromoacetic acid (1.99 g, 14.3 mmol, 1.0 eq.) and thiophenol (1.47 mL, 14.3 mmol, 1.0 eq.). 6 M aqueous NaOH (5.0 mL, 30.0 mmol, 2.1 eq.) was added at room temperature and the solution stirred for 22 h. The solution was acidified with dilute 1 M aqueous HCl and extracted with EtOAc (3 x 30 mL). The combined organic extracts were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure by rotary evaporation to afford the title compound SI 4 (2.39 g, 4.21 mmol, 99%) as a white solid.

The data is in accordance with previously reported work.²⁷

**TLC: R_f = 0.50 (1:1 EtOAc/n-heptane + 1% AcOH)**

**LCMS (ESI) [M]+** m/z calcd for C₉H₇O₂S: 167.0172, m/z found: 166.83 [M]+

R_t: 1.04 min (total run time: 2.6 min), purity >99%

**¹H NMR** (400 MHz, CDCl₃): δ 10.22 (s, 1H), 7.49 – 7.41 (m, 2H), 7.38 – 7.31 (m, 2H), 7.31 – 7.27 (m, 1H), 3.70 (s, 2H)

**¹³C NMR** (101 MHz, CDCl₃): δ 175.9, 134.6, 130.2, 129.3, 127.4, 36.7
Hemithioindigo (SI 6)

To an oven-dried reaction tube were added thiophenoxy acetic acid SI 1 (1.92 g, 11.4 mmol, 1.0 eq.) and DCM (20 mL, 0.570 M). The solution was purged with nitrogen for 5 min. Triflic acid (5.0 mL, 56.6 mmol, 5.0 eq.) was carefully added and the reaction tube transferred to a pre-warmed oil bath set to 40°C and stirred for 44 h. The reaction mixture was allowed to cool to room temperature before carefully poured into icy H₂O (200 mL). The aqueous phase was extracted with EtOAc (2 x 100 mL) and the combined organic extracts were washed with a saturated aqueous NaHCO₃ (100 mL) and brine (50 mL), dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure by rotary evaporation to afford the title compound SI 6 (1.09 g, 6.66 mmol, 58%) as an orange solid.

Important note: Store in a freezer under inert atmosphere to prevent oxidation and prolong shelf life.

The data is in accordance with previously reported work.²⁸

**TLC:** \( R_f = 0.80 \) (1:1 EtOAc/n-heptane + 1% AcOH)

**LCMS (ESI) [M+H]+**

\( m/z \) calcd for C₉H₇OS⁺: 151.0212, \( m/z \) found: 150.86 [M+H]+

**Rₜ:** 1.11-1.21 min (total run time: 2.6 min), purity >90%

**¹H NMR** (400 MHz, CDCl₃): \( \delta \) 7.78 (d, \( J = 6.7 \) Hz, 1H), 7.55 (t, \( J = 7.6 \) Hz, 1H), 7.43 (d, \( J = 8.0 \) Hz, 1H), 7.22 (t, \( J = 7.4 \) Hz, 1H), 3.80 (s, 2H)

**¹³C NMR** (101 MHz, CDCl₃): \( \delta \) 200.2, 154.4, 135.8, 131.1, 126.8, 124.9, 124.8, 39.4
(2-Naphthylthio)acetic acid (SI 3)

To a 100 mL round-bottomed flask were added deionized H$_2$O (30 mL), EtOH (20 mL), 2-bromoacetic acid (2.00 g, 14.4 mmol, 1.0 eq.) and 2-naphthalenethiol (2.00 mL, 14.5 mmol, 1.0 eq.). 6 M aqueous NaOH (5.0 mL, 30.0 mmol, 2.1 eq.) was added at room temperature and the solution stirred for 4.5 h. The reaction mixture was filtered and the filtrate acidified with dilute 2 M aqueous HCl. Another filtration was performed and the residues combined, washed with n-heptane (3 x 20 mL) and concentrated under reduced pressure by rotary evaporation to afford the (naphthylthio)acetic acid SI 3 (2.99 g, 13.7 mmol, 95%) as a white solid.

**TLC:** $R_f = 0.45$ (1:1 EtOAc/n-heptane + 1% AcOH)

**LCMS (ESI)** [M+H]$^+$ $m/z$ calcd for C$_{12}$H$_{11}$O$_2$S$: 219.0474 , m/z found: 218.91 [M+H]$^+$

$R_t$: 1.41 min (total run time: 2.6 min), purity >90%

**$^1$H NMR** (400 MHz, CD$_3$OD): δ 7.81 – 7.71 (m, 4H), 7.48 – 7.35 (m, 3H), 3.73 (s, 2H)

**$^{13}$C NMR** (101 MHz, CD$_3$OD): δ 175.7, 136.4, 135.4, 133.0, 129.2, 128.6, 128.0, 127.6, 127.5, 126.4, 39.0

**$^1$H NMR** (400 MHz, DMSO-d$_6$): δ 7.82 (d, $J = 8.1$ Hz, 1H), 7.78 (d, $J = 3.6$ Hz, 1H), 7.76 (d, $J = 3.1$ Hz, 1H), 7.72 (bs, 1H), 7.46 (ddd, $J = 8.2$, 6.8, 1.4 Hz, 1H), 7.43 – 7.36 (m, 2H), 3.67 (s, 2H)

**$^{13}$C NMR** (101 MHz, DMSO-d$_6$): δ 170.2, 136.4, 133.5, 130.6, 127.8, 127.5, 126.7, 126.5, 125.9, 125.0, 123.4, 38.1
**Naphtho[2,1-b]thiophen-1(2H)-one (SI 5)**

To an oven-dried reaction tube were added (2-naphthylthio)acetic acid 3 (1.00 g, 4.58 mmol, 1.0 eq.) and DCM (7.0 mL, 0.654 M). Triflic acid (2.0 mL, 22.9 mmol, 5.0 eq.) was carefully added, the solution purged with Ar for 5 min and the reaction tube transferred to a pre-warmed oil bath set to 40°C and stirred for 22 h. The reaction mixture was allowed to cool to room temperature before carefully poured onto iced H₂O (100 mL). The aqueous phase was extracted with DCM (3 x 30 mL) and the combined organic extracts were washed with a saturated aqueous NaHCO₃ (30 mL) and brine (30 mL), dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure by rotary evaporation to afford the title compound SI 5 (0.816 g, 4.08 mmol, 89%) as a dark orange solid.

Important note: Store in a freezer under inert atmosphere to prevent oxidation and prolong shelf life.

**TLC:** Rᵣ = 0.38 (1:6 EtOAc/n-heptane)

**LCMS (ESI)** [M+H]⁺ m/z calcld for C₁₂H₉OS⁺: 201.0369, m/z found: 200.93 [M+H]⁺

Rᵣ: 1.59 min (total run time: 2.6 min), purity >98%

**¹H NMR** (400 MHz, DMSO-d₆): δ 10.65 (s, 1H, enol-OH), 9.10 (d, J = 8.3 Hz, 1H), 7.99 (dd, J = 8.0, 1.4 Hz, 1H), 7.88 (d, J = 8.7 Hz, 1H), 7.78 (d, J = 8.7, 1H), 7.63 – 7.57 (m, 1H), 7.57-7.51 (m, 1H), 6.67 (s, 1H)

**¹³C NMR** (101 MHz, DMSO-d₆): δ 151.9, 135.6, 130.9, 129.2, 128.0, 126.0, 125.4, 125.1, 125.1, 123.6, 121.6, 98.5

Note: NMR spectroscopy in DMSO-d₆ resulted in the enol tautomer.
**1H,1'H-2,2'-Bipyrrrole (SI 8)**

To an oven-dried round-bottomed flask were added pyrrole (0.52 mL, 7.49 mmol, 1.0 eq.) in DCM (100 mL, 0.0745 M), PIFA (1.07 g, 2.48 mmol, 0.33 eq.) and TMSBr (0.65 mL, 4.97 mmol, 0.66 eq.) at -78°C. The reaction mixture was stirred for 80 min, allowed to slowly heat to room temperature and saturated aqueous NaHCO₃ (120 mL) was added. This was stirred vigorously for 30 min. The aqueous phase was extracted with DCM (5 x 30 mL) and the combined organic extracts were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure by rotary evaporation. Purified by DCVC (5% to 25% EtOAc in n-hexane with 1% increments) to afford the title compound **SI 8** (192 mg, 3.73 mmol, 39%).

The data is in accordance with previously reported work.²⁹

**LCMS** (ESI) [M+H]⁺/m/z calcd for C₈H₉N₂⁺: 133.0760, m/z found: 132.95 [M+H]⁺

Rₜ: 1.08 min (total run time: 2.6 min), purity >99%

**¹H NMR** (400 MHz, CDCl₃): δ 8.31 (bs, 2H), 6.81 – 6.71 (m, 2H), 6.29 – 6.19 (m, 4H)

**¹³C NMR** (101 MHz, CDCl₃): δ 126.1, 117.7, 109.6, 103.7
1H,1'H-[2,2'-Bipyrrole]-5-carbaldehyde (SI 9)

To an oven-dried round-bottomed flask was added bipyrrrole 5 (151 mg, 1.14 mmol, 1.0 eq.) and DMF (7.5 mL, 0.152 M). The solution was cooled to 0°C, and POCl₃ (0.10 mL, 1.07 mmol, 1.0 eq.) was added using a Hamilton syringe. The reaction mixture was stirred at 0°C for 2 h and saturated aqueous Na₂CO₃ (40 mL) was added. The mixture was heated to 70°C for 30 min, cooled to room temperature and filtered. The residue was washed with H₂O, cold MeOH, cold Et₂O and cold n-pentane to afford the title compound SI 9 (52.6 mg, 0.328 mmol, 29%) as a crystalline green-yellow solid.

Data is in accordance with previously reported work.³⁰

TLC: Rᵢ = 0.52 (1:1 EtOAc/n-heptane)

LCMS (ESI) [M+H⁺] m/z calcd for C₉H₉N₂O⁺: 161.0709 , m/z found: 160.94 [M+H⁺]

Rᵢ: 1.00 min (total run time: 2.6 min), purity >99%

¹H NMR (400 MHz, DMSO-d₆): δ 11.97 (s, 1H), 11.23 (s, 1H), 9.34 (s, 1H), 7.00 (d, J = 3.9 Hz, 1H), 6.88 (q, J = 2.1 Hz, 1H), 6.75 – 6.70 (m, 1H), 6.53 (d, J = 3.9 Hz, 1H), 6.11 (q, J = 3.1, 2.5 Hz, 1H)

¹³C NMR (101 MHz, DMSO-d₆): δ 177.4, 134.6, 132.0, 123.5, 119.9, 109.2, 107.5, 106.2

Note: There is one quaternary carbon signal missing from the ¹³C NMR spectrum.
5 Specific reaction procedures and analyses of photoswitches

(Z)-2-(Naphthalen-1-ylmethylene)benzo[b]thiophen-3(2H)-one (2)

Prepared according to general procedure A.

Hemithioindigo SI 6 (109 mg, 0.727 mmol, 1.0 eq.), benzene (4.0 mL, 0.182 M), 1-naphthaldehyde (1.04 mL, 0.726 mmol, 1.0 eq.). The aldehyde was added in two portions with stirring for 45 min under N₂ at 100°C in between. Stirring continued for 2 h at 100°C and 17 h at room temperature. Purified by flash column chromatography (0% to 15% EtOAc in n-heptane) to afford the title compound (Z/E)-1 (64.3 mg, 0.223 mmol, 31%) as an orange solid.

TLC: Rᵣ = 0.38 (1:6 EtOAc/n-heptane)

LCMS (ESI) [M+H]⁺ m/z calcd for C₁₉H₁₃OS⁺: 289.0682, m/z found: N/A [M+H]⁺

Rᵣ: 3.39 min (total run time: 5.2 min), purity >99%

¹H NMR (800 MHz, CD₂Cl₂): δ 8.71 (s, 1H, H-9), 8.27 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 7.1 Hz, 1H), 7.97 – 7.96 (m, 1H), 7.96 – 7.95 (m, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.65 – 7.57 (m, 4H), 7.54 (dd, J = 7.9, 1.8 Hz, 1H), 7.34 (td, J = 7.4, 1.6 Hz, 1H)

¹³C NMR (101 MHz, CD₂Cl₂): δ 188.5, 147.0, 135.9, 134.3, 133.7, 132.8, 132.0, 131.4, 131.2, 130.1, 129.4, 128.2, 127.6, 127.4, 127.1, 126.2, 126.0, 124.6, 124.1

HRMS-ESI [M+H]⁺ m/z calcd for C₁₉H₁₃OS⁺: 289.0682, m/z found: 289.0678 [M+H]⁺ (ppm error: -1.34)

(E)-1:

¹H NMR (400 MHz, CD₂Cl₂): δ 7.98 (m, 1H), 7.96 – 7.90 (m, 3H), 7.88 (s, 1H, H-9), 7.74 (ddd, J = 7.7, 1.4, 0.7 Hz, 1H), 7.63 – 7.56 (m, 2H), 7.56 – 7.52 (m, 2H), 7.51 – 7.48 (m, 1H), 7.26 (ddd, J = 8.1, 7.2, 1.0 Hz, 1H)

Note: A 1:5 (Z/E)-ratio was observed for (E)-10 by ¹H NMR.
UV-Vis spectroscopy

HTI 1-naphthalene (2) (33 μM in DCM)

\[ \lambda_{\max} (Z) = 447 \text{ nm} \]
\[ \varepsilon = 11170 \text{ L·mol}^{-1}·\text{cm}^{-1} \]

HTI 1-naphthalene (2) (33 μM in n-hexane/iPrOH 9:1)

\[ \lambda_{\max} (E) = 450 \text{ nm} \]
\[ \varepsilon = 4697 \text{ L·mol}^{-1}·\text{cm}^{-1} \]
HTI 1-naphthalene (2) (33 µM in PhMe)

![Absorption spectrum for HTI 1-naphthalene (2) with and without irradiation at 470 nm for 5 minutes.](image)

- $\lambda_{\text{max}}(\mathbf{Z}) = 447$ nm
- $\lambda_{\text{max}}(\mathbf{E}) = 453$ nm
UV-Vis thermal relaxation spectroscopy

HTI 1-naphthalene (2) (33 µM in PhMe)

**Note:** Concentrations of isomers were calculated using $\lambda_{\text{max}} (Z) = 447$ nm and 320 nm as representative for $\lambda_{\text{max}} (E) = 453$ nm.
HPLC conditions

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
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<td>ChiralPak AD-H column (5 µm, 250 x 4.6 mm)</td>
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<tr>
<td>Mobile Phase</td>
<td>90:10 n-hexane/iPrOH (isocratic, 1 mL/min)</td>
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<td>Isosbestic Point</td>
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<td>$t_R$(E)</td>
<td>11.88 min</td>
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<td>$t_R$(Z)</td>
<td>9.95 min</td>
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Solution composition (%E-isomer)

Initial solution composition before irradiation: E-isomer (0.00%) / Z-isomer (100.00%)

<table>
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<th>Time</th>
<th>530 nm</th>
</tr>
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<tr>
<td>5 min</td>
<td>85.60%</td>
<td>10 min</td>
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</tr>
<tr>
<td>10 min</td>
<td>86.14%</td>
<td>20 min</td>
<td>14.17%</td>
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Representative HPLC traces
(Z)-2-(Naphthalen-2-ylmethylene)benzo[b]thiophen-3(2H)-one (3)

Prepared according to general procedure A.

Hemithioindigo Si 6 (95.0 mg, 0.633 mmol, 1.0 eq.), benzene (4.0 mL, 0.158 M), 2-naphthaldehyde (88.9 mg, 0.569 mmol, 0.90 eq.). Stirred for 14 h under N2 at 100°C. Upon cooling to room temperature precipitation occurred. Purified by DCVC (0% to 10% EtOAc in n-heptane with 1% increments) to afford the title compound (Z)-3 (145 mg, 0.503 mmol, 88%) as an orange solid.

The data is in accordance with previously reported work.31 No photophysical properties reported.

**TLC:** 
$R_f = 0.70$ (1:1 EtOAc/n-heptane)

**LCMS** (ESI) [M+H]$^+$ m/z calcd for C$_{19}$H$_{13}$OS$: 289.0682$, m/z found: 288.97 [M+H]$^+$

R$_t$: 2.28 min (total run time: 2.6 min), purity >97%

$^1$H NMR (400 MHz, CDCl$_3$): δ 8.21 (s, 1H, H-15), 8.14 (s, 1H, H-9), 7.98 (d, J = 6.6 Hz, 1H, H-6), 7.96 – 7.91 (m, 2H), 7.89 – 7.84 (m, 1H), 7.81 (dd, J = 8.6, 1.8 Hz, 1H), 7.63 – 7.52 (m, 4H, H-1, H-3), 7.33 (td, J = 7.3, 1.0 Hz, 1H, H-2)

$^{13}$C NMR (101 MHz, CDCl$_3$): δ 188.8 (C-8), 146.3 (C-5), 135.4 (C-1), 134.0 (C-10/C-14), 133.9 (C-9), 133.4, 132.1 (C-15), 132.0, 130.7, 130.6, 129.0, 128.9, 127.9, 127.9, 127.3, 127.3, 127.0, 125.8 (C-2), 124.1

**HRMS-ESI** [M+H]$^+$ m/z calcd for C$_{19}$H$_{13}$OS$: 289.0682$, m/z found: 289.0684 [M+H]$^+$ (ppm error: 0.726)
UV-Vis spectroscopy

HTI 2-naphthalene (3) (33 µM in DCM)

HTI 2-naphthalene (3) (33 µM in n-hexane/iPrOH 9:1)
HTI 2-naphthalene (3) (33 μM in PhMe)

- λ_{max} (Z) = 444 nm
- λ_{max} (E) = 451 nm
UV-Vis thermal relaxation spectroscopy

HTI 2-naphthalene (3) (33 µM in PhMe)

Note: Concentrations of isomers were calculated using \( \lambda_{\text{max}} (Z) = 444 \) nm and 470 nm as representative for \( \lambda_{\text{max}} (E) = 451 \) nm.
HPLC conditions

<table>
<thead>
<tr>
<th>Column:</th>
<th>ChiralPak AD-H column (5 µm, 250 x 4.6 mm)</th>
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</thead>
<tbody>
<tr>
<td>Mobile Phase</td>
<td>90:10 n-hexane/iPrOH (isocratic, 1 mL/min)</td>
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<tr>
<td>Isosbestic Point</td>
<td>451 nm (in HPLC mobile Phase)</td>
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<tr>
<td>$t_R(E)$</td>
<td>12.42 min</td>
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<tr>
<td>$t_R(Z)$</td>
<td>11.38 min</td>
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Solution composition (%E-isomer)

Initial solution composition before irradiation: E-isomer (5.80%) / Z-isomer (94.20%)

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<th>Time</th>
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</tr>
<tr>
<td>10 min</td>
<td>82.25</td>
<td>4.03</td>
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Representative HPLC traces
(Z)-2-Benzylidenenaphtho[2,1-b]thiophen-1(2H)-one (4)

Prepared according to general procedure A.

Hemithioindigo derivative SI 5 (81.2 mg, 0.405 mmol, 1.0 eq.), benzene (4.0 mL, 0.101 M), benzaldehyde (0.36 mL, 0.354 mmol, 0.9 eq.). Stirred for 3 h under N₂ at 100°C. Purified by DCVC (0% to 5% EtOAc in n-heptane with 0.5% increments) to afford the title compound (Z)-4 (27 mg, 0.354 mmol, 26%) as a yellow orange solid.

TLC: Rᵢ = 0.40 (1:1 EtOAc/n-heptane)

LCMS (ESI) [M+H]+ m/z calcd for C₁₉H₁₃OS⁺: 289.0682, m/z found: 289.01 [M+H]+

Rᵢ: 3.55 min (total run time: 5.2 min), purity >99%

¹H NMR (400 MHz, DMSO-d₆): δ 9.25 (d, J = 8.4 Hz, 1H), 8.33 (d, J = 8.6 Hz, 1H), 8.10 (d, J = 8.1 Hz, 1H), 8.05 (s, 1H, H-13), 7.93 (d, J = 8.6 Hz, 1H), 7.88 (m, 1H, H-15/19), 7.86 (m, 1H, H-15/19), 7.83 – 7.77 (m, 1H), 7.69 – 7.50 (m, 4H)

¹³C NMR (101 MHz, DMSO-d₆): δ 188.0 (C-11), 149.7, 136.9, 133.8 (C-13), 133.8, 131.5, 130.9 (C-15/19), 130.9 (C-15/19), 130.7, 130.4, 130.2, 129.9, 129.4 (C-16/18), 129.4 (C-16/18), 129.1, 126.6, 122.3, 122.2, 122.1

HRMS-ESI [M+H]+ m/z calcd for C₁₉H₁₃OS⁺: 289.0682, m/z found: 289.0684 [M+H]+ (ppm error: 0.726)

Note: The ¹³C NMR peaks at 130.9 ppm and 129.4 ppm both correspond to 2 carbon signals each disclosed by 2D NMR.
UV-Vis spectroscopy

Phenyl HTI derivative (4) (33 µM in DCM)

Phenyl HTI derivative (4) (33 µM in n-hexane/iPrOH 9:1)
Phenyl HTI derivative (4) (33 µM in PhMe)

\[ \lambda_{\text{max}} (Z) = 442 \text{ nm} \]

\[ \lambda_{\text{max}} (E) = 461 \text{ nm} \]
**UV-Vis thermal relaxation spectroscopy**

Phenyl HTI derivative (4) (33 μM in PhMe)

**Note:** Concentrations of isomers were calculated using $\lambda_{\text{max}} (Z) = 442$ nm and 480 nm as representative for $\lambda_{\text{max}} (E) = 461$ nm.
HPLC conditions

<table>
<thead>
<tr>
<th>Column:</th>
<th>ChiralPak AD-H column (5 µm, 250 x 4.6 mm)</th>
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<tbody>
<tr>
<td>Mobile Phase</td>
<td>90:10 n-hexane/iPrOH (isocratic, 1 mL/min)</td>
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<tr>
<td>Isosbestic Point</td>
<td>467 nm (in HPLC mobile Phase)</td>
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<tr>
<td>t_R(E)</td>
<td>8.05 min</td>
</tr>
<tr>
<td>t_R(Z)</td>
<td>9.37 min</td>
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Solution composition (%E-isomer)

Initial solution composition before irradiation: E-isomer (0.00%) / Z-isomer (100.00%)

<table>
<thead>
<tr>
<th>Time</th>
<th>470 nm</th>
<th>530 nm</th>
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<tr>
<td>10 min</td>
<td>59.77</td>
<td>12.17</td>
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<tr>
<td>20 min</td>
<td>75.00</td>
<td>11.28</td>
</tr>
<tr>
<td>30 min</td>
<td>77.13</td>
<td>11.31</td>
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</table>

Note: The sample was irradiated in DCM following a direct injection.

Representative HPLC traces
(Z)-2-(Naphthalen-2-ylmethylene)naphtho[2,1-b]thiophen-1(2H)-one (5)

Prepared according to general procedure A. Hemithioindigo derivative SI 5 (83.1 mg, 0.415 mmol, 1.0 eq.), benzene (4.0 mL, 0.104 M), 2-naphthaldehyde (63.8 mg, 0.408 mmol, 1.0 eq.). Stirred for 2.5 h under N₂ at 100°C. Compound was judged sufficiently pure after work-up. Afforded the title compound (Z)-5 (70 mg, 0.207 mmol, 51%) as an orange-brown solid.

**TLC:** $R_f = 0.57$ (1:1 EtOAc/n-heptane)

$R_f$: 1.62 min (84%) + 2.17 min (16%) (total run time: 2.6 min)

**$^1$H NMR** (400 MHz, DMSO-$d_6$): $\delta$ 9.26 (dd, $J = 8.1$, 0.9 Hz, 1H), 8.44 (m, 1H), 8.32 (d, $J = 8.6$ Hz, 1H), 8.18 (s, 1H, H-13), 8.09 (m, 3H), 8.02 – 7.99 (m, 1H), 7.95 (m, 1H), 7.93 (m, 1H), 7.80 (ddd, $J = 8.4$, 6.9, 1.3 Hz, 1H), 7.68 – 7.61 (m, 3H)

**$^{13}$C NMR** (101 MHz, DMSO-$d_6$): $\delta$ 188.0 (C-12), 149.7, 137.0, 133.9 (C-13), 133.5, 132.9, 132.0, 131.6, 131.4, 130.5, 130.0, 129.1, 129.0, 128.8, 128.2, 127.8, 127.2, 126.7, 126.6, 122.4, 122.3, 122.1

**HRMS-ESI** [M+H]$^+$ $m/z$ calcd for C$_{23}$H$_{15}$OS$: 339.0838$, $m/z$ found: 339.0837 [M+H]$^+$ (ppm error: -0.295)

Note: There is one quaternary carbon signal missing from the $^{13}$C NMR spectrum. Performing 2D NMR did not disclose the missing peak.
UV-Vis spectroscopy

2-Naphthyl HTI derivative (5) (33 µM in DCM)

2-Naphthyl HTI derivative (5) (33 µM in n-hexane/iPrOH 9:1)
2-Naphthyl HTI derivative (5) (33 μM in PhMe)

[Graph]

Absorbance [a.u.]
Wavelength [nm]

λ_{max} (Z) = 462 nm
λ_{max} (E) = 468 nm

No irradiation
λ irradiation 470 nm 5 min
UV-Vis thermal relaxation spectroscopy

2-Naphthyl HTI derivative (5) (33 µM in PhMe)

**Note**: Concentrations of isomers were calculated using $\lambda_{\text{max}} (Z) = 462$ nm and 410 nm as representative for $\lambda_{\text{max}} (E) = 468$ nm.
**HPLC conditions**

<table>
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<tr>
<th><strong>Column:</strong></th>
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<tbody>
<tr>
<td><strong>Mobile Phase</strong></td>
<td>90:10 n-hexane/iPrOH (isocratic, 1 mL/min)</td>
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<td><strong>Isosbestic Point</strong></td>
<td>475 nm (in HPLC mobile Phase)</td>
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<td>$t_R(E)$</td>
<td>15.32 min</td>
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<td>$t_R(Z)$</td>
<td>12.90 min</td>
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**Solution composition (%E-isomer)**

Initial solution composition before irradiation: $E$-isomer (0.78%) / $Z$-isomer (99.22%)

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<tr>
<td>5 min</td>
<td>74.17</td>
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<td>10 min</td>
<td>75.09</td>
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Note: The sample (1 mg/mL) was irradiated in DCM following a direct injection.

Representative HPLC traces
**Z**-2-[[1H-Pyrrol-2-yl]methylene]benzo[b]thioph-3(2H)-one (6)

Prepared according to general procedure A.

Hemithioindigo SI 6 (87.0 mg, 0.582 mmol, 1.0 eq.), EtOH (2.0 mL, 0.291 M), 1H-pyrrole-2-carbaldehyde (56.0 mg, 0.593 mmol, 1.0 eq.). The solution was purged with N₂ for 10 min before piperidine was added. Stirred for 22 h under Ar at 40°C. Purified by DCVC (0% to 50% EtOAc in n-heptane with 5% increments) to afford the title compound (Z)-6 (70.0 mg, 0.308 mmol, 53%) as an orange solid.

The data is in accordance with previously reported work.²⁸

**TLC:** Rₛ = 0.41 (2:3 EtOAc/n-heptane)

**LC-MS (ESI)** [M+H]⁺ m/z calcd for C₁₃H₁₀NOS⁺: 228.0478, m/z found: 228.45 [M+H]⁺

Rₛ: 1.69 min (total run time: 2.6 min), purity >98%

**¹H NMR** (800 MHz, DMSO-d₆): δ 11.84 (s, 1H, H-14), 7.87 (s, 1H, H-9), 7.82 – 7.80 (m, 1H, H-6), 7.77 – 7.74 (m, 1H, H-3), 7.68 (ddd, J = 8.2, 7.1, 1.4 Hz, 1H, H-1), 7.37 (m, 1H, H-2), 7.28 (td, J = 2.6, 1.2 Hz, 1H, H-13), 6.79 – 6.76 (m, 1H, H-11), 6.42 (dt, J = 4.2, 2.3 Hz, 1H, H-12)

**¹³C NMR** (201 MHz, DMSO-d₆): δ 186.8 (C-8), 144.4 (C-5), 135.2 (C-1), 131.0 (C-4), 128.2 (C-10), 126.1 (C-6), 125.9 (C-2), 125.7 (C-13), 124.6 (C-3), 123.6 (C-9), 122.9 (C-7), 115.3 (C-11), 112.6 (C-12)

**HRMS-ESI** [M+H]⁺ m/z calcd for C₁₃H₁₀NOS⁺: 228.0478, m/z found: 228.0483 [M+H]⁺ (ppm error: 2.19)

**E-14:**

**¹H NMR** (800 MHz, DMSO-d₆): δ 13.31 (s, 1H, H-14), 7.90 (ddd, J = 7.8, 1.3, 0.7 Hz, 1H, H-6), 7.76 (tt, J = 3.6, 0.8 Hz, 1H, H-3), 7.68 (ddd, J = 8.1, 7.0, 1.3 Hz, 2H, H-1), 7.64 (s, 1H, H-9), 7.45 – 7.43 (m, 1H, H-13), 7.39 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H, H-2), 6.93 (dt, J = 3.6, 1.7 Hz, 1H, H-11), 6.45 (dt, J = 3.7, 2.3 Hz, 1H, H-12)

**¹³C NMR** (201 MHz, DMSO-d₆): δ 184.7 (C-8), 145.1 (C-5), 134.4 (C-1), 132.6 (C-4), 130.5 (C-10), 130.0 (C-9), 127.0 (C-13), 126.2 (C-6), 125.0 (C-2), 124.1 (C-3), 122.0 (C-11), 121.4 (C-7), 112.8 (C-12)

Note: A 1:2 (Z/E)-ratio was observed for (E)-14 by ¹H NMR.
UV-Vis spectroscopy

HTI pyrrole (6) (33 µM in DCM)

\[ \lambda_{\text{max}} (Z) = 457 \text{ nm} \]
\[ \varepsilon = 25770 \text{ L\cdotmol}^{-1}\cdot\text{cm}^{-1} \]

\[ \lambda_{\text{max}} (E) = 503 \text{ nm} \]
\[ \varepsilon = 21391 \text{ L\cdotmol}^{-1}\cdot\text{cm}^{-1} \]

HTI pyrrole (6) (33 µM in n-hexane/iPrOH 1:1)

\[ \lambda_{\text{max}} (Z) = 473 \text{ nm} \]

\[ \lambda_{\text{max}} (E) = 502 \text{ nm} \]
HTI pyrrole (6) (33 μM in n-hexane/iPrOH 9:1)

\[ \lambda_{\text{max}} (Z) = 475 \text{ nm} \]

\[ \lambda_{\text{max}} (E) = 500 \text{ nm} \]

HTI pyrrole (6) (33 μM in PhMe)

\[ \lambda_{\text{irradiation}} 415 \text{ nm 5 min} \]

\[ \lambda_{\text{max}} (Z) = 457 \text{ nm} \]

\[ \lambda_{\text{max}} (E) = 505 \text{ nm} \]
Fluorescence spectroscopy

HTI pyrrole (6) (33 μM in DCM)

No irradiation ExWL 370 nm
λ irradiation 415 nm 5 min ExWL 370 nm

λ_{max} (Z) = 485 nm
λ_{max} (E) = 541 nm

Stokes shift: 37 nm
Stokes shift: 28 nm

Excitation
Emission
UV-Vis thermal relaxation spectroscopy

HTI pyrrole (6) (33 µM in PhMe)

\[
\lambda_{\text{max}} (Z) = 457 \text{ nm}
\]

\[
\lambda_{\text{max}} (E) = 505 \text{ nm}
\]

\[
y = 32.933e^{-0.0000212x}
\]

\[
R^2 = 0.776
\]

\[
T_{\frac{1}{2}} = \text{nd}
\]
HPLC conditions

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<tr>
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<td>Isosbestic Point</td>
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<tr>
<td>$t_R(Z)$</td>
<td>12.38 min</td>
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Solution composition (%E-isomer)

Initial solution composition before irradiation: E-isomer (0.86%) / Z-isomer (99.14%)

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<tr>
<td>20 min</td>
<td>95.93</td>
<td>3.75</td>
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Representative HPLC traces
(Z)-2-((1H-Indol-2-yl)methylene)benzo[b]thiophen-3(2H)-one (7)

Prepared according to general procedure A.

Hemithioindigo SI 6 (89.0 mg, 0.594 mmol, 1.0 eq.), benzene (2.0 mL, 0.297 M), indole-2-carbaldehyde (73.0 mg, 0.504 mmol, 0.85 eq.). The solution was purged with N₂ for 10 min before piperidine was added. Stirred for 17 h under Ar at 40°C. Purified by DCVC (0% to 100% EtOAc in n-heptane with 5% increments) to afford the title compound (Z)-7 (116 mg, 0.419 mmol, 83%) as a bordeaux red solid.

TLC: \( R_f = 0.24 \) (1:3 EtOAc/n-heptane)

LCMS (ESI) [M+H]^+ m/z calcd for C₁₇H₁₂NOS⁺: 278.0634, m/z found: 278.50 [M+H]^+

\( R_f: 2.09 \text{ min (total run time: 2.6 min), purity} >98\%

\(^1\)H NMR (800 MHz, DMSO-d₆): \( \delta 11.75 \) (s, 1H, H-14), 7.95 (m, 1H, H-9), 7.87 (ddd, \( J = 7.6, 1.3, 0.6 \) Hz, 1H, H-6), 7.82 (d, \( J = 7.8 \) Hz, 1H, H-3), 7.74 (ddd, \( J = 8.0, 7.2, 1.3 \) Hz, 1H, H-1), 7.71 (dd, \( J = 8.0, 1.0 \) Hz, 1H, H-18), 7.46 (dd, \( J = 8.2, 1.0 \) Hz, 1H, H-15), 7.42 (td, \( J = 7.4, 0.9 \) Hz, 1H, H-2), 7.25 (dd, \( J = 8.1, 6.9, 1.1 \) Hz, 1H, H-17), 7.09 (ddd, \( J = 7.9, 6.9, 1.0 \) Hz, 1H, H-16), 7.07 (m, 1H, H-11)

\(^{13}\)C NMR (201 MHz, DMSO-d₆): \( \delta 187.0 \) (C-8), 144.5 (C-5), 137.9 (C-12), 135.9 (C-1), 133.1 (C-10), 130.3 (C-4), 128.7 (C-7), 128.6 (C-13), 126.3 (C-6), 124.7 (C-3), 124.7 (C-17), 122.9 (C-9), 121.6 (C-18), 120.5 (C-16), 112.0 (C-15), 107.4 (C-11)

HRMS-ESI [M+H]^+ m/z calcd for C₁₇H₁₂NOS⁺: 278.0634, m/z found: 278.0636 [M+H]^+ (ppm error: 0.719)

(E)-15:

\(^1\)H NMR (400 MHz, DMSO-d₆): \( \delta 12.56 \) (s, 1H, H-14), 7.93 (m, 1H), 7.81 (m, 1H), 7.77 (m, 1H), 7.73 (ddd, \( J = 8.1, 6.2, 1.3 \) Hz, 1H), 7.70 – 7.67 (m, 2H), 7.42 (m, 1H), 7.32 (ddd, \( J = 8.2, 6.9, 1.1 \) Hz, 1H), 7.20 (m, 1H), 7.11 (ddd, \( J = 8.1, 7.0, 0.9 \) Hz, 1H)

Note: A sample of (Z)-7 was irradiated in an LCMS vial in DCM followed by a solvent exchange to DMSO-d₆. A 1:4 (Z/E)-ratio was observed for (E)-7 by \(^1\)H NMR. Photoisomerization of an NMR sample performed directly in DMSO-d₆ did not produce the desired (E)-isomer in greater than Z/E 9:1. Switching directly in CD₂Cl₂ afforded the (E)-isomer cleanly, however with a loss in \(^1\)H NMR spectrum quality.
UV-Vis spectroscopy

HTI indole (7) (33 μM in DCM)

\[ \lambda_{\text{max}} (Z) = 468 \text{ nm} \]
\[ \varepsilon = 21655 \text{ L} \cdot \text{ mol}^{-1} \cdot \text{ cm}^{-1} \]

\[ \lambda_{\text{max}} (E) = 516 \text{ nm} \]
\[ \varepsilon = 16991 \text{ L} \cdot \text{ mol}^{-1} \cdot \text{ cm}^{-1} \]

No wavelengths at hand facilitated backswitching to produce the (Z)-isomer

HTI indole (7) (33 μM in n-hexane/iPrOH 9:1)

\[ \lambda_{\text{max}} (Z) = 488 \text{ nm} \]

No wavelengths at hand facilitated backswitching to produce the (Z)-isomer
HTI indole (7) (33 µM in iPrOH). The apparent lack of an isosbestic point is likely due to photodegradation with prolonged irradiation times.

Irradiation with 530 nm produced only minor backswitching to the (Z)-isomer though potentially due to thermal relaxation.

Irradiation with 470 nm produced the same excitation spectrum for the (E)-isomer. No wavelengths at hand facilitated backswitching to produce the (Z)-isomer.
HTI indole (7) (33 μM in PhMe)

No wavelengths at hand facilitated backswitching to produce the (Z)-isomer.

HTI indole (7) (33 μM in DMSO)
HTI indole (7) (33 μM in DMSO/H$_2$O 1:1, T = 20 °C)

- $\lambda_{\text{max}} (Z) = 481$ nm
- $\lambda_{\text{max}} (E) = 518$ nm
Fluorescence spectroscopy

HTI indole (7) (33 µM in DCM)

![Graph showing fluorescence intensity vs. wavelength for HTI indole (7) under different conditions.]

1. **λ<sub>max</sub> (Z) = 499 nm**
2. **λ<sub>max</sub> (E) = 552 nm**

**Stokes shift:**
- **Z-HTI indole (7):** 32 nm
- **E-HTI indole (7):** 37 nm
UV-Vis thermal relaxation spectroscopy

HTI indole (7) (33 µM in DMSO)

\[ y(t) = 0.4085 \cdot \exp(-0.06981 \cdot t) \]

\[ R^2 = 0.9958 \]

\[ T_{1/2} = 9.93 \text{ h} \]
HTI indole (7) (33 μM in DMSO, T = 28 °C, first 75 minutes)

The linear fit gives the first order rate constant $k = 4.62 \cdot 10^{-6} \text{ s}^{-1}$. This corresponds to a Gibbs energy of activation of $\Delta G^\ddagger = 105 \text{ kJ mol}^{-1} = 25.0 \text{ kcal mol}^{-1}$. 

\[
y(t) = 4.622 \cdot 10^{-6} \cdot t \\
R^2 = 0.9947
\]
HTI indole (7) (33 µM in PhMe)

\[ \lambda_{\text{max}} (Z) = 519 \text{ nm} \]

\[ \lambda_{\text{max}} (E) = 468 \text{ nm} \]

\[ y = 32.904e^{-0.00000305x} \]

\[ R^2 = 0.705 \]

\[ T_{\text{H}} = \text{nd} \]
HTI indole (7) (33 μM in DMSO/H$_2$O 1:1, T = 20 °C, measurement every 20 minutes for 24 hours)

\[ y(t) = 0.3866 \cdot \exp(-0.003058 \cdot t) \]

\[ R^2 = 0.9954 \]

\[ T_{1/2} = 226.7 \text{ min} \]
Kinetic analysis of thermal $E$-to-$Z$ isomerisation

HTI indole (7) (33 μM in DMSO/H$_2$O 1:1, T = 20 °C, first 183 minutes)

The linear fit gives the first order rate constant $k = 2.56 \cdot 10^{-5}$ s$^{-1}$. This corresponds to a Gibbs energy of activation of $\Delta G^\ddagger = 97.5$ kJ·mol$^{-1} = 23.3$ kcal·mol$^{-1}$. 
HPLC conditions

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Column:</strong></td>
<td>ChiralPak AD-H column (5 µm, 250 x 4.6 mm)</td>
</tr>
<tr>
<td><strong>Mobile Phase</strong></td>
<td>90:10 n-hexane/iPrOH (isocratic, 1 mL/min)</td>
</tr>
<tr>
<td><strong>Isosbestic Point</strong></td>
<td>498 nm (in HPLC mobile Phase)</td>
</tr>
<tr>
<td><strong>t_R(E)</strong></td>
<td>8.82 min</td>
</tr>
<tr>
<td><strong>t_R(Z)</strong></td>
<td>17.05 min</td>
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Solution composition (%E-isomer)

Initial solution composition before irradiation: E-isomer (2.60%) / Z-isomer (97.40%)

<table>
<thead>
<tr>
<th>Time</th>
<th>415 nm</th>
<th>530 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 min</td>
<td>98.43</td>
<td>94.79</td>
</tr>
<tr>
<td>20 min</td>
<td>99.21</td>
<td>96.16</td>
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Representative HPLC traces
HPLC conditions

<table>
<thead>
<tr>
<th>Column:</th>
<th>ChiralPak AD-H column (5 µm, 250 x 4.6 mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobile Phase</td>
<td>90:10 n-hexane/iPrOH (isocratic, 1 mL/min)</td>
</tr>
<tr>
<td>Isosbestic Point</td>
<td>498 nm (in HPLC mobile Phase)</td>
</tr>
<tr>
<td>$t_R(E)$</td>
<td>8.37-8.65 min</td>
</tr>
<tr>
<td>$t_R(Z)$</td>
<td>14.6-15.75 min</td>
</tr>
</tbody>
</table>

Solution composition (%$E$-isomer)

Initial solution composition before irradiation: $E$-isomer (1.64%) / $Z$-isomer (98.36%)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>415 nm</th>
<th>590 nm</th>
</tr>
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<tbody>
<tr>
<td>10 min</td>
<td>97.88</td>
<td>86.74</td>
</tr>
<tr>
<td>20 min</td>
<td>-</td>
<td>80.82</td>
</tr>
<tr>
<td>30 min</td>
<td>-</td>
<td>70.83</td>
</tr>
<tr>
<td>40 min</td>
<td>-</td>
<td>63.14</td>
</tr>
</tbody>
</table>

Note: Sample prepared (0.66 mg/mL), filtered, irradiated in and measured directly from iPrOH.

Representative HPLC traces
$^1$H NMR thermal relaxation spectroscopy

HTI indole (7) (CD$_2$Cl$_2$)

Note: Indole-NH of the (E)-7 at 12.78 ppm plotted vs. time (relaxation).
(Z)-7:

$^1H$ NMR (800 MHz, CD$_2$Cl$_2$): \( \delta 8.61 \) (s, 1H), 7.93 (s, 1H), 7.91 (m, 1H), 7.70 (dq, \( J = 8.0, 1.0 \) Hz, 1H), 7.63 (m, 1H), 7.59 (dt, \( J = 7.8, 0.9 \) Hz, 1H), 7.46 (dq, \( J = 8.2, 0.9 \) Hz, 1H), 7.35 (ddd, \( J = 7.9, 7.1, 1.0 \) Hz, 1H), 7.31 (ddd, \( J = 8.1, 6.9, 1.1 \) Hz, 1H), 7.16 (ddd, \( J = 7.9, 7.0, 1.0 \) Hz, 1H), 7.12 (m, 1H)

(E)-7:

$^1H$ NMR (800 MHz, CD$_2$Cl$_2$): \( \delta 12.78 \) (s, 1H), 7.97 (ddd, \( J = 7.8, 1.3, 0.7 \) Hz, 1H), 7.66 (dq, \( J = 8.1, 1.0 \) Hz, 1H), 7.63 (ddd, \( J = 8.3, 7.1, 1.3 \) Hz, 1H), 7.55 (m, 1H), 7.54 (dt, \( J = 7.9, 0.9 \) Hz, 1H), 7.36 (s, 1H), 7.35 (m, 1H), 7.33 (m, 1H), 7.13 (ddd, \( J = 7.9, 6.8, 0.9 \) Hz, 1H), 7.96 (m, 1H)
**(Z)-2-((1H-Pyrrol-2-yl)methylene)naphtho[2,1-b]thiophen-1(2H)-one (8)**

Prepared according to general procedure B.

Hemithioindigo derivative SI 5 (93.5 mg, 0.467 mmol, 1.0 eq.), PhMe (2.0 mL, 0.234 M) and pyrrole-2-carbaldehyde (44.4 mg, 0.467 mmol, 1.0 eq.). Stirred for 3 h under Ar at 40°C. Afforded the title compound (Z)-8 (107 mg, 0.385 mmol, 82%) as an orange solid.

**TLC:** $R_f = 0.61$ (1:1 EtOAc/n-heptane)

**LCMS (ESI) [$M+H]^+$ m/z** calcd for C$_{17}$H$_{12}$NOS$: 278.0634, m/z found: 278.27 [$M+H]^+$

$R_t$: 2.10 min (total run time: 2.6 min), purity >99%

**$^1H$ NMR** (800 MHz, DMSO-$d_6$): $\delta$ 11.90 (s, 1H, H-18), 9.29 (d, $J = 8.3$ Hz, 1H, H-6), 8.23 (d, $J = 8.6$ Hz, 1H, H-10), 8.05 (d, $J = 8.1$ Hz, 1H, H-3), 7.95 (s, 1H, H-13), 7.87 (d, $J = 8.6$ Hz, 1H, H-9), 7.74 (t, $J = 7.6$ Hz, 1H, H-1), 7.60 (t, $J = 7.4$ Hz, 1H, H-2), 7.31 (s, 1H, H-15), 6.84 (s, 1H, H-17), 6.45 (s, 1H, H-16)

**$^{13}$C NMR** (201 MHz, DMSO-$d_6$): $\delta$ 187.3 (C-12), 148.0 (C-8), 135.7 (C-10), 131.4 (C-4/5), 130.5 (C-4/5), 129.4 (C-1), 128.8 (C-3), 128.1 (C-14), 126.2 (C-2), 125.7 (C-15), 124.2 (C-13), 123.4 (C-7/11), 123.4 (C-7/11), 122.3 (C-9), 122.1 (C-6), 115.1 (C-17), 112.6 (C-16)

**HRMS-ESI [$M+H]^+$ m/z** calcd for C$_{17}$H$_{12}$NOS$: 278.0634, m/z found: 278.0635 [$M+H]^+$ (ppm error: 0.360)

**Melting point:** 245-250°C (decomposes)
UV-Vis spectroscopy

2-Pyrrole HTI derivative (8) (33 µM in DCM)

Irradiation with 530 nm produced the same excitation spectrum for the (Z)-isomer as dark state before irradiation.

2-Pyrrole HTI derivative (8) (33 µM in n-hexane/iPrOH 9:1)
2-Pyrrole HTI derivative (8) (33 μM in PhMe)

![Absorption spectrum of 2-Pyrrole HTI derivative (8) in PhMe.]

2-Pyrrole HTI derivative (8) (33 μM in DMSO, T = 18 °C)

![Absorption spectrum of 2-Pyrrole HTI derivative (8) in DMSO.]

\( \lambda_{\text{max}} (Z) = 477 \text{ nm} \)
\( \lambda_{\text{max}} (E) = 515 \text{ nm} \)

\( \lambda_{\text{max}} (Z) = 488 \text{ nm} \)
\( \lambda_{\text{max}} (E) = 516 \text{ nm} \)
Fluorescence spectroscopy

2-Pyrrole HTI derivative (8) (33 µM in DCM)
UV-Vis thermal relaxation spectroscopy

2-Pyrrole HTI derivative (8) (33 µM in DCM)

\[ \lambda_{\text{max}} (Z) = 478 \, \text{nm} \]

\[ \lambda_{\text{max}} (E) = 513 \, \text{nm} \]

\[ y = 32.178e^{-0.0000560x} \]

\[ R^2 = 0.866 \]

\[ T_{1/2} = \text{nd} \]
2-Pyrrole HTI derivative (8) (33 µM in PhMe)

\[ \lambda_{\text{max}} (Z) = 477 \text{ nm} \]

\[ \lambda_{\text{max}} (E) = 515 \text{ nm} \]

\[ y = 32.904e^{-0.0000881x} \]

\[ R^2 = 0.383 \]

\[ T_{1/2} = \text{nd} \]
2-Pyrrole HTI derivative (8) (33 μM in DMSO, T = 18 °C, measurement every 10 minutes for 18 hours)

\[ y(t) = 0.7667 \cdot \exp(-0.001636 \cdot t) \]

\[ R^2 = 1.000 \]

\[ T_{1/2} = 423.6 \text{ min} \]
Kinetic analysis of thermal $E$-to-$Z$ isomerisation

2-Pyrrole HTI derivative (8) (33 μM in DMSO, T = 18 °C, first 331 minutes)

The linear fit gives the first order rate constant $k = 2.07 \cdot 10^{-5}$ s$^{-1}$. This corresponds to a Gibbs energy of activation of $\Delta G^\ddagger = 97.4$ kJ mol$^{-1} = 23.3$ kcal mol$^{-1}$. 
HPLC conditions

<table>
<thead>
<tr>
<th>Column:</th>
<th>ChiralPak AD-H column (5 µm, 250 x 4.6 mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobile Phase</td>
<td>90:10 n-hexane/iPrOH (isocratic, 1 mL/min)</td>
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<tr>
<td>Isosbestic Point</td>
<td>502 nm (in HPLC mobile Phase)</td>
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<tr>
<td>( t_R(E) )</td>
<td>7.63 min</td>
</tr>
<tr>
<td>( t_R(Z) )</td>
<td>11.52 min</td>
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</table>

Solution composition (%E-isomer)

Initial solution composition before irradiation: \( E \)-isomer (0.48%) / \( Z \)-isomer (99.52%)

<table>
<thead>
<tr>
<th>Time</th>
<th>470 nm</th>
<th>Time</th>
<th>530 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 min</td>
<td>86.86</td>
<td>10 min</td>
<td>60.03</td>
</tr>
<tr>
<td>20 min</td>
<td>87.61</td>
<td>30 min</td>
<td>27.92</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>50 min</td>
<td>26.10</td>
</tr>
</tbody>
</table>

Note: The sample (1 mg/mL) was irradiated in DCM following a direct injection.

Representative HPLC traces
(Z)-2-((1H-Indol-2-yl)methylene)naphtho[2,1-b]thiophen-1(2H)-one (9)

Prepared according to general procedure B.

Hemithioindigo derivative SI 5 (101 mg, 0.505 mmol, 1.0 eq.), PhMe (2.0 mL, 0.253 M) and indole-2-carbaldehyde (66.6 mg, 0.468 mmol, 0.93 eq.). Stirred for 3 h under Ar at 40°C. Afforded the title compound (Z)-9 (86.6 mg, 0.265 mmol, 57%) as a red solid.

TLC: $R_f = 0.78$ (1:1 EtOAc/n-heptane + 1% TEA)

LCMS (ESI) [M+H]+ m/z calcd for C_{21}H_{14}NOS$: 328.0791, m/z found: 328.01 [M+H]+

Rf: 3.41-4.28 min broad peak (total run time: 5.2 min), purity >N/A

$^1$H NMR (800 MHz, DMSO-$d_6$): $\delta$ 11.81 (s, 1H, H-18), 9.26 (d, $J = 8.3$ Hz, 1H, H-6), 8.30 (d, $J = 8.5$ Hz, 1H, H-10), 8.08 (d, $J = 8.0$ Hz, 1H, H-3), 8.03 (s, 1H, H-13), 7.92 (d, $J = 8.5$ Hz, 1H, H-9), 7.78 (ddd, $J = 8.3, 6.8, 1.3$ Hz, 1H, H-1), 7.72 (d, $J = 7.9$ Hz, 1H, H-22), 7.63 (ddd, $J = 8.0, 6.8, 1.2$ Hz, 1H, H-2), 7.48 (d, $J = 8.1$ Hz, 1H, H-19), 7.26 (ddd, $J = 8.0, 6.7, 1.1$ Hz, 1H, H-20), 7.14 (s, 1H, H-15), 7.10 (t, $J = 7.4$ Hz, 1H, H-21)

$^{13}$C NMR (151 MHz, DMSO-$d_6$): $\delta$ 187.5 (C-12), 148.6 (C-8), 137.9 (C-16), 136.6 (C-10), 133.0 (C-14), 131.5 (C-4/5), 130.5 (C-4/5), 129.8 (C-1), 129.1 (C-11), 129.0 (C-3), 128.6 (C-17), 126.5 (C-2), 124.6 (C-20), 123.7 (C-13), 122.9 (C-7), 122.3 (C-9), 122.1 (C-6), 121.6 (C-22), 120.5 (C-21), 111.9 (C-19), 107.4 (C-15)

$^1$H NMR (800 MHz, C$_6$H$_6$O): 11.03 (s, 1H, H-18), 9.66 (d, $J = 8.4$ Hz, 1H, H-6), 8.40 (d, $J = 8.5$ Hz, 1H), 8.26 (s, 1H, H-13), 8.21 (d, $J = 8.0$ Hz, 1H), 7.97 (d, $J = 8.5$ Hz, 1H), 7.94 (t, $J = 7.6$ Hz, 1H), 7.92 (d, $J = 8.0$ Hz, 1H), 7.80 (t, $J = 7.4$ Hz, 1H), 7.67 (d, $J = 8.1$ Hz, 1H), 7.47 (t, $J = 7.5$ Hz, 1H), 7.40 (d, $J = 2.1$ Hz, 1H), 7.33 (t, $J = 7.4$ Hz, 1H)

HRMS-ESI [M+H]+ m/z calcd for C$_{21}$H$_{14}$NOS$: 328.0791, m/z found: 328.0789 [M+H]+ (ppm error: -0.610

Melting point: 287-289°C

(E)-9:

$^1$H NMR (800 MHz, DMSO-$d_6$): $\delta$ 12.84 (s, 1H, H-18), 9.48 (d, $J = 7.8$ Hz, 1H), 8.28 (d, $J = 8.5$ Hz, 1H), 8.10 – 8.07 (m, 1H), 7.94 (t, 1H), 7.88 (d, $J = 8.5$ Hz, 1H), 7.81 (ddd, $J = 8.3, 6.8, 1.3$ Hz, 1H), 7.79 – 7.75 (m, 1H), 7.74 – 7.71 (m, 1H), 7.66 – 7.61 (m, 1H), 7.36 (ddd, $J = 8.1, 6.8, 1.1$ Hz, 1H), 7.28 – 7.25 (m, 1H), 7.15 – 7.12 (m, 1H)

$^1$H NMR (800 MHz, C$_6$H$_6$O): $\delta$ 13.41 (s, 1H, H-18), 9.83 (d, $J = 8.3$ Hz, 1H, H-6), 8.37 (d, $J = 8.5$ Hz, 1H), 8.21 (d, $J = 8.0$ Hz, 1H), 7.99 (t, $J = 7.7$ Hz, 1H), 7.92 – 7.87 (m, 4H), 7.82 (t, $J = 7.4$ Hz, 1H), 7.58 (t, $J = 7.6$ Hz, 1H), 7.34 (t, $J = 7.4$ Hz, 1H), 7.32 – 7.29 (m, 1H)

Note: A 1.5:1 (Z/E)-ratio was observed for (E)-9 in DMSO, whereas THF afforded clean (E)-9 by $^1$H NMR.
UV-Vis spectroscopy

2-Indole HTI derivative (9) (33 µM in DCM)

No irradiation
λ irradiation 470 nm 10 min

λ<sub>max</sub> (Z) = 486 nm
ε = 25121 L·mol<sup>-1</sup>·cm<sup>-1</sup>

λ<sub>max</sub> (E) = 526 nm
ε = 24333 L·mol<sup>-1</sup>·cm<sup>-1</sup>

No wavelengths at hand facilitated backswitching to produce the (Z)-isomer

Irradiation with 530 nm produced the same excitation spectrum for the (E)-isomer

2-Indole HTI derivative (9) (33 µM in n-hexane/iPrOH 9:1)

No irradiation
λ irradiation 530 nm 20 min

λ<sub>max</sub> (Z) = 505 nm

λ<sub>max</sub> (E) = 526 nm

Irradiation with 470 nm produced the same excitation spectrum for the (E)-isomer. A drifting baseline, likely due to poor solubility, is observed for the (Z)-isomer
2-Indole HTI derivative (9) (33 µM in iPrOH)

No wavelengths at hand facilitated backswitching to produce the (Z)-isomer. A drifting baseline, likely due to poor solubility, is observed for the (Z)-isomer.

2-Indole HTI derivative (9) (33 µM in THF)

Irradiation with 530 nm produced the same excitation spectrum for the (E)-isomer.
2-Indole HTI derivative (9) (33 µM in PhMe)

Irradiation with 530 nm produced the same excitation spectrum for the (E)-isomer

2-Indole HTI derivative (9) (33 µM in DMSO)

Irradiation with 530 nm produced the same excitation spectrum for the (E)-isomer
Fluorescence spectroscopy

2-Indole HTI derivative (9) (33 µM in DCM)
UV-Vis thermal relaxation spectroscopy

2-Indole HTI derivative (9) (33 µM in DMSO)

\[ y(t) = 0.6182 \cdot \exp(-0.007753 \cdot t) \]

\[ R^2 = 0.9994 \]

\[ T_{1/2} = 89.4 \text{ min} \]

\( \lambda_{\text{max}} (Z) = 492 \text{ nm} \)

\( \lambda_{\text{max}} (E) = 528 \text{ nm} \)
Kinetic analysis of thermal E-to-Z isomerisation

2-Indole HTI derivative (9) (33 μM in DMSO, T = 28 °C, first 80 minutes)

The linear fit gives the first order rate constant $k = 1.13 \cdot 10^{-4} \text{ s}^{-1}$. This corresponds to a Gibbs energy of activation of $\Delta G^\ddagger = 96.6 \text{ kJ mol}^{-1} = 23.1 \text{ kcal mol}^{-1}$. 
2-Indole HTI derivative (9) (33 µM in PhMe)

\[
\lambda_{\text{max}}(Z) = 487 \text{ nm}
\]

\[
\lambda_{\text{max}}(E) = 531 \text{ nm}
\]

\[
y = 32.781e^{-0.0000116x}
\]

R² = 0.982
(Z)-2-(1H,1'H-[2,2'-Bipyrrl]-5-ylmethylene)benzo[b]thiophen-3(2H)-one (10)

Prepared according to general procedure B.

Hemithioindigo Si 6 (53 mg, 0.353 mmol, 1.0 eq.), PhMe (2.0 mL, 0.176 M) and bipyrrrole-5-carbaldehyde (46.0 mg, 0.287 mmol, 0.81 eq.). Stirred for 2.5 h under Ar at 100°C. Afforded the title compound (Z)-10 (31.7 mg, 0.108 mmol, 38%) as a dark purple solid.

TLC: R_f = 0.52 (1:1 EtOAc/n-heptane + 1% TEA)

LCMS (ESI) [M+H]^+ m/z calcd for C_{21}H_{14}NOS^+: 328.0791, m/z found: 328.01 [M+H]^+

R_t: 3.41-4.28 min broad peak (total run time: 5.2 min)

$^1{H}$ NMR (800 MHz, DMSO-$d_6$): δ 11.88 (s, 1H, H-14/19), 11.35 (s, 1H, H-14/19), 7.85 (s, 1H, H-9), 7.80 (d, J = 7.7 Hz, 1H, H-6), 7.76 (d, J = 7.9 Hz, 1H, H-3), 7.66 (t, J = 7.5 Hz, 1H, H-2), 7.37 (t, J = 7.4 Hz, 1H, H-1), 6.90 (d, J = 2.5 Hz, 1H, H-18), 6.84 (d, J = 4.2 Hz, 1H, H-11), 6.72 (d, J = 4.4 Hz, 1H, H-12), 6.53 (s, 1H, H-16), 6.15 (q, J = 2.8 Hz, 1H, H-17)

$^{13}$C NMR (201 MHz, DMSO-$d_6$): δ 185.8 (C-8), 143.8 (C-5), 134.5 (C-2), 133.3 (C-13), 131.4 (C-4), 127.9 (C-10), 125.7 (C-6), 125.6 (C-1), 124.4 (C-3), 123.8 (C-15), 122.7 (C-9), 121.4 (C-7), 119.9 (C-16/18), 117.4 (C-11), 109.3 (C-17), 108.8 (C-12), 106.1 (C-16/18)

HRMS-ESI [M+H]^+ m/z calcd for C_{17}H_{13}N_{2}OS^+: 293.0743, m/z found: 293.0744 [M+H]^+ (ppm error: 0.341)

Melting point: 273-275°C (decomposes)
UV-Vis spectroscopy

Bipyrrole HTI (10) (33 µM in DCM)

Irradiation with 530 nm gradually produced the (Z)-isomer with a drifting baseline likely caused by poor solubility.

λ\text{max}(E) = 577 nm

Bipyrrole HTI (10) (33 µM in n-hexane/iPrOH 9:1)

λ\text{max}(Z) = 475 nm

λ\text{max}(E) = 605 nm
Bipyrrrole HTI (10) (33 μM in iPrOH)

\[ \lambda_{\text{max}}(Z) = 549 \text{ nm} \]

\[ \lambda_{\text{max}}(E) = 596 \text{ nm} \]

Bipyrrrole HTI (10) (33 μM in THF)

\[ \lambda_{\text{max}}(Z) = 519 \text{ nm} \]

\[ \varepsilon = 27524 \text{ L} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1} \]

\[ \lambda_{\text{max}}(E) = 581 \text{ nm} \]

\[ \varepsilon = 25675 \text{ L} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1} \]

Irradiation with 625 nm produced the (Z)-isomer
Bipyrrrole HTI (10) (33 µM in PhMe)

Irradiation with 625 nm produced the (Z)-isomer as well.

\[ \lambda_{\text{max}}(E) = 581 \text{ nm} \]

\[ \lambda_{\text{max}}(Z) = 511 \text{ nm} \]

Bipyrrrole HTI (10) (33 µM in DMSO)

Irradiation with 625 nm produced the (Z)-isomer as well.

\[ \lambda_{\text{max}}(E) = 589 \text{ nm} \]

\[ \lambda_{\text{max}}(Z) = 537 \text{ nm} \]
Bipyrrrole HTI (10) (33 µM in acetone)

\[ \lambda_{\text{max}}(Z) = 516 \text{ nm} \]

\[ \lambda_{\text{max}}(E) = 576 \text{ nm} \]
UV-Vis thermal relaxation spectroscopy

Bipyrrrole HTI (10) (33 µM in THF)

\[ y(t) = 0.9829 \cdot \exp(-0.005773 \cdot t) \]
\[ R^2 = 0.9954 \]
\[ T_{1/2} = 120.1 \text{ min} \]
Kinetic analysis of thermal E-to-Z isomerisation

Bipyrrrole HTI (10) (33 μM in THF, T = 28 °C, first 30 minutes)

\[ y(t) = 5.325 \cdot 10^{-5} \cdot t \]
\[ R^2 = 0.9259 \]

The linear fit gives the first order rate constant \( k = 5.33 \cdot 10^{-5} \text{ s}^{-1} \). This corresponds to a Gibbs energy of activation of \( \Delta G^\ddagger = 98.4 \text{ kJ mol}^{-1} = 23.5 \text{ kcal mol}^{-1} \).
Bipyrrrole HTI (10) (33 μM in PhMe)

**Note:** Concentrations of isomers were calculated using 480 nm as representative for $\lambda_{\text{max}}(Z) = 511$ nm and $\lambda_{\text{max}}(E) = 581$ nm. An apparent lack of isosbestic points could be due to the difference in solubility between the two isomers, with the (E)-isomer being significantly more soluble in toluene.
Bipyrrrole HTI (10) (33 μM in DMSO, T = 18 °C, measurement every 30 seconds for 30 minutes)

\[
y(t) = 0.8530 \cdot \exp(-0.002208 \cdot t)
\]

\[
R^2 = 1.000
\]

\[
T_{1/2} = 313.9 \text{ s}
\]
Kinetic analysis of thermal E-to-Z isomerisation

Bipyrrrole HTI (10) (33 μM in DMSO, T = 18 °C, first 480 seconds)

The linear fit gives the first order rate constant \( k = 1.52 \cdot 10^{-3} \, \text{s}^{-1} \). This corresponds to a Gibbs energy of activation of \( \Delta G^\ddagger = 87.0 \, \text{kJ\,mol}^{-1} = 20.8 \, \text{kcal\,mol}^{-1} \).
UV-Vis photobleaching spectroscopy

Bipyrrrole HTI (10) (33 µM in THF)

Note: Red marker is after irradiation with 625 nm (1 Amp) for 3 minutes, whereas blue marker is after irradiation with 470 nm (1 Amp) for 2 minutes, reaching the photostationary state in both cases.
6 Appendix

Nuclear magnetic resonance spectroscopy

$^1$H NMR, $^{13}$C NMR
(2-Naphthylthio)acetic acid (SI 3)
Naphtho[2,1-b]thiophen-1(2H)-one (SI 4)
(Z)-2-(Naphthalen-1-ylmethylene)benzo[b]thiophen-3(2H)-one (2)
Note: Compound (Z) in 1:3 (Z/E)
(Z)-2-(Naphthalen-2-ylmethylene)benzo[b]thiophen-3(2H)-one (3)
(Z)-2-benzylidenenaphtho[2,1-b]thiophen-1(2H)-one (4)
(Z)-2-(naphthalen-2-ylmethylene)naptho[2,1-b]thiophen-1(2H)-one (5)
(Z)-2-((1H-Pyrrol-2-yl)methylene)benzo[b]thiophen-3(2H)-one (6)
Note: Compound (6) in 1:2 (Z/E)
(Z)-2-((1H-Indol-2-yl)methylene)benzo[b]thiophen-3(2H)-one (7)
Note: Compound (7) in 1:4 (Z/E)
Note: Compound (7) in >99 (E)-isomer used for $^1$H NMR thermal relaxation spectroscopy
(Z)-2-((1H-pyrrol-2-yl)methylene)naphtho[2,1-b]thiophen-1(2H)-one (8)
(Z)-2-((1H-indol-2-yl)methylene)naphtho[2,1-b]thiophen-1(2H)-one (9)
Note: Compound (9) in 1.5:1 (Z/E)
Note: Compound (Z-9) with double solvent suppression of the THF proton signals

Note: Compound (E-9) with double solvent suppression of the THF proton signals
(Z)-2-(1H,1'H-[2,2'-bipyrrrol]-5-ylmethylene)benzo[b]thiophen-3(2H)-one (10)
7 References

15624–15632.


