Iminobispyrazole (IBP) Photoswitches: Two Pyrazole Rings Can Be Better Than One

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We recently demonstrated that suitably functionalised aryliminopyrazoles can exhibit useful photoswitching properties. In this study, we investigate the photoswitching potential of iminobispyrazoles (IBPs). We find that the regiochemistry of the IBPs strongly dictates their photoswitching properties, most notably, the λ_{max}, the photostationary state and the thermal half-life of the Z-isomer.
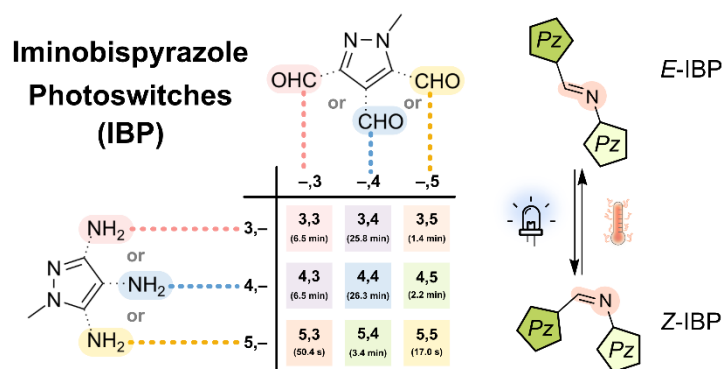
Photochromic imines[1–4] based on an aryliminopyrazole (AIP) motif have recently emerged as an interesting class of photoswitch, featuring a C=N bond that can photoisomerize while also exhibiting dynamic-covalent (DC) properties.[1,5] Specifically, AIPs functionalised with *ortho*-pyrrolidine units exhibit quantitative *E*-to-*Z* photoisomerism under visible light, with thermal half-lives ($t_{1/2}$) of the metastable *Z*-isomer exceeding 19 hours at room temperature.[1] In a subsequent study, we demonstrated that the DC properties of these imine-based photoswitches could be harnessed: coupling a thermal equilibrium reaction to a reversible photochemical transformation enabled the generation of a non-equilibrium steady state (NESS)[6] of the transimination reaction[7] under photoirradiation.[5] This system exhibited behaviour consistent with an information ratchet,[8] operating continuously under light irradiation.[9,10] Building on these foundations and inspired by the diversity in structures and properties found in the azoheteroarene field,[11,12] we postulate that iminobispyrazole (IBPs), where both arene rings are pyrazoles, could also show useful photoswitching properties without the need for *ortho*-amination.

The groups of Li,[13] Fuchter[14] and Han have demonstrated the utility of azobispyrazoles in terms of their photoswitching properties and strengths in energy-storage applications.[14] Inspired by the work on azobisheteroarenes, we investigate the photoswitching properties of corresponding imine-based systems. We hypothesise that the potential diversity in properties of these chemically similar structures could render IBPs compelling candidates in DC systems.[15] Lehn and co-workers have already demonstrated network behaviours of DC systems,[16,17] which may be well suited to these IBPs.

In this communication, we present the photoswitching properties of a select library, a [3×3] matrix, of IBPs. The entries in this library are positional isomers, specifically, regioisomers. We analyse their photoswitching properties, noting that several derivatives exhibit significantly improved $t_{1/2}$ values (over 120 times longer) compared to their non-functionalised AIP analogues. Trends of the E-isomer's λ_{max} and the thermal stability of the Z-isomer are rationalised according to the IBP structure. This communication provides an overview of the photoswitching properties of IBPs and highlights how the regiochemistry of the pyrazole ring impacts these properties.

The nine IBPs shown in Figure 1 were prepared from commercially available precursors following our previously reported procedure.[1] Specific details of the synthesis and characterisation data are provided in the Supporting Information. The IBPs were prepared quantitatively, as determined by ^{1}H NMR, but their subsequent purification on neutralised silica gel to remove excess amine revealed that the IBPs are less stable to column chromatography than their AP counterparts. The IBPs were isolated as the thermodynamically stable E-isomers and stored in the dark prior to photoswitching studies. A single crystal suitable for X-ray diffraction of E-**4,4** was obtained by slow evaporation of solvent. The X-ray crystal structure indicates that the IBP was successfully formed, and that the E-isomer is the thermodynamically stable structure (Figure 2a). The structure is relatively planar, showing only a twist from planarity of the N-pyrazole ring due to steric clash with the adjacent imine bond, similar to the behaviour of the previously reported AIPs.[1]
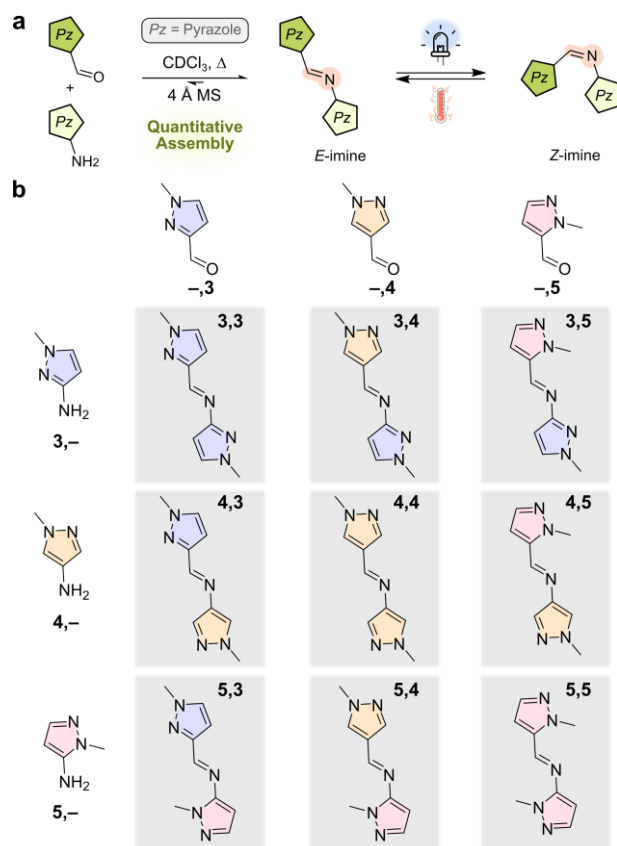
Fig. 1 (a) Schematic of the imine condensation of commercially available amine and aldehyde precursors, in CDCl$_3$, to yield iminobispyrazole (IBP) photoswitches. Monitoring the condensation by ^{1}H NMR indicates quantitative formation of the imine. (b) Overview of the IBP photoswitches explored in this study. Colour coding refers to the site of substitution, names are given based on the site of substitution for amine:aldehyde precursors.

The photoswitching properties of the IBPs were investigated spectroscopically in acetonitrile. Compared to *E*-AIPs, the *E*-IBPs exhibited a larger extinction coefficient at λ_{max}, ranging from 11,000 to 15,000 M^{-1} cm^{-1} (Table 1). The position of the λ_{max} for the *E*-IBPs varied depending on the regiochemistry of the photoswitch. Notably, the IBPs formed from the **5,−** precursor exhibited the largest red-shift in λ_{max}, following the order: **5,5** > **5,4** > **5,3**, **4,5** > **3,5** > **4,3**, > **4,4** > **3,4** > **3,3**. We rationalised this trend by considering the extent of conjugation across the relatively planar *E*-isomer (Figure 2a,b, Section 5 of the Supporting Information). For the 5-substituted pyrazoles, the position of the *N*-methyl motif in the pyrazole ring relative to the imine bond allows more extensive conjugation of the lone-pair across the molecule compared to the other regioisomers.[18] In line with the nomenclature used for azo-based photoswitches,[13,18,19] we refer to the degree of conjugation in the 5-substituted derivatives as "complete" conjugation, and in the 3- and 4- regioisomers as "partial" conjugation (Figure 2b). Simply put, the greater the π-conjugation, the greater the bathochromic shift of the π-

π* transition. The three compounds with the longest absorption wavelengths are *E*-**5,5** (324 nm), *E*-**5,4** (320 nm) and *E*-**5,3** (315 nm). Common to these compounds is that the 5-subsitution is located on the former amine component. These findings indicate that the use of 5-aminopyrazole is more critical for achieving the bathochromic shift than the corresponding aldehyde moiety.
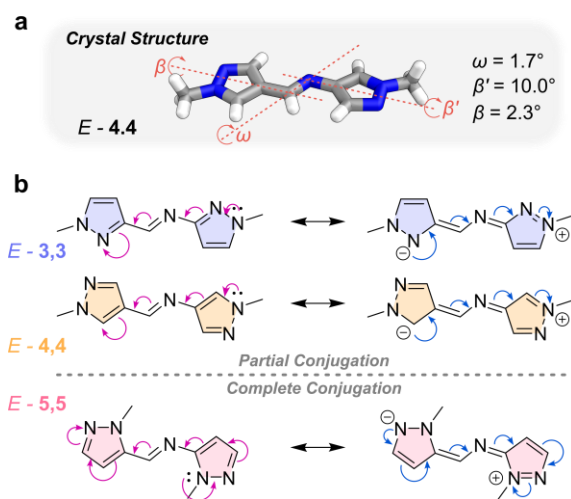

Fig. 2 (a) Proposed reasoning for the variation in λ_{max} for the different regioisomers. (b) The X-ray crystal structure of *E*-**4,4** showing a relatively planar conformation, with the exception of the *N*-pyrazole ring twisting away from planarity (*β'*) due to steric clash between the C−H of the *N*-pyrazole and the C−H of the imine. Colour code in panel (a): C, grey; N, blue; H, white. CCDC 2370061.

Next, we investigated the photoisomerism of these IBPs in acetonitrile solution at 20 °C. The amount of *Z*-isomer generated under photoirradiation, and at the photostationary state (PSS) for compounds that exhibit a sufficiently stable *Z*-isomer (Table 1),[1] was determined using a diode array setup (Figure S1). Photoisomerism was monitored by following the changes in the UV/vis absorption spectra when the IBPs were irradiated with 340 and 365 nm LEDs; longer wavelengths, notably 385 nm and 405 nm afforded negligible photoswitching, except for **5,4**. The proportion of *Z*-isomer generated and the predicted spectra of the pure *Z*-isomer were calculated using the UV/vis spectroscopic approach reported by Fischer.[20] The largest amount of *Z*-isomer generated at a PSS was for **5,4**, achieving up to 76% of the *Z*-isomer at the 340 nm PSS. In general, the percentage of the *Z*-isomer formed at the 340 nm PSS for the IBPs is similar to their *ortho*-aminated AIP counterparts when irradiated at 340 nm,[1] while the 365 nm PSS values of the IBPs are significantly lower. We attribute this to the poor spectral overlap of the LEDs' emission with the UV/vis absorption spectrum of the *E*-isomers (Table S1). Regarding the quantum yields of photoisomerism for the IBPs, they are similar in magnitude to those of the previously reported AIPs (Section 4.4 of the Supporting Information).[1] Comparing the spectra of the *E*-isomers with the predicted

spectra of the *Z*-isomers, and the similarity in the QY values to AIPs, we envisage that investigations with different photoirradiation wavelengths may enhance the fraction of *Z*-isomer generated, if necessary for the intended application.

The UV/vis absorption spectra of the *Z*-isomers display two relatively intense absorption bands: one near the λ_{max} of the *E*-isomer (the lowest energy transition of the *E*-isomer corresponds to a $\pi \rightarrow \pi^*$ transition, Figure S32), which is significantly lower in intensity, and one hypsochromically shifted to *ca.* 250 nm (Figure 3a). A weaker absorption band is also observed, red-shifted with respect to the longest wavelength of absorption of the *E*-isomer, attributed to an $n \rightarrow \pi^*$ transition (Figure S32). Thus, these IBPs exhibit positive photochromism, whereby $\lambda_{max}(E) < \lambda_{max}(Z)$. While quantitative *E*-to-*Z* photoisomerism is not achieved for the IBPs under the LED wavelengths investigated here, it should be noted that the amount of *Z*-isomer generated at the PSS
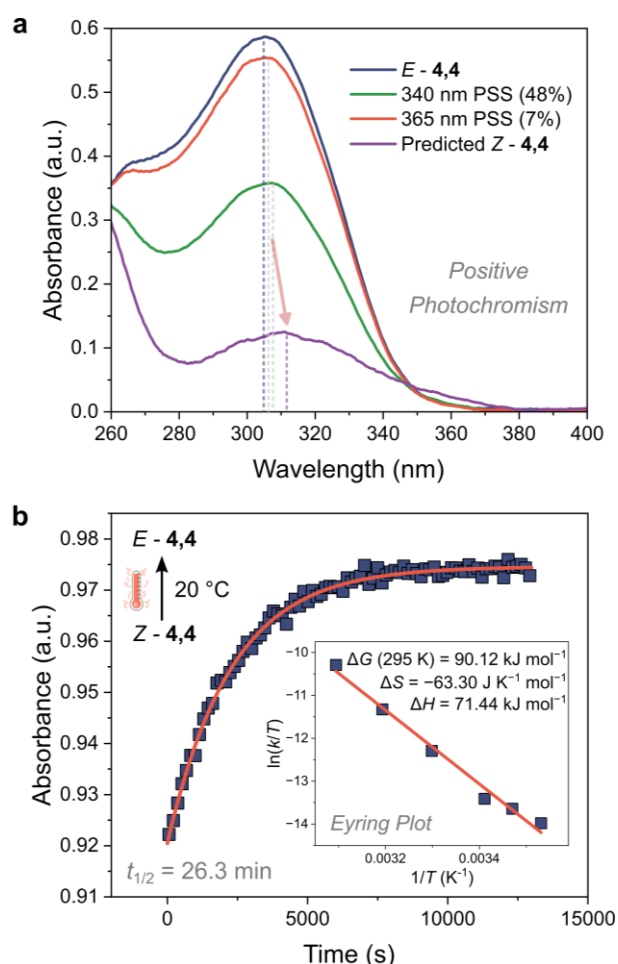

Fig. 2 (a) UV/vis absorption spectra of **4,4** (40 µM, 20 °C, MeCN) as the *E*-isomer, at the 340 nm and 365 nm PSS, and the predicted spectrum of the *Z*-isomer obtained as described in Section 4.3 of the Supporting Information. Note the low-energy absorption band for the *Z*-isomer, which results in the positive photochromic properties. (b) The rate of thermal Z-to-*E* isomerism at 20 °C. (inset) Eyring plot of the rate of thermal reversion at different temperatures, with thermodynamic values reported.

is greater than that of non-functionalised AIPs[1] and previously reported arylimine-based photoswitches.[2,21,22] Furthermore, the IBPs showed good resistance to fatigue; **4,4** could be switched back and forth between the 340 nm and 365 nm PSS reversibly with no observable degradation after 10 cycles (Figure S30).

The thermal stability of the metastable Z-isomers exhibited a broad range of $t_{1/2}$ values dependent on the regiochemistry. IBP **4,4** shows the longest $t_{1/2}$ of 26.3 minutes, followed by **3,4** with a half-life of 25.7 minutes. These $t_{1/2}$ values are significantly longer than those of previously reported arylimine switches,[2,21,22] only surpassed in duration by the AIP containing two *ortho*-pyrrolidine units.[1] This highlights the potential to achieve imine-based photoswitches with longer $t_{1/2}$ values compared to previous reports of arylimine derived photoswitches,[2,21,22] without the need for *ortho*-amination. Interestingly, the IBPs with the most bathochromically shifted UV/vis absorption bands, *i.e.*, the 5-substituted derivatives, generally show the lowest thermal stability of their Z-isomers (with $t_{1/2}$ values of less than 1.3 min at 20 °C). Similar observations for azo-based switches have been previously rationalised based on the polarisation of the photochromic double bond, where greater electron donation from a heteroaryl ring can decrease the bond order.[18] A summary of the key photoswitching properties for this [3×3] matrix of IBPs is presented in Table 1.

Table 1. Overview of the photoswitching properties of the IBP photoswitches; the processed data can be found in the Supporting Information. The λ_{max} and the corresponding extinction coefficient (ε) is measured for the E-isomer.

	λ_{max} (nm)	ε (M^{-1} cm^{-1})	$t_{1/2}$	%Z at PSS		
				340 nm	365 nm	385 nm
3,3	296	14980	6.5 min	26%	6%	—
3,4	301	13080	25.8 min	58%	15%	—
3,5	307	14920	1.4 min	54%	28%	—
4,3	305	15530	6.5 min	35%	10%	—
4,4	304	14570	26.3 min	48%	6%	—
4,5	315	12470	2.2 min	36%	15%	—
5,3[a]	315	11260	50.4 s	—[b]	—[b]	—
5,4	316	11520	3.4 min	76%	54%	18%
5,5[a]	324	13890	17.0 s	—[b]	—[b]	—

[a] Note that the short $t_{1/2}$ values preclude the measurement of the % Z at the PSS under these conditions. [b] The PSS could not be determined at 20 °C.

Computational investigations were conducted to determine the optimised geometries of the *E, Z* and transition state (TS) structures using the ωB97X-D4/def2-TZVPP level of theory and a CPCM solvation model for acetonitrile.[1] The predicted conformation of

E-**4,4** correlates well with the single crystal X-ray structure (Figure 2a, S37). All *E*-IBPs exhibited a small twist away from planarity due to steric clash of the C−H bonds of the *N*-pyrazole ring with the C−H of the imine bond. For the TSs, the IBPs adopt either a planar or perpendicular TS structure[2] and exhibit a linearisation of the imine motif (C=N−C), consistent with an inversion isomerisation pathway.[1,2] In terms of preference, the **5,−** IBPs exhibit a perpendicular TS, the **4,−** IBPs adopt planar TS conformations, while the **3,−** analogues adopt a perpendicular TS geometry.

For the *Z*-isomers, the majority of the IBPs adopted a near T-shape conformation. Exceptions included *Z*-**5,5** and *Z*-**4,5** which is attributed to a preferred twisted structure that enables greater conjugation across the molecule. Interestingly, *Z*-**4,3** adopts a planar structure, potentially stabilised by an intramolecular hydrogen bond (2.2 Å distance, Figure S31). This observation agrees with the azobispyrazoles reported by Li and co-workers.[13] It is interesting to note that *Z*-**3,4** does not adopt a planar geometry, indicating the diversity arising from the regiochemistry of these systems.

For the derivatives that adopt a near T-shape conformation, the C−H bond of the aldehyde fragment is directed towards the π-system of the *N*-pyrazole ring. The close proximity of the C−H bond to the centroid of the *N*-pyrazole ring, 2.6 Å for *Z*-**4,4**, may enable stabilising CH-π interactions, with some indication shown in the non-covalent interaction plot (Figure S32).[1,13,18] In the case of *Z*-**5,5**, the twisted geometry appears to significantly destabilise the *Z*-isomer compared to the *E*-isomer, indicated by a ΔG_{Z-E} of 30 kJ mol^{-1}. In comparison to the AIPs where the $t_{1/2}$ appeared to be dominated by a stabilisation of the *Z*-isomer, the IBPs show a more balanced effect between TS destabilisation and *Z*-isomer stabilisation; on-going work is attempting to elucidate this behaviour.

In summary, we have prepared a [3×3] library of nine iminobispyrazoles and characterised their photoswitching properties. While the overall amount of the metastable isomer generated under photoirradiation is less than that achieved for *ortho*-aminated AIPs, the fraction of *Z*-isomer formed is improved compared to the previously reported arylimines. The greatest fraction of *Z*-isomer generated under the conditions explored here was 76% for **5,4**. Moreover, while relatively long $t_{1/2}$ values were only achieved upon *ortho*-functionalisation of the AIPs, we show that the IBPs, specifically **4,4** and **3,4** exhibit enhanced stabilities of the *Z*-isomer. Efforts are currently underway to explore the use of this accessible and diverse photoswitch library in the

context of systems chemistry by exploiting the dynamic-covalent character of the imine bond.

Conflicts of interest
There are no conflicts to declare.

Author contributions
J.W. and C.L. performed the synthesis, characterisation and photoswitching experiments. L.K. conducted the computational investigations. J.W. and J.L.G. prepared the manuscript, with input from all authors. J.L.G. conceived the project and supervised the research.

Acknowledgements

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