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Protoisomerization of indigo di- and monoimines

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Received 00th January 20xx, Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Indigo di- and monoimines can be protonated to form stable salts in which the central C=C bond has isomerized from a trans to cis configuration. Deprotonation of these salts regenerates the neutral trans species. The protonation chemistry of indigo is also explored.

Cis-trans isomerization of alkenes is a fundamental component of their chemistry and is featured in a number of biological systems (e.g. bacteriorhodopsin, green fluorescent protein). Olefin interconversion can be triggered by light or by a wide range of catalysts (protons, Lewis acids, transition metals) and occur via many different mechanistic pathways. Among the many different classes of conjugated olefinic species which have been investigated in this context are the indigos (Figure 1). The two prototypical species, indigo and thioindigo, have markedly different isomerization characteristics: whereas thioindigo undergoes trans→cis photoisomerism, indigo does not due to its intramolecular NH-O hydrogen bonds which instead lead to rapid and efficient excited state intramolecular proton transfer. N,N'-disubstituted indigo derivatives, lacking H-bonding capabilities, do undergo photoisomerization.

We recently reported the synthesis of indigo diimine (‘Nindigo’) derivatives. These more soluble indigo analogues have been shown by us and others to possess a rich coordination chemistry. Herein we report the discovery that Nindigos can be protonated and that protonation is accompanied by trans→cis isomerization about the central C=C bond. This process is fully reversible: treatment of the protonated Nindigo compounds with base regenerates the neutral Nindigo itself.

Figure 1. Trans/cis isomerization in indigoid compounds.

Nindigo 1 reacts instantly with strong acids (HCl, HBF₄, CF₃CO₂H, but not acetic acid or benzoic acids) to give intense green solutions from which pure crystalline products can be obtained in excellent yields (92% of 2a and 79% for 2b) (Scheme 1). The reaction is fully reversible: reaction of the protonated species with base (e.g., DBU, NEt₃) rapidly regenerates the neutral Nindigo 1. Control experiments indicate that, unlike thioindigo photoisomerization, light is not required to trigger this photosomerization process. The structures of 2a (Figure 2) and 2b (ESI) reveals that the protonated Nindigo has undergone trans→cis isomerization with respect to the central C=C bond. The additional proton is located on one of the two imine nitrogens (N2) and appears to engage in an intramolecular hydrogen bond to the other imine group (N4). The protonation induces a small but statistically significant degree of asymmetry in the protonated structure. This is evidenced by the protonation-induced changes in C2v vs C1 symmetry, which may arise either from a change in the protonation site or from the formation of a single position symmetrically bridged by the two.

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eElectronic Supplementary Information (ESI) available Synthesis and characterization data for new compounds and crystallographic data (CIF format). See DOI: 10.1039/x0xx00000x

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The unexpected trans→cis isomerization of Nindigo 1 raised the question as to whether indigo itself reacts similarly with strong acids. Indigo was unreactive towards most of the acids that protoizomerize Nindigo (e.g. CF₃COOH, HBF₄, HC). Sulfuric and trifluoromethanesulfonic acids react with indigo in dilute CHCl₃ to give persistent green solutions (Scheme 2). With sulfuric acid, the resulting green solution (λ_max 623 nm) gradually fades and leads to a blue precipitate which dissolves in water. This blue material is a mixture of sulfonated indigo derivatives 3 (indigo can be controllably sulfonated under different conditions to produce from mono- to tetrasulfonated compounds[1]). In contrast, the green solutions (λ_max 642 nm) resulting from indigo and triflic acid revert back to indigo. Attempts to isolate the green solution species generated from either acid were thwarted by the instability of these solutions; the solution instability also prevents us from determining if the presumed protonated indigo has isomerized (4) or remains as a trans olefin[5].

The substantial differences in protonation chemistry between Nindigo and indigo prompted us to explore the properties of the corresponding indigo mono-imine – a hybrid of indigo and Nindigo. Modification of the synthetic procedures for Nindigo 1 facilitated the preparation of indigo mono-imine 6. Protonation of 6 could be carried out with the same set of acids that were used in the protonation of dimine 1 (Scheme 3). In this instance, HCl proved to be the most practical acid because the hydrochloride salt crystallizes readily from solution. The 1H NMR spectrum of 7 presents three distinct NH signals at 11.8, 12.4 and 14.8 ppm; solution NMR cannot be used to determine the configuration about the central CC bond because the cis and trans isomers of 7 have the same (C₃) symmetry. X-ray crystallography studies on the indigo mono-imine 6 and its HCl salt 7 (Figure 3) reveal them to be trans and cis olefins respectively. The protonation site in 7 is the imine nitrogen, and an intramolecular hydrogen bond to the proximal carbonyl group is apparent.
Indigo bis(aryl imines) (i.e. Nindigos) were originally reported over a century ago\(^\text{(a)}\) (although the specific synthetic route has not been reproducible\(^\text{(b)}\)). Included in this original report were reactions of indigo bis(phenylimine) with strong acids (HCl, H\(_2\)SO\(_4\), picric acid) which gave green solutions or crystalline materials. Herein we have elucidated the structural details of the reaction of Nindigo with strong acids. Unlike the cis isomers of neutral indigo, thiindigo, etc, the protonated species presented here are indefinitely stable. The reversible “protoisomerization” of Nindigo complements the vast majority of olefin isomerization pathways (vide supra). In fact the only other example of proton-dependent alkene isomerism of which we are aware occurs in the natural product Noradione A.\(^\text{(c)}\)

Chemically-induced indigoid isomerization is not without precedent. The reactions of indigo with either dihaloalkanes or oxalyl chloride produces the fused cis indigo species \(^8\) and \(^9\) respectively. More recently, transition metal complexes \(^10\) and \(^11\) contain cis Nindigo derivatives in reactions starting from the trans configuration of the ligand. The protoisomerization of Nindigo presented herein is distinguished by each of these examples by its facile reversibility.

In conclusion, we have presented a highly unusual protoisomerization process for indigo diimines and their corresponding mono-imines. The protonated species are a new class of dyes based on indigo: Given the burgeoning interest in exploiting indigo’s properties – it’s blue, flat, and cheap – in a variety of organic electronics applications (e.g. transistors, solar cells),\(^\text{(d)}\) the notion of making chemical derivatives of indigo for organic materials research is still in its infancy.\(^\text{(e)}\) Future work will aim to further develop the chemistry of protonated Nindigos and to understand the mechanism by which this unusual protoisomerization occurs.

**Acknowledgements**

We thank the Natural Sciences and Engineering Research Council of Canada and the University of Victoria for Support.

**Notes and references**


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