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Protoisomerization of indigo di- and monoimines

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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[1] and is featured in a number of biological systems (e.g. bacteriorhodopsin,[2] green fluorescent protein[3]). 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.[4] Among the many different classes of conjugated olefinic species which have been investigated in this context are the indigoids (Figure 1). The two prototypical species, indigo and thioindigo, have markedly different isomerization characteristics: whereas thioindigo undergoes *trans→cis* photoisomerism,[5, 6] indigo does not[7] due to its intramolecular NH-O hydrogen bonds which instead lead to rapid and efficient excited state intramolecular proton transfer.[8] *N,N'*-disubstituted indigo derivatives, lacking H-bonding capabilities, do undergo photoisomerization.[6, 9]

We recently reported the synthesis of indigo diimine ('Nindigo') derivatives.[10, 11]. These more soluble indigo analogues have been shown by us[12] and others[13, 14] 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 compound in its *trans* configuration. We further generalize this discovery by demonstrating analogous processes in indigo *mono*imines (reported here for the first time) and

investigate the possibility of protonation/isomerization in indigo itself.

X, Y = **O, S** (thioindigo)
O, NH (indigo)
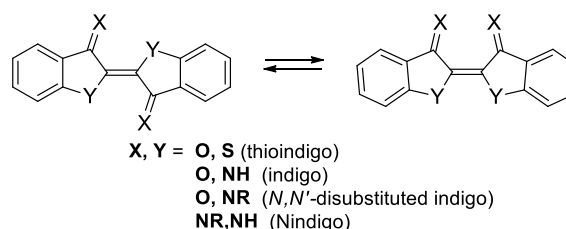**O, NR** (*N,N'*-disubstituted indigo)
NR,NH (Nindigo)

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 photoisomerization 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 (in the structures of neutral Nindigo derivatives **1** the two halves of the molecule are crystallographically equivalent). For example, the protonated imine C=N bond (C2-N2) is longer than the unprotonated imine(C18-N4), and there are differences between other pairs of nominally equivalent bonds (e.g. C1-N1 *vs.* C17-N3; C1-C2 vs C17-C18). The differences in bond lengths between the two halves of the molecule can be rationalized based on resonance structure **2'** (Figure 3). The solution ¹H NMR spectra suggest higher (C_{2v}) symmetry, which may arise either from a structure in which the proton occupies a single position symmetrically bridged by the two

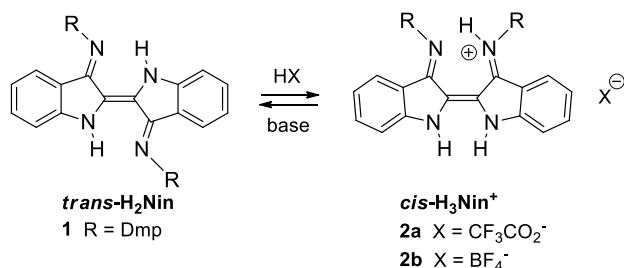[a.] Department of Chemistry, University of Victoria, PO Box 3065 STN CSC, Victoria BC V8W 3V6, Canada
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imines, or more likely from a rapidly interconverting mixture of tautomers in which the proton is bound to either of the two imines.

Scheme 1. Protoisomerization of Nindigo **1** (Dmp = 2,6-dimethylphenyl).

trans-H_2Nin
1 R = Dmp

cis-H_3Nin$^+$
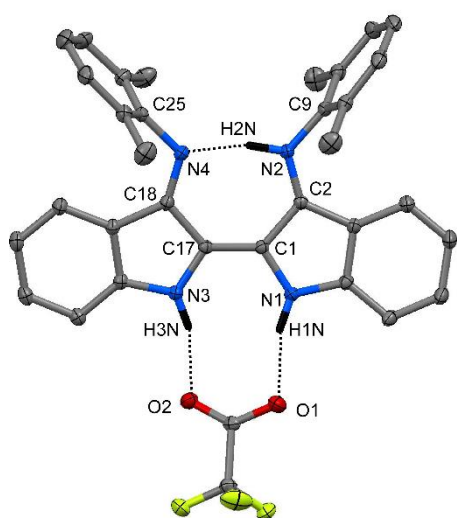**2a** X = $CF_3CO_2^-$
2b X = BF_4^-

Figure 2. X-ray structure of **2a**. Hydrogen atoms except N-H hydrogens omitted for clarity. Thermal ellipsoids represented at 50%.

The indole-type NH protons are hydrogen-bonded to the trifluoroacetate counter-ion in **2a** (Figure 2) (d(NH-O) 1.872 and 1.847 Å). In the corresponding BF_4 salt **2b** somewhat longer N-H- - F contacts (1.980 and 2.060 Å) are evident. These cation/anion interactions are also evident in solution in **2a:** the indole-type proton chemical shifts in the ^{1}H NMR spectra **2a** and **2b** are markedly different (13.07 $vs.$ 9.71 ppm respectively) reflecting the different hydrogen bond capabilities of the counter-anions. In contrast, the chemical shifts of the imine-bound proton are relatively close (16.02 for **2a** vs. 16.47 ppm for **2b**).

Table 1. Selected bond lengths in derivatives of **2** and **1** (Mes = mesityl and Dipp = 2,6-diisopropylphenyl)

bond	**2a**	**2b**	**1** (R=Mes)[11]	**1** (R=Dipp)[10]
C1-C17	1.3852(14)	1.3800(15)	1.366(4)	1.356(3)
C1-C2	1.4678(14)	1.4649(15)	1.455(3)	1.4638(17)
C17-C18	1.4838(14)	1.4836(15)	-	-
C1-N1	1.3807(13)	1.3881(14)	1.378(3)	1.3753(17)
C17-N3	1.3695(13)	1.3716(15)	-	-
C2-N2	1.3153(13)	1.3142(14)	1.301(3)	1.2939(17)
C18-N4	1.3007(14)	1.2974(15)	-	-

The unexpected $trans{\rightarrow}cis$ 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. CF_3CO_2H, HBF_4, HCl). Sulfuric and trifluoromethanesulfonic acids react with indigo in dilute $CHCl_3$ 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[15]). 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**).
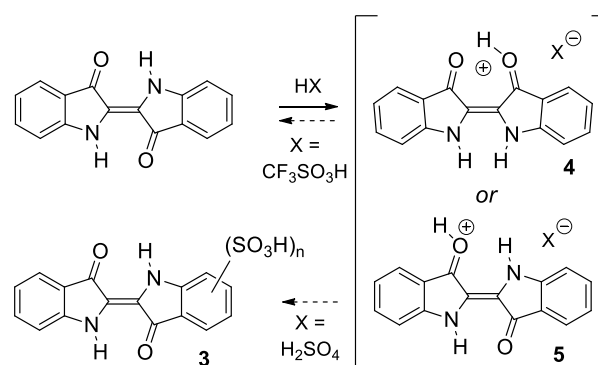
Scheme 2. Reactivity of indigo towards H_2SO_4 and CF_3SO_3H.

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 diimine **1** (Scheme 3). In this instance, HCl proved to be the most practical acid because the hydrochloride salt crystallized readily from solution. The ^{1}H 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 (C_s) 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.

6

7
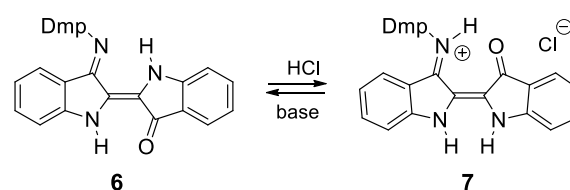
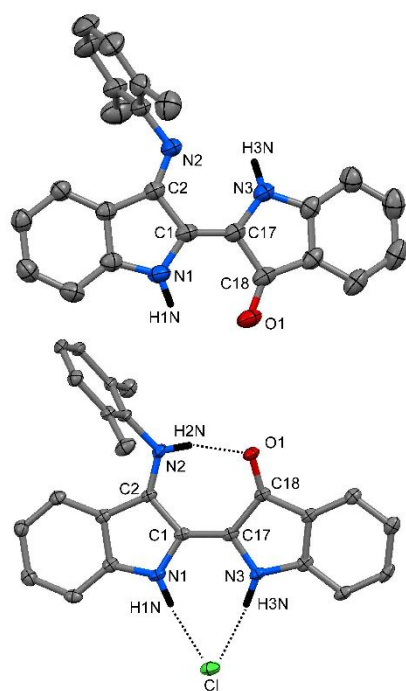**Scheme 3**. Protonation of indigo mono-imine **6**.

Figure 3. Structure of **6** (top) and **7** (bottom). Hydrogen atoms except N-H hydrogens omitted for clarity. Thermal ellipsoids represented at 50%. [a]bond metrics for each of the two independent molecules of **6** in the unit cell.

Table 2. Selected bond lengths for 6 and 7.

bond	6	7
C1-C17	1.354(2), 1.356(2)[a]	1.377(3)
C1-C2	1.4765(19), 1.466(2)	1.454(3)
C17-C18	1.4876(19), 1.467(2)	1.502(3)
C1-N1	1.3753(18), 1.377(2)	1.378(3)
C17-N3	1.3754(19), 1.382(2)	1.366(3)
C2-N2	1.2905(18), 1.2864(19)	1.323(2)
C18-O1	1.2392(17), 1.2429(19)	1.231(3)

Indigo bis(aryl imines) (i.e. Nindigos) were originally reported over a century ago[16] (although the specific synthetic route has not been reproducible[10, 17]). Included in this original report were reactions of indigo bis(phenylimine) with strong acids (HCl, H_2SO_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, thioindigo, 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 Norbadione A.[18]

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**[19] and **9**[20] respectively. More recently, transition metal complexes **10**[11] and **11**[14] 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.
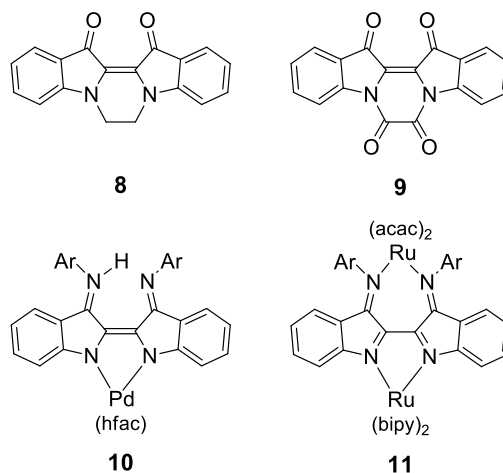
In conclusion, we have presented a highly unusual protoisomerization process for indigo diimines and their corresponding mono-imines. The protonated species are a new class of dyes based on indigo: Given the burgeoning interest in exploiting indigo's properties – it's blue, flat, and cheap – in a variety of organic electronics applications (e.g. transistors, solar cells),[21] the notion of making chemical derivatives of indigo for organic materials research is still in its infancy.[22] Future work will aim to further develop the chemistry of protonated *cis* Nindigos and to understand the mechanism by which this unusual protoisomerization occurs.

Acknowledgements

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