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Evidence for Intramolecular C-H···O Hydrogen Bonds Determining *N,N'*-Diacylindigo Crystal Structure Conformations

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The debate over C-H···O hydrogen bonds lasted for many years before Taylor and Kennard surveyed the Cambridge Structural Database in 1982 and extracted strong statistical evidence in favor of such attractive interactions.[1] Further work by a number of other groups have concluded that although C-H···O bonds are much weaker than traditional hydrogen bonds (X-H···X, where X = O or N) they are nonetheless ubiquitous in crystal structures.[2-5] The current consensus is that C-H···O bonds are weakly attractive, electrostatic interactions, with a moderate degree of directionality, that decrease with $1/r$ and consequently extend well beyond the conventional van der Waals limit. Desiraju has also shown that the C···O distance decreases with increased C-H acidity.[5] At present there is no strong evidence correlating C···O distance with O basicity; the general feeling is that, like traditional X-H···X hydrogen bonds, the interaction is relatively insensitive to the basicity of the hydrogen bond acceptor.[6] In general, any experimental study of the factors determining C-H···O bond strengths is destined to be problematic due to the difficulty delineating such a weak interaction from the influence of stronger interactions. Correlations based on statistical surveys have proved to be an effective way to cancel out these environmental effects as "random noise". In this report, we compare three related crystal structures that provide insight into how a molecule with an excess of hydrogen bond acceptors attempts to counter these acceptors in the solid state by forming intramolecular C-H···O hydrogen bonds. Moreover, the relative order of the observed C···O distances is rationalized in terms of the CH acidities and O basicities.

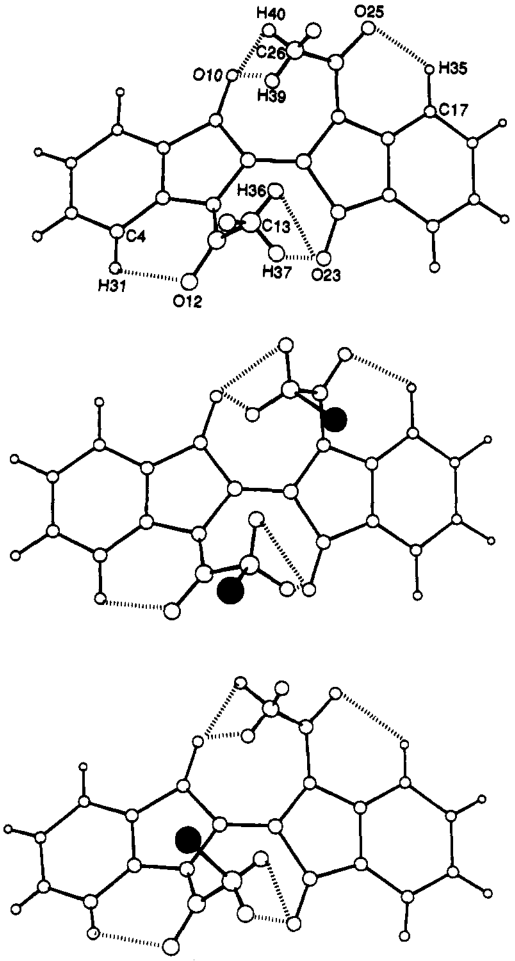

Figure 1. Ball and stick representations of the X-ray structures of **1** (top), **2** (middle), and **3** (bottom). For clarity only the relevant atom numbers for structure **1** are shown; the atom numbers for structures **2** and **3** correspond to the same positions. Putative intramolecular CH···O interactions are depicted by the hashed lines and chlorine atoms are shaded black.

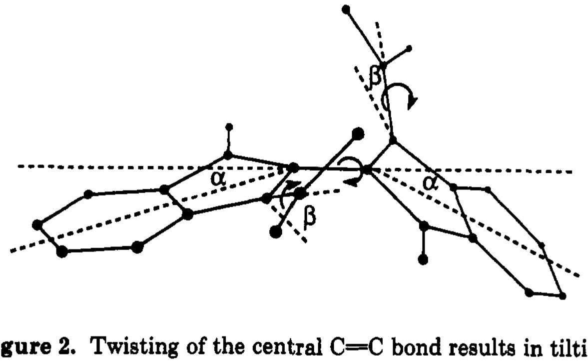

Figure 2. Twisting of the central C═C bond results in tilting of the two planar halves by angle α. Rotation of the *N*-acyl groups around their N–C bonds results in tilting by angle β.

We have recently characterized the structure and photochemistry of a number of *N,N'*-diacylindigo dye derivatives.[7,8] This report focuses on the crystal structures of *N,N'*-diacetylindigo (**1**), *N,N'*-bis(chloroacetyl)indigo (**2**), and *N*-acetyl-*N'*-chloroacetylindigo (**3**), which are depicted in Figure 1 and Scheme I. Steric crowding in these compounds is alleviated by two torsional mechanisms, twisting of the central C═C bond, and rotation of the N–C bonds of the *N*-acyl groups (Figure 2).[7,9] These torsions induce changes in the hybridization of the attached atoms which are manifested as intramolecular tilts. For example, twisting of the central C═C bond changes the hybridization of the attached carbons from sp^2 toward sp^3 which allows the two planar halves of the molecules to tilt

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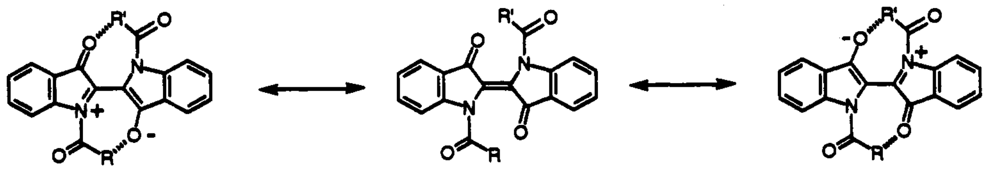
0022-3263/93/1958-6905$04.00/0

Scheme I



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1 R = R' = CH_3
2 R = R' = CH_2Cl
3 R = CH_3, R' = CH_2Cl

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Table I. C···O and H···O Distances (Å)[a]

compd	C_{26}–O_{10}	H_{39}–O_{10}	H_{40}–O_{10}	C_{13}–O_{23}	H_{36}–O_{23}	H_{37}–O_{23}	C_{17}–O_{25}	H_{35}–O_{25}	C_4–O_{12}	H_{31}–O_{12}
1	3.040(1)	3.04(2)	2.62(2)	2.944(1)	2.87(2)	2.66(2)	2.852(1)	2.34(2)	2.852(1)	2.31(2)
2	2.981(2)	3.26	2.52	2.914(2)	3.23	2.26	2.902(2)	2.36	2.845(2)	2.33
3	2.925(4)	2.84(3)	2.51(3)	2.869(4)	2.63(2)	3.10(3)	2.848(4)	2.33(3)	2.905(4)	2.31(3)

[a] Where valid, the standard deviation of the final digit is given in parentheses.

away from coplanarity by angle α (Figure 2).[10] Similarly, rotation of the *N*-acyl groups around the N–C bonds forces the nitrogens to become more sp^3 hybridized, resulting in the *N*-acyl groups tilting away from coplanarity by an angle β. In all of the derivatives we have so far examined, the *N*-acyl side chains adopt conformations placing their R groups *syn* to the central C═C bond. NMR studies have shown that these conformations are strongly retained in solution.[7] By adopting these *N*-acyl conformations, repulsive acyl carbonyl–indigo carbonyl interactions are avoided and attractive CH···O interactions are formed. Initially, we obtained the X-ray structures of 1 and 2. The skeletal structures of these two compounds are essentially the same; the only significant differences concern the *N*-acyl groups as reflected by the four sets of CH···O distances summarized in Table I.[11] In each molecule, both of the *N*-acyl groups are involved in "double C–H···O hydrogen bond relays"; the *N*-acyl CH's are bifurcated hydrogen bond donors with the indigo carbonyls and the *N*-acyl carbonyls are hydrogen bond acceptors with the adjacent indigo aryl CH's. Focusing the discussion on the more reliable C···O distances, the C26···O10 and C13···O23 distances are shorter for 2 than for 1, whereas the C17···O25 distances show the reverse trend and the C4···O12 distances are approximately equal. The Cl substituents in 2 adopt positions that have very little steric interaction with the rest of the molecule, suggesting that their major influence on the molecular structure is an inductive, withdrawing effect. Thus, a plausible explanation for the observed difference in C···O distances is that the electronegative Cl's make the *N*-chloroacetyl CH's more acidic and therefore capable of stronger CH···O interactions whereas the N-chloroacetyl carbonyls are less basic and form weaker CH···O interactions.[12]

To further probe if this substituent effect is truly operative, the asymmetric *N*-acetyl-*N'*-chloroacetyl derivative 3 was synthesized and its X-ray structure determined. We reasoned that if intramolecular CH···O interactions were significant in the solid state, then 3 should adopt a structure where the relative order of C···O distances can be predicted by simply considering the CH acidities and O basicities. This appears to be the case. The more acidic *N'*-chloroacetyl CH's form a stronger CH···O interaction than the *N*-acetyl CH's as judged by the C13–O23 distance of 2.869(4) Å being significantly shorter than the C26–O10 distance of 2.925(4) Å (Table I). Conversely, the less basic *N'*-chloroacetyl carbonyl forms a weaker CH···O interaction than the *N*-acetyl carbonyl as judged by the C4···O12 distance of 2.905(4) Å being longer than the C17···O25 distance of 2.848(4) Å. Since 3 and 1 differ by a single, sterically unobtrusive but inductively important Cl substituent, we were interested in how the structure of 3 with its altered C–H···O bonding strengths compared to that of 1. A computer-graphics examination of 3 overlaid on 1 (not shown) indicated that transformation of the skeleton of 1 into 3 is not achieved by any single movement such as rotation of the *N*-chloroacetyl group but results from a combination of the two major torsion mechanisms and their associated intramolecular tilts as described above.

Although C–H···O hydrogen bonds can be observed in the solid state, an important question is do they have any significance in solution?[13] In terms of the *N,N'*-diacylindigo dyes described here, the question is do the intramolecular C–H···O hydrogen bonds observed in the solid state affect the dye's solution-state electronic absorption properties? The nature of the *N,N'*-diacylindigo ground and excited states have been well characterized.[14] It is known from semiempirical calculations that the excited singlet state of the chromophore, obtained by direct irradiation, has more zwitterionic character than the ground state due to increased participation of the resonance structures 4 and 5 depicted in Scheme I.[15] If the steric effect of Cl substitution is considered negligible, the excitation energy is likely to be affected, inductively, in two ways. The more

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[11] As well as the distances quoted in Table I, the *N*-acetyl C═O bonds were observed to be 0.015 Å longer than the *N*-chloroacetyl C═O bonds whereas the C–CH_3 bonds were about 0.015 Å shorter than the C–CH_2Cl bonds. To ensure that the observed differences in CH···O distances were not simply due to these changes in *N*-acyl bond lengths, the deviation of the CH···O distances due to different *N*-acyl bond lengths for structures 1–3 was determined by computer graphics. It was found that changing the *N*-acyl bond lengths by 0.015 Å had essentially no effect on any of the measured CH···O distances.

[12] When comparing 1 and 2, the correlation of C···O distance with carbonyl basicity is not as certain as it is for CH acidity, in agreement with the conclusion that CH acidity is more important than carbonyl basicity.[6]

[13] The recent reports by Steiner and Saenger discussing C–H···O bonding in carbohydrates indicate that if an excess of hydrogen bond acceptors are placed in a hydrocarbon environment then C–H···O bonding is a serviceable way to satisfy coordination geometries. Their work suggests that C–H···O bonding may be a significant interaction in certain types of host/guest complexation systems. An illustrative example is when an oxygen-rich guest molecule, such as water, is complexed inside a hydrophobic cyclodextrin cavity.[4]

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withdrawing *N′*-chloroacetyl group should destabilize the zwitterionic excited state relative to the *N*-acetyl group, producing a red-shifted absorbance.[15] On the other hand, increased C–H···O hydrogen bonding by the *N′*-chloroacetyl CH's should provide a stabilizing influence on the zwitterionic excited state and have a countering blue-shift effect (Scheme I).[16] Thus, the observed inductive effect upon Cl substitution should really be considered an apparent effect that is the sum of these two counteractive factors. The absolute contributions of each of the factors cannot be determined from this work. The absorption maxima for **1**, **2**, and **3** in benzene solution occur at 562, 556, and 561 nm, respectively. Although the spread of wavelengths is quite small, a possible explanation why **3** has an absorption maximum closer to **1** than **2** is that its resonance structure **4** is the dominant tautomer in the excited state; the alternative resonance structure **5** is less favored as it places the cationic nitrogen adjacent to the more withdrawing *N′*-chloroacetyl group. The excitation energy to produce resonance structure **4** is, therefore, expected to be similar for compounds **1** and **3** and higher for compound **2**.

In conclusion, these X-ray structures show a correlation of increased intramolecular C–H···O hydrogen bond strength with increased CH acidity and increased O basicity. The evidence is circumstantial; a coincidental alignment of other crystal packing forces cannot be ruled out as the true origin of the correlation, although it is unlikely. The characterization of weak, noncovalent interactions is currently an active area of chemical research. CH···X interactions[17] like other weak, directional, electrostatic interactions, such as π–π,[18] XH···π[19] and XH···C,[20] are becoming increasingly important secondary considerations in the design and evaluation of supramolecular systems.

Experimental Section

Synthesis. The syntheses of *N,N′*-diacetylindigo (**1**) and *N,N′*-bis(chloroacetyl)indigo (**2**) have already been described.[8] *N*-Acetyl-*N′*-(chloroacetyl)indigo (**3**) was obtained by stirring *N*-acetylindigo (0.08 mM)[21] and chloroacetyl chloride (0.12 mM) in pyridine (10 mL) at 90 °C for 6 h. After removing the solvent, the desired product was recrystallized from hexane/methylene chloride (mp >260 °C).

X-ray Crystallography.[22] Crystal data for **1**: $C_{20}H_{14}N_2O_4$, $M = 346.35$, monoclinic $P2_1/n$ (no. 14), $a = 13.707(2)$, $b = 8.516(1)$, $c = 14.768(2)$ Å, $\beta = 112.13(1)°$, $V = 1596.7(5)$ Å^3, $Z = 4$, $D_c = 1.44$g/cm^3 (294 K), μ(Cu Kα) = 8.01 cm^{-1}, $R_{\text{merge}}(I) = 0.022$, 3377 unique reflections, 2768 with $Fo > 3\sigma(Fo)$, coordinates of all hydrogen atoms refined $R_1 = 0.039$, $R_2 = 0.052$, gof = 1.84.

Crystal data for **2** has been reported before:[7] $C_{20}H_{12}N_2O_4Cl_2$, $M = 415.24$, monoclinic $C2/c$ (no. 15), $a = 23.226(2)$, $b = 8.404(1)$, $c = 18.677(1)$ Å, $\beta = 96.15(1)°$, $V = 3622.7(8)$ Å^3, $Z = 8$, $D_c = 1.52$g/cm^3 (294 K), μ(Cu Kα) = 35.45 cm^{-1}, $R_{\text{merge}}(I) = 0.019$, 3836 unique reflections, 3116 with $Fo > 3\sigma(Fo)$, hydrogen atoms included only in the F_c calculation $R_1 = 0.044$, $R_2 = 0.061$, gof = 2.12.

Crystal data for **3**: $C_{20}H_{13}N_2O_4Cl$, $M = 380.79$, monoclinic $C2/c$ (no. 15), $a = 25.084(4)$, $b = 8.404(3)$, $c = 16.530(3)$ Å, $\beta = 95.56(1)°$, $V = 3468(2)$ Å^3, $Z = 8$, $D_c = 1.459$g/cm^3 (293 K), μ(Mo Kα) = 2.458 cm^{-1}, $R_{\text{merge}}(I) = 0.019$, 2347 unique reflections, 1641 with $Fo^2 > 3\sigma(Fo)^2$, coordinates of all hydrogen atoms refined $R_1 = 0.035$, $R_2 = 0.047$, gof = 1.558.

All data collected on an Enraf Nonius CAD4 diffractometer. Solutions and refinements via Enraf Nonius SDP/VAX software. The Chem3D Plus computer graphics program was used for drawing and comparing the final structures.

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(22) The authors have deposited atomic coordinates for **1**–**3** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.