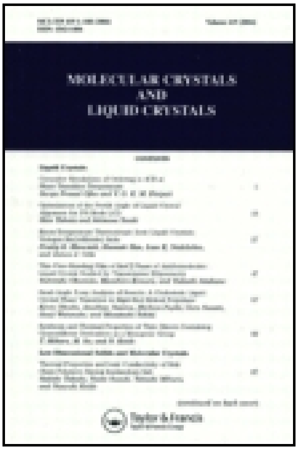


Molecular Crystals and Liquid Crystals
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gmcl20

Hydrogen Bonding in Glyoxylamides

David StC. Black [a], Glenn C. Condie [a], Donald C. Craig [a] & Darryl B. McConnell [a]

[a] School of Chemistry, The University of New South Wales, Sydney, Australia

Version of record first published: 31 Aug 2006

To cite this article: David StC. Black, Glenn C. Condie, Donald C. Craig & Darryl B. McConnell (2005): Hydrogen Bonding in Glyoxylamides, Molecular Crystals and Liquid Crystals, 440:1, 141-146

To link to this article: http://dx.doi.org/10.1080/15421400590958205

Mol. Cryst. Liq. Cryst., Vol. 440, pp. 141–146, 2005
Copyright © Taylor & Francis Inc.
ISSN: 1542-1406 print/1563-5287 online
DOI: 10.1080/15421400590958205

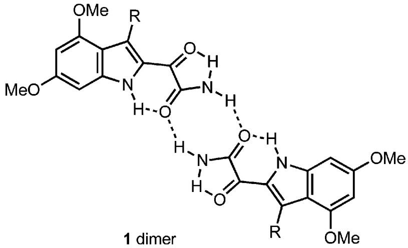
Hydrogen Bonding in Glyoxylamides

David StC. Black
Glenn C. Condie
Donald C. Craig
Darryl B. McConnell
School of Chemistry, The University of New South Wales,
Sydney, Australia

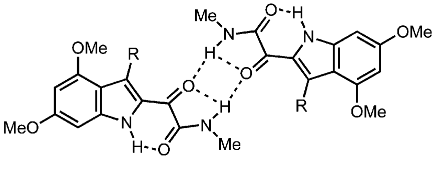
A range of secondary 2-amidophenylglyoxylamides self-assemble by intermolecular hydrogen bonding between the secondary amide proton and the 2-amidophenyl carbonyl oxygen atom.

Keywords: amides; hydrogen bonding; self-assembled dimers; X-ray crystal structures

The glyoxylamide structural fragment has been shown to display rather different hydrogen bonding features from simple amides. Primary and secondary amides usually form tape networks and chain motifs respectively. However, the primary and secondary indol-2-ylglyoxylamides **1,2** undergo self-assembly to give dimeric structures exhibiting new hydrogen bond motifs [1]. On the other hand, the related tertiary indol-7-ylglyoxylamide **3** dimerises as the result of unique intermolecular hydrogen bonding, which makes use of π-hydrogen bonds from the indole NH to an amide carbonyl acceptor [2].



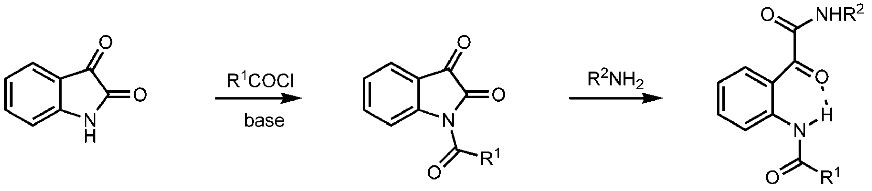
1 dimer



2 dimer

R = 4-ClC_6H_4

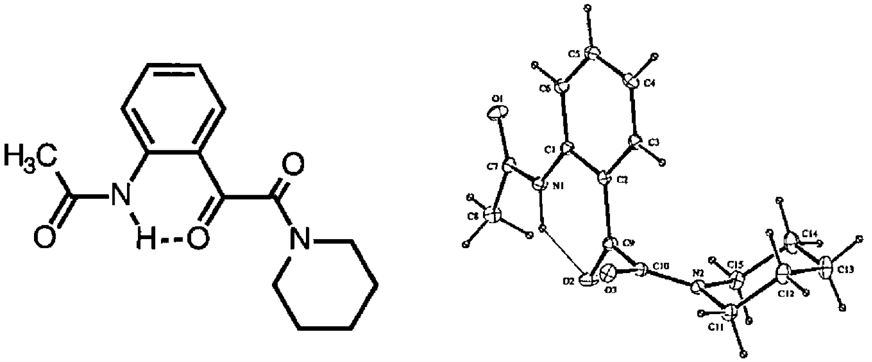
Address correspondence to David StC. Black, School of Chemistry, The University of New South Wales, Sydney 2052, Australia. E-mail: d.black@unsw.edu.au



SCHEME 1 The synthesis of 2-amidoglyoxylamides from N-acylisatins.

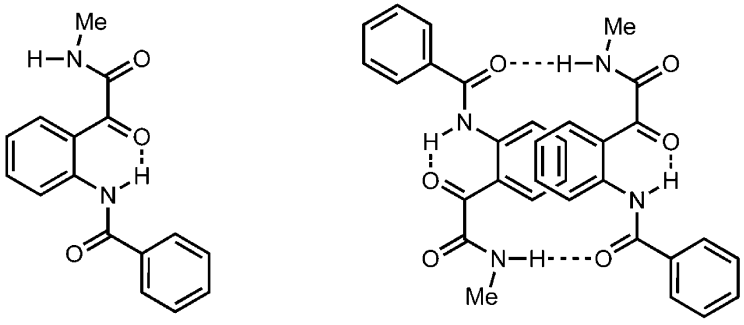
The formation of hydrogen bonded dimers by the self-assembly of pyridones [3], homo-peptides [4] and amido-lactams [5] has been reported earlier. We now report that a range of simple 2-amidophenylglyoxylamides also self-assemble by intermolecular hydrogen bonding, but in a completely different way from the glyoxylamides **1** and **2**. The 2-amidophenylglyoxylamides can be readily synthesized by the nucleophilic addition of amines to N-acylisatins [6] (Scheme 1).

The tertiary 2′-amidophenylglyoxylamide, *N*-[2-(oxo-1-piperidinylacetyl)phenyl]acetamide **3** exists as a monomer in the solid state, which is not unexpected since there is only a single free amide NH proton available for hydrogen bonding and that proton is strongly hydrogen bonded to the α-carbonyl oxygen atom forming a six-membered ring S(6). The crystal structure of glyoxylamide **3** shows the strong intramolecular hydrogen bonding between the C2′ amido NH proton and the α-carbonyl oxygen. Another interesting feature is that the torsional angle O2-C9-C10-O3 about the glyoxyl moiety is –94.8°. The ^{1}H NMR spectrum of glyoxylamide **3** displays a highly deshielded NH proton at 11.29 ppm belonging to the acetamide.



3 and X-ray structure

The secondary 2′-benzamidophenylglyoxylamide **4** was observed to exist as dimer in the solid state. Each monomer unit retains the strong intramolecular hydrogen bond S(6), evident in the tertiary derivative, and in this case, the torsional angle O2-C14-C15-O3 about the glyoxyl moiety is –89.1°. The X-ray crystal structure is shown in Figure 1



4 and dimer

Dimerization of the secondary derivative exists through intermolecular hydrogen bonds between the C2′ amide carbonyl oxygen atom and the glyoxylamide NH proton, forming an eighteen membered ring, $R^{2}_{2}(18)$, which was not possible in the tertiary derivative. Each monomer contains an approximately planar portion encompassing the C2′ amide, the central phenyl ring, and the α-carbonyl group. With respect

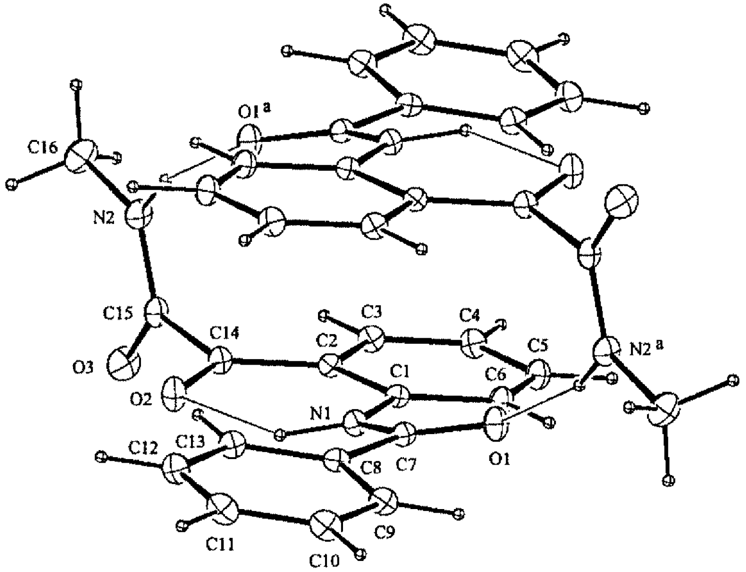
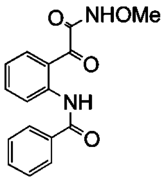


FIGURE 1 X-ray crystal structure of compound **4**.

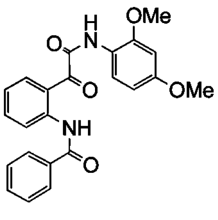
to this planarity, the two monomers are antiparallel, head to tail, one above the other and offset, suggesting a π–π interaction.

The ^{1}H NMR spectrum of glyoxylamide **4** displays a highly deshielded NH proton at 11.97 ppm, belonging to the benzamide, shifted even further downfield than the acetamide NH proton of glyoxylamide **3**. The glyoxylamide NH proton is present at 7.02 ppm due to its involvement in the S(6) motif.

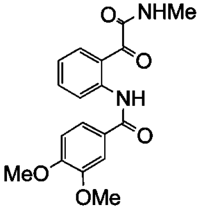
The self-assembly dimerisation was found to be quite general for secondary glyoxylamides and examples such as compounds **5–12** have been prepared.



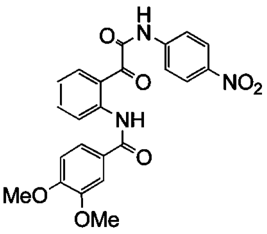
5



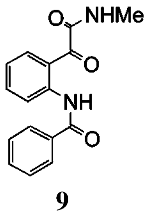
6



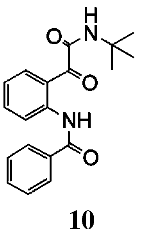
7



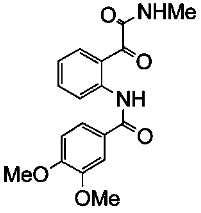
8



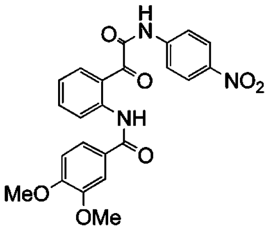
9



10

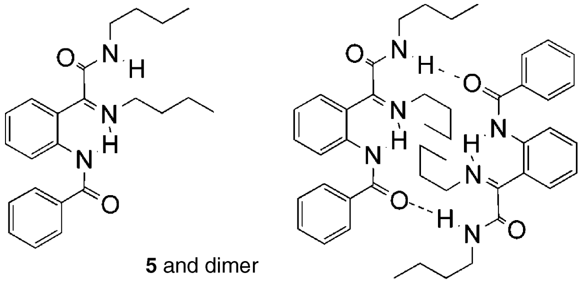


11



12

The crystal structure (Fig. 2) of an imine derivative **5**, prepared *via* addition of n-butylamine to the related glyoxylamide, or alternatively by the addition of two equivalents of n-butylamine to *N*-benzoylisatin, also shows dimer formation, with an eighteen-membered ring R $^2_2$(18).



5 and dimer

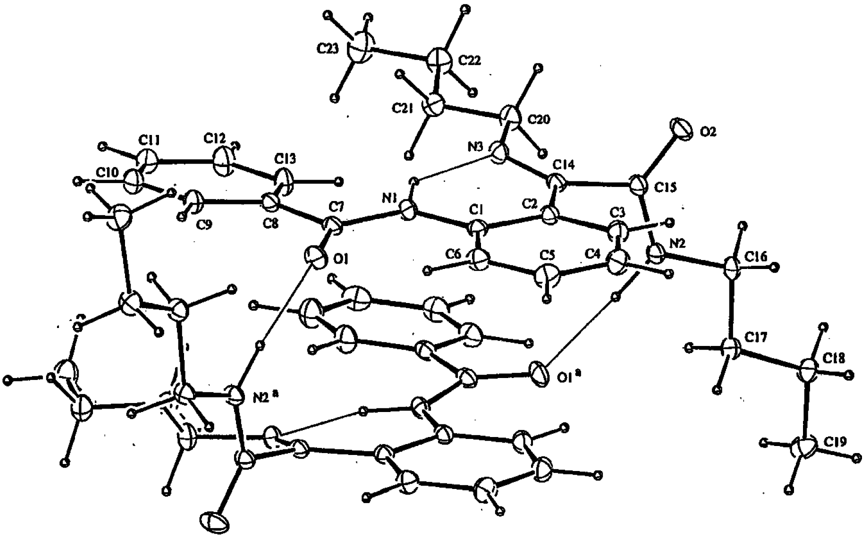
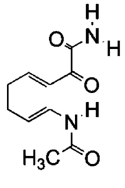


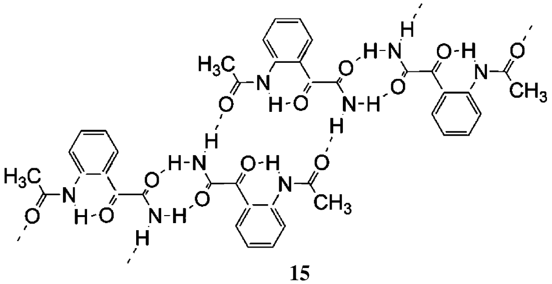
FIGURE 2 X-ray crystal structure of compound **5**.

Each monomer retains the strong intramolecular hydrogen bond, thus forming a six-membered ring, S(6), however in this case the acceptor is an imine. The presence of the imine seems to make little difference to the hydrogen bonding and the torsional angle N3-C14-C15-O2 about the glyoxyl moiety is 81.0°, slightly rotated from an expected 90°. Dimerization again exists through intermolecular hydrogen bonds between the C2′ amide carbonyl oxygen atom and the glyoxylamide NH proton, $R_2^2(18)$.

The primary 2′-amidophenylglyoxylamide, 2′-acetamidophenylglyoxylamide **14** was prepared but a suitable crystal could not be obtained. It is possible that the primary amide derivative could exhibit further inter- and intra-molecular hydrogen bonding and might therefore exist as an aggregate of dimer **15**. The ^{1}H NMR spectrum of the primary amide **14** indicates that the C2′ amide NH proton, at 10.90 ppm, is strongly intramolecularly hydrogen bonded to the α-carbonyl group, suggesting the presence of the S(6) motif. The primary amide NH protons are not equivalent, and two very broad signals are observed at 6.66 and 5.66 ppm, indicating that each is uniquely hydrogen bonded. Of these two, the downfield NH proton is likely to be involved in a hydrogen bonded system. It is unclear to what extent the upfield proton is also involved in hydrogen bonding.

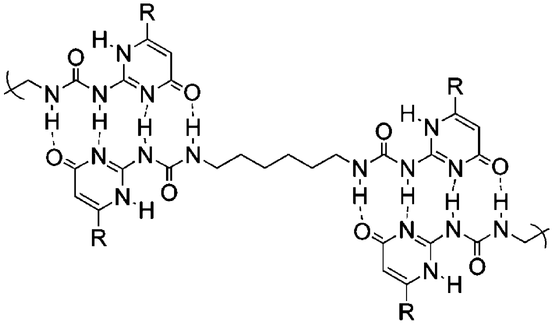


14



15

It is possible that the construction of suitable dimeric secondary glyoxylamides could allow the formation of polymeric self-assembled structures. The 2-ureido-4-pyrimidone moiety, with its array of four parallel hydrogen bonds, exists as a self-assembled polymer **16** [6].



16

REFERENCES

[1] Black, D. StC., Craig, D. C., & McConnell, D. B. (1996). The indol-2-ylglyoxylamide moiety: A new building block for the design and self-assembly of hydrogen bond networks. *J. Am. Chem. Soc.*, *118*, 8148–8149.

[2] Black, D. StC., Craig, D. C., & McConnell, D. B. (1997). Self-assembly of an indolylglyoxylamide by unusual hydrogen bonding. *Tetrahedron Lett.*, *38*, 4287–4290.

[3] Ducharme, Y. & Wuest, J. D. (1988). Use of hydrogen bonds to control molecular aggregation. Extensive, complementary arrays of donors and acceptors. *J. Org. Chem.*, *53*, 5787–5789.

[4] Bisson, A. P. & Hunter, C. A. (1996). Cooperativity in the assembly of zipper complexes. *Chem. Commun.*, 1723–1724.

[5] Nadin, A., Derrer, S., McGeary, R. P., Goodman, J. M., Raithby, P. R., Holmes, A. B., O'Hanlon, P. J., & Pearson, N. D. (1995). Seven-membered lactams as constraints for amide self-recognition. *J. Am. Chem. Soc.*, *117*, 9768–9769.

[6] Sijbesma, R. P., Beijer, F. H., Brunsveld, L., Folmer, B. J. B., Hirschberg, J. J. K. K., Lange, R. F. M., Lowe, J. K. L., & Meijer, E. W. (1997). Reversible polymers formed from self-complementary monomers using quadruple hydrogen bonding. *Science*, *278*, 1601–1604.