Supporting information for "An experiment in crystal structure prediction by popular vote"

Information on the small manual screen for crystals

Molecule I

Crystallization was attempted from water, toluene, hexanes, chloroform, THF, DMSO, acetonitrile, methanol, ethanol, t-butanol, isopropanol, from acetone:water and methanol:water mixtures, and by sublimation.

The best crystals were obtained from a 1:1 acetone:water solution, allowed to evaporate slowly, and these were used for single crystal XRD structure solution. Crystals of the same crystal form (as verified by powder XRD) were obtained by crystallization from THF and by sublimation of the material received from Aldrich. There was no evidence of other polymorphs.

Molecule II

The same solvents as used for molecule I were used for crystallization of molecule II. The crystals used to solve the structure initially were grown from a toluene solution, prepared warm and at high supersaturation. The structure was solved by single crystal XRD from one of these crystals. Crystals of the same crystal form were also obtained by crystallization from: benzene, acetonitrile, nitromethane, isopropanol, chloroform and an acetone:water mixture (as verified by powder XRD). There was no evidence of other polymorphs.

Some of the crystals grown from acetonitrile were of better quality than those originally used (from toluene) and the structure was solved again after the test, to obtain a better quality structure. This structure is reported in the paper (Table I).

Details of the computational search of the lattice energy surface

The first step in the crystal structure prediction calculations was to calculate molecular structures to be used as rigid building blocks in the lattice energy search for low energy crystal structures. Both molecules were optimised using density functional theory within the program Dmol3, using the PW91 functional and DNP basis set.

Crystal structures were generated using the Monte Carlo simulated annealing algorithm implemented in the Cerius2 Polymorph Predictor module.[S1] Crystal structures were generated in the nine space groups $P2_1/c$, $P\bar{1}$, $P2_1$, $P2_12_12_1$, $C2/c$, $Pbca$, $Pna2_1$, $Pbcn$ and $Pnma$ with Z' = 1 and the simulated annealing was repeated 4 times in each space group to ensure convergence of the set of generated structures. The empirically derived W99 model potential [S2] was used during the search, along with atomic charges fitted to the molecular electrostatic potential calculated for the optimised molecules in Dmol3.[S3] All crystal structures in the lowest 10 kJ/mol were then re-minimized using a higher quality model potential: the W99 potential with atomic multipoles up to hexadecapole on each atom. For molecule I, fluorine parameters were taken from Williams' parameterization to perfluorocarbon crystal structures [S4] and geometric combining rules were used for F…X interactions. The multipoles were calculated using a distributed multipole analysis [S5] of a B3P91/6-

31G** wavefunction calculated using the program CADPAC [S6] and the lattice energy minimizations were performed using the crystal structure modeling program DMAREL.[S7] Structures were tested for mechanical stability by calculating the elastic stiffness tensor and **k** = 0 phonons were calculated to check stability. Any unstable crystal structures were re-minimized with space group symmetry constraints removed to allow minimization to a stable local minimum. The final set of crystal structures was then clustered to remove any duplicates, using the COMPACK algorithm.[S8]

Our earlier assessment of such rigid molecule lattice energy minimizations with this model potential showed that this methodology provides reliable predictions of crystal structures of similar molecules (references 1 and 8 in the main text). There might be slightly larger errors in the lattice energy calculations because: i) molecule I contains fluorine, which was not parameterized in the W99 model potential and ii) molecule II has the possibility of flexibility of the OH group. Concerning (i): our experience with supplementing the W99 potential by Williams' older fluorine parameters [S9] has lead to predictions of as good quality as for non-fluorinated molecules (i.e. the observed crystal structure typically amongst the lowest few predicted crystal structures). Concerning (ii): it is difficult to assess the error introduced by the rigid molecule approximation, but it gives us confidence that the OH orientation in the DFT optimized and XRD determined molecular structures are almost identical. The H-O-C angle is 107.7° in the DFT optimized molecular model and 109.5° in the XRD determined structure, while the H-O-C-H dihedral angles are 56.8° in both DFT optimized and XRD determined molecular structures. The similarity of the isolated molecule (DFT) and the molecule in the crystal structure suggest that packing effects on the OH geometry are small.

S1. (a) Cerius2, version 4.6, Accelrys Inc.: San Diego, 1997; (b) P. Verwer and F. J. J. Leusen, *Rev. Comput. Chem.* (1998), 12, 327.

S2. (a) D. E. Williams, *J. Comput. Chem.* (2001), 22, 1; (b) D. E. Williams, *J. Comput. Chem.* (2001), 22, 1154.

S3. B. Delley, *J. Chem. Phys.* (199), 92, 508.

S4. D. E. Williams and D. J. Houpt, *Acta Cryst.* (1986), B42, 286.

S5. (a) A. J. Stone, *Chem. Phys. Lett.* (1981), 83, 233; (b) A. J. Stone and M. Alderton, *Mol. Phys.* (1985), 56, 1047.

S6. Amos, R. D.; with contributions from Alberts, I. L.; Andrews, J. S.; Colwell, S. M.; Handy, N. C.; Jayatilaka, D.; Knowles, P. J.; Kobayashi, R.; Koga, N.; Laidig, K. E.; Maslen, P. E.; Murray, C. W.; Rice, J. E.; Sanz, J.; Simandiras, E. D.; Stone, A. J.; Su, M.-D. *CADPAC*, version 6.0; University of Cambridge: Cambridge, 1995.

S7. S. L. Price, D. J. Willock, M. Leslie and G. M. Day, *DMAREL*, version 3.1, 2001.

S8. J. A. Chisholm and S. Moterwell, *J. Appl. Cryst.* (2005), 38, 228.

S9. Unpublished results.

form for 5-fluoro-2-oxindole

Date:
Name:
contact email (optional):

Start time:
Finish time:

5 computer-generated crystal structures are provided. A lattice energy search for the lowest energy crystal structures was performed, using the most common methods currently applied to crystal structure prediction. These are a sample of the structures in the lowest 6 kJ/mol of the results from this search and we are testing whether the experiences eye can distinguish the observed structure from the other 4, which are (as yet) unobserved in the lab.

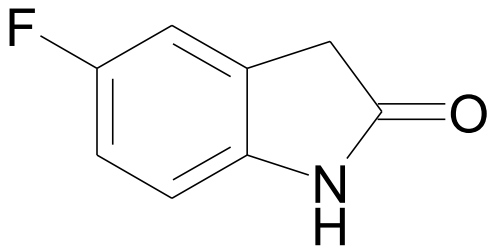
Please take up to a maximum of 15 min. to assess the structures.

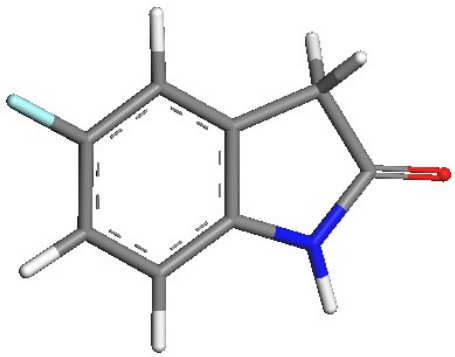
Please answer a few questions:
1) What is your research field?

_____

2) How many years experience do you have in crystallography-related research?
a) solving structures from XRD/PXRD: ___ years
b) analysing packing crystal structures: ___ years
c) modelling of crystal structures: ___ years
d) What types of crystals do you work with? (tick all that apply)
organic ___
metallo-organic ___
inorganic ___

5-fluoro-2-oxindole:





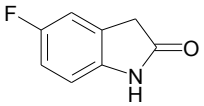
slow evaporation from a 1:1 acetone:water solution

Three packing diagrams are provided for each of the 5 computer-generated crystal structures. One of these structures is the one that we found in a small manual screen of crystallisation conditions.

Please give your three best predictions for the real crystal structure in the box below. Rank 1 is the structure you judge as most likely, 2 is your second prediction, 3 is your third guess.

As well as the ranking, please give a rationalisation of your ranking and a measure of your confidence in making the predictions.

5-fluoro-2-oxindole:



(circle one letter for each rank)
rank 1: A B C D E
rank 2: A B C D E
rank 3: A B C D E

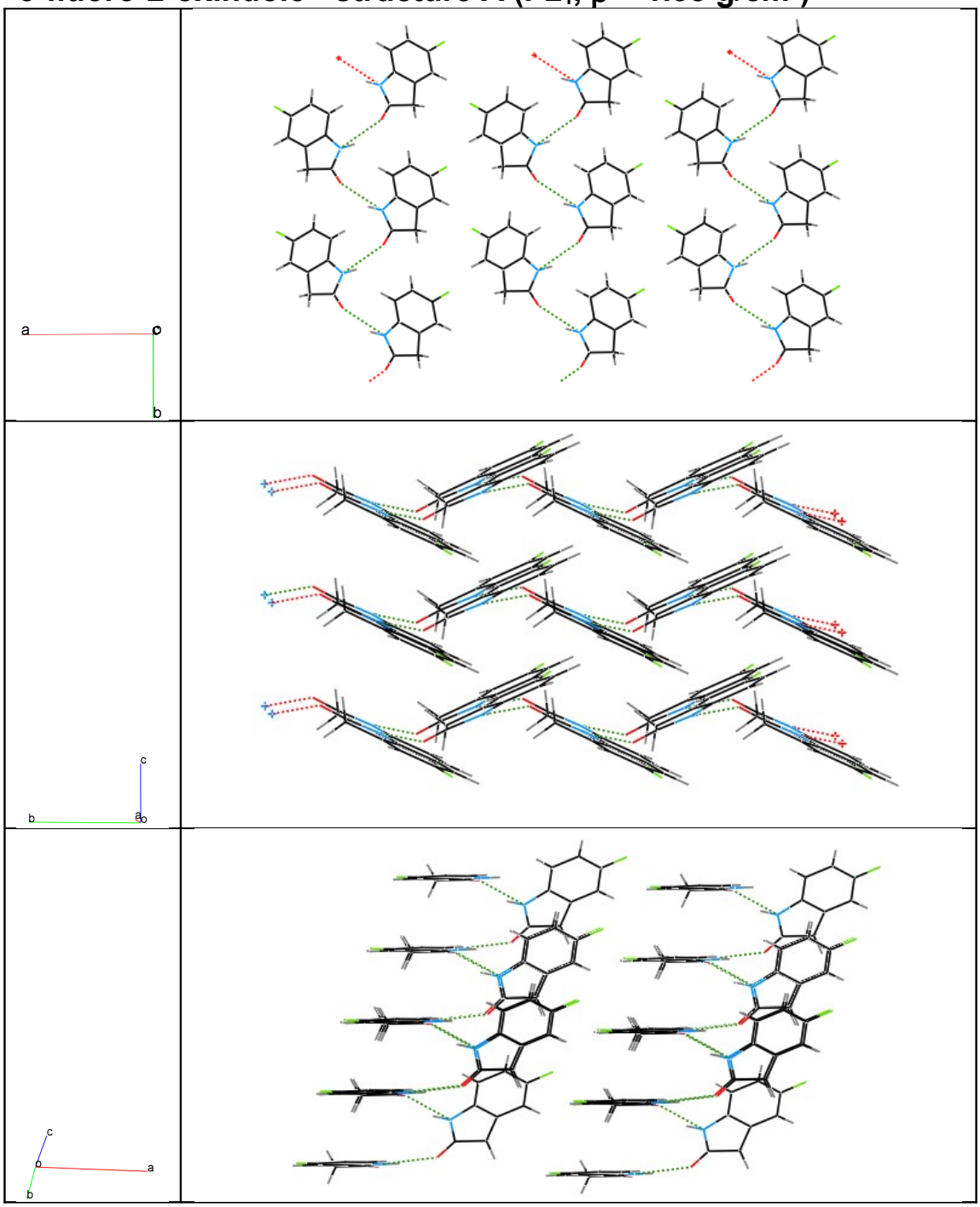
confidence in ranking (circle one): low medium high

Did you use of the printed packing diagrams, 3-D visualisation in Mercury, or both?

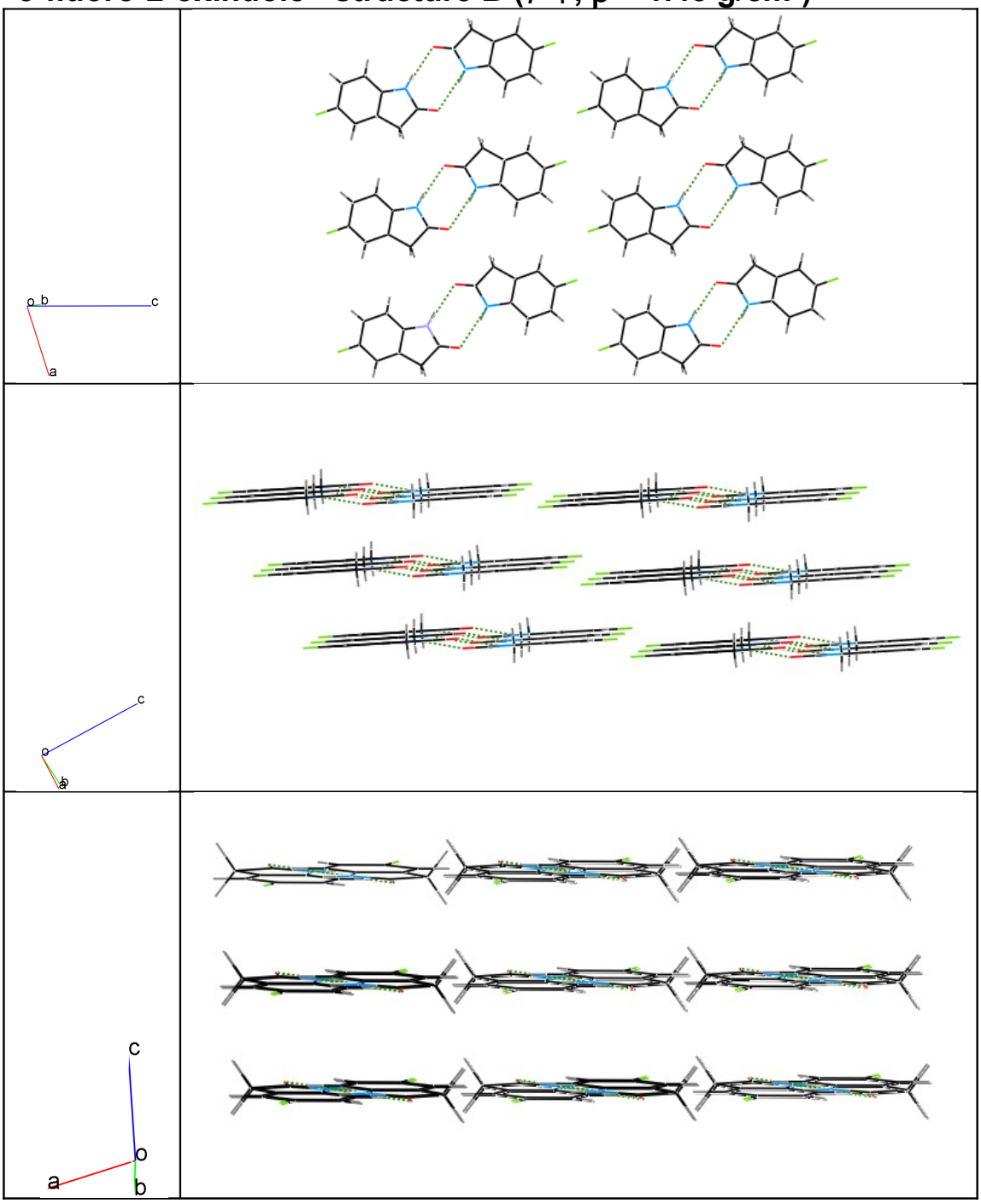
Do you use Mercury regularly (circle one)? Yes No

Would any additional features in the visualiser have helped in analysing the structures?

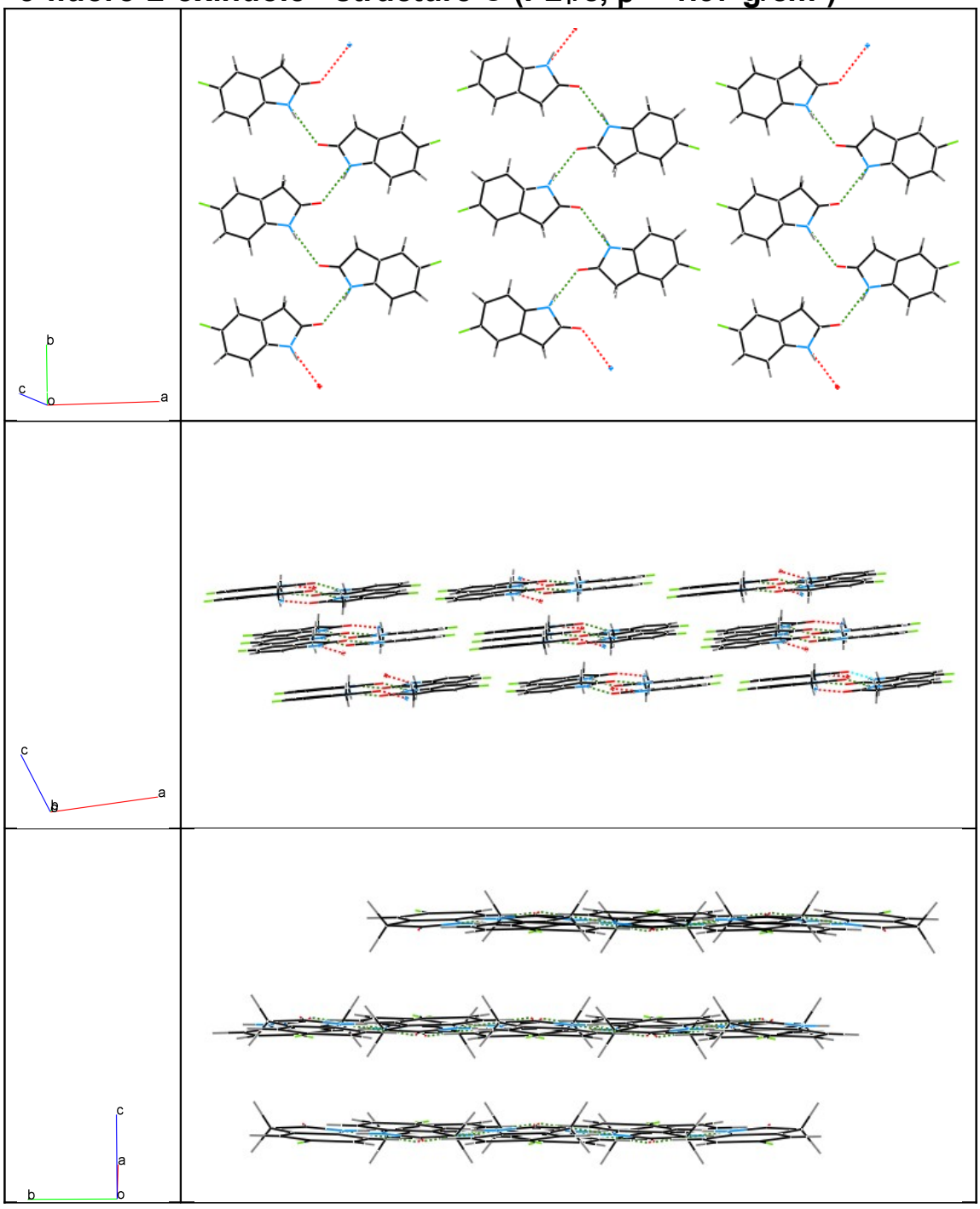
5-fluoro-2-oxindole - structure A ($P2_1$, ρ = 1.38 g/cm^3)



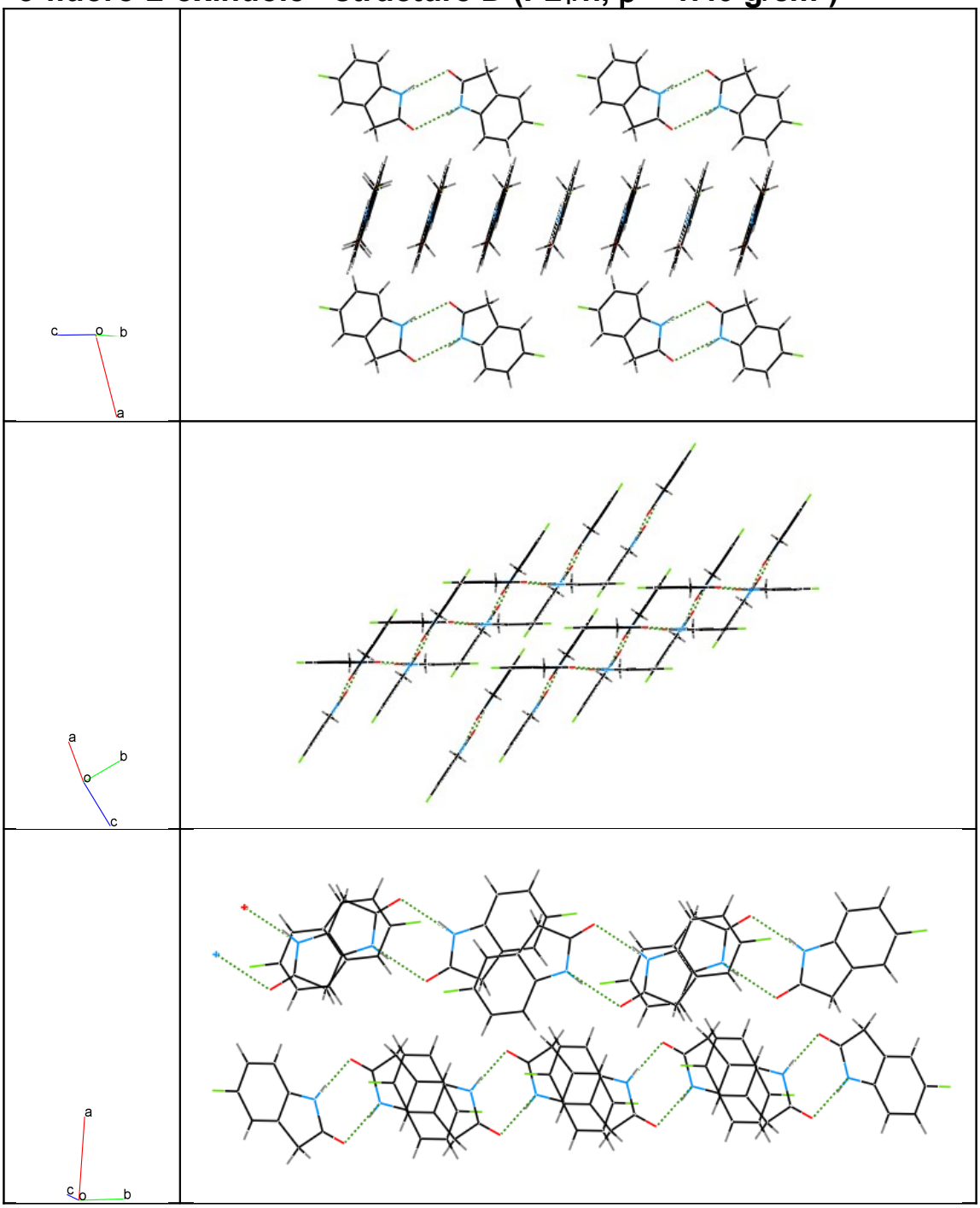
5-fluoro-2-oxindole - structure B ($P\bar{1}$, ρ = 1.45 g/cm^3)



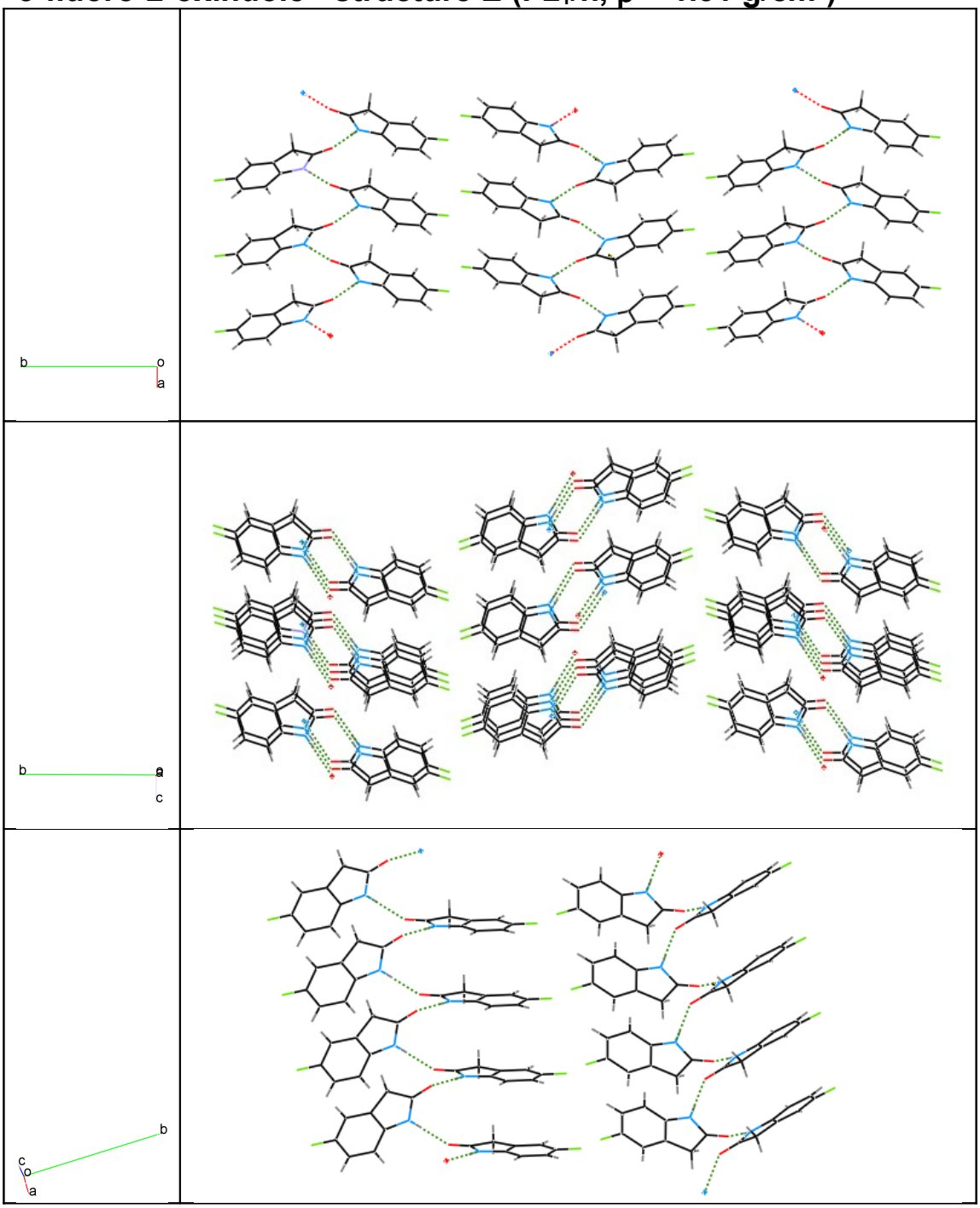
5-fluoro-2-oxindole - structure C ($P2_1/c$, ρ = 1.37 g/cm^3)



5-fluoro-2-oxindole - structure D ($P2_1/n$, ρ = 1.40 g/cm^3)



5-fluoro-2-oxindole - structure E ($P2_1/n$, ρ = 1.31 g/cm^3)



form for 3-quinuclidinol

Date:
Name:
contact email (optional):

Start time:
Finish time:

5 computer-generated crystal structures are provided. A lattice energy search for the lowest energy crystal structures was performed, using the most common methods currently applied to crystal structure prediction. These are a sample of the structures in the lowest 6 kJ/mol of the results from this search and we are testing whether the experiences eye can distinguish the observed structure from the other 4, which are (as yet) unobserved in the lab.

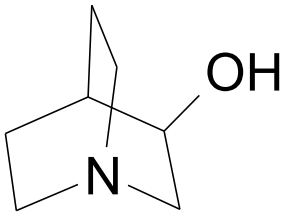
Please take up to a maximum of 15 min. to assess the structures.

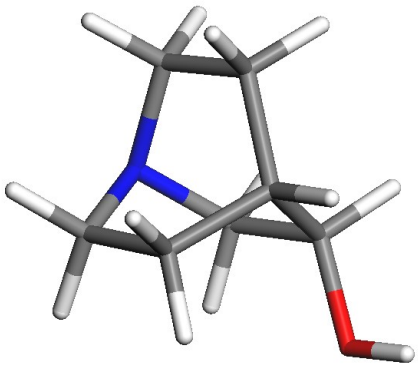
Please answer a few questions:
1) What is your research field?

_____

2) How many years experience do you have in crystallography-related research?
a) solving structures from XRD/PXRD: ___ years
b) analysing packing crystal structures: ___ years
c) modelling of crystal structures: ___ years
d) What types of crystals do you work with? (tick all that apply)
organic ___
metallo-organic ___
inorganic ___

3-quinuclidinol:





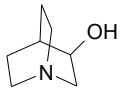
racemate - grown from a toluene solution at high supersaturation

Three packing diagrams are provided for each of the 5 computer-generated crystal structures. One of these structures is the one that we found in a small manual screen of crystallisation conditions.

Please give your three best predictions for the real crystal structure in the box below. Rank 1 is the structure you judge as most likely, 2 is your second prediction, 3 is your third guess.

As well as the ranking, please give a rationalisation of your ranking and a measure of your confidence in making the predictions.

3-quinuclidinol:



(circle one letter for each rank)
rank 1: A B C D E
rank 2: A B C D E
rank 3: A B C D E

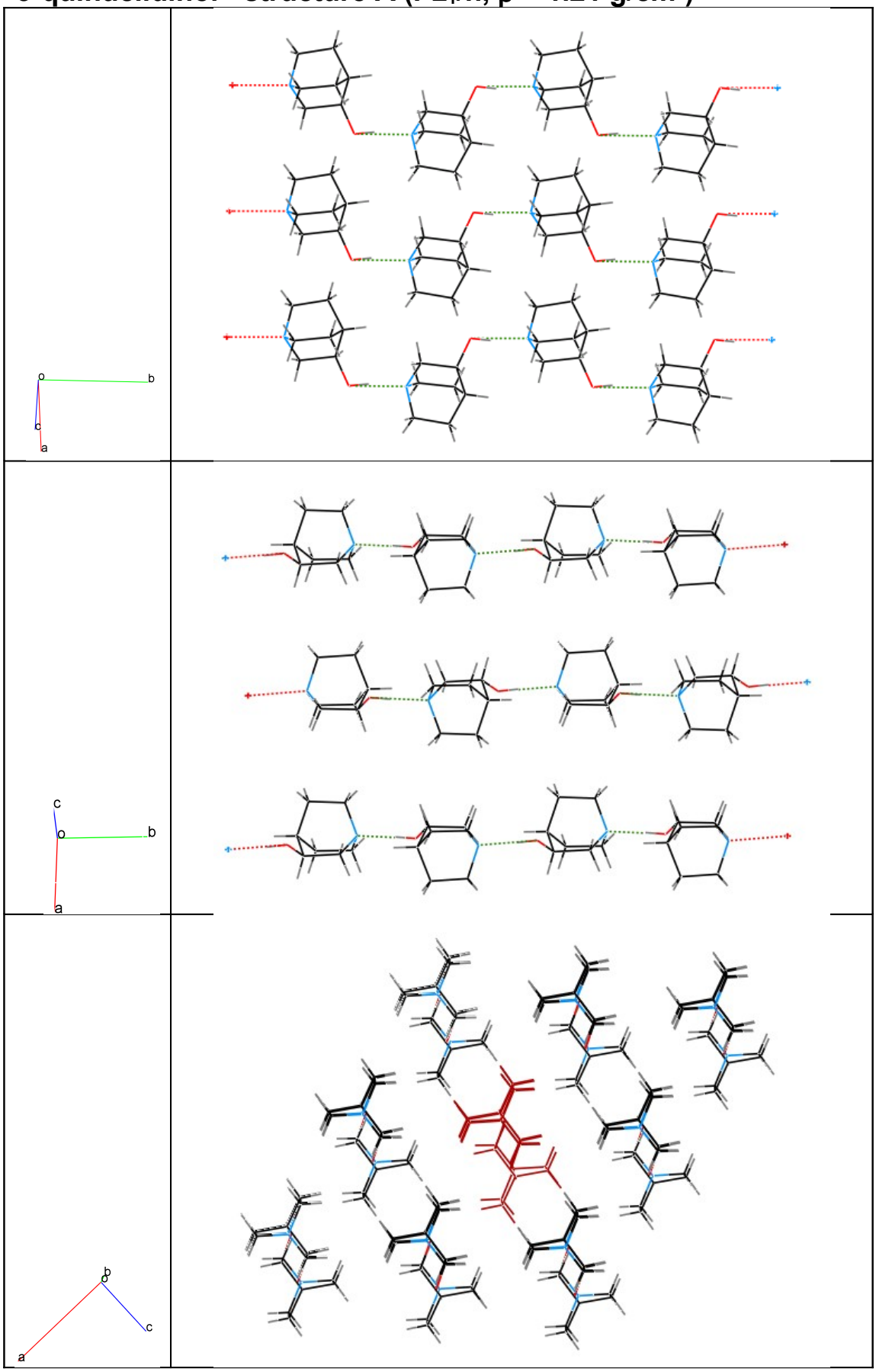
confidence in ranking (circle one): low medium high

Did you use of the printed packing diagrams, 3-D visualisation in Mercury, or both?

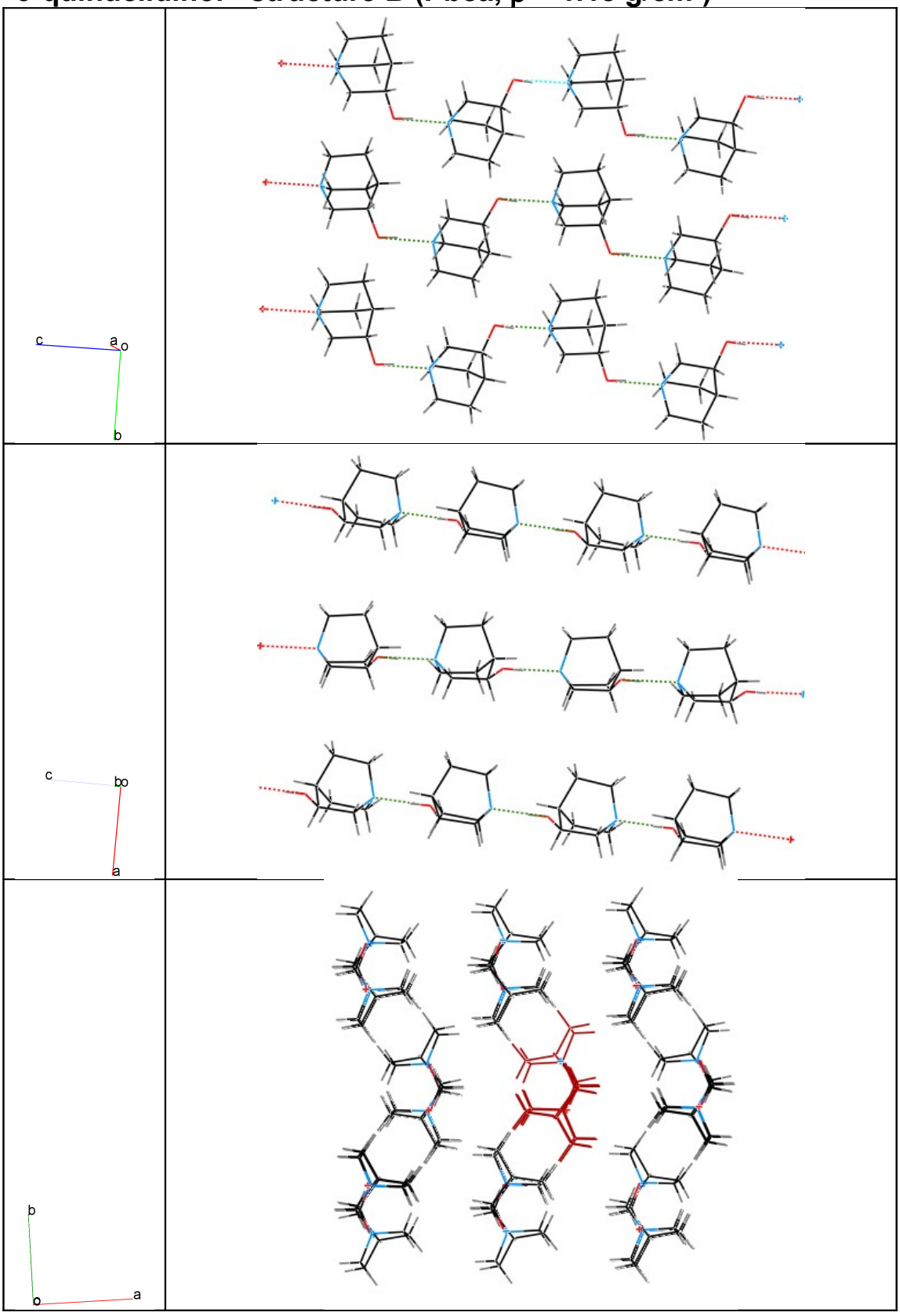
Do you use Mercury regularly (circle one)? Yes No

Would any additional features in the visualiser have helped in analysing the structures?

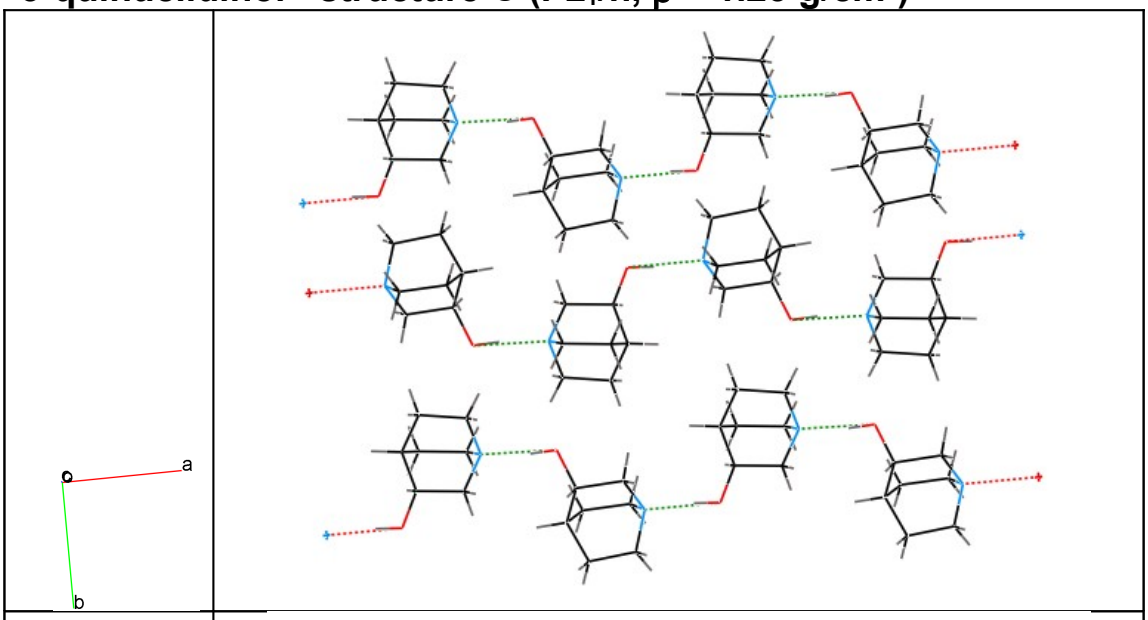
3-quinuclidinol - structure A ($P2_1/n$, ρ = 1.21 g/cm^3)

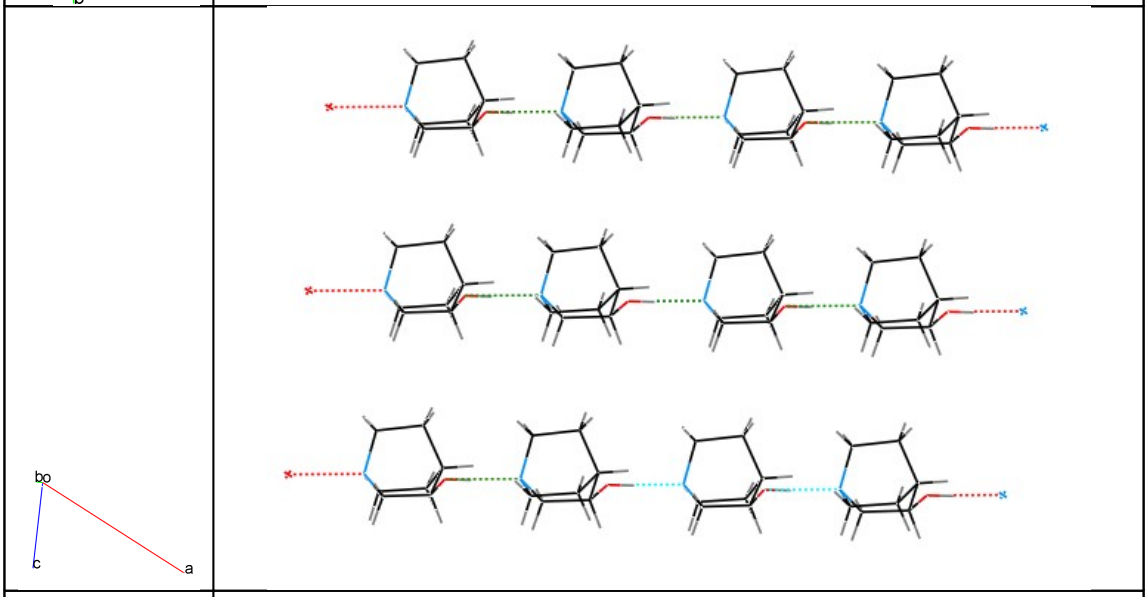


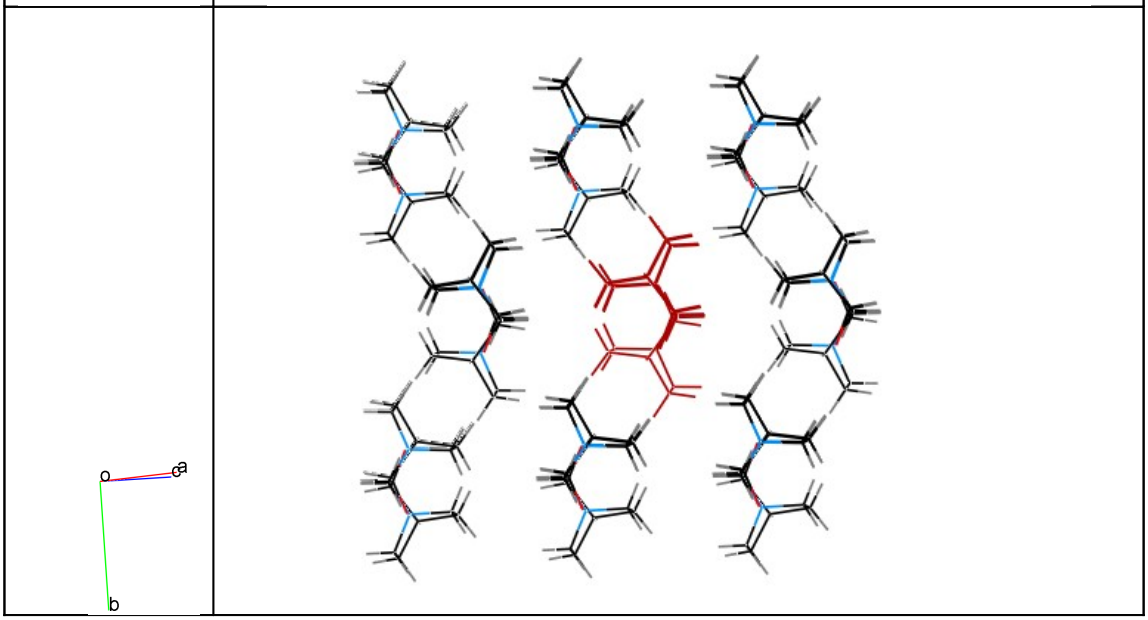
3-quinuclidinol - structure B (Pbca, ρ = 1.18 g/cm^3)



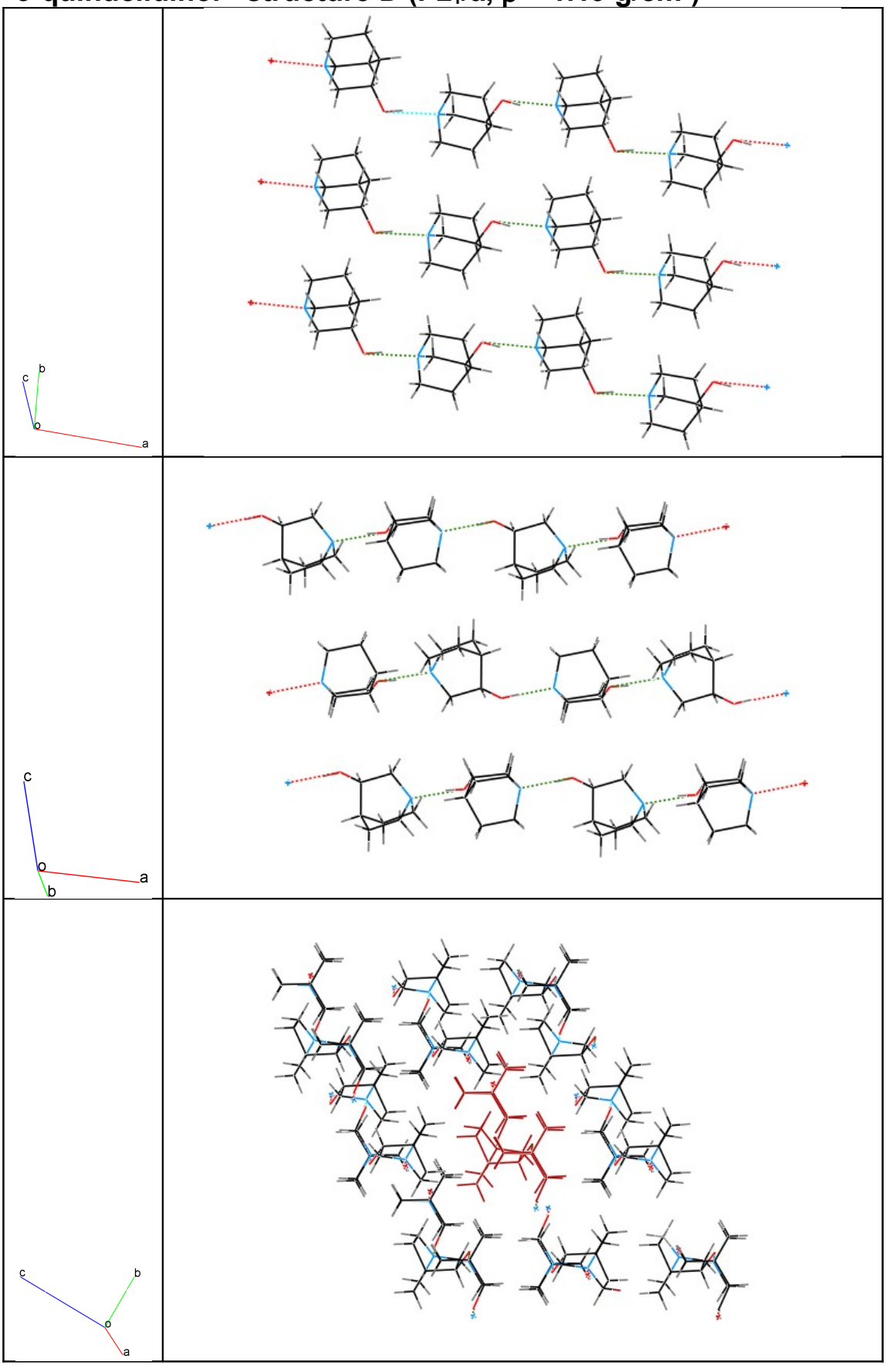
3-quinuclidinol - structure C ($P2_1/n$, ρ = 1.23 g/cm^3)







3-quinuclidinol - structure D ($P2_1/a$, ρ = 1.19 g/cm^3)



3-quinuclidinol - structure E ($P2_1/n$, ρ = 1.22 g/cm^3)