Experimental and theoretical studies on six-membered ring hydrogen bond systems in crystalline drug substances

Rutian Jin

Master of Philosophy

September 2006

Acknowledgement

I wish to thank my supervisor Dr Carl H Schwalbe for his patient and warm teaching and attention to my progress through my studies at Aston University.

Thanks are also due to Dr Yongfeng Wang and Dr Kejun Zhao for the supply of sample and knowledgeable support.

I am grateful for the assistance of all my friends and staff in the School of Life and Health Sciences in the Aston University.

Finally I want to thank my parents
This work would not have been possible without my parents' continued love and encouragement.

Contents

Summary

Crystals of five compounds that are capable of forming a six-membered ring held together by intramolecular hydrogen bonding have been investigated in the Aston University laboratory. The geometry of the six-membered intramolecular hydrogen bonded ring in these structures and related molecules in the Cambridge Structural Database (CSD) has been surveyed.

Analysis of the five potential drugs provides proof of their structures and also gives important information for drug design. Knowledge of H-bond geometries, directionalities and motif formation which is vital in crystal engineering has been obtained.

An intramolecular hydrogen bonded N-C-C-C-O-H ring with saturated carbon atoms was found in both structures of the 1-dimethylaminomethyl-2-hydroxycyclohexane derivatives ZK-42 and ZK-43 but is rare in the CSD.

This study has shown that in small organic molecules hydrogen bonding can have a very strong influence upon the conformation adopted.

Tables and Schemes

Figures

Chapter 1 Introduction

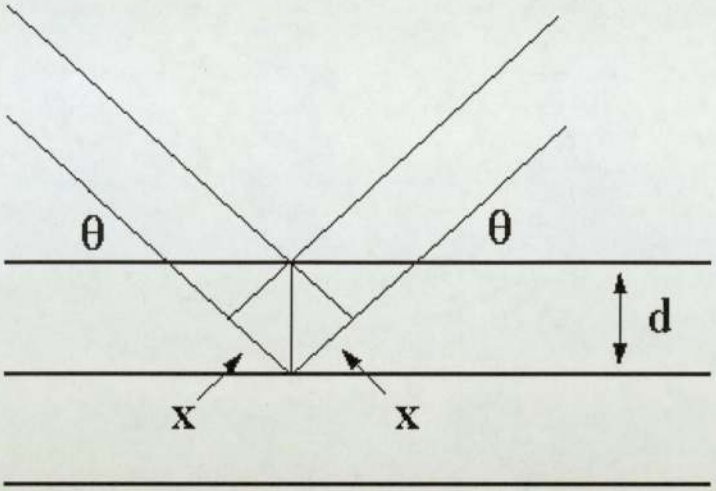
1.1 The definition of a crystal

A crystal is, by definition, a solid that has a regularly repeating internal structure (arrangement of atoms). The most obvious feature of crystal is the presence of facets, and well-formed crystals are found to be completely bounded by flat surfaces---- flat to a degree of precision capable of giving high-quality plane-mirror images. But it is not sufficient to describe a solid as crystalline based on macroscopic observable properties such as flat faces; it must have a regular internal structure at the molecular level to satisfy the definition just given. For example, no matter how much glass is ground or polished to produce flat faces, it cannot be called crystal.

1.2 X-ray crystallography

X-ray crystal structure determination involves the analysis of the diffraction pattern produced when a crystal is irradiated with X-rays. Because the spacing between the repeating units of a crystal is comparable to the wavelength of X-rays, a crystal can diffract X-rays. Unfortunately the direct analysis of a three-dimensional diffraction pattern is infeasible in practice, but there is an easier alternative. The repeat unit that generates the crystal is called the unit cell. Stacks of planes can be imagined to cut through the unit cell, intersecting an axis 0, 1, 2, or another integral number of times. The process of three-dimensional diffraction is equivalent to reflection from these stacks of planes and that this reflection only occurs when reflected beams from successive planes in the stack interfere constructively. Constructive interference is only possible if the path difference between such beams is an integral number of wavelengths. Mathematically, $n\lambda=2d\sin\theta$ where n is an integer equivalent to the order of diffraction, usually 1, λ is the wavelength of the x-rays, d is the perpendicular distance between planes in the stack, and θ is the angle between either the incoming beam or the reflected beam and the plane surface.

The Bragg equation describes x-ray diffraction



Path difference = $2x = 2d\sin\theta$

Thus, for diffraction to occur $n\lambda = 2d\sin\theta$

Diagram from http://materials.binghamton.edu/444/Part_I/sld032.htm

Measurement of θ values yields the unit cell dimensions. From measurements of the intensity of reflection from each stack of planes, it is possible to calculate the electron density, from which the location of each atom in each molecule in the unit cell can be found. However, the phase of each reflection must be supplied, and it cannot be measured. The phase of a wave determines whether a reference point is at a crest, a trough, or in between. Most frequently the phases are determined by a computerised process called direct methods. The atomic positions thus found, and parameters representing thermal motion, are refined by least squares to give a final model that best fits the data.

1.3 Hydrogen bonds

The **hydrogen bond**, usually characterized as A-H...B[1], is a weak electrostatic interaction that forms between a hydrogen atom (H) [covalently bonded to an electronegative atom (A)] and another atom (B) that is basic, that is one that has lone pairs of electrons and is fairly electronegative. In chemistry, a hydrogen bond is a type of attractive intermolecular force that exists between two partial electric charges of opposite polarity. Although stronger than most other intermolecular forces, the typical hydrogen bond is much weaker than both the ionic bond and the covalent bond.

The easier it is to remove the hydrogen atom in the form of H^+ from AH, the stronger is the hydrogen bond H...B. The terminology for a hydrogen bond is confusing with respect to the terms "donor" and "acceptor." Atoms A and B are either considered in terms of donors and acceptors of lone pairs (B the donor and A the acceptor) or as proton donors (A the donor and B the acceptor). When reading articles on hydrogen bonding, it is important to be sure which definition of donor and acceptor has been used. This report will use the convention for a hydrogen bond A-H...B that A is the proton donor, and B is the proton acceptor.

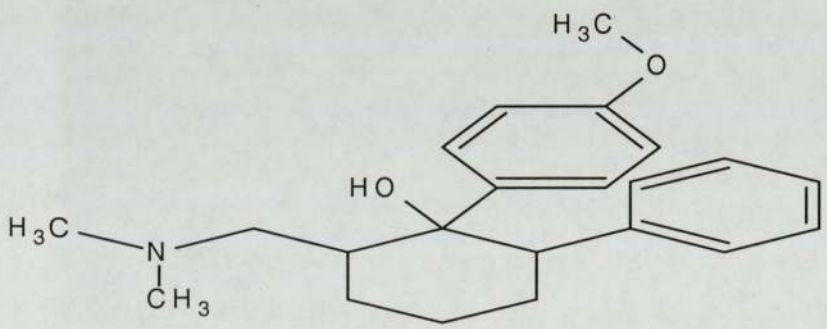
Now that hydrogen atoms can be well located by neutron diffraction or good X-ray diffraction studies, there is a large amount of information available on hydrogen bonding (see examples in Table 1)

A-H...B	H...B distance(Å)
O-H...COO^-	1.35-1.85
N-H^+...O	1.70-2.22
O-H...OH^-	1.70-2.15
O_w-H...O*	1.75-2.06
O-H...Cl^-	1.95-2.15
N-H+...Cl^-	2.05-2.22
*Ow= oxygen of water	

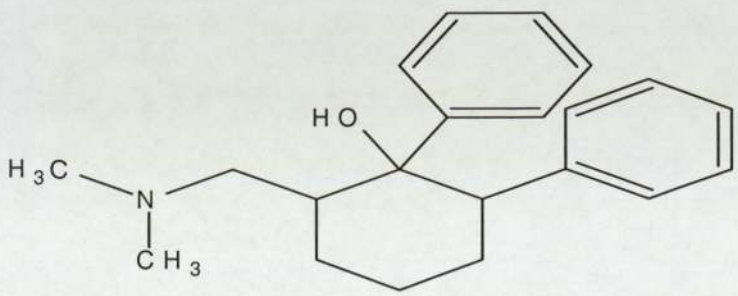
Table 1 Hydrogen bonds in crystal structures [2]

1.4 The compounds under investigation

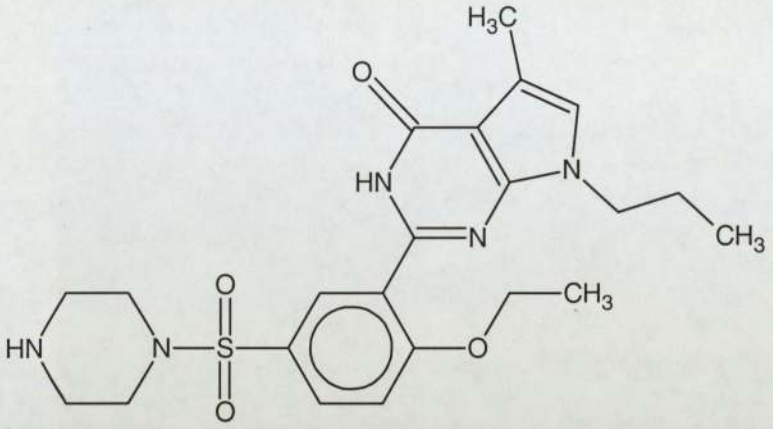
Crystal structures of the following five compounds were determined. Confirmation of structure was needed by the collaborating chemists for a variety of reasons, but all five compounds are capable of forming a six-membered ring held together by intramolecular hydrogen bonding, either N-H...O, O-H...N or O-H...O. It was considered unlikely that all molecules in the series would hydrogen bond in this way, in view of a careful survey of intramolecular hydrogen bonding by Bilton et al. (2004)[3]. They found that for the highest probability of occurrence the hydrogen bond donor and acceptor groups had to be linked by conjugated bonds that enforced coplanarity. Such complete conjugation is not present in any of the compounds under study here. Nevertheless, all five structures were compared to see how many, if any, displayed cyclic intramolecular hydrogen bonds.



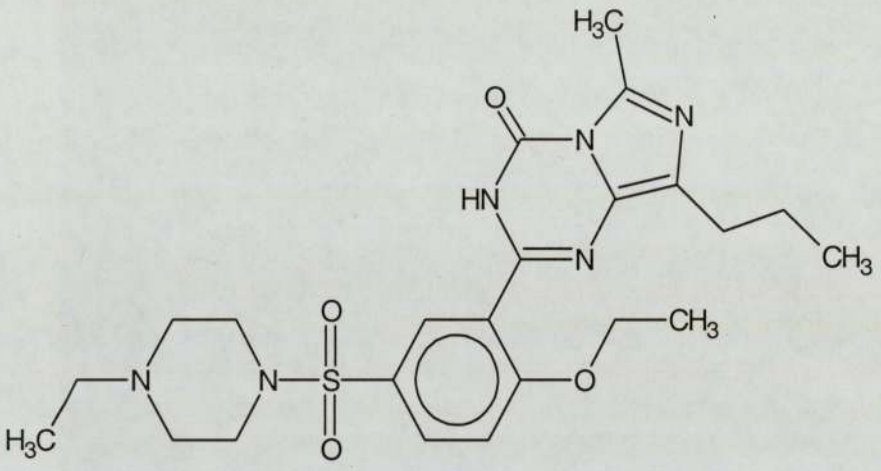
Scheme 1. Chemical Structure of ZK-42



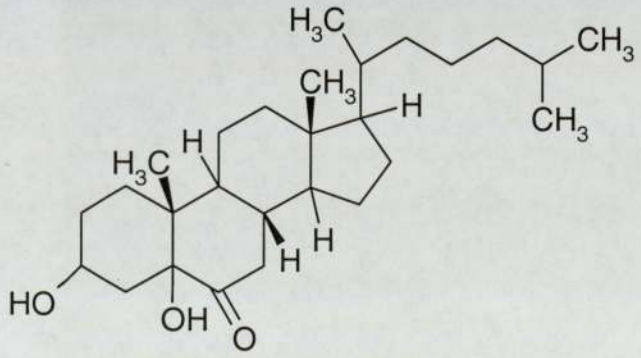
Scheme 2. Chemical structure of ZK-43



Scheme 3. Chemical structure of WZA001



Scheme 4. Chemical structure of WZA002



Scheme 5. Chemical structure of Sterol1

1.5 Quality of the structure determinations

A successful crystal structure determination depends on collecting accurate data and refining a correct model of the structure. When intensities have been measured for some reflections that are supposed to be equivalent by symmetry, they can be averaged and a discrepancy index can be calculated:

$R_{int} = \Sigma |F_o^2 - F_o^2 (mean)| / \Sigma F_o^2$

where the sum is taken over all reflections with multiple observations and F_o = observed structure factor = $\sqrt{}$ (intensity) after necessary corrections have been made.

A low R_{int} implies consistent data. Once all atoms in the structure have been located and refined, it is possible to calculate what the value of each structure factor should be, F_c. Two further discrepancy indices R1 and wR2 indicate how well this model of the structure matches the observed data:

$R1 = \Sigma |F_o - F_c| / \Sigma |F_o|$

where the sum is usually taken only over reflections with sufficient measured intensity that F_o is greater than 4 times its own standard deviation, and

$wR2 = \Sigma w|F_o^2 - F_c^2| / \Sigma w|F_o^2|$

where the sum is taken over all reflections.

Since the usual reason for determining a crystal structure is to define the molecular geometry, the estimated standard deviation of a typical bond distance is another measure of success. Finally, a difference electron density map should be calculated. If atoms have been correctly placed, the model should account for all the observed electron density and any residual peaks and holes should be negligible.

1.6 Hydrogen bonds in supramolecular organisation

Hydrogen bonds play a crucial role in supramolecular organisation. Knowledge of H-bond geometries, directionalities and motif formation is vital in the modelling of protein-ligand interactions, in crystal engineering and in *ab initio* crystal structure prediction. The crystallography database has been used to identify the most common motifs and to establish their probabilities of formation, and hence identify the most robust and reproducible intermolecular H-bonded motif that might act as supramolecular synthons in crystal engineering applications.[4-10]

Chapter 2 Experimental Work and Results

2.1 General Method

Samples of crystals were examined under a polarising microscope. A crystal was chosen for further work if its edges appeared smooth and it went light and dark uniformly as it was rotated between crossed polarisers. The chosen specimen was mounted to a glass fibre with epoxy cement, and the fibre was attached to a goniometer head.

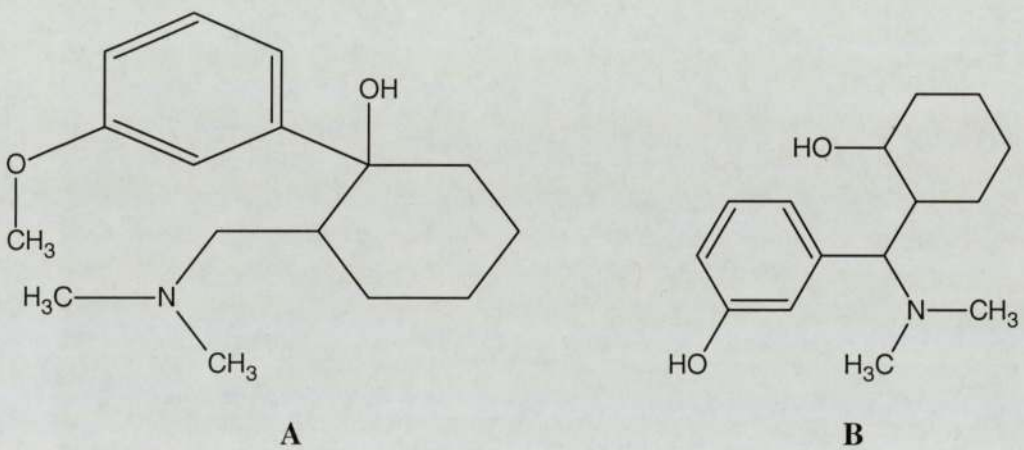
X-ray data were collected on an Enraf-Nonius CAD4 diffractometer at 293(2) K with MoKα radiation (λ = 0.71073 Å). Unit cell dimensions were calculated by least squares analysis of the setting angles of 25 reflections with the Enraf-Nonius LS routine. Whenever availability of time and durability of the crystal permitted, more than one asymmetric unit of intensity data were collected, so that equivalent data could be averaged for greater accuracy. At the end of data collection a psi scan (rotating the crystal in a plane that is set to diffract X-rays) was made on a suitable reflection for use in calculating an absorption correction.

Each structure was solved by the direct methods program SHELXS [11]. Positions of non-hydrogen atoms were located in the resulting map and refined, along with displacement parameters, by least squares with the program SHELXL [12]. Hydrogen atoms were introduced in calculated positions, confirmed whenever possible by peaks in difference electron density maps. The final stages of refinement adjusted positions and anisotropic displacement parameters for the non-hydrogen atoms, while hydrogen atoms were assumed to ride on their attached atom. Reflections were weighted according to the scheme recommended by SHELXL. Pictures of the molecules and their mode of packing were drawn with ORTEP[13].

2.2 ZK structures

Zk4-2 and ZK4-3 are the two structural analogues of Tramadol.

Tramadol is a centrally acting analgesic agent used in the treatment of mild to moderate pain. Showing a low affinity to opioid receptors, it inhibits the reuptake of norepinephrine and serotonin. Ciramadol has similar activity. Aside from the hydrobromide salt of ciramadol (BARGEG)[14], no crystal structure has appeared in the Cambridge Structural Database for either drug. To explore the conformational preferences and hydrogen bonding motifs of such drugs, unperturbed by strong ionic interactions, the crystal structures of two analogues, codenamed ZK42 and ZK43, have been determined in free base form.



A B

Scheme 6. Chemical structure of Tramadol and Ciramadol

A Tramadol , B Ciramadol

2.2.1 ZK-42

Crystal Growing

ZK-42 (0.5 g) was placed in a 25ml sample tube. Taking the sample tube, with its cover on it, a nail was used to drill 5 holes in it. As solvent 2ml ethanol were added, then shaken in the 40°C water bath. Dropwise addition of ethanol was continued until the chemical has been completely dissolved. At this end point the solvent consisted of

approximately 10ml ethanol. Shaking in the 40°C water bath was continued for 5 minutes.

Then the solution was gradually cooled to room temperature, keeping the solution in a well-ventilated cabinet. Ten days later, several crystals could be found in the flask bottom. Using a minimum amount of ethanol to wash the crystals, the required sample crystal was obtained.

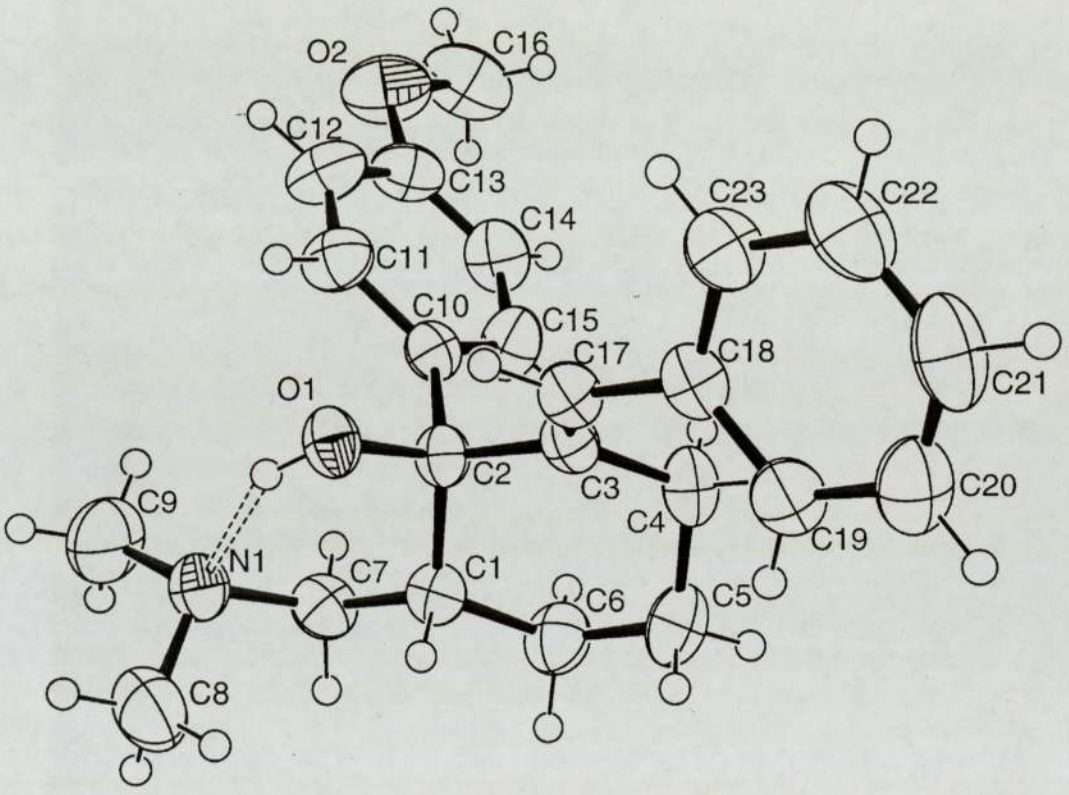


Figure 1. Crystal structure and atom numbering scheme for ZK42. In this ORTEP drawing and subsequent ones the displacement ellipsoids are drawn at the 50% probability level.

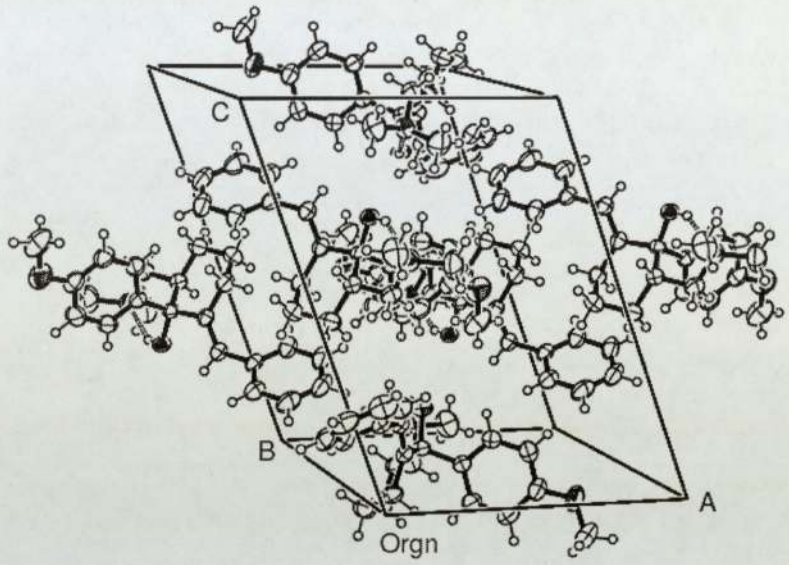


Figure 2. Packing of molecules of ZK42 in the unit cell

Report of Zk-42 structure:

The structure of ZK-42 is shown of Figure 1 and Figure 2. The crystal structure of ZK-42 has been determined from three-dimensional X-ray diffraction data at 298K, There are four molecule in asymmetry unit, and the hydrogen bond length is 1.9797 Å. The Unit cell parameters are a(Å)=11.2670, b(Å)=12.2951, c(Å)=15.2400, $\alpha(°)$ = 90.00, $\beta(°)$ = 111.271, $\gamma(°)$ = 90.00, Cell volume: 1967.36.

2.2.2 ZK-43

Crystal Growing

Zk-43 (0.5 g) was placed in a 25ml sample tube. Taking the sample tube, with its cover on it, a nail was used to drill 5 holes in it. As solvent 2ml ethanol were added, then shaken in the 40°C water bath. Dropwise addition of ethanol was continued until the chemical has been completely dissolved. At this end point the solvent consisted of approximately 10ml ethanol. Shaking in the 40°C water bath was continued for 5

minutes.

Then the solution was gradually cooled to room temperature, keeping the solution in a well-ventilated cabinet. Ten days later, several crystals could be found in the flask bottom. Using a minimum amount of ethanol to wash the crystals, the required sample crystal was obtained.

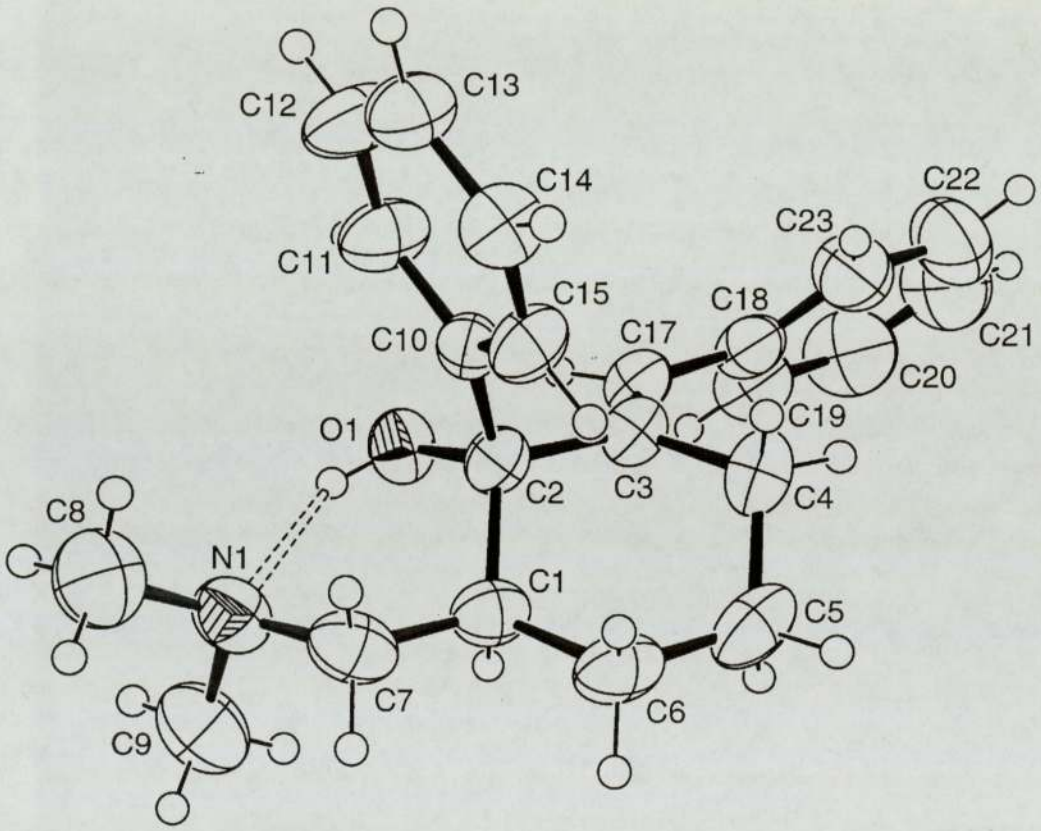


Figure 3. The molecular structure of ZK43 showing the atom numbering scheme.

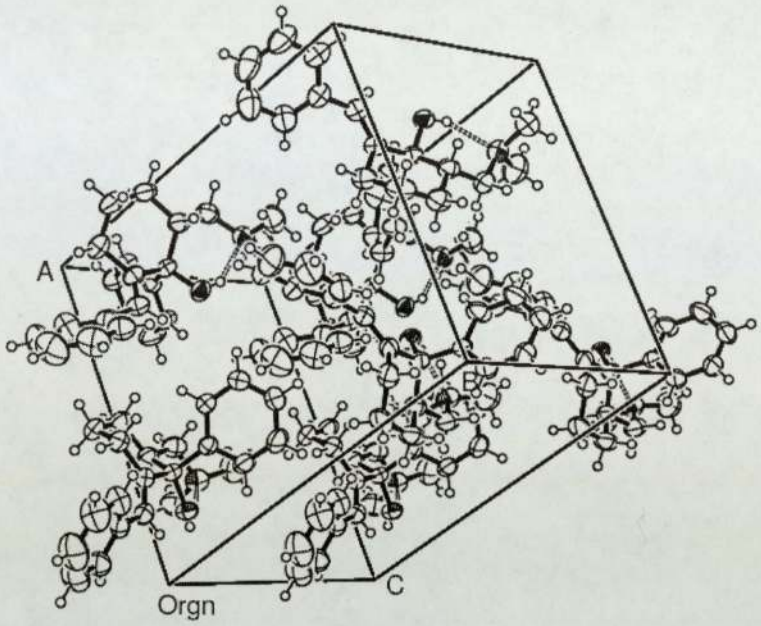


Figure 4. Packing of molecules of ZK43 in the unit cell.

Report of Zk-43 structure:

The structure of ZK-43 is shown of Figure 3 and Figure 4. The crystal structure of ZK-43 has been determined from three-dimensional X-ray diffraction data at 298K, There are four molecule in asymmetry unit, and the hydrogen bond length is 1.9894 Å. The Unit cell parameters are a(Å)=12.3609, b(Å)=15.830, c(Å)=10.0810, $\alpha(°)$ = 90.00, $\beta(°)$ = 90.00, $\gamma(°)$ = 90.00, Cell volume: 1879.50.

2.3 WZA structures

Structure determination for the two "WZ" compounds was undertaken initially as an analytical technique that would confirm the expected structures with complete certainty. However, it was noted that these molecules, like the other three in the thesis, had the potential to make a 6-membered ring held together by an intramolecular hydrogen bond. One N-H group on the heterocycle could act as the proton donor, while the available acceptors included an ether oxygen atom on one

side of the adjacent aromatic ring or sulfonyl oxygen atoms on the other side.

2.3.1 WZA001

Crystal growth

WZA001 (0.5 g) was placed in a 25ml sample tube. Taking the sample tube, with its cover on it, a nail was used to drill 5 holes in it. As solvent 2ml dichloromethane and 2ml ethyl acetate were added, then shaken in the 40°C water bath. Dropwise addition of dichloromethane and ethyl acetate was continued until the chemical has been completely dissolved. At this end point the solvent consisted of approximately 5ml dichloromethane and 5ml ethyl acetate. Shaking in the 40°C water bath was continued for 5 minutes.

Then the solution was gradually cooled to room temperature, keeping the solution in a well-ventilated cabinet. Ten days later, numerous crystals could be found in the flask bottom. Using a minimum amount of dichloromethane to wash the crystals, the required sample crystal was obtained.

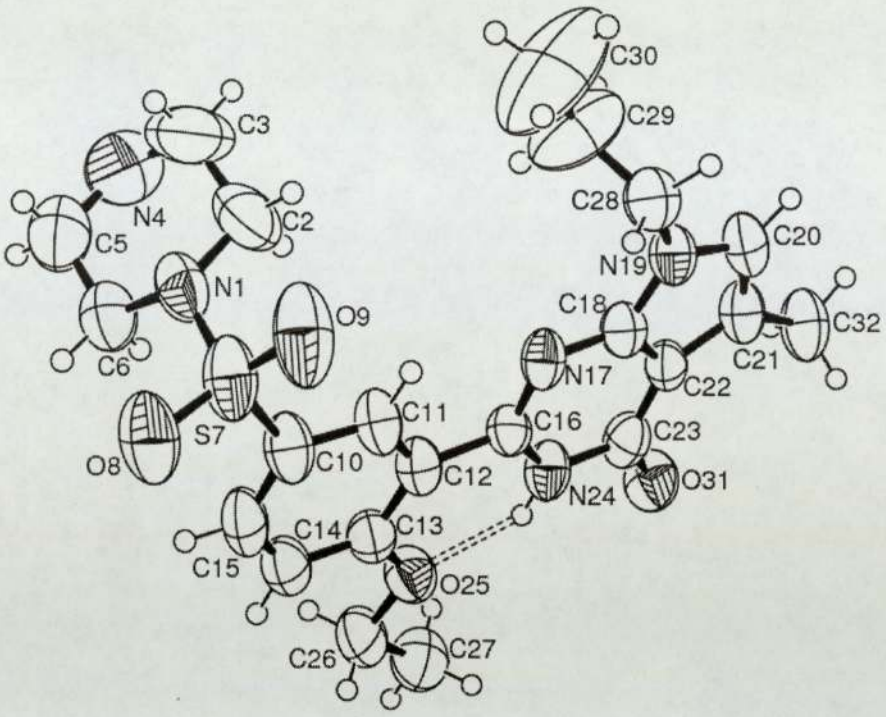


Figure 5. The molecular structure of WZA001showing the atom numbering scheme.

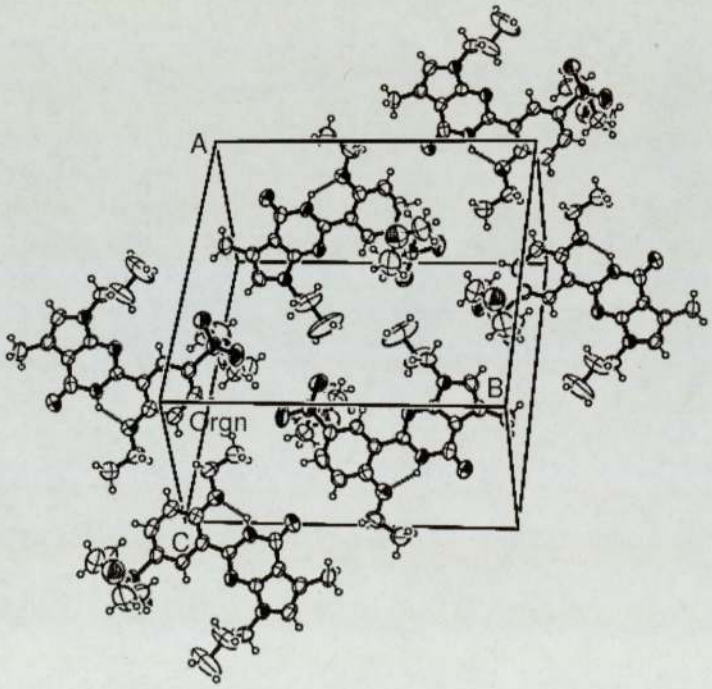


Figure 6. Packing of molecules of WZA001 in the unit cell.

Report of WZA001 structure:

The structure of WZA001 is shown of Figure 5 and Figure 6. The crystal structure of WZA001 has been determined from three-dimensional X-ray diffraction data at 298K, There are four molecule in asymmetry unit. The Unit cell parameters are a(Å)=12.3609, b(Å)=15.830, c(Å)=10.0810, α(°) = 90.00, β(°) = 90.00, γ(°) = 90.00, Cell volume: 1879.50.

2.3.2 WZA002

Crystal growth

WZA002 (0.5 g) was placed in a 25ml sample tube. Taking the sample tube, with its cover on it, a nail was used to drill 5 holes in it. As solvent 2ml dichloromethane and 2ml methanol were added, then shaken in the 40°C water bath. Dropwise addition of dichloromethane and methanol was continued until the chemical has been completely dissolved. At this end point the solvent consisted of approximately 5ml dichloromethane and 5ml methanol. Shaking in the 40°C water bath was continued for 5 minutes.

Then the solution was gradually cooled to room temperature, keeping the solution in a well-ventilated cabinet. Ten days later, several crystals could be found in the flask bottom. Using a minimum amount of dichloromethane to wash the crystals, the required sample crystal was obtained.

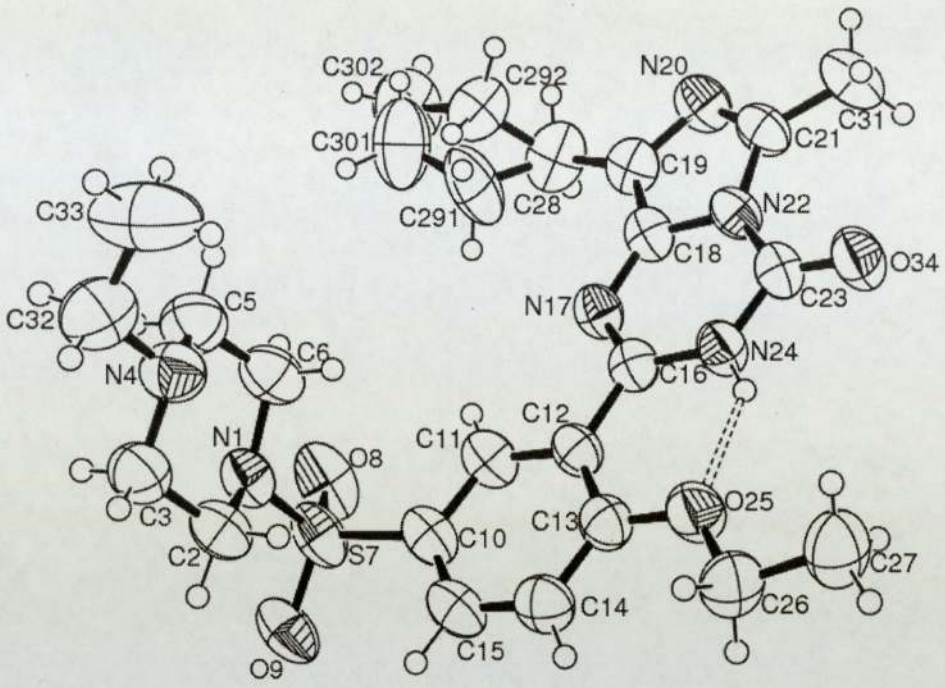


Figure 7. The molecular structure of WZA002 showing the atom numbering scheme. The two alternative positions for the disordered ethyl group are designated C291-C301 and C292-C302.

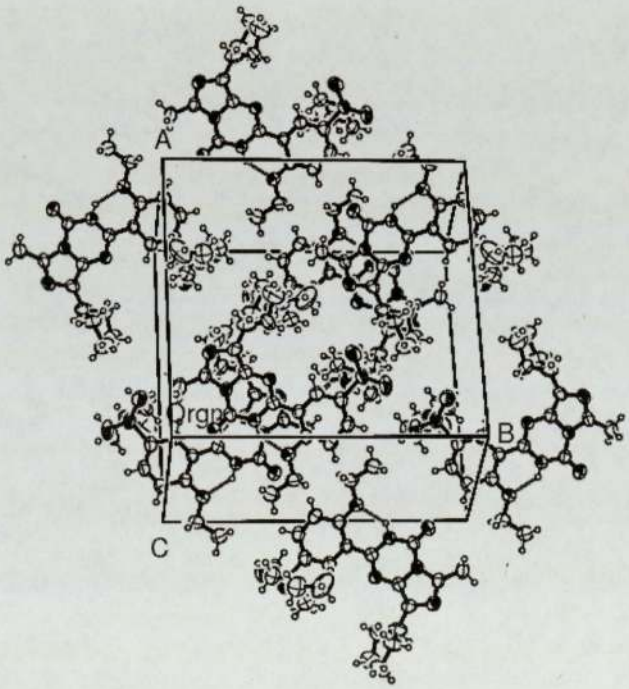


Figure 8. Packing of molecules of WZA002 in the unit cell.

Report of WZA002 structure:

The structure of WZA002 is shown of Figure 7 and Figure 8. The crystal structure of WZA002 has been determined from three-dimensional X-ray diffraction data at 298K, There are four molecule in asymmetry unit. The Unit cell parameters are a(Å)=17.2263, b(Å)=17.3122, c(Å)=8.4721, $\alpha(°) = 90.00$, $\beta(°) = 99.1972$, $\gamma(°) = 90.00$, Cell volume: 2491.22..

2.4 Steroids

Steroids represent a large group of naturally occurring organic molecules of biochemical and medical interest, which are extensively distributed in the animal and plant kingdoms. They form a group of lipids resistant to saponification found in an appreciable quantity in all animal and vegetal tissues. Such nonsaponifiable matter may include one or more of a variety of molecules belonging to the category of C27-C30 crystalline alcohols.

The term steroid is generally applied to compounds containing the same fundamental four hydrocarbon-rings skeleton. Since many of these compounds are alcohols, sometimes, the name sterol is used for the whole class. However, sterol is better reserved for the substance that are actually alcohols (Roberts et al 1974)[15]. The basic structural feature of steroids is that they are tetracyclic hydrocarbons, usually saturated.

Although many oxidized sterols can be included in the group of oxygenated derivatives of cholesterol, oxysterols especially refer to those compounds having a similar carbon skeleton structure to cholesterol but containing one or more oxygen atoms in addition to the oxygen at C-3 (www.atherognic.com). Therefore, sometimes

they were also called cholesterol oxidation products.

A number of studies have concerned the cytotoxicity of various oxygenated sterols. But their results cannot necessarily be extrapolated to systemic human effects. There is frequently no clear differentiation of toxic action due to the primary or secondary effects of compounds and actions due to the induction of apoptotic (apoptotic means disintegration of cells into membrane-bouns particles that are then eliminated by phagocytosis or by shedding) changes that might be natural, physiological actions of some of the compounds concerned. A variety of changes have frequently been taken as indicative of cytotoxicity including changes in cell growth, cell viability, cell detachment, plating efficiency of various aspects of morphology, transport of small molecules (i.e., 2-deoxyglucose, uridine, thymidine), protein synthesis, and DNA synthesis.

Crystal growth

Sterol1 (0.5 g) was placed in a 25ml sample tube. Taking the sample tube, with its cover on it, a nail was used to drill 5 holes in it. As solvent 2ml dichloromethane and 2ml methanol were added, then shaken in the 40°C water bath. Dropwise addition of dichloromethane and methanol was continued until the chemical has been completely dissolved. At this end point the solvent consisted of approximately 5ml dichloromethane and 5ml methanol. Shaking in the 40°C water bath was continued for 5 minutes.

Then the solution was gradually cooled to room temperature, keeping the solution in a well ventilated cabinet. Ten days later, several crystals could be found in the flask bottom. Using a minimum amount of dichloromethane to wash the crystals, the required sample crystal was obtained.

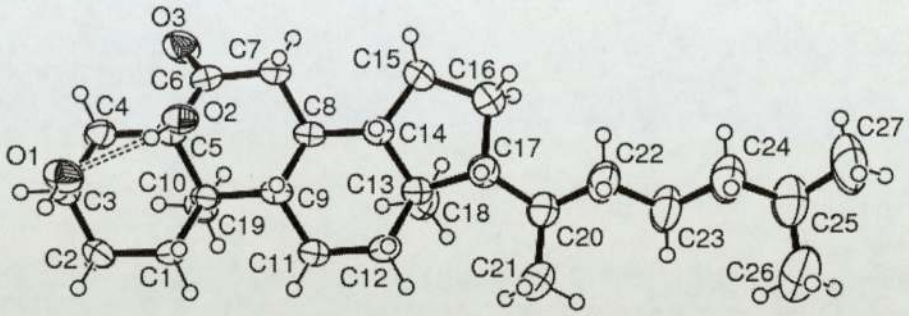


Figure 9. The molecular structure of STEROL1 showing the atom numbering scheme

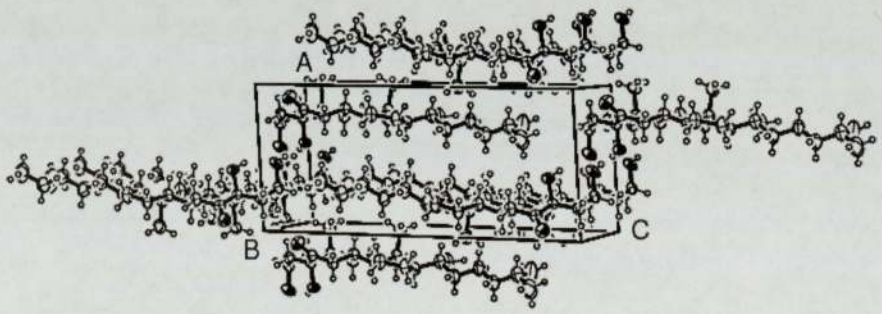


Figure 10. Packing of molecules of STEROL1 in the unit cell.

Report of Steroid1 structure:

The structure of Steroid1 is shown of Figure 9 and Figure 10. The crystal structure of Steroid1 has been determined from three-dimensional X-ray diffraction data at 298K, There are four molecule in asymmetry unit. The hydrogen bond length is 2.04 Å. The Unit cell parameters are a(Å)=8.6610, b(Å)=7.6240, c(Å)=19.5759, $\alpha(°)$ = 90.00, $\beta(°)$ = 93.8801, $\gamma(°)$ = 90.00, Cell volume: 1282.22.

Chapter 3 Discussion and Conclusions

3.1 Analysis of the data

The quality of WZA001 is clearly the worst. Already at the stage of averaging equivalent reflections the agreement is poor. The crystal appears to have diffracted weakly, and thus the signal-to-noise ratio is not adequate. Only 1617 data out of the 4658 measured were intense enough to be included in the calculation of R1. Thus the structural formula has been made clear, but comparison with other molecules to look for small differences in geometry is difficult.

The drawing of WZA002 (Figure 7) shows a problem with the refinement model: the ethyl group C29-C30 is disordered almost equally over two alternative sites C291-C301 and C292-C302. In such cases it is often difficult to refine a model that correctly fits the electron density. Nevertheless, all the measures of quality are reasonable.

The quality of the other three structure determinations is good to excellent, as shown by the values below 0.05 for the discrepancy index R1. Indeed, the 0.0312 for ZK43 is outstanding.

3.2 Comparison of structures of related molecules

3.2.1 ZK42 and ZK43

Description of the molecular structures

In both ZK42 and ZK43 N1 is *gauche* to C2, which bears the hydroxyl group responsible for the hydrogen bonding described below. Torsion angle N1-C7-C1-C2 is –60.7(2)° in ZK42 and 58.0(3)° in ZK43. The 172.1° torsion angle in ciramadol hydrobromide, where the N atom is protonated, moves the N and O apart. Both ZK42 and ZK43 have two phenyl rings, which intersect at angles of 81.10(5) and 80.96(9)° respectively.They got similarities in molecular geometry in single molecular, but the unit cell and space group are entirely different.

3.2.2. WZA001 and WZA002

WZA001 and WZA002 differ in the placement of nitrogen atoms in the heterocyclic ring: in particular, at the points where the 6-membered ring and the 5-membered ring are fused, both atoms are carbon in WZA001 but one atom (with label 22) is nitrogen in WZA002. There is a large difference in the bond distances to the adjacent carbonyl carbon C23: in WZA001 C(22)-C(23) is 1.432(7) Å, while in WZA002 is 1.374(5) Å. The shortening can be attributed to electron donation from N22 to the carbonyl group which is not possible when this atom is carbon.

Wza001		Wza002	
C22-C18	1.377(7)	N22-C18	1.409(5)
C22-C21	1.402(7)	N22-C21	1.388(5)
C22-C23	1.432(7)	N22-C23	1.374(5)

Table 2. The comparison of the C22 and N22 bond lengths in WZA001 and WZA002

3.2.3 Sterol1

The crystal structures of cholesterol and its monohydrate, ethanol solvate and methanol solvate have each been determined several times. A characteristic feature seems to be that there are multiple molecules in the asymmetric unit of the unit cell. For instance, Z'=16 for CHOEST21[16], 8 for CHOLES20[17] and for CHOLEU10[18], 4 for CHOLME02[19]. When polar groups like OH

And C=O are introduced, the number of molecules in the asymmetric unit drops, usually to 1. Possibly the strengthened intermolecular forces impose one conformation on all the molecular forces impose one conformation on all the molecules. I A CSD search search on the steroid ring system with OH at the bridgehead position where we have OH and C=O next to it, and this gave 6 hits: COMXIL[20], with R=11% too inaccurate to locate hydrogen atoms; COQCAM[21], with geometry perturbed by an epoxide group; HXSPEO[22], much more polar; LOBSTB[23], which may actually be useful as a comparison structure, for instance to compare C=O and C-O bond distances; and YACMIY[24], ZINSEU[25] and ZZZMCM[26], for which no coordinates are available.

3.3 Hydrogen bonding patterns

A six-membered intramolecularly hydrogen-bonded ring is formed in each case. With the exception of STEROL1 there is no intermolecular hydrogen bonding even though possible acceptor atoms are available. STEROL1 does have an

intermolecular hydrogen bond O1-H1...O2 hydrogen bond in addition to the intramolecular O2-H2...O1 interaction, the keto oxygen atom remaining unused. The resulting infinite chain composed of alternating intra- and intermolecular hydrogen bonds is similar to the chains formed by the OH groups of andrographolide[27] and 14-acetylandrographolide[28]. The structure data LOBSTB compare of sterol1, also has an intramolecular O-H...O hydrogen bond with H...O distance 2.04 Å, acceptor and the other OH is the proton donor. This is the opposite way round from Sterol1.

		Intramolecular	Intermolecular
Compound	Donor	Acceptor	Acceptor(s) [not] Used
Wza001	N_2H-H	O_{25}	[N_1(amide)] [N_4(tertiary amine)] [N_{17},N_{20},N_{22} (ring nitrogen)], [O_7,O_8(sulfonyl),O_{25}(methoxy), O_{34}(keto)]
Wza002	N_2H-H	O_{25}	
Sterol1	O_1-H O_2-H	------ O_1	[O_1(hydroxy)],O_2(hydroxy),[O_3(keto)]
Zk42	O_1-H	N_1	[O_1(hydrohy),O_2(methoxy),N_1(tertiary amine)]
Zk43	O_1-H	N_1	[O_1,N_1]

Table 3. Packing and list of hydrogen bonding.

3.3.1 O-H...N hydrogen bonding

Both ZK42 and ZK43 form a 6-membered intramolecularly hydrogen bonded ring with N1 as acceptor. It prevails in the face of strong competition from the oxygen atoms. We used the program GAMESS[29] to calculate Löwdin charges. This sort of quantum mechanical calculation provides you with wave functions. When squared, these give the probability of finding an election in a given region of space. To get to the simpler and more useful concept of charges on atoms, the electron density has to

be divided up among the atoms. The oldest and most straightforward way is the method of Mulliken, but this calculation tends to yield very large charges, sometimes larger than + or – 1. the Löwdin scheme gives charges that seem more realistic. Mulliken populations and charges are the simplest division of the electron density between orbitals. The Löwdin sheme divides the electron density in a way that more reflects the difference in electronegativity of the atoms. We have been using the Löwdin population analysis instead of usual Mulliken analysis to avoid the tendence of Mulliken analysis to put all of the charge on the oxygen atom. In ZK42 the Löwdin charges are only –0.285 for N1 but –0.426 on hydroxyl oxygen O1 and –0.295 on methoxyl oxygen O2. This agrees with Etter's (1990) original rule[30] that " six-membered ring intramolecular hydrogen bonds form in preference to intermolecular hydrogen bonds." However, Bilton et al. (2000) subsequently restricted it to " planar conjugated systems which may be stabilized by resonance-assisted hydrogen bonding." Although their N-C-C-C-O-H search group with one double and one aromatic bond gave the eighth highest probability of intramolecular hydrogen bonding, the search group in the present study with sp^3 hybridised carbon atoms did not figure in their "50 greatest hits".

This search group without limits on the N..H distance finds 620 hits. With a maximum limit of 2.75Å, the sum of van der Waals radii, there are 18 hits[31-48], giving a probability of 2.9 %. As found by Bilton et al. (2000), the distribution of N..H distances is bimodal (Fig. 13). The "strong" hydrogen bonds can be identified by using their criterion d < 2.30Å, leaving 13 structures with 15 independent molecules. With sp3 atoms present, ring puckering is to be expected. The strongly negative correlation (r = -0.942) between torsion angles O-H-N-C and C-O-H-N suggests that this puckering is not random (Fig. 14).

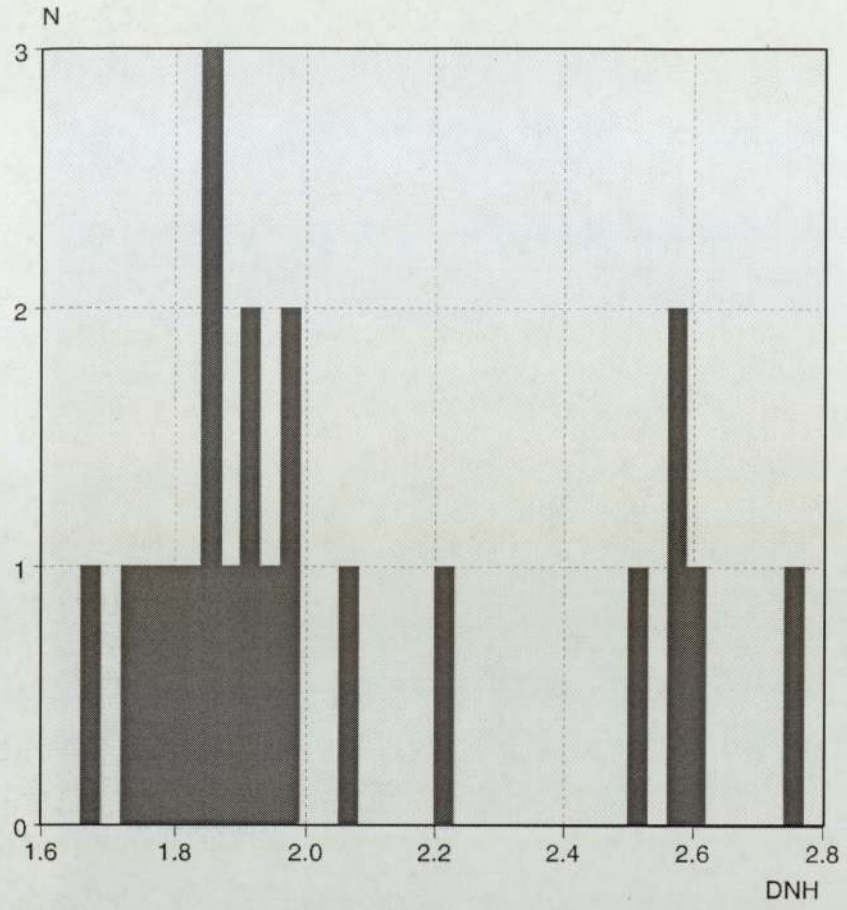


Figure 11. Histogram of N..H distances up to the sum of van der Waals radii

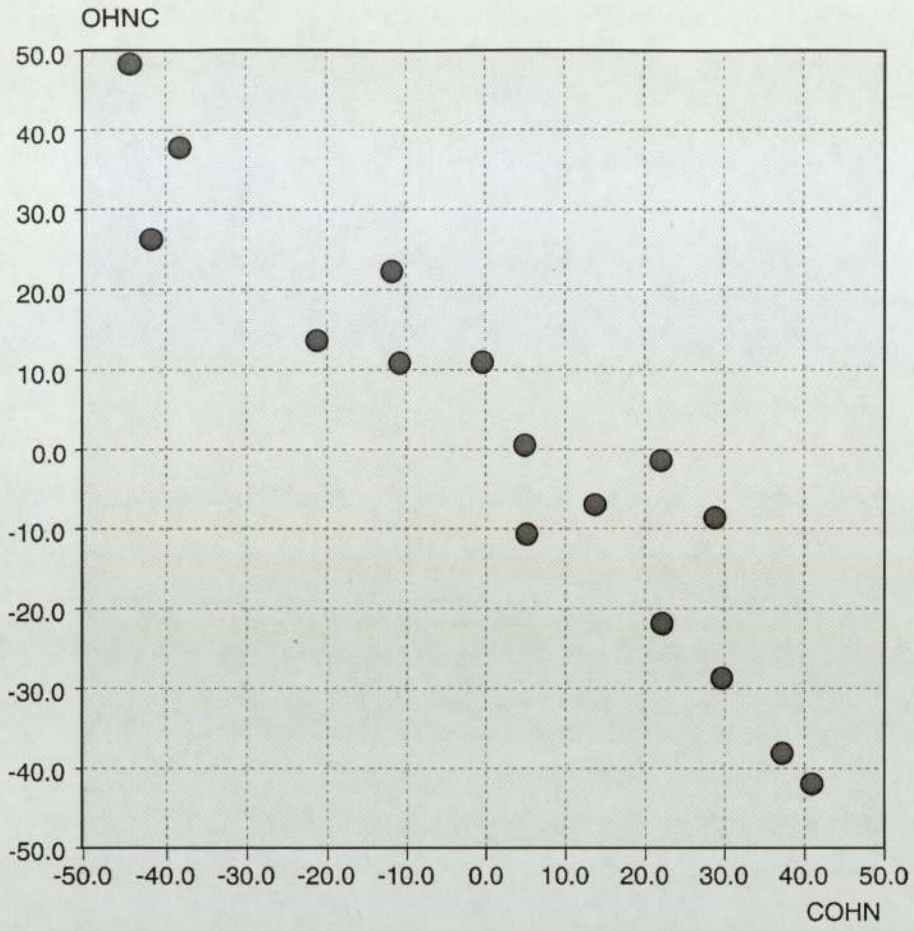


Figure 12. Graph of the torsion angle OHNC about the hydrogen bond versus torsion angle COHN defining hydroxyl group rotatio

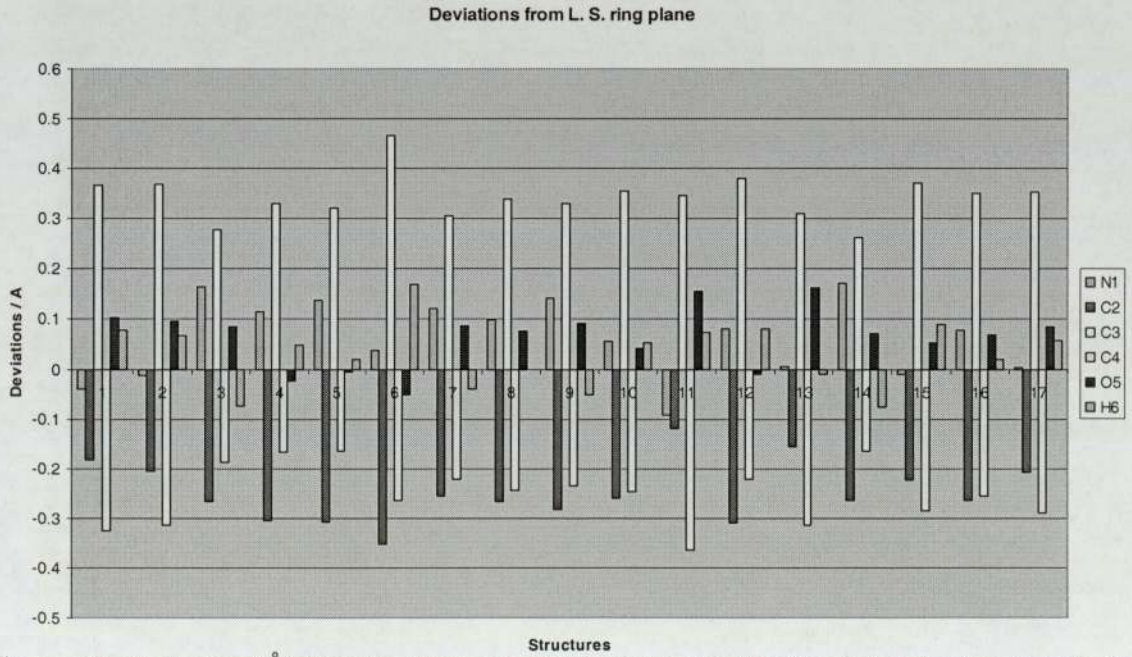


Figure 13. Deviations (Å) from the least-squares plane through the ring for each atom type in the search group.The first two structures are ZK42 and ZK43, followed by hits from theCSD.

ZK42 and ZK43 have many structural features in common, which differ from the protonated form of the comparison drug ciramadol. The intramolecularly hydrogen bonded N-C-C-C-O-H ring with saturated carbon atoms found in both structures is rare; but when it does occur, it seems to define the ring puckering. Flattening of the ring around the hydrogen bonded atoms keeps the partially negative N and O apart. The middle carbon atom in the chain of three is normally the most out-of-plane. A well-defined plane of symmetry through this carbon and the opposite hydrogen atom is consistent with a sofa conformation for the ring.

Despite the weakness of an individual hydrogen bond, hydrogen bonding can have important structural consequences, such as maintaining the structure of proteins and double-helical DNA. This study has shown that also in small organic molecules hydrogen bonding can have a very strong influence upon the conformation adopted.

References

1. Allen, L.C. *J. Amer. Chem. Soc.*,1975, **97**, 6921-6940.

2. Glusker, J.P., Rossi, M., Lewis, M. *Crystal Structure Analysis for Chemists and Biologists*', New York, Wiley, Edition - October 1994

3. Bilton, C., Allen, F.H., Shields, G.P., Howard, J.A. *Acta Crystallographica B.*, 2000, **56** ,849-56.

4. Jeffrey, G.A. '*An Introduction to Hydrogen Bonding*', New York, Oxford University Press.Edition-1997

5. Taylor, R. and Kennard, O. *Acc. Chem. Res.*, 1984, **17**, 320-326.

6. Murray-Rust, P. and Glusker, J.P. *J. Am. Chem. Soc.*, 1984, **106**, 1018-1025

7. Tintelnot, M. & Andrews, P. *J. Comput. Aided Molec. Design*, 1989,**3**,67-84.

8. Aakeroy, C.B.. *Acta Cryst., B*,1997,**53**, 569-586.

9. Aakeroy,C. B. & Seddon, K.R. *Chem. Soc. Rev.*, 1993,**22**, 397-407.

10. Desiraju, G.R. *Crystal Engineering. The design of organic solids.* Amsterdam: Elsevier 1989

11. Sheldrick, G.M. (1986). SHELXS-86. Program for the Solution of Crystal Structures. Univ. of Göttingen, Germany.

12. Sheldrick, G.M. (1997). SHELXL-97. Program for Crystal Structure Refinement. Univ. of Göttingen, Germany.

13. Johnson, C.K. (1976). ORTEPII. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

14. Stallings Junior W., J. Donohue *J. Cryst.Mol.Struct.* 1981,**11**,59.

15. Roberts, Stewart, Caserio, Organic chemistry, methane to macromolecules, W.A.Benjamin California.1974

16. Hsu,L.Y., Kampf, J.W., Nordman, C.E. *Acta Crystallogr., Sect. B*: 2002, **58**, 260.

17. Craven, B.M. *Acta Crystallogr., Sect. B*: 1979, **35**, 1123.

18. Shieh, H.S., Hoard, L.G., Nordman, C.E. *Acta Crystallogr., Sect. B*:1982, **38**, 2411.

19. Shieh, H.S., Nordman, C.E. *Acta Crystallogr., Sect. B*:2002, **58**, o79.

20. Shklover, V.E., Lindeman, S.V., Struchkov, Y. T. ,Kamernitskii, A.V., Reshetova, I.G.

Bioorg.Khim.(Russ.)(Bioorg.Chem.):1984, **10**,265.

21. Hanson ,J.R., Hitchcock, P.B., Nagaratnam, S., *J.Chem.Res.*:1999,**22**,319.

22. Miyahara, K. ,Kumamoto, F. Kawasaki, T. *Tetrahedron Lett.*1980,**21**,83.

23. Losman, D. ,Karlsson, R. ,Declercq, J.P., Germain, G.,*Acta Crystallogr., Sect. B*:1976, **32**, 2513

24.Li Ping, Kitamura, Y. , Kaneko, K. ,Shiro, M. Xu G.J., Chen Yuh-Pan, Hsu Hong-Yen *Phytochemistry* 1992,**31**,2190.

25. Chiplunkar, Y.G. ,Nagasampagi, B.A., Tavale, S.S., Puranik, V.G., *Phytochemistry* 1993,**33**,901.

26 Bernal. Philos. *Trans.R.Soc.London, Ser.B*.1940,**239**,135

27. Spek, A. L., Duisenberg, A. J. M., Labadie, R. P., Ratnayake, S., Abeysekera, A.& De Silva, K. T. D. Andrographolide, *Acta Cryst. C*,1987,**43**, 530-532.

28. Jada, S.R., McMillan, K., Hamzah, A.S., Saad, M.S., Lajis, N.H., Stevens, M.F.G., Schwalbe, C.H., and Stanslas, J. *J. Chem. Cryst.*, February 2006, **36**. 93-97(5)

29.Schmidt, M.W., Baldridge, K.K., Boatz, J.A.,Jensen, J.H.,Koseki, S., Gordon, M. S., Nguyen, K. A., Windus, T.L.&Elbert, S.T.*QCPE Bulletin*1990,**10**,52-54.

30. Etter, M.C. *Acc. Chem. Res.* , 1990,**23**, 120.

31. Szmuszkovicz, J., Kane,M.P., Laurian, L.G., Chidester, C.G., Scahill, T.A. *J.Org.Chem.*,1981,**46**,3562

32. Perez, S., A Lopez-Castro, Marquez, R., *Acta Cryst., .B.*,1978,**34**,2341

33. Lgarashi, M., Nakamura, H., Takeuchi, T.,*J.Antibiot.*, 1997,**50**,1026

34. Gaudiano, G., Sweeney, K., Haltiwanger, R.C., Koch, T.H., *J.Am.Chem.Soc.*,1984,**106**,7628

35. Clarke, C. ,Fleming, I. Fortinak, J.M.D., Gallagher, P.T., Honan, M.C., Nubling, C.O., Raithby, P.R., Wolff, J.J., *Tetrahedron* , 1988,**44**,3931

36. Chyuan-Der Hwang, Biing-Jiun Uang, *J.Org.Chem.*, 1988,**63**,6762

37 . Weber, B., Kolczewski, S. , Frohlich, R., Hoppe, D., *synthesis*, 1999,1593

38. Baillie, L.C., Beader, J.R., Li, Wang-Shi, Sherringham, J.A., Whiting, D.A., *J. Chem. Soc., Perkin Trans.*, 1998,**1** ,4047

39. Vorwerk, S., Vasella, A., *Angew. Chem., Int. Ed.* 1998,**37**,1732

40. Beckmann, C., Jones, P.G., Kirby, A.J. *Acta Cryst E.*, 2003,**59**,564

41. Hong Zhang, Wei-Fen Li, Kui-Wu Wang, Yuan Jiang Pan,

Acta Cryst.,E 2004,**60**, 299

42. Donohoe, T.J., Blades, K., Moore, P.R., Waring, M.J., Winter, J.J.G., Helliwell, M., Newcombe, N.J., Stemp, G., *J. Org. Chem.*, 2002,**67**,7946

43. Yamauchi, Y., Katagiri, T., Uneyama , K.,*Organic Letters* ,2002,**4**,173

44. Fiorelli, C., Maini, L., Martelli, G., Savoia, D., Zazzetta , C.,*Tetrahedron* ,2002,**58**,8679

45. McMahon, C.N., Bott, S.G., Barron, A.R., *J. Chem. Soc.,Dalton Trans.* ,1997,3129

46. Tessler, L., Goldberg , I., *Acta Cryst., E:*,**60**,o1868

47. Bowman, W.R., Brown, D.S., Burns, C.A., Crosby, D. *J. Chem. Soc., Perkin Trans.* 1993,**1** ,2099

48. Guarnieri, W., Sendzik, M., Frohlich, R., Hoppe, D., *Synthesis* ,1998,1274

Appendix (Detailed crystal data)

Crystal data 1 Zk-42

Appendix 1. Crystal data and structure refinement for zk42.

Identification code	zk42
Empirical formula	C23 H29 N O2
Formula weight	351.47
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system	monoclinic
Space group	P21/c
Unit cell dimensions	a = 11.267(2) A alpha = 90 deg.
	b = 12.2951(14) A beta = 111.271(12)deg.
	c = 15.240(3) A gamma = 90 deg.
Volume	1967.4(5) A^3
Z	4
Density (calculated)	1.187 Mg/m^3
Absorption coefficient	0.075 mm^-1
F(000)	760
Crystal size	0.7 x 0.4 x 0.3 mm
Theta range for data collection	2.19 to 25.38 deg.
Index ranges	-13<=h<=0, -14<=k<=5, -17<=l<=18
Reflections collected	5625
Independent reflections	3616 [R(int) = 0.0173]
Refinement method	Full-matrix least-squares on F^2

Data / restraints / parameters	3616 / 0 / 239
Goodness-of-fit on F^2	1.010
Final R indices [I>2sigma(I)]	R1 = 0.0385, wR2 = 0.1026
R indices (all data)	R1 = 0.0675, wR2 = 0.1209
Largest diff. peak and hole	0.165 and -0.198 e.A^-3

Appendix 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for zk42. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

---

	x	y	z	U(eq)
O(1)	3307(1)	3182(1)	1978(1)	41(1)
O(2)	6721(1)	1295(1)	-123(1)	78(1)
N(1)	3538(1)	5103(1)	1181(1)	48(1)
C(1)	1878(2)	3707(1)	443(1)	40(1)
C(2)	2695(1)	2764(1)	1048(1)	36(1)
C(3)	1807(1)	1847(1)	1105(1)	38(1)
C(4)	842(2)	1493(1)	178(1)	50(1)
C(5)	39(2)	2446(2)	-355(1)	58(1)
C(6)	863(2)	3360(2)	-490(1)	54(1)
C(7)	2714(2)	4612(1)	294(1)	48(1)
C(8)	2867(2)	5948(2)	1480(2)	77(1)
C(9)	4699(2)	5548(2)	1107(2)	80(1)
C(10)	3726(1)	2340(1)	685(1)	37(1)
C(11)	4994(2)	2358(2)	1277(1)	52(1)
C(12)	5959(2)	2005(2)	991(1)	63(1)
C(13)	5691(2)	1611(1)	93(1)	53(1)

C(14)	4446(2)	1591(2)	-514(1)	56(1)
C(15)	3490(2)	1952(2)	-218(1)	53(1)
C(16)	6486(3)	804(2)	-1010(2)	85(1)
C(17)	1885(1)	1439(1)	1936(1)	40(1)
C(18)	1048(2)	607(1)	2109(1)	42(1)
C(19)	-276(2)	708(1)	1761(1)	51(1)
C(20)	-1039(2)	-65(2)	1950(1)	62(1)
C(21)	-509(2)	-953(2)	2490(1)	66(1)
C(22)	801(2)	-1062(2)	2852(1)	67(1)
C(23)	1570(2)	-288(1)	2667(1)	54(1)

Appendix 3. Bond lengths [A] and angles [deg] for zk42.

O(1)-C(2)	1.4277(17)
O(1)-H(1)	0.8200
O(2)-C(13)	1.372(2)
O(2)-C(16)	1.416(3)
N(1)-C(8)	1.453(2)
N(1)-C(9)	1.460(2)
N(1)-C(7)	1.463(2)
C(1)-C(7)	1.526(2)
C(1)-C(6)	1.528(2)
C(1)-C(2)	1.558(2)
C(1)-H(1A)	0.9800
C(2)-C(3)	1.530(2)
C(2)-C(10)	1.547(2)
C(3)-C(17)	1.335(2)

C(3)-C(4)	1.501(2)
C(4)-C(5)	1.522(3)
C(4)-H(4A)	0.9700
C(4)-H(4B)	0.9700
C(5)-C(6)	1.519(3)
C(5)-H(5A)	0.9700
C(5)-H(5B)	0.9700
C(6)-H(6A)	0.9700
C(6)-H(6B)	0.9700
C(7)-H(7A)	0.9700
C(7)-H(7B)	0.9700
C(8)-H(8A)	0.9600
C(8)-H(8B)	0.9600
C(8)-H(8C)	0.9600
C(9)-H(9A)	0.9600
C(12)-H(12)	0.9300
C(9)-H(9B)	0.9600
C(9)-H(9C)	0.9600
C(10)-C(11)	1.386(2)
C(10)-C(15)	1.389(2)
C(11)-C(12)	1.379(2)
C(11)-H(11)	0.9300
C(12)-C(13)	1.379(3)
C(13)-C(14)	1.371(3)
C(14)-H(14)	0.9300
C(15)-H(15)	0.9300
C(16)-H(16A)	0.9600
C(16)-H(16B)	0.9600
C(16)-H(16C)	0.9600

C(17)-C(18)	1.479(2)
C(17)-H(17)	0.9300
C(18)-C(23)	1.385(2)
C(18)-C(19)	1.395(2)
C(19)-C(20)	1.380(2)
C(19)-H(19)	0.9300
C(20)-C(21)	1.367(3)
C(20)-H(20)	0.9300
C(21)-C(22)	1.382(3)
C(21)-H(21)	0.9300
C(22)-C(23)	1.383(3)
C(22)-H(22)	0.9300
C(23)-H(23)	0.9300

C(2)-O(1)-H(1)	109.5
C(13)-O(2)-C(16)	117.90(17)
C(8)-N(1)-C(9)	109.81(16)
C(8)-N(1)-C(7)	110.88(15)
C(9)-N(1)-C(7)	111.71(15)
C(7)-C(1)-C(6)	111.08(13)
C(7)-C(1)-C(2)	111.58(13)
C(6)-C(1)-C(2)	115.14(13)
C(7)-C(1)-H(1A)	106.1
C(6)-C(1)-H(1A)	106.1
C(2)-C(1)-H(1A)	106.1
O(1)-C(2)-C(3)	107.45(11)
O(1)-C(2)-C(10)	108.73(11)
C(3)-C(2)-C(10)	111.33(12)
O(1)-C(2)-C(1)	106.72(11)

C(3)-C(2)-C(1)	108.94(12)
C(10)-C(2)-C(1)	113.40(11)
C(17)-C(3)-C(4)	124.07(14)
C(17)-C(3)-C(2)	120.72(13)
C(4)-C(3)-C(2)	115.16(12)
C(3)-C(4)-C(5)	111.52(13)
C(3)-C(4)-H(4A)	109.3
C(5)-C(4)-H(4A)	109.3
C(3)-C(4)-H(4B)	109.3
C(5)-C(4)-H(4B)	109.3
H(4A)-C(4)-H(4B)	108.0
C(6)-C(5)-C(4)	111.57(14)
C(6)-C(5)-H(5A)	109.3
C(4)-C(5)-H(5A)	109.3
C(6)-C(5)-H(5B)	109.3
C(4)-C(5)-H(5B)	109.3
H(5A)-C(5)-H(5B)	108.0
C(5)-C(6)-C(1)	111.64(14)
C(5)-C(6)-H(6A)	109.3
C(1)-C(6)-H(6A)	109.3
C(5)-C(6)-H(6B)	109.3
C(1)-C(6)-H(6B)	109.3
H(6A)-C(6)-H(6B)	108.0
N(1)-C(7)-C(1)	112.48(12)
N(1)-C(7)-H(7A)	109.1
C(1)-C(7)-H(7A)	109.1
N(1)-C(7)-H(7B)	109.1
C(1)-C(7)-H(7B)	109.1
H(7A)-C(7)-H(7B)	107.8

N(1)-C(8)-H(8A)	109.5
N(1)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
N(1)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
N(1)-C(9)-H(9A)	109.5
N(1)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
N(1)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(11)-C(10)-C(15)	115.57(15)
C(11)-C(10)-C(2)	119.53(13)
C(15)-C(10)-C(2)	124.88(14)
C(12)-C(11)-C(10)	122.31(16)
C(12)-C(11)-H(11)	118.8
C(10)-C(11)-H(11)	118.8
C(13)-C(12)-C(11)	120.64(17)
C(13)-C(12)-H(12)	119.7
C(11)-C(12)-H(12)	119.7
C(14)-C(13)-O(2)	125.50(17)
C(14)-C(13)-C(12)	118.57(16)
O(2)-C(13)-C(12)	115.91(17)
C(13)-C(14)-C(15)	120.11(17)
C(13)-C(14)-H(14)	119.9
C(15)-C(14)-H(14)	119.9
C(14)-C(15)-C(10)	122.78(16)
C(14)-C(15)-H(15)	118.6

C(10)-C(15)-H(15)	118.6
O(2)-C(16)-H(16A)	109.5
O(2)-C(16)-H(16B)	109.5
H(16A)-C(16)-H(16B)	109.5
O(2)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5
C(3)-C(17)-C(18)	126.99(14)
C(3)-C(17)-H(17)	116.5
C(18)-C(17)-H(17)	116.5
C(23)-C(18)-C(19)	117.46(15)
C(23)-C(18)-C(17)	120.19(15)
C(19)-C(18)-C(17)	122.29(15)
C(20)-C(19)-C(18)	121.37(18)
C(20)-C(19)-H(19)	119.3
C(18)-C(19)-H(19)	119.3
C(21)-C(20)-C(19)	120.41(19)
C(21)-C(20)-H(20)	119.8
C(19)-C(20)-H(20)	119.8
C(20)-C(21)-C(22)	119.22(17)
C(20)-C(21)-H(21)	120.4
C(22)-C(21)-H(21)	120.4
C(21)-C(22)-C(23)	120.57(19)
C(21)-C(22)-H(22)	119.7
C(23)-C(22)-H(22)	119.7
C(22)-C(23)-C(18)	120.95(19)
C(22)-C(23)-H(23)	119.5
C(18)-C(23)-H(23)	119.5

Appendix 4. Anisotropic displacement parameters (A^2 x 10^3) for zk42.

The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
O(1)	52(1)	41(1)	31(1)	-4(1)	15(1)	-8(1)
O(2)	71(1)	96(1)	81(1)	5(1)	46(1)	26(1)
N(1)	47(1)	42(1)	56(1)	0(1)	19(1)	-7(1)
C(1)	42(1)	43(1)	36(1)	0(1)	15(1)	-1(1)
C(2)	40(1)	39(1)	30(1)	-3(1)	13(1)	-5(1)
C(3)	42(1)	35(1)	40(1)	-4(1)	21(1)	-2(1)
C(4)	56(1)	51(1)	44(1)	-12(1)	23(1)	-18(1)
C(5)	49(1)	74(1)	44(1)	-7(1)	8(1)	-14(1)
C(6)	53(1)	61(1)	41(1)	4(1)	8(1)	-2(1)
C(7)	56(1)	44(1)	45(1)	8(1)	21(1)	0(1)
C(8)	78(1)	63(1)	93(2)	-26(1)	33(1)	-7(1)
C(9)	61(1)	77(1)	103(2)	5(1)	31(1)	-21(1)
C(10)	43(1)	35(1)	37(1)	2(1)	18(1)	-3(1)
C(11)	50(1)	64(1)	40(1)	1(1)	15(1)	9(1)
C(12)	47(1)	85(1)	56(1)	6(1)	16(1)	16(1)
C(13)	58(1)	51(1)	59(1)	9(1)	34(1)	11(1)
C(14)	66(1)	61(1)	50(1)	-10(1)	32(1)	-5(1)
C(15)	48(1)	70(1)	45(1)	-12(1)	21(1)	-8(1)
C(16)	110(2)	79(2)	96(2)	-1(1)	73(2)	19(1)
C(17)	44(1)	38(1)	43(1)	-1(1)	21(1)	-1(1)
C(18)	54(1)	40(1)	40(1)	-5(1)	26(1)	-5(1)
C(19)	54(1)	51(1)	58(1)	-4(1)	31(1)	-3(1)

C(20)	61(1)	71(1)	68(1)	-16(1)	41(1)	-18(1)
C(21)	90(2)	64(1)	62(1)	-14(1)	50(1)	-34(1)
C(22)	98(2)	51(1)	62(1)	10(1)	39(1)	-11(1)
C(23)	64(1)	52(1)	51(1)	6(1)	26(1)	-4(1)

Appendix 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for zk42.

	x	y	z	U(eq)
H(1)	3580	3794	1949	62
H(1A)	1419	4027	816	49
H(4A)	290	946	287	59
H(4B)	1277	1167	-201	59
H(5A)	-536	2198	-965	70
H(5B)	-472	2719	-9	70
H(6A)	328	3979	-775	65
H(6B)	1273	3121	-917	65
H(7A)	3237	4318	-33	57
H(7B)	2173	5172	-101	57
H(8A)	2666	6536	1035	116
H(8B)	3396	6212	2090	116
H(8C)	2094	5656	1513	116
H(9A)	4480	6091	622	120
H(9B)	5170	4975	955	120
H(9C)	5210	5871	1697	120
H(11)	5203	2618	1887	62
H(12)	6799	2033	1409	76

H(14)	4245	1334	-1125	67
H(15)	2653	1935	-643	64
H(16A)	5952	178	-1075	127
H(16B)	7279	585	-1056	127
H(16C)	6068	1316	-1501	127
H(17)	2537	1707	2463	48
H(19)	-652	1308	1395	62
H(20)	-1919	19	1709	75
H(21)	-1024	-1477	2612	79
H(22)	1169	-1662	3222	81
H(23)	2450	-370	2921	65

Structure data 2 ZK-43

Appendix 6. Crystal data and structure refinement for zk43.

Identification code	zk43
Empirical formula	C22 H27 N O
Formula weight	321.45
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system	orthorhombic
Space group	Pna21
Unit cell dimensions	a = 12.361(3) A alpha = 90 deg.
	b = 15.083(2) A beta = 90 deg.
	c = 10.0810(17) A gamma = 90 deg.
Volume	1879.5(6) A^3
Z	4

Density (calculated)	1.136 Mg/m^3
Absorption coefficient	0.069 mm^-1
F(000)	696
Crystal size	0.6 x 0.5 x 0.4 mm
Theta range for data collection	2.43 to 25.96 deg.
Index ranges	-15<=h<=4, -18<=k<=18, -12<=l<=0
Reflections collected	5159
Independent reflections	1950 [R(int) = 0.0510]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1950 / 1 / 221
Goodness-of-fit on F^2	1.027
Final R indices [I>2sigma(I)]	R1 = 0.0312, wR2 = 0.0844
R indices (all data)	R1 = 0.0433, wR2 = 0.0912
Absolute structure parameter	-0.1(17)
Extinction coefficient	0.017(2)
Largest diff. peak and hole	0.118 and -0.110 e.A^-3

Appendix 7. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for zk43. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1)	8517(1)	8802(1)	5106(1)	50(1)
N(1)	7174(2)	9414(1)	7033(2)	60(1)
C(1)	6655(2)	9123(1)	4679(2)	52(1)
C(2)	7582(2)	8442(1)	4483(2)	43(1)
C(3)	7832(2)	8333(1)	2998(2)	47(1)

C(4)	6860(2)	8162(2)	2136(2)	57(1)
C(5)	6007(2)	8882(2)	2316(3)	67(1)
C(6)	5676(2)	9009(2)	3753(3)	63(1)
C(7)	6293(2)	9177(2)	6129(3)	60(1)
C(8)	7011(3)	9049(2)	8370(3)	90(1)
C(9)	7311(3)	10376(2)	7119(3)	79(1)
C(10)	7366(1)	7508(1)	5060(2)	40(1)
C(11)	8175(2)	7088(2)	5754(3)	62(1)
C(12)	8036(2)	6248(2)	6259(3)	78(1)
C(13)	7073(2)	5797(1)	6094(3)	61(1)
C(14)	6260(2)	6198(1)	5402(2)	55(1)
C(15)	6402(2)	7042(1)	4896(2)	52(1)
C(17)	8846(2)	8438(1)	2565(2)	51(1)
C(18)	9258(2)	8329(1)	1202(2)	55(1)
C(19)	9972(2)	8956(2)	687(3)	67(1)
C(20)	10375(3)	8871(2)	-579(3)	91(1)
C(21)	10102(3)	8158(3)	-1337(3)	104(1)
C(22)	9426(3)	7523(2)	-849(3)	96(1)
C(23)	9000(3)	7608(2)	417(3)	73(1)

Appendix 8. Bond lengths [A] and angles [deg] for zk43.

O(1)-C(2)	1.423(2)
O(1)-H(1)	0.8200
N(1)-C(9)	1.462(3)
N(1)-C(7)	1.465(3)
N(1)-C(8)	1.470(4)

C(1)-C(7)	1.531(3)
C(1)-C(6)	1.538(3)
C(1)-C(2)	1.552(3)
C(1)-H(1A)	0.9800
C(2)-C(3)	1.537(3)
C(2)-C(10)	1.548(3)
C(3)-C(17)	1.336(3)
C(3)-C(4)	1.506(3)
C(4)-C(5)	1.524(3)
C(5)-C(6)	1.517(4)
C(9)-H(9B)	0.9600
C(9)-H(9C)	0.9600
C(10)-C(11)	1.375(3)
C(10)-C(15)	1.394(3)
C(11)-C(12)	1.377(3)
C(11)-H(11)	0.9300
C(12)-C(13)	1.382(3)
C(12)-H(12)	0.9300
C(13)-C(14)	1.364(3)
C(13)-H(13)	0.9300
C(14)-C(15)	1.383(3)
C(14)-H(14)	0.9300
C(15)-H(15)	0.9300
C(17)-C(18)	1.474(3)
C(17)-H(17)	0.9300
C(18)-C(23)	1.382(3)
C(18)-C(19)	1.394(3)
C(19)-C(20)	1.375(4)
C(19)-H(19)	0.9300

C(20)-C(21)	1.362(5)
C(20)-H(20)	0.9300
C(21)-C(22)	1.362(5)
C(21)-H(21)	0.9300
C(22)-C(23)	1.387(4)
C(22)-H(22)	0.9300
C(23)-H(23)	0.9300

C(2)-O(1)-H(1)	109.5
C(9)-N(1)-C(7)	111.4(2)
C(9)-N(1)-C(8)	109.5(2)
C(7)-N(1)-C(8)	112.1(2)
C(7)-C(1)-C(6)	110.83(18)
C(7)-C(1)-C(2)	111.89(18)
C(6)-C(1)-C(2)	115.43(18)
C(7)-C(1)-H(1A)	106.0
C(6)-C(1)-H(1A)	106.0
C(2)-C(1)-H(1A)	106.0
O(1)-C(2)-C(3)	107.91(15)
O(1)-C(2)-C(10)	108.76(15)
C(3)-C(2)-C(10)	107.66(15)
O(1)-C(2)-C(1)	106.90(15)
C(3)-C(2)-C(1)	110.10(16)
C(10)-C(2)-C(1)	115.30(15)
C(17)-C(3)-C(4)	125.46(19)
C(17)-C(3)-C(2)	119.61(18)
C(4)-C(3)-C(2)	114.83(18)
C(3)-C(4)-C(5)	111.15(19)
C(3)-C(4)-H(4A)	109.4

C(5)-C(4)-H(4A)	109.4
C(3)-C(4)-H(4B)	109.4
C(5)-C(4)-H(4B)	109.4
H(4A)-C(4)-H(4B)	108.0
C(6)-C(5)-C(4)	113.02(19)
C(6)-C(5)-H(5A)	109.0
C(4)-C(5)-H(5A)	109.0
C(6)-C(5)-H(5B)	109.0
C(4)-C(5)-H(5B)	109.0
H(5A)-C(5)-H(5B)	107.8
C(5)-C(6)-C(1)	112.43(19)
C(5)-C(6)-H(6A)	109.1
C(1)-C(6)-H(6A)	109.1
C(5)-C(6)-H(6B)	109.1
C(1)-C(6)-H(6B)	109.1
H(6A)-C(6)-H(6B)	107.8
N(1)-C(7)-C(1)	112.91(18)
N(1)-C(7)-H(7A)	109.0
C(1)-C(7)-H(7A)	109.0
N(1)-C(7)-H(7B)	109.0
C(1)-C(7)-H(7B)	109.0
H(7A)-C(7)-H(7B)	107.8
N(1)-C(8)-H(8A)	109.5
N(1)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
N(1)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
N(1)-C(9)-H(9A)	109.5

N(1)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
N(1)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(11)-C(10)-C(15)	116.82(18)
C(11)-C(10)-C(2)	118.98(17)
C(15)-C(10)-C(2)	124.18(16)
C(10)-C(11)-C(12)	121.4(2)
C(10)-C(11)-H(11)	119.3
C(12)-C(11)-H(11)	119.3
C(11)-C(12)-C(13)	121.1(2)
C(11)-C(12)-H(12)	119.5
C(13)-C(12)-H(12)	119.5
C(14)-C(13)-C(12)	118.6(2)
C(14)-C(13)-H(13)	120.7
C(12)-C(13)-H(13)	120.7
C(13)-C(14)-C(15)	120.2(2)
C(13)-C(14)-H(14)	119.9
C(15)-C(14)-H(14)	119.9
C(14)-C(15)-C(10)	121.9(2)
C(14)-C(15)-H(15)	119.1
C(10)-C(15)-H(15)	119.1
C(3)-C(17)-C(18)	128.0(2)
C(3)-C(17)-H(17)	116.0
C(18)-C(17)-H(17)	116.0
C(23)-C(18)-C(19)	117.8(2)
C(23)-C(18)-C(17)	122.8(2)
C(19)-C(18)-C(17)	119.3(2)

C(20)-C(19)-C(18)	120.8(3)
C(20)-C(19)-H(19)	119.6
C(18)-C(19)-H(19)	119.6
C(21)-C(20)-C(19)	120.3(3)
C(21)-C(20)-H(20)	119.9
C(19)-C(20)-H(20)	119.9
C(20)-C(21)-C(22)	120.3(3)
C(20)-C(21)-H(21)	119.9
C(22)-C(21)-H(21)	119.9
C(21)-C(22)-C(23)	120.1(3)
C(21)-C(22)-H(22)	120.0
C(23)-C(22)-H(22)	120.0
C(18)-C(23)-C(22)	120.8(3)
C(18)-C(23)-H(23)	119.6
C(22)-C(23)-H(23)	119.6

Appendix 9. Anisotropic displacement parameters (A^2 x 10^3) for zk43.

The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
O(1)	38(1)	60(1)	51(1)	-5(1)	-2(1)	-7(1)
N(1)	56(1)	62(1)	61(1)	-8(1)	5(1)	3(1)
C(1)	42(1)	46(1)	67(1)	2(1)	-4(1)	1(1)
C(2)	31(1)	50(1)	47(1)	2(1)	-4(1)	-2(1)
C(3)	44(1)	49(1)	46(1)	7(1)	-4(1)	-2(1)
C(4)	54(1)	70(1)	47(1)	8(1)	-9(1)	-10(1)

C(5)	52(1)	71(1)	79(2)	20(1)	-25(1)	-5(1)
C(6)	42(1)	59(1)	89(2)	2(1)	-13(1)	8(1)
C(7)	46(1)	56(1)	78(2)	-9(1)	8(1)	4(1)
C(8)	97(2)	100(2)	71(2)	2(2)	10(2)	9(2)
C(9)	79(2)	72(2)	87(2)	-18(2)	11(2)	-12(2)
C(10)	36(1)	47(1)	39(1)	-2(1)	2(1)	4(1)
C(11)	42(1)	54(1)	91(2)	6(1)	-18(1)	-1(1)
C(12)	63(2)	58(1)	112(2)	17(2)	-31(2)	7(1)
C(13)	65(1)	48(1)	70(1)	10(1)	-3(1)	1(1)
C(14)	49(1)	55(1)	62(1)	5(1)	0(1)	-8(1)
C(15)	41(1)	57(1)	60(1)	9(1)	-9(1)	-1(1)
C(17)	45(1)	56(1)	51(1)	7(1)	-4(1)	5(1)
C(18)	52(1)	61(1)	50(1)	11(1)	2(1)	14(1)
C(19)	55(1)	78(2)	68(1)	11(1)	12(1)	3(1)
C(20)	86(2)	105(2)	81(2)	21(2)	34(2)	3(2)
C(21)	129(3)	119(3)	65(2)	8(2)	36(2)	18(3)
C(22)	133(3)	88(2)	67(2)	-13(2)	9(2)	9(2)
C(23)	92(2)	64(1)	63(1)	6(1)	6(1)	1(2)

Appendix 10. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for zk43.

	x	y	z	U(eq)
H(1)	8350	9008	5831	74
H(1A)	6965	9704	4467	62
H(4A)	6550	7590	2361	69
H(4B)	7082	8142	1213	69

H(5A)	6288	9437	1975	81
H(5B)	5373	8728	1799	81
H(6A)	5258	8500	4039	76
H(6B)	5217	9529	3820	76
H(7A)	5721	9614	6206	72
H(7B)	5997	8608	6393	72
H(8A)	6339	9262	8723	134
H(8B)	7595	9232	8935	134
H(8C)	6994	8413	8323	134
H(9A)	7929	10509	7659	119
H(9B)	6676	10634	7509	119
H(9C)	7416	10615	6246	119
H(11)	8831	7379	5884	75
H(12)	8600	5979	6718	93
H(13)	6980	5232	6447	73
H(14)	5609	5902	5270	66
H(15)	5837	7307	4432	63
H(17)	9354	8600	3201	61
H(19)	10179	9437	1205	80
H(20)	10836	9302	-918	109
H(21)	10377	8105	-2192	125
H(22)	9252	7033	-1365	115
H(23)	8534	7175	741	88

Crystal Data 3 WZA001

Appendix 11. Crystal data and structure refinement for wza001na.

Identification code	wza001na
Empirical formula	C24 H33 N5 O4 S
Formula weight	487.61
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system	monoclinic
Space group	P21/c
Unit cell dimensions	a = 17.987(2) A alpha = 90 deg.
	b = 17.1743(16) A beta = 96.559(13) deg.
	c = 8.4317(18) A gamma = 90 deg.
Volume	2587.6(7) A^3
Z	4
Density (calculated)	1.252 Mg/m^3
Absorption coefficient	0.163 mm^-1
F(000)	1040
Crystal size	0.4 x 0.4 x 0.2 mm
Theta range for data collection	2.28 to 25.23 deg.
Index ranges	-21<=h<=21, -20<=k<=20, 0<=l<=10
Reflections collected	9809
Independent reflections	4658 [R(int) = 0.1354]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4658 / 0 / 301
Goodness-of-fit on F^2	0.940
Final R indices [I>2sigma(I)]	R1 = 0.0709, wR2 = 0.1985
R indices (all data)	R1 = 0.2310, wR2 = 0.2730
Largest diff. peak and hole	0.461 and -0.241 e.A^-3

Appendix 12. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for wza001na. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
N(1)	2770(3)	3686(3)	6647(6)	77(2)
C(2)	3268(4)	4359(4)	6958(10)	112(3)
C(3)	3912(5)	4130(6)	8174(16)	149(4)
N(4)	3650(4)	3881(5)	9685(11)	137(3)
C(5)	3169(5)	3204(5)	9342(11)	120(3)
C(6)	2518(4)	3386(4)	8160(8)	87(2)
S(7)	2112(1)	3762(1)	5158(2)	85(1)
O(8)	1740(3)	3022(2)	5013(5)	99(2)
O(9)	2455(3)	4070(3)	3849(6)	113(2)
C(10)	1480(4)	4452(3)	5727(6)	70(2)
C(11)	1611(3)	5233(3)	5535(6)	66(2)
C(12)	1166(3)	5805(3)	6094(6)	61(2)
C(13)	556(3)	5562(3)	6859(6)	63(2)
C(14)	396(4)	4779(4)	7023(7)	70(2)
C(15)	856(4)	4231(4)	6477(7)	76(2)
C(16)	1393(3)	6626(3)	5861(6)	52(1)
N(17)	1997(2)	6745(2)	5189(5)	56(1)
C(18)	2171(3)	7503(3)	5056(6)	53(1)
N(19)	2787(3)	7759(3)	4408(5)	60(1)
C(20)	2815(4)	8554(4)	4509(6)	69(2)
C(21)	2212(4)	8816(3)	5216(6)	67(2)

C(22)	1811(3)	8149(3)	5564(6)	54(1)
C(23)	1145(3)	8013(3)	6301(7)	63(2)
N(24)	985(2)	7220(3)	6391(5)	64(1)
O(25)	125(2)	6129(2)	7415(5)	74(1)
C(26)	-460(4)	5912(4)	8367(8)	85(2)
C(27)	-809(4)	6671(4)	8860(9)	98(2)
C(28)	3282(3)	7252(4)	3639(7)	72(2)
C(29)	3841(4)	6841(5)	4739(9)	134(3)
C(30)	4314(7)	6291(7)	3809(13)	243(8)
O(31)	717(2)	8491(2)	6830(5)	82(1)
C(32)	2027(4)	9665(3)	5595(8)	87(2)
C(33)	4301(7)	3774(9)	11200(20)	298(9)

Appendix 13. Bond lengths [A] and angles [deg] for wza001na.

Atom	Bond angle
N(1)-C(2)	1.466(8)
N(1)-C(6)	1.494(7)
N(1)-S(7)	1.630(5)
C(2)-C(3)	1.509(11)
C(3)-N(4)	1.472(12)
N(4)-C(5)	1.458(10)
N(4)-C(33)	1.642(14)
C(5)-C(6)	1.481(9)
S(7)-O(9)	1.426(4)
S(7)-O(8)	1.436(4)
S(7)-C(10)	1.745(6)

C(10)-C(11)	1.375(7)
C(10)-C(15)	1.402(8)
C(11)-C(12)	1.383(7)
C(12)-C(13)	1.399(7)
C(12)-C(16)	1.486(7)
C(13)-O(25)	1.360(6)
C(14)-C(15)	1.367(8)
C(16)-N(17)	1.298(6)
C(16)-N(24)	1.361(6)
N(17)-C(18)	1.347(6)
C(18)-N(19)	1.363(6)
C(18)-C(22)	1.377(7)
N(19)-C(20)	1.368(7)
N(19)-C(28)	1.450(7)
C(20)-C(21)	1.372(7)
C(13)-C(14)	1.386(8)
C(21)-C(22)	1.402(7)
C(21)-C(32)	1.538(8)
C(22)-C(23)	1.432(7)
C(23)-O(31)	1.242(6)
C(23)-N(24)	1.395(7)
O(25)-C(26)	1.444(6)
C(26)-C(27)	1.526(8)
C(28)-C(29)	1.469(9)
C(29)-C(30)	1.543(10)

C(2)-N(1)-C(6)	111.0(6)
C(2)-N(1)-S(7)	116.7(5)
C(6)-N(1)-S(7)	114.9(4)

N(1)-C(2)-C(3)	108.8(7)
N(4)-C(3)-C(2)	111.5(7)
C(5)-N(4)-C(3)	107.5(8)
C(5)-N(4)-C(33)	114.8(8)
C(3)-N(4)-C(33)	115.7(8)
N(4)-C(5)-C(6)	111.8(7)
C(5)-C(6)-N(1)	110.7(6)
O(9)-S(7)-O(8)	120.1(3)
O(9)-S(7)-N(1)	106.5(3)
O(8)-S(7)-N(1)	106.6(3)
O(9)-S(7)-C(10)	108.3(3)
O(8)-S(7)-C(10)	108.2(3)
N(1)-S(7)-C(10)	106.3(3)
C(11)-C(10)-C(15)	118.2(6)
C(11)-C(10)-S(7)	120.3(5)
C(15)-C(10)-S(7)	121.3(5)
C(10)-C(11)-C(12)	122.7(5)
C(11)-C(12)-C(13)	117.4(5)
C(11)-C(12)-C(16)	116.8(5)
C(13)-C(12)-C(16)	125.8(5)
O(25)-C(13)-C(14)	121.8(5)
O(25)-C(13)-C(12)	116.9(5)
C(14)-C(13)-C(12)	121.2(6)
C(15)-C(14)-C(13)	119.6(6)
C(14)-C(15)-C(10)	120.9(6)
N(17)-C(16)-N(24)	122.3(5)
N(17)-C(16)-C(12)	117.6(5)
N(24)-C(16)-C(12)	120.1(5)
C(16)-N(17)-C(18)	113.8(4)

N(17)-C(18)-N(19)	123.6(5)
N(17)-C(18)-C(22)	129.1(5)
N(19)-C(18)-C(22)	107.3(5)
C(18)-N(19)-C(20)	108.8(5)
C(18)-N(19)-C(28)	123.6(5)
C(20)-N(19)-C(28)	127.4(5)
N(19)-C(20)-C(21)	109.2(5)
C(20)-C(21)-C(22)	105.9(5)
C(20)-C(21)-C(32)	127.0(5)
C(22)-C(21)-C(32)	127.1(6)
C(18)-C(22)-C(21)	108.8(5)
C(18)-C(22)-C(23)	116.8(5)
C(21)-C(22)-C(23)	134.5(5)
O(31)-C(23)-N(24)	119.1(5)
O(31)-C(23)-C(22)	129.1(5)
C(13)-O(25)-C(26)	119.1(5)
O(25)-C(26)-C(27)	106.3(5)
N(19)-C(28)-C(29)	114.7(5)
C(28)-C(29)-C(30)	110.6(6)
N(24)-C(23)-C(22)	111.8(5)
C(16)-N(24)-C(23)	126.3(5)

Appendix 14. Anisotropic displacement parameters (A^2 x 10^3) for wza001na.

The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

U11	U22	U33	U23	U13	U12

N(1)	86(4)	60(3)	91(4)	-2(3)	34(3)	-1(3)
C(2)	89(6)	105(6)	151(8)	7(5)	52(6)	-17(5)
C(3)	64(6)	149(9)	232(12)	-12(8)	13(7)	-15(5)
N(4)	104(6)	145(7)	160(7)	4(6)	4(5)	1(5)
C(5)	116(6)	114(7)	128(7)	26(6)	0(6)	3(6)
C(6)	90(5)	90(5)	83(4)	13(4)	16(4)	-5(4)
S(7)	125(2)	62(1)	73(1)	-4(1)	30(1)	4(1)
O(8)	157(4)	56(3)	86(3)	-15(2)	15(3)	-6(3)
O(9)	176(5)	90(3)	85(3)	7(2)	68(4)	16(3)
C(10)	96(5)	60(4)	56(3)	-4(3)	17(4)	-2(3)
C(11)	80(4)	62(4)	58(3)	5(3)	13(3)	-6(3)
C(12)	70(4)	60(4)	52(3)	2(3)	9(3)	0(3)
C(13)	63(4)	70(4)	55(3)	2(3)	0(3)	-3(3)
C(14)	78(4)	74(4)	59(3)	6(3)	4(3)	-11(3)
C(15)	100(5)	70(4)	55(4)	10(3)	-4(4)	-15(4)
C(16)	51(3)	61(3)	45(3)	0(3)	8(3)	5(3)
N(17)	70(3)	51(3)	48(2)	-1(2)	6(2)	4(2)
C(18)	61(3)	57(3)	41(3)	0(3)	6(3)	3(3)
N(19)	75(3)	62(3)	47(3)	3(2)	16(3)	1(3)
C(20)	83(5)	73(4)	52(4)	9(3)	11(3)	-14(3)
C(21)	83(4)	65(4)	51(3)	9(3)	8(3)	0(4)
C(22)	55(3)	57(3)	46(3)	11(3)	-4(3)	-3(3)
C(23)	68(4)	53(4)	65(4)	0(3)	-1(3)	6(3)
N(24)	65(3)	63(3)	67(3)	4(2)	20(3)	6(2)
O(25)	65(3)	81(3)	79(3)	6(2)	19(2)	-3(2)
C(26)	76(4)	92(5)	91(5)	19(4)	28(4)	-2(4)
C(27)	80(5)	113(6)	104(5)	4(5)	27(4)	8(4)
C(28)	76(4)	93(5)	50(3)	0(3)	17(3)	-4(4)
C(29)	113(6)	199(9)	89(5)	-25(6)	16(5)	77(6)

C(30)	271(15)	314(17)	154(10)	8(11)	64(10)	210(14)
O(31)	83(3)	69(3)	97(3)	-7(2)	21(3)	15(2)
C(32)	110(6)	61(4)	92(5)	7(4)	19(4)	4(4)
C(33)	161(11)	303(17)	390(20)	127(18)	-114(13)	15(12)

Appendix 15. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for wza001na.

	x	y	z	U(eq)
H(2A)	2995	4790	7359	134
H(2B)	3455	4523	5976	134
H(3A)	4189	3708	7750	178
H(3B)	4249	4569	8374	178
H(5A)	2992	3024	10323	144
H(5B)	3457	2787	8934	144
H(6A)	2207	3773	8599	105
H(6B)	2220	2919	7936	105
H(11)	2014	5383	5007	80
H(14)	-22	4627	7501	85
H(15)	754	3705	6605	91
H(20)	3184	8867	4154	83
H(24)	591	7094	6822	77
H(26A)	-255	5620	9301	102
H(26B)	-832	5592	7748	102
H(27A)	-435	6980	9470	147
H(27B)	-1205	6557	9497	147

H(27C)	-1008	6953	7924	147
H(28A)	3541	7561	2911	87
H(28B)	2981	6870	3009	87
H(29A)	3591	6541	5496	160
H(29B)	4166	7216	5332	160
H(30A)	3992	6016	3011	365
H(30B)	4572	5924	4534	365
H(30C)	4671	6590	3305	365
H(32A)	2474	9975	5635	131
H(32B)	1833	9689	6608	131
H(32C)	1660	9863	4778	131
H(33A)	4586	4246	11353	446
H(33B)	4627	3354	10983	446
H(33C)	4072	3659	12146	446
H(33D)	4271	3260	11635	446
H(33E)	4230	4152	12005	446
H(33F)	4785	3847	10842	446

Crystal Data WZA002

Appendix 16. Crystal data and structure refinement for wza002.

Identification code	wza002
Empirical formula	C23 H32 N6 O4 S
Formula weight	488.61
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system	monoclinic

Space group	P21/c
Unit cell dimensions	a = 17.206(4) A alpha = 90 deg.
	b = 17.312(3) A beta = 99.197(12) deg.
	c = 8.4721(8) A gamma = 90 deg.
Volume	2491.2(7) A^3
Z	4
Density (calculated)	1.303 Mg/m^3
Absorption coefficient	0.171 mm^-1
F(000)	1040
Crystal size	0.5 x 0.5 x 0.3 mm
Theta range for data collection	2.35 to 25.22 deg.
Index ranges	-20<=h<=20, -3<=k<=20, -10<=l<=0
Reflections collected	5729
Independent reflections	4452 [R(int) = 0.0588]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4452 / 4 / 331
Goodness-of-fit on F^2	1.018
Final R indices [I>2sigma(I)]	R1 = 0.0579, wR2 = 0.1569
R indices (all data)	R1 = 0.1689, wR2 = 0.2033
Largest diff. peak and hole	0.278 and -0.227 e.A^-3

Appendix 17. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for wza002. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
N(1)	2886(2)	6239(2)	2153(4)	64(1)

C(2)	2580(3)	6623(2)	3491(5)	72(1)
C(3)	3239(3)	6757(3)	4842(6)	79(1)
N(4)	3607(2)	6043(2)	5381(4)	75(1)
C(5)	3961(3)	5704(3)	4104(6)	83(1)
C(6)	3348(3)	5530(3)	2685(5)	76(1)
S(7)	2250(1)	6145(1)	505(1)	72(1)
O(8)	2665(2)	5831(2)	-676(4)	94(1)
O(9)	1846(2)	6869(2)	226(3)	85(1)
C(10)	1557(3)	5459(2)	933(4)	65(1)
C(11)	1708(3)	4677(2)	719(4)	62(1)
C(12)	1224(2)	4109(2)	1189(4)	54(1)
C(13)	578(2)	4342(2)	1889(5)	59(1)
C(14)	422(3)	5127(2)	2058(5)	67(1)
C(15)	911(3)	5674(2)	1586(5)	67(1)
C(16)	1452(2)	3293(2)	918(4)	53(1)
N(17)	2056(2)	3170(2)	238(4)	56(1)
C(18)	2270(2)	2409(2)	91(4)	54(1)
C(19)	2880(2)	2077(2)	-492(4)	60(1)
N(20)	2848(2)	1283(2)	-277(4)	68(1)
C(21)	2245(3)	1133(2)	407(5)	60(1)
N(22)	1845(2)	1805(2)	671(3)	54(1)
C(23)	1184(3)	1929(2)	1354(5)	57(1)
N(24)	1018(2)	2701(2)	1437(4)	58(1)
O(25)	122(2)	3781(2)	2382(3)	73(1)
C(26)	-512(3)	3976(3)	3216(5)	74(1)
C(27)	-871(3)	3233(3)	3660(6)	91(2)
C(28)	3505(3)	2455(3)	-1244(6)	86(2)
C(291)	3770(14)	3164(9)	-750(20)	107(7)
C(301)	4590(16)	3365(19)	-1210(40)	123(12)

C(292)	4230(7)	2696(11)	-346(10)	79(5)
C(302)	4819(18)	3100(17)	-1260(40)	119(9)
C(31)	2007(3)	349(2)	885(6)	82(1)
C(32)	4173(4)	6126(4)	6877(7)	106(2)
C(33)	4372(4)	5378(4)	7696(7)	142(3)
O(34)	780(2)	1435(2)	1798(4)	75(1)

Appendix 18. Bond lengths [A] and angles [deg] for wza002.

N(1)-C(2)	1.482(5)
N(1)-C(6)	1.492(5)
N(1)-S(7)	1.637(4)
C(2)-C(3)	1.496(6)
C(2)-H(2A)	0.9700
C(2)-H(2B)	0.9700
C(3)-N(4)	1.431(6)
C(3)-H(3A)	0.9700
C(3)-H(3B)	0.9700
N(4)-C(5)	1.447(5)
N(4)-C(32)	1.476(6)
C(5)-C(6)	1.498(6)
C(5)-H(5A)	0.9700
C(5)-H(5B)	0.9700
C(6)-H(6A)	0.9700
C(6)-H(6B)	0.9700
S(7)-O(8)	1.426(3)
S(7)-O(9)	1.434(3)

S(7)-C(10)	1.761(4)
C(10)-C(15)	1.370(6)
C(10)-C(11)	1.397(5)
C(11)-C(12)	1.387(5)
C(11)-H(11)	0.9300
C(12)-C(13)	1.399(6)
C(12)- C(16)	1.493(5)
C(13)-O(25)	1.356(5)
C(13)-C(14)	1.396(6)
C(14)-C(15)	1.370(6)
C(14)-H(14)	0.9300
C(15)-H(15)	0.9300
C(16)-N(17)	1.285(5)
C(16)-N(24)	1.381(5)
N(17)-C(18)	1.378(5)
C(18)-C(19)	1.357(5)
C(18)-N(22)	1.409(5)
C(19)-N(20)	1.389(5)
C(19)-C(28)	1.486(6)
N(20)-C(21)	1.292(5)
C(21)-N(22)	1.388(5)
C(21)-C(31)	1.492(6)
N(22) -C(23)	1.374(5)
C(23)-O(34)	1.199(4)
C(23)-N(24)	1.371(5)
N(24)-H(24)	0.8600
O(25)-C(26)	1.430(5)
C(26)-C(27)	1.501(6)
C(26)-H(26A)	0.9700

C(26)-H(26B)	0.9700
C(27)-H(27A)	0.9600
C(27)-H(27B)	0.9600
C(27)-H(27C)	0.9600
C(28)-C(291)	1.354(11)
C(28)-C(292)	1.417(10)
C(28)-H(28A)	0.9700
C(28)-H(28B)	0.9700
C(291)-C(301)	1.56(2)
C(291)-H(29A)	0.9700
C(291)-H(29B)	0.9700
C(301)-H(30A)	0.9600
C(301)-H(30B)	0.9600
C(301)-H(30C)	0.9600
C(292)-C(302)	1.54(2)
C(292)-H(29C)	0.9700
C(292)-H(29D)	0.9700
C(302)-H(30D)	0.9600
C(302)-H(30E)	0.9600
C(302)-H(30F)	0.9600
C(31)-H(31A)	0.9600
C(31)-H(31B)	0.9600
C(31)-H(31C)	0.9600
C(32)-C(33)	1.484(8)
C(32)-H(32A)	0.9700
C(32)-H(32B)	0.9700
C(33)-H(33A)	0.9600
C(33)-H(33B)	0.9600
C(33)-H(33C)	0.9600

C(2)-N(1)-C(6)	112.1(3)
C(2)-N(1)-S(7)	115.2(3)
C(6)-N(1)-S(7)	115.3(3)
N(1)-C(2)-C(3)	109.6(4)
N(1)-C(2)-H(2A)	109.7
C(3)-C(2)-H(2A)	109.7
N(1)-C(2)-H(2B)	109.7
C(3)-C(2)-H(2B)	109.7
H(2A)-C(2)-H(2B)	108.2
N(4)-C(3)-C(2)	110.7(4)
N(4)-C(3)-H(3A)	109.5
C(2)-C(3)-H(3A)	109.5
N(4)-C(3)-H(3B)	109.5
C(2)-C(3)-H(3B)	109.5
H(3A)-C(3)-H(3B)	108.1
C(3)-N(4)-C(5)	109.2(4)
C(3)-N(4)-C(32)	112.7(4)
C(5)-N(4)-C(32)	112.6(4)
N(4)-C(5)-C(6)	110.8(4)
N(4)-C(5)-H(5A)	109.5
C(6)-C(5)-H(5A)	109.5
N(4)-C(5)-H(5B)	109.5
C(6)-C(5)-H(5B)	109.5
H(5A)-C(5)-H(5B)	108.1
N(1)-C(6)-C(5)	110.5(4)
N(1)-C(6)-H(6A)	109.5
C(5)-C(6)-H(6A)	109.5
N(1)-C(6)-H(6B)	109.5

C(5)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6B)	108.1
O(8)-S(7)-O(9)	120.1(2)
O(8)-S(7)-N(1)	107.2(2)
O(9)-S(7)-N(1)	107.10(18)
O(8)-S(7)-C(10)	108.56(19)
O(9)-S(7)-C(10)	107.2(2)
N(1)-S(7)-C(10)	105.88(18)
C(15)-C(10)-C(11)	119.7(4)
C(15)-C(10)-S(7)	121.3(3)
C(11)-C(10)-S(7)	118.8(3)
C(12)-C(11)-C(10)	121.2(4)
C(12)-C(11)-H(11)	119.4
C(10)-C(11)-H(11)	119.4
C(11)-C(12)-C(13)	118.1(4)
C(11)-C(12)-C(16)	116.2(4)
C(13)-C(12)-C(16)	125.7(4)
O(25)-C(13)-C(14)	122.2(4)
O(25)-C(13)-C(12)	117.5(4)
C(14)-C(13)-C(12)	120.2(4)
C(15)-C(14)-C(13)	120.3(4)
C(15)-C(14)-H(14)	119.8
C(13)-C(14)-H(14)	119.8
C(10)-C(15)-C(14)	120.4(4)
C(10)-C(15)-H(15)	119.8
C(14)-C(15)-H(15)	119.8
N(17)-C(16)-N(24)	122.4(3)
N(17)-C(16)-C(12)	118.5(3)
N(24)-C(16)-C(12)	119.0(3)

C(16)-N(17)-C(18)	116.5(3)
C(19)-C(18)-N(17)	132.2(4)
C(19)-C(18)-N(22)	106.6(3)
N(17)-C(18)-N(22)	121.1(3)
C(18)-C(19)-N(20)	108.8(3)
C(18)-C(19)-C(28)	128.6(4)
N(20)-C(19)-C(28)	122.6(4)
C(21)-N(20)-C(19)	108.0(3)
N(20)-C(21)-N(22)	110.9(4)
N(20)-C(21)-C(31)	125.5(4)
N(22)-C(21)-C(31)	123.6(4)
C(23)-N(22)-C(21)	131.6(3)
C(23)-N(22)-C(18)	122.8(3)
C(21)-N(22)-C(18)	105.6(3)
O(34)-C(23)-N(24)	122.9(4)
O(34)-C(23)-N(22)	125.6(4)
N(24)-C(23)-N(22)	111.5(3)
C(23)-N(24)-C(16)	125.5(3)
C(23)-N(24)-H(24)	117.2
C(16)-N(24)-H(24)	117.2
C(13)-O(25)-C(26)	120.6(3)
O(25)-C(26)-C(27)	107.4(4)
O(25)-C(26)-H(26A)	110.2
C(27)-C(26)-H(26A)	110.2
O(25)-C(26)-H(26B)	110.2
C(27)-C(26)-H(26B)	110.2
H(26A)-C(26)-H(26B)	108.5
C(26)-C(27)-H(27A)	109.5
C(26)-C(27)-H(27B)	109.5

H(27A)-C(27)-H(27B)	109.5
C(26)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5
C(291)-C(28)-C(292)	48.7(7)
C(291)-C(28)-C(19)	119.8(6)
C(292)-C(28)-C(19)	122.3(5)
C(291)-C(28)-H(28A)	107.4
C(292)-C(28)-H(28A)	60.1
C(19)-C(28)-H(28A)	107.4
C(291)-C(28)-H(28B)	107.4
C(292)-C(28)-H(28B)	130.3
C(19)-C(28)-H(28B)	107.4
H(28A)-C(28)-H(28B)	106.9
C(28)-C(291)-C(301)	113.3(14)
C(28)-C(291)-H(29A)	108.9
C(301)-C(291)-H(29A)	108.9
C(28)-C(291)-H(29B)	108.9
C(301)-C(291)-H(29B)	108.9
H(29A)-C(291)-H(29B)	107.7
C(28)-C(292)-C(302)	117.3(16)
C(28)-C(292)-H(29C)	108.0
C(302)-C(292)-H(29C)	108.0
C(28)-C(292)-H(29D)	108.0
C(302)-C(292)-H(29D)	108.0
H(29C)-C(292)-H(29D)	107.2
C(292)-C(302)-H(30D)	109.5
C(292)-C(302)-H(30E)	109.5
H(30D)-C(302)-H(30E)	109.5

C(292)-C(302)-H(30F)	109.5
H(30D)-C(302)-H(30F)	109.5
H(30E)-C(302)-H(30F)	109.5
C(21)-C(31)-H(31A)	109.5
C(21)-C(31)-H(31B)	109.5
H(31A)-C(31)-H(31B)	109.5
C(21)-C(31)-H(31C)	109.5
H(31A)-C(31)-H(31C)	109.5
H(31B)-C(31)-H(31C)	109.5
N(4)-C(32)-C(33)	112.8(5)
N(4)-C(32)-H(32A)	109.0
C(33)-C(32)-H(32A)	109.0
N(4)-C(32)-H(32B)	109.0
C(33)-C(32)-H(32B)	109.0
H(32A)-C(32)-H(32B)	107.8
C(32)-C(33)-H(33A)	109.5
C(32)-C(33)-H(33B)	109.5
H(33A)-C(33)-H(33B)	109.5
C(32)-C(33)-H(33C)	109.5
H(33A)-C(33)-H(33C)	109.5
H(33B)-C(33)-H(33C)	109.5

Appendix 19. Anisotropic displacement parameters (A^2 x 10^3) for wza002.

The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

U11	U22	U33	U23	U13	U12

N(1)	77(2)	54(2)	65(2)	-2(2)	23(2)	-4(2)
C(2)	88(3)	56(2)	73(3)	-9(2)	20(3)	9(2)
C(3)	86(3)	67(3)	80(3)	-8(2)	-1(3)	6(3)
N(4)	76(2)	72(3)	77(2)	-3(2)	14(2)	9(2)
C(5)	74(3)	82(4)	96(4)	-1(3)	25(3)	9(3)
C(6)	90(3)	65(3)	80(3)	-5 (2)	36(3)	13(2)
S(7)	110(1)	50(1)	62(1)	3(1)	28(1)	-9(1)
O(8)	147(3)	75(2)	72(2)	-7(2)	59(2)	-17(2)
O(9)	132(3)	49(2)	74(2)	12(1)	13(2)	2(2)
C(10)	91(3)	50(2)	54(2)	-1(2)	12(2)	-1(2)
C(11)	82(3)	55(3)	50(2)	-3(2)	18(2)	0(2)
C(12)	66(3)	47(2)	48(2)	-5(2)	9(2)	-1(2)
C(13)	63(3)	55(3)	58(2)	-3(2)	8(2)	-2(2)
C(14)	74(3)	64(3)	62(3)	-11(2)	11(2)	5(2)
C(15)	91(3)	47(3)	62(3)	-6(2)	14(2)	6(2)
C(16)	60(2)	54(2)	45(2)	-2(2)	6(2)	-4(2)
N(17)	68(2)	50(2)	54(2)	-6(1)	19(2)	-4(2)
C(18)	69(3)	53(2)	40(2)	-4(2)	8(2)	-5(2)
C(19)	68(3)	67(3)	45(2)	-15(2)	15(2)	-2(2)
N(20)	86(3)	58(2)	62(2)	-14(2)	23(2)	4(2)
C(21)	80(3)	45(2)	56(2)	-7(2)	11(2)	5(2)
N(22)	71(2)	44(2)	49(2)	-1(1)	15(2)	2(2)
C(23)	67(3)	48(2)	57(2)	-3(2)	10(2)	-8(2)
N(24)	65(2)	47(2)	66(2)	-4(2)	22(2)	-4(2)
O(25)	73(2)	60(2)	93(2)	-5(2)	36(2)	1(2)
C(26)	70(3)	80(3)	78(3)	-9(2)	29(3)	-1(2)
C(27)	89(4)	92(4)	98(4)	-8(3)	36(3)	-14(3)
C(28)	84(4)	115(5)	65(3)	-26(3)	30(3)	-12(3)
C(291)	145(17)	66(9)	128(11)	2(8)	82(12)	-25(9)

C(301)	150(20)	140(20)	91(12)	-38(14)	36(15)	-56(19)
C(292)	72(8)	115(11)	52(5)	9(5)	19(5)	-8(7)
C(302)	125(14)	130(20)	116(16)	20(15)	59(11)	-17(14)
C(31)	113(4)	51(3)	85(3)	1(2)	23(3)	9(3)
C(32)	100(4)	110(5)	103(4)	4(3)	-4(4)	7(4)
C(33)	165(7)	153(7)	101(5)	6(4)	1(4)	77(6)
O(34)	86(2)	53(2)	91(2)	4(2)	31(2)	-7(2)

Appendix 20. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for wza002.

	x	y	z	U(eq)
H(2A)	2180	6302	3849	86
H(2B)	2340	7113	3132	86
H(3A)	3625	7098	4494	95
H(3B)	3037	7006	5719	95
H(5A)	4231	5231	4481	99
H(5B)	4347	6058	3795	99
H(6A)	3600	5338	1817	91
H(6B)	2997	5132	2961	91
H(11)	2140	4534	253	74
H(14)	-18	5278	2494	80
H(15)	804	6196	1709	80
H(24)	610	2827	1848	70
H(26A)	-902	4283	2537	89
H(26B)	-317	4272	4169	89
H(27A)	-1010	2920	2721	136

H(27B)	-1334	3342	4119	136
H(27C)	-498	2960	4424	136
H(28A)	3955	2110	-1112	103
H(28B)	3313	2489	-2382	103
H(29A)	3810	3191	409	128
H(29B)	3390	3548	-1203	128
H(30A)	4980	3013	-694	185
H(30B)	4732	3884	-886	185
H(30C)	4561	3323	-2352	185
H(29C)	4487	2246	182	95
H(29D)	4115	3044	483	95
H(30D)	5098	2719	-1775	178
H(30E)	5187	3394	-524	178
H(30F)	4541	3440	-2051	178
H(31A)	2418	-14	786	124
H(31B)	1532	195	202	124
H(31C)	1917	362	1974	124
H(32A)	3950	6469	7594	128
H(32B)	4651	6363	6637	128
H(33A)	3897	5112	7822	213
H(33B)	4679	5471	8729	213
H(33C)	4670	5068	7068	213

Crystal data 5 sterol1

Appendix 21. Crystal data and structure refinement for sterol1.

Identification code	sterol1

Empirical formula	C27 H46 O3
Formula weight	418.64
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system	monoclinic
Space group	P21
Unit cell dimensions	a = 8.6110(8) A alpha = 90 deg.
	b = 7.624(3) A beta = 93.880(9) deg.
	c = 19.576(2) A gamma = 90 deg.
Volume	1282.2(5) A^3
Z	2
Density (calculated)	1.084 Mg/m^3
Absorption coefficient	0.068 mm^-1
F(000)	464
Crystal size	0.45 x 0.32 x 0.16 mm
Theta range for data collection	2.09 to 25.18 deg.
Index ranges	0<=h<=10, -1<=k<=9, -23<=l<=23
Reflections collected	3091
Independent reflections	2859 [R(int) = 0.0266]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2859 / 1 / 278
Goodness-of-fit on F^2	1.003
Final R indices [I>2sigma(I)]	R1 = 0.0436, wR2 = 0.1061
R indices (all data)	R1 = 0.1335, wR2 = 0.1342
Absolute structure parameter	-1(2)
Largest diff. peak and hole	0.174 and -0.182 e.A^-3

Appendix 22. Atomic coordinates (x 10^4) and equivalent isotropic

displacement parameters (A^2 x 10^3) for sterol1. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1)	5446(3)	3826(4)	-338(2)	55(1)
O(2)	5868(3)	5666(4)	806(1)	44(1)
O(3)	9097(3)	8074(4)	765(2)	59(1)
C(1)	7409(5)	2222(6)	861(2)	42(1)
C(2)	7648(5)	2032(6)	95(2)	43(1)
C(3)	7110(4)	3613(6)	-320(2)	42(1)
C(4)	7819(5)	5290(6)	-16(2)	43(1)
C(5)	7527(4)	5486(6)	736(2)	35(1)
C(6)	8221(5)	7147(6)	1062(2)	40(1)
C(7)	7820(5)	7461(6)	1787(2)	47(1)
C(8)	8284(5)	5898(6)	2239(2)	42(1)
C(9)	7665(5)	4149(5)	1921(2)	41(1)
C(10)	8155(4)	3881(5)	1173(2)	36(1)
C(11)	8105(6)	2620(6)	2396(2)	54(1)
C(12)	7591(6)	2876(6)	3129(2)	58(1)
C(13)	8181(5)	4596(6)	3446(2)	46(1)
C(14)	7679(5)	6076(6)	2951(2)	45(1)
C(15)	8003(6)	7750(6)	3354(2)	57(1)
C(16)	7680(6)	7222(7)	4100(2)	65(1)
C(17)	7408(5)	5220(6)	4099(2)	50(1)
C(18)	9969(5)	4523(8)	3596(2)	63(1)
C(19)	9938(4)	3780(7)	1156(2)	51(1)
C(20)	7864(6)	4359(7)	4797(2)	59(1)
C(21)	7669(7)	2384(8)	4781(3)	82(2)
C(22)	6958(6)	5183(8)	5356(2)	69(2)

C(23)	7543(6)	4661(9)	6083(2)	76(2)
C(24)	6669(5)	5533(10)	6634(2)	80(2)
C(25)	7271(7)	5151(10)	7368(3)	87(2)
C(26)	7163(11)	3189(13)	7521(3)	149(3)
C(27)	6425(7)	6211(12)	7871(2)	119(3)

Appendix 23. Bond lengths [A] and angles [deg] for sterol1.

O(1)-C(3)	1.440(4)
O(1)-H(1)	0.8200
O(2)-C(5)	1.451(4)
O(2)-H(2)	0.8200
O(3)-C(6)	1.210(5)
C(1)-C(10)	1.527(6)
C(1)-C(2)	1.535(5)
C(1)-H(1A)	0.9700
C(1)-H(1B)	0.9700
C(2)-C(3)	1.508(6)
C(2)-H(2A)	0.9700
C(2)-H(2B)	0.9700
C(3)-C(4)	1.521(6)
C(3)-H(3)	0.9800
C(4)-C(5)	1.519(5)
C(4)-H(4A)	0.9700
C(4)-H(4B)	0.9700
C(5)-C(6)	1.521(6)
C(5)-C(10)	1.568(5)

C(6)-C(7)	1.503(6)
C(7)-C(8)	1.522(6)
C(7)-H(7A)	0.9700
C(7)-H(7B)	0.9700
C(8)-C(14)	1.526(5)
C(8)-C(9)	1.551(6)
C(8)-H(8)	0.9800
C(9)-C(11)	1.523(6)
C(9)-C(10)	1.565(5)
C(9)-H(9)	0.9800
C(10)-C(19)	1.539(5)
C(11)-C(12)	1.542(6)
C(11)-H(11A)	0.9700
C(11)-H(11B)	0.9700
C(12)-C(13)	1.523(6)
C(12)-H(12A)	0.9700
C(12)-H(12B)	0.9700
C(13)-C(14)	1.531(6)
C(13)-C(18)	1.549(6)
C(13)-C(17)	1.556(6)
C(14)-C(15)	1.516(6)
C(14)-H(14)	0.9800
C(15)-C(16)	1.559(6)
C(15)-H(15A)	0.9700
C(15)-H(15B)	0.9700
C(16)-C(17)	1.544(7)
C(16)-H(16A)	0.9700
C(16)-H(16B)	0.9700
C(17)-C(20)	1.543(6)

C(17)-H(17)	0.9800
C(18)-H(18A)	0.9600
C(18)-H(18B)	0.9600
C(18)-H(18C)	0.9600
C(19)-H(19A)	0.9600
C(19)-H(19B)	0.9600
C(19)-H(19C)	0.9600
C(20)-C(21)	1.515(8)
C(20)-C(22)	1.522(7)
C(20)-H(20)	0.9800
C(21)-H(21A)	0.9600
C(21)-H(21B)	0.9600
C(21)-H(21C)	0.9600
C(22)-C(23)	1.529(6)
C(22)-H(22A)	0.9700
C(22)-H(22B)	0.9700
C(23)-C(24)	1.512(7)
C(23)-H(23A)	0.9700
C(23)-H(23B)	0.9700
C(24)-C(25)	1.522(7)
C(24)-H(24A)	0.9700
C(24)-H(24B)	0.9700
C(25)-C(27)	1.499(8)
C(25)-C(26)	1.529(12)
C(25)-H(25)	0.9800
C(26)-H(26A)	0.9600
C(26)-H(26B)	0.9600
C(26)-H(26C)	0.9600
C(27)-H(27A)	0.9600

C(27)-H(27B)	0.9600
C(27)-H(27C)	0.9600
C(3)-O(1)-H(1)	109.5
C(5)-O(2)-H(2)	109.5
C(10)-C(1)-C(2)	112.9(3)
C(10)-C(1)-H(1A)	109.0
C(2)-C(1)-H(1A)	109.0
C(10)-C(1)-H(1B)	109.0
C(2)-C(1)-H(1B)	109.0
H(1A)-C(1)-H(1B)	107.8
C(3)-C(2)-C(1)	113.2(4)
C(3)-C(2)-H(2A)	108.9
C(1)-C(2)-H(2A)	108.9
C(3)-C(2)-H(2B)	108.9
C(1)-C(2)-H(2B)	108.9
H(2A)-C(2)-H(2B)	107.8
O(1)-C(3)-C(2)	111.9(3)
O(1)-C(3)-C(4)	106.7(3)
C(2)-C(3)-C(4)	111.2(3)
O(1)-C(3)-H(3)	109.0
C(2)-C(3)-H(3)	109.0
C(4)-C(3)-H(3)	109.0
C(5)-C(4)-C(3)	111.9(3)
C(5)-C(4)-H(4A)	109.2
C(3)-C(4)-H(4A)	109.2
C(5)-C(4)-H(4B)	109.2
C(3)-C(4)-H(4B)	109.2
H(4A)-C(4)-H(4B)	107.9

O(2)-C(5)-C(4)	109.2(3)
O(2)-C(5)-C(6)	104.1(3)
C(4)-C(5)-C(6)	113.7(3)
O(2)-C(5)-C(10)	109.2(3)
C(4)-C(5)-C(10)	112.3(3)
C(6)-C(5)-C(10)	108.1(3)
O(3)-C(6)-C(7)	123.4(4)
O(3)-C(6)-C(5)	121.7(4)
C(7)-C(6)-C(5)	114.8(4)
C(6)-C(7)-C(8)	110.9(3)
C(6)-C(7)-H(7A)	109.5
C(8)-C(7)-H(7A)	109.5
C(6)-C(7)-H(7B)	109.5
C(8)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	108.0
C(7)-C(8)-C(14)	111.7(3)
C(7)-C(8)-C(9)	111.7(3)
C(14)-C(8)-C(9)	108.3(3)
C(7)-C(8)-H(8)	108.4
C(14)-C(8)-H(8)	108.4
C(9)-C(8)-H(8)	108.4
C(11)-C(9)-C(8)	110.4(3)
C(11)-C(9)-C(10)	113.6(3)
C(8)-C(9)-C(10)	112.4(3)
C(11)-C(9)-H(9)	106.7
C(8)-C(9)-H(9)	106.7
C(10)-C(9)-H(9)	106.7
C(1)-C(10)-C(19)	110.1(3)
C(1)-C(10)-C(9)	110.5(3)

C(19)-C(10)-C(9)	111.1(3)
C(1)-C(10)-C(5)	107.9(3)
C(19)-C(10)-C(5)	109.6(3)
C(9)-C(10)-C(5)	107.7(3)
C(9)-C(11)-C(12)	113.3(4)
C(9)-C(11)-H(11A)	108.9
C(12)-C(11)-H(11A)	108.9
C(9)-C(11)-H(11B)	108.9
C(12)-C(11)-H(11B)	108.9
H(11A)-C(11)-H(11B)	107.7
C(13)-C(12)-C(11)	112.3(4)
C(13)-C(12)-H(12A)	109.2
C(11)-C(12)-H(12A)	109.2
C(13)-C(12)-H(12B)	109.2
C(11)-C(12)-H(12B)	109.2
H(12A)-C(12)-H(12B)	107.9
C(12)-C(13)-C(14)	107.8(3)
C(12)-C(13)-C(18)	110.3(4)
C(14)-C(13)-C(18)	112.4(4)
C(12)-C(13)-C(17)	116.7(4)
C(14)-C(13)-C(17)	100.2(3)
C(18)-C(13)-C(17)	109.2(3)
C(15)-C(14)-C(8)	119.2(4)
C(15)-C(14)-C(13)	104.9(3)
C(8)-C(14)-C(13)	114.4(3)
C(15)-C(14)-H(14)	105.8
C(8)-C(14)-H(14)	105.8
C(13)-C(14)-H(14)	105.8
C(14)-C(15)-C(16)	103.4(4)

C(14)-C(15)-H(15A)	111.1
C(16)-C(15)-H(15A)	111.1
C(14)-C(15)-H(15B)	111.1
C(16)-C(15)-H(15B)	111.1
H(15A)-C(15)-H(15B)	109.0
C(17)-C(16)-C(15)	106.9(4)
C(17)-C(16)-H(16A)	110.3
C(15)-C(16)-H(16A)	110.3
C(17)-C(16)-H(16B)	110.3
C(15)-C(16)-H(16B)	110.3
H(16A)-C(16)-H(16B)	108.6
C(20)-C(17)-C(16)	112.9(4)
C(20)-C(17)-C(13)	120.0(4)
C(16)-C(17)-C(13)	103.3(4)
C(20)-C(17)-H(17)	106.6
C(16)-C(17)-H(17)	106.6
C(13)-C(17)-H(17)	106.6
C(13)-C(18)-H(18A)	109.5
C(13)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(13)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(10)-C(19)-H(19A)	109.5
C(10)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(10)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5

C(21)-C(20)-C(22)	111.4(5)
C(21)-C(20)-C(17)	112.5(4)
C(22)-C(20)-C(17)	110.4(4)
C(21)-C(20)-H(20)	107.4
C(22)-C(20)-H(20)	107.4
C(17)-C(20)-H(20)	107.4
C(20)-C(21)-H(21A)	109.5
C(20)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(20)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(20)-C(22)-C(23)	114.1(4)
C(20)-C(22)-H(22A)	108.7
C(23)-C(22)-H(22A)	108.7
C(20)-C(22)-H(22B)	108.7
C(23)-C(22)-H(22B)	108.7
H(22A)-C(22)-H(22B)	107.6
C(24)-C(23)-C(22)	113.6(4)
C(24)-C(23)-H(23A)	108.8
C(22)-C(23)-H(23A)	108.8
C(24)-C(23)-H(23B)	108.8
C(22)-C(23)-H(23B)	108.8
H(23A)-C(23)-H(23B)	107.7
C(23)-C(24)-C(25)	115.8(5)
C(23)-C(24)-H(24A)	108.3
C(25)-C(24)-H(24A)	108.3
C(23)-C(24)-H(24B)	108.3
C(25)-C(24)-H(24B)	108.3

H(24A)-C(24)-H(24B)	107.4
C(27)-C(25)-C(24)	111.5(5)
C(27)-C(25)-C(26)	111.1(6)
C(24)-C(25)-C(26)	110.5(6)
C(27)-C(25)-H(25)	107.8
C(24)-C(25)-H(25)	107.8
C(26)-C(25)-H(25)	107.8
C(25)-C(26)-H(26A)	109.5
C(25)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26B)	109.5
C(25)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5
C(25)-C(27)-H(27A)	109.5
C(25)-C(27)-H(27B)	109.5
H(27A)-C(27)-H(27B)	109.5
C(25)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5

Appendix 24. Anisotropic displacement parameters (A^2 x 10^3) for sterol1.

The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
O(1)	51(2)	44(2)	69(2)	-8(2)	-18(1)	-3(2)
O(2)	38(1)	37(2)	56(2)	1(2)	2(1)	5(1)

O(3)	69(2)	41(2)	67(2)	-7(2)	13(2)	-17(2)
C(1)	56(3)	26(2)	45(2)	5(2)	1(2)	5(2)
C(2)	48(2)	34(3)	47(2)	-10(2)	1(2)	-1(2)
C(3)	50(2)	37(3)	40(2)	-4(2)	-1(2)	0(2)
C(4)	48(2)	36(3)	46(2)	3(2)	0(2)	-9(2)
C(5)	34(2)	29(2)	41(2)	1(2)	2(2)	-2(2)
C(6)	44(2)	30(2)	48(2)	8(2)	2(2)	3(2)
C(7)	65(3)	29(3)	46(3)	0(2)	1(2)	1(2)
C(8)	50(2)	28(3)	49(2)	0(2)	3(2)	5(2)
C(9)	47(2)	26(3)	49(2)	1(2)	3(2)	-1(2)
C(10)	40(2)	25(2)	41(2)	0(2)	0(2)	2(2)
C(11)	87(3)	31(3)	44(2)	-2(2)	-4(2)	7(2)
C(12)	93(3)	32(3)	47(3)	6(2)	-3(2)	-2(3)
C(13)	59(3)	34(3)	44(2)	1(2)	0(2)	4(2)
C(14)	56(2)	34(3)	43(2)	0(2)	1(2)	1(2)
C(15)	88(3)	38(3)	46(2)	-6(2)	4(2)	-2(3)
C(16)	94(4)	52(4)	49(3)	-5(3)	1(2)	8(3)
C(17)	55(3)	50(3)	44(2)	-1(2)	-1(2)	7(2)
C(18)	69(3)	72(4)	48(2)	2(3)	-6(2)	12(3)
C(19)	46(2)	50(3)	56(2)	-8(3)	-5(2)	10(3)
C(20)	75(3)	55(3)	45(3)	1(3)	-4(2)	-1(3)
C(21)	128(5)	67(4)	49(3)	15(3)	-5(3)	1(4)
C(22)	83(3)	81(4)	43(2)	10(3)	3(2)	15(3)
C(23)	85(3)	102(5)	40(2)	9(3)	5(2)	15(3)
C(24)	84(3)	107(5)	50(3)	9(3)	6(2)	18(4)
C(25)	84(4)	122(6)	54(3)	-1(4)	-2(3)	6(4)
C(26)	225(9)	148(9)	78(4)	29(6)	43(5)	30(8)
C(27)	135(5)	168(9)	52(3)	-17(5)	-3(3)	34(6)

Appendix 25. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for sterol1.

	x	y	z	U(eq)
H(1)	5021	2926	-485	83
H(2)	5391	5042	522	66
H(1A)	6302	2242	925	51
H(1B)	7850	1207	1102	51
H(2A)	8744	1839	37	52
H(2B)	7083	1008	-81	52
H(3)	7423	3478	-789	51
H(4A)	8931	5284	-67	52
H(4B)	7377	6290	-267	52
H(7A)	6710	7663	1796	56
H(7B)	8356	8502	1964	56
H(8)	9423	5839	2289	50
H(9)	6526	4226	1893	49
H(11A)	9225	2466	2417	65
H(11B)	7633	1557	2206	65
H(12A)	6463	2856	3118	69
H(12B)	7979	1909	3413	69
H(14)	6543	5991	2884	54
H(15A)	7315	8688	3188	69
H(15B)	9074	8124	3325	69
H(16A)	8563	7523	4413	78
H(16B)	6769	7831	4244	78
H(17)	6285	5042	4011	60
H(18A)	10228	3588	3912	95

H(18B)	10327	5617	3792	95
H(18C)	10460	4319	3177	95
H(19A)	10311	2738	1388	77
H(19B)	10400	4791	1380	77
H(19C)	10213	3748	689	77
H(20)	8970	4605	4908	70
H(21A)	6644	2096	4591	123
H(21B)	7811	1928	5238	123
H(21C)	8430	1877	4503	123
H(22A)	5873	4847	5284	83
H(22B)	7013	6449	5315	83
H(23A)	7454	3399	6129	91
H(23B)	8637	4962	6151	91
H(24A)	5588	5170	6578	96
H(24B)	6697	6792	6563	96
H(25)	8371	5485	7416	105
H(26A)	7719	2939	7952	223
H(26B)	7612	2535	7165	223
H(26C)	6091	2863	7543	223
H(27A)	5360	5836	7861	178
H(27B)	6465	7429	7750	178
H(27C)	6910	6045	8322	178

2