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Weak C–H…O hydrogen bonds in alkaloids: An overview

RAJNIKANT*, DINESH and KAMNI
Post Graduate Department of Physics, University of Jammu, Jammu Tawi 180 006, India

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Abstract. An overview of general classification scheme, medicinal importance and crystal structure analysis with emphasis on the role of hydrogen bonding in some alkaloids is presented in this paper. The article is based on a general kind of survey while crystallographic analysis and role of hydrogen bonding are limited to only those alkaloids whose three-dimensional structure has been reported by us. The C–H…O hydrogen bonding in the solid state in alkaloids has been found to be predominant and this observation makes the role of hydrogen bonding in organic molecular assemblies very important.

Keywords. Alkaloids; crystallography; crystal structure; hydrogen bond.

1. Introduction

Defining what the term alkaloid means today is no easy task. The reason is that over 5000 alkaloids of all structural types are known. No other class of natural products possesses such an enormous variety of structures. Steroids, for example, are all modeled on a few skeletal types. The same holds true for triterpenes, flavonoids, coumarins, biphenyls or polysaccharides. But alkaloids exhibit dozens of different skeletal types. This situation causes an extraordinary difficulty in defining alkaloids so that they may be readily recognized and differentiated from other classes of nitrogen-containing compounds.

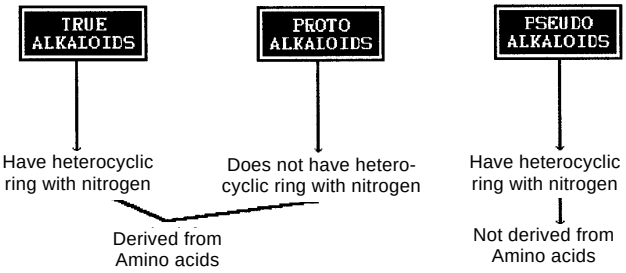
The term alkaloid was first coined in 1819 by a pharmacist, W. Meissner and meant simply, *alkalilike* (Middle English alcaly, from Medieval Latin *alkali*, from Arabic *alqaliy* = ashes of saltwort, from *qualey*, to fry). The first modern definition by Winterstein and Trier (1910) describes these substances in a broad sense as basic, nitrogen-containing compounds of either plant or animal origin. "True alkaloids" were defined as compounds meeting the four additional qualifications that are (i) nitrogen atom may or may not be a part of a heterocyclic system, (ii) they have a complex molecular structure, (iii) these compounds manifests significant pharmacological activity and (iv) these are restricted to the plant kingdom.

Alkaloids occur as salts of plant acids such as *malic*, *meconic* or *quinic* acid. Some alkaloids occur in plants combined with sugars, whereas others are present as amides. Compounds satisfying the definition of true alkaloids are restricted to certain families and genera of plant kingdom, rarely being distributed in large group of plants. Though about 40% of all plant families contain atleast one alkaloid-bearing species, alkaloids have been reported in only 9% of over 10,000 plant genera. Chemical, pharmacological and botanical properties are usually considered when classifying a compound as an alkaloid. Other heterocyclic nitrogenous bases not classified as alkaloids by some authorities include the purines, of which caffeine, xanthine and bromine are few examples.

In view of the complexity of the compounds involved and for some historical reasons, the nomenclature of alkaloids has not been systematized even today. The two commonly used systems classify alkaloids either according to the plant genera in which they occur or on the basis of similarity in their molecular structures.

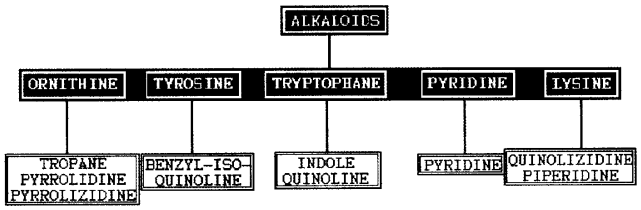
1.1 *General classification of alkaloids*

The concept regarding classification of alkaloids has changed now with the changing scientific out-look and scenario and the modern concept classify alkaloids into three main kinds as shown in the following diagrammatic scheme.



*Author for correspondence (rkantverma@rediffmail.com)

On the basis of chemical classification, numerous classes of alkaloids are possible:



Although majority of alkaloids or their derivatives are colourless, crystalline, non-volatile solids, a few such as *contine* and *nicotine* are liquids and few are even coloured, e.g. *berberine* is yellow. The free bases (i.e. alkaloids themselves) are insoluble in water but soluble in most of the organic solvents. Most of the alkaloids are laevo-rotatory (optically active), although a few are dextro-rotatory (optically inactive) e.g. *conine*, *papaverine* etc. Generally, the alkaloids are bitter in taste and have pronounced physiological activity. Many of the alkaloids possess curative properties and are of much importance and relevance in medicines, but they are powerful poisons as well (Baker *et al* 1961).

1.2 *Isolation and pharmacological activity*

Many of the earliest isolated pure compounds with biological activity were alkaloids and it was due to the ease in the procedure of isolation. The nitrogen generally makes the compound basic and the compound exists in the plant as a salt. Thus alkaloids are often extracted with water or mild acid and then recovered as crystalline material by treatment with base. Most of them are nitrogen heterocycles which occur mainly in plants as their salts of common carboxylic acids such as citric, lactic, oxalic, acetic, malic and tartaric acids as well as fumaric, benzoic, aconitic and veratric acids. Their amine character produces an alkaline solution in water and hence the origin of their name—alkaloids.

The concentration of alkaloids in plants depend upon the season, age and its locality. It is interesting to note that closely related alkaloids generally occur together in the same plant. For instance, twenty alkaloids have been isolated from opium (Anshu Sawhney 2003). It is also observed that different genera of the same family may contain the same or structurally related alkaloids. It is found that simple alkaloids are often found in different plants whereas the complex alkaloids in one species or genus of a family.

Alkaloids are renowned for their potent and diverse pharmacological activities which include their clinical use such as analgesics, anti-malarial, anti-spasmotics, for pupil dilation, for the treatment of hypertension, mental disorders and tumours (Babita 1994). Many alkaloids have very great value in medical sciences because of the specific pharmacological action. A number of pyrrolizidine alkaloids have been found to cause severe lesions in the liver and lungs of both men and animals (Sharma 1985). The pyrrolizidine alkaloids have been investigated as anti-tumour agents and correlation between the lesions as cancer has also been studied (Mclean 1970). Morphine and some of its related compounds are the best known reagents for the relief of pain. Quinazoline derivatives possess hypotensive, analgesic and anticoagulant activities (Bergman *et al* 1986). Quinine, a poisonous derivative of alkaloid, is extensively used as antimalarial drug (Baker *et al* 1961). Quinazoline derivatives have been found effective against parasites (Berg and Lucas 1961). In addition to the uses of quinazoline in drugs, certain quinazoline derivatives particularly when condensed with amino anthraquinolines, act as useful dye-stuffs (Ebel *et al* 1958). Recent studies have shown some remarkable properties exhibited by a variety of quinazoline derivatives and most notable among these have found place in analgesics, antiallergic, anti-inflammatory, secretion, anticoagulant (Babita 1994), etc.

Alkaloids are used for the treatment of asthma, cough, tuberculosis (Thappa *et al* 1996), etc. Alkaloids are also widely being abused as a recreational drug. It causes a variety of pharmacological effects on the central nervous systems. The well known example is that of cocaine which when inhaled results in increased heart rate and blood pressure (Byke and Vandyke 1997). Carpaine is another such substance which is reported to be a kind of heart poison and it lowers the pulse frequency and depresses the central nervous system (Rajnikant 1988; Joshi *et al* 1996). It has also been seen that the nitrogen is an important component which plays an important role in the determination of activity of alkaloids.

1.3 *Aim of the present work*

The paper has been designed keeping in view not only the chemical or pharmacological aspects of alkaloids but the main thrust is to make a review of X-ray crystallographic studies, their findings and interpretation of the role of hydrogen bonding in this particular class of organic compounds. It is now an admitted fact that all those materials which exist in single crystal form need to be examined for knowing their internal architecture and the well accepted and known technique for determining the three-dimensional structure is X-ray crystallography. We have been working in this direction for the last over ten years and felt the need to put the whole data in the form of a compendium on a comparative scale so that the results may speak about what is missing in the literature. It appears to be an attempt of first of its kind where alkaloids are being discussed with particular reference to

their X-ray crystallographic investigations and also with the following aims and objectives:

(I) Precise presentation of the crystal data of each molecule so as to know whether alkaloids do have any preference to exist in a particular crystal system or space group.
(II) To ascertain whether the phenomenon of multiple molecules (asymmetric or crystallographically independent molecules) does exist in this class of materials.
(III) A comparison of some important structural and geometrical features of alkaloids.
(IV) A brief exposition of the possible role of nitrogen in alkaloids and their crystallographic comparison on a comparative scale.
(V) To examine the role of intra- and intermolecular hydrogen bonded interactions in alkaloids and find reasons for the predominance of one over another.
(VI) Determine the distance and angle cut-off criteria in case of various hydrogen bonds in alkaloids in the light of work as reported by Desiraju and Steiner (1999) and other researchers (Nishio and Hirota 1989; Aakeroy and Seddon 1993a,b; Nishio *et al* 1995, 1998; Aakeroy 1997).

2. Brief crystallographic description about alkaloids and comparative crystallographic findings

Presented below is the IUPAC name, chemical formula and reference of the alkaloids whose structures have been investigated and reported by us (Rajnikant *et al* 1993, 1996, 1998a,b, 2000, 2001a,b, 2002a,b; Magotra *et al* 1996).

2.1 *General experimental procedure involved in structure determination and refinement*

The preliminary X-ray photographic techniques such as oscillation, rotation and Weissenberg are employed to ascertain the crystalline nature of any grown material and this provides a first hand information to a crystallographer to move ahead for the collection of X-ray diffraction data using a computer-controlled single crystal X-ray diffractometer. Three-dimensional intensity data of a chosen crystal is collected on CAD-4 diffractometer by using either CuKα (λ = 1·5418 Å) or MoKα radiation (λ = 0·71069 Å). $\omega/2\theta$ scan mode is employed for data collection. The cell parameters are usually refined from accurately determined 25 reflections in a given θ range. Two reference reflections are generally monitored of every 100 reflections to check for crystal deterioration, if any, during beam exposure to the sample. The reflection data so obtained is usually raw in nature and is generally cleaned by applying various corrections. The reduced data thus becomes an input for structure determination by employing direct methods (Stout and Jensen 1968).

The molecular structures (mol. I–X) have been solved by direct methods using SHELXS86 software (Sheldrick 1986). Full-matrix least-squares refinement of organic structure is generally carried out by using SHELXL93 (Sheldrick 1993) and SHELXL97 (Sheldrick 1997a,b) softwares. The least-squares refinement of the positional (x, y, z) and thermal parameters ($U_{eq's}$) provide precision in location of various atoms and their thermal amplitudes. Statistically, the refinement technique provides treatment to our data so that precision in the observed and calculated values for various structural and geometrical parameters is obtained. This treatment helps us in obtaining a good model of the structure which should have a high level of confidence i.e. the chemical and computed structure should match at a level of confidence as close to 95–97% or in other words the reliability index i.e. R-factor, for a well refined structure should have a value between 3 and 5%. All non-hydrogen atoms of the molecule are located from the E-map and all hydrogen atoms are either located or fixed stereo-chemically. Further refinement of the molecule with anisotropic thermal parameters provides the final yield of R-factor. In other words, R-factor is the average per cent error between observed and calculated $|F|$ or F^2's and it is expressed as

$$R = \frac{\sum \| F_o | - | F_c \|}{\sum | F_o |},$$

where F_o and F_c are the magnitudes of the observed and

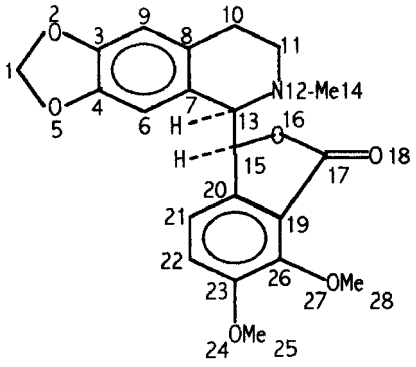
Mol. no.	IUPAC name	Chemical formula	Reference
I	*b*-hydrastine	$C_{21}H_{21}NO_6$	Rajnikant *et al* (1993)
II	Water solvated tetrahydropalmatine hydrochloride	$[C_{21}H_{26}NO_4]^+ \cdot Cl^- \cdot H_2O$	Rajnikant *et al* (1996)
III	7-methoxyvascinone hydrate	$C_{12}H_{12}N_2O_3 \cdot H_2O$	Magotra *et al* (1996)
IV	1,2,3,4,5-pentahydro-azpino(2,1-b)quinazolin-11(1H)-one hydrochloride	$C_{13}H_{14}N_2O$ HCl H_2O	Rajnikant *et al* (1998a)
V	Carpaine	$C_{28}H_{50}N_2O_4$	Rajnikant *et al* (1998b)
VI	5N-ethyl,8-carboxy,9-oxo-11-methyl-pyridol[2,1-b] quinazoline	$C_{16}H_{16}N_2O_3$	Rajnikant *et al* (2000)
VII	Royline monohydrate	$C_{25}H_{41}NO_7 \cdot H_2O$	Rajnikant *et al* (2001a)
VIII	Methyl-3,4-dihydro-3-(p-methylphenyl)-4-oxo-2-quinazolinyl thiopropionate	$C_{19}H_{18}N_2O_3S$	Rajnikant *et al* (2001b)
IX	2-methyl-4-phenyl-3,4-dihydro-quinazolinium chloride	$C_{15}H_{14}N_2 \cdot HCl$	Rajnikant *et al* (2002a)
X	4-phenylquinolin-2(1H)-one	$C_{15}H_{11}NO$	Rajnikant *et al* (2002b)

calculated structure factors. The weighing scheme is generally employed to have a flat analysis of variance in terms of F_c^2. Atomic scattering factors are taken from International tables for Crystallography (1992, Vol. C, Tables 4·2·6·8 and 6·1·1·4). Structural parameters such as bond distances, bond angles, torsion angles, dihedral angles between various planes of a given molecule etc are obtained from the PARST software (Nardelli 1983) and molecular modeling i.e. to obtain a general view of the molecule and plotting the molecules in the three dimensional environment in a unit cell is carried out with ORTEP software (Farrugia 1997).

2.2 *Brief crystallographic description of each investigated alkaloid*

A precise description of all the ten alkaloids is presented with more emphasis on the activity, medicinal importance, brief crystallographic data and some unique observations about each structure. Some selected C–N(Å) bond distances and C–N–C(°) bond angles are presented in table 1, while the data on hydrogen bonding is listed in tables 3 and 4, respectively. The general view and molecular packing have not been included since these details are already reported (Rajnikant *et al* 1993, 1996, 1998a,b, 2000, 2001a,b, 2002a,b; Magotra *et al* 1996).

(i) *b-hydrastine*: *b*-hydrastine (I) is a naturally occurring phthalideisoquinoline alkaloid and is used as an antiseptic and as a uterine hemostatic. It is isolated from *Fumaria parviflora*, crystallized as transparent prisms from alcohol (Rajnikant *et al* 1993). It is closely related to (–) *a*-narcotine (Moss and Watson 1984) and bicuculline (Gorinsky and Moss 1973).

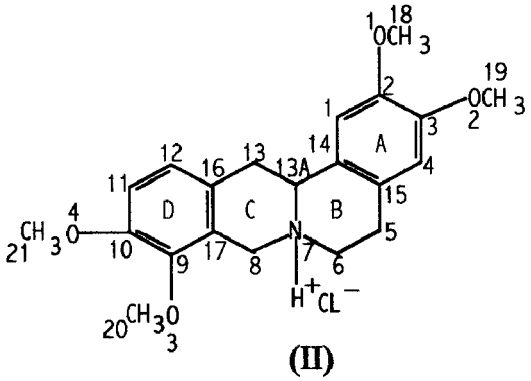


(I)

Chemical formula: $C_{21}H_{21}NO_6$; cell parameters: a = 7·542(2), c = 33·266(2) Å; unit cell volume: 1892 Å^3; crystal system/space group: tetragonal/$P4_3$; no. of molecules per unit cell (Z): 4; radiation used (CuKa, l): 1·5405 Å; no. of measured reflections: 2129; R-factor: 0·061.

The N-heterocyclic ring has bond distances and angles comparable with the literature values (Cameron *et al* 1974; Bruderer *et al* 1976; Wong and Nyburg 1979). Molecular packing in the unit cell is typical of tetragonal system (Rajnikant *et al* 1993). In hydrastine the dihedral angle between plane 1 [C1–O2–C3–C9–C8–C10–C11–N12–C13–C7–C6–C4–O5] and plane 2 [C15–O16–C17–C19–C26–C23–C22–C21–C20] is 42·9°, while the magnitude of torsion present along C13–C15 bond is – 55·2°. This may be due to the presence of N–CH_3 group and a five-membered ring at C15 position.

(ii) *Water solvated tetrahydro–palmatine hydrochloride*: The compound (II) has been isolated from the roots of *Stephania glabra* (Gupta and Banerjee 1994), a shrub growing in tropical and temperate Himalayas at an altitude of 7,000 ft. above the sea level. The roots of this shrub are considered to be useful in the treatment of tuberculosis, asthma, dysentery and intestinal complaints. It is widely used by the hill tribes of Assam in India as a household remedy for the said disease (Chopra 1958).

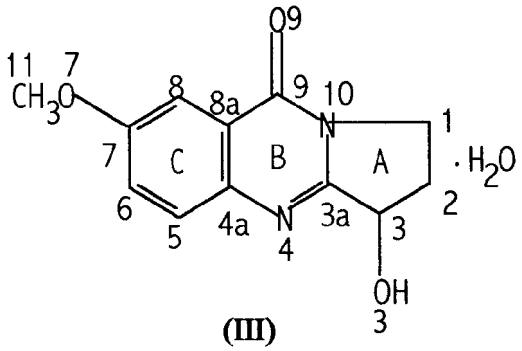


(II)

Chemical formula: $[C_{21}H_{26}NO_4]^+ \cdot Cl^- \cdot 2H_2O$; cell parameters: a = 6·879(1), b = 11·977(1), c = 13·088 Å, b = 95·33(1)°; unit cell volume: 1073·65 Å^3; crystal system/space group: Monoclinic/$P2_1$; no. of molecules per unit cell (Z): 2; radiation used (MoKa, l): 0·71073 Å; no. of measured reflections: 2050; R-factor: 0·051.

The two phenyl rings *A* and *D* having methoxy substitutions at C2, C3 and C9, C10 are planar. Ring-B exists in half-chair conformation with the rotational axes bisecting the C6–N7 and C14–C15 bonds with asymmetry parameter ΔC_2(C6–N7) = 3·31 (Duax and Norton 1975). Ring C also adopts half-chair conformation with the rotational axis bisecting the N7–C13A and C16–C17 bonds; ΔC_2 (N7–C13A) = 4·01. The C18, C19 and C21 methoxyl groups are nearly coplanar with their respective phenyl rings, *A* and *D*, while C20 is rotated out of the plane of ring D by 114·0(6)°. The cation and chloride anion are connected by a hydrogen bond involving H7 at N7. Intra- and intermolecular C–H…O hydrogen bonds contribute to the stability of molecules in the unit cell (Rajnikant *et al* 1996).

(iii) *7-Methoxyvasicinone hydrate*: The compound (III) has been isolated from the leaves of *Adhatoda vasica* (Nees), a highly reputed ayurvedic medicinal plant used for the treatment of asthma, bronchitis and tuberculosis (Mehta *et al* 1963). Leaves of *Adhatoda vasica* were extracted with ethanol at room temperature (Magotra *et al* 1996).



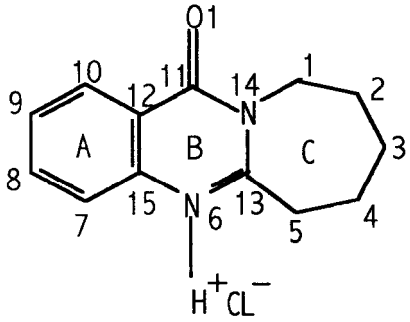
(III)

Chemical formula: $C_{12}H_{12}N_2O_3{\cdot}H_2O$; cell parameters: a = 7·630(1), b = 35·156(5), c = 8·505(1) Å; unit cell volume: 2281·4 Å^3; crystal system/space group: orthorhombic/*Pbca*; no. of molecules per unit cell (Z): 8; radiation used (MoKa, l): 0·71073 Å; no. of measured reflections: 3145; R-factor: 0·049.

The C3a–N4 bond [1·288(4)Å] displays typical double bond character. The N–C–N angle is 125·2(3)°. Generally this bond angle has been found to be greater than 120° in most pyrimidine and quinazoline compounds (Stroud 1973). The least-squares planes and torsion angle calculations indicate strict planarity for the phenyl ring and the methoxy group is coplanar with it. The pyrimidine ring deviates slightly from planarity [with a maximum deviation from the plane of 0·023(4) Å for C9]. The five-membered ring has an intermediate half-chair/envelope conformation with a phase angle of pseudorotation d = 53·95° and a maximum torsion angle of 27·72°. Atom O3 attached to C3 is 1·472(3) Å above the plane defined by the atoms of the fused ring system. The crystal structure is stabilized by two O–H…O type intermolecular contacts involving water molecule of crystallization (Magotra *et al* 1996).

(iv) *1,2,3,4,5-Pentahydroazepino (2,1-b) quinazolin–11 (1H)–one hydrochloride with water molecule*: The compound (IV) has been synthesized by condensing *d*-valerolac–tam(2-piperidone) and caprolactam (6-aminocaproic acid lactam), respectively, with anthranilic acid in the presence of P_2O_5 and xylene (Rajnikant *et al* 1998a). It possesses potent bronchodilatory activity (Atal 1980).

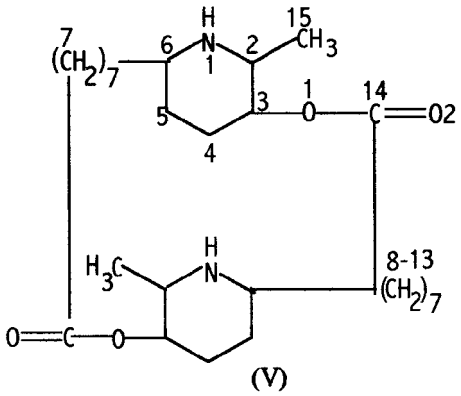
The rings A and B are planar. The length of C13–N6 bond [1·335(1)Å] indicates the double bond character. The N–C–N bond angle (120·7°) is considerably less in magnitude as compared to the values reported for some analogous structures (Kistenmacher and Shigematsu 1974; Picorari *et al* 1992; Sharma *et al* 1993). However, the bond angles C13–N6–C15 [122·1(8)°] and C11–N14–C13[122·4(8)°] possess slightly large values. The mean value of bond length and bond angle for the seven-membered heterocyclic ring C is 1·482(15)Å and 116·2(9)°, respectively. This ring deviates significantly from planarity (maximum deviation being 0·272(12)Å for C4) and hence the deviation makes this ring to exist in chair conformation with a pseudo mirror through C3 and bisecting the C13–N14 bond. The dihedral angle between the plane of ring A and B is 3·5(4)° while it is 25·7(3)° between the plane of ring B and C. The chlorine atom of the hydrochloride is not involved in any intermolecular interaction and the crystal structure is stabilized by van der Waals interactions (Rajnikant *et al* 1998a).



(IV)

Chemical formula: $C_{13}H_{14}N_2O$ HCl H_2O; cell parameters: a = 6·251, b = 10·383, c = 19·970 Å; unit cell volume: 1296·14 Å^3; crystal system/space group: orthorhombic/$P2_12_12_1$; no. of molecules per unit cell (Z): 4; radiation used (CuKa, l): 1·5418 Å; no. of measured reflections: 1152; R-factor: 0·069.

(v) *Carpaine*: Isolation of carpaine (V) has been reported from the leaves of *Carica papaya* L family Enphorpiaceae, a subherbaceous and almost branchless tree found throughout India (Govindachari *et al* 1965). Carpaine, an alkaloid present in papaya leaves, can be used as a heart-rate depressant. It is also reported to be a potent amoebicide and diuretic (Choudhary and Panda 2003).

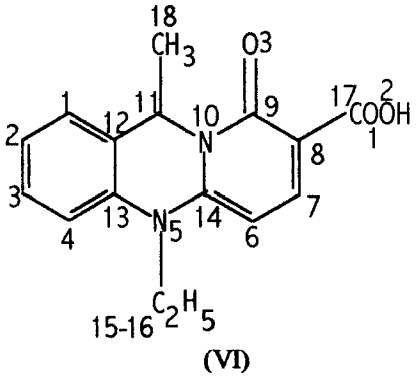


(V)

Chemical formula: $C_{28}H_{50}N_2O_4$; cell parameters: a = 18·695(2), b = 14·474(2), c = 5·474(1) Å; unit cell volume: 1481·2 Å^3; crystal system/space group: orthorhombic/$P2_12_12_1$; no. of molecules per unit cell (Z): 2; radiation used (MoKa, l): 0·71073 Å; no. of measured reflections: 1558; R-factor: 0·050.

The stereochemistry of the side chain at C6 and the presence of CH_3 at C2 in carpaine molecule is reported to be *cis* (Govindachari and Narasimhan 1955). Models suggested by Govindachari *et al* (1965) indicate that the dimeric carpaine molecule is flexible and the two piperidine rings can assume the chair forms without restraint. The asymmetric parameter calculation for the piperidine ring clearly indicates that this ring adopts chair conformation with best rotational axis bisecting N1–C6 and C3–C4 bonds, with ΔC_2(N1–C6) = 3·183 Å and the best mirror passing through N1 and C4, with ΔC_S (N1–C4) = 1·278(38). In nature, there exists only half of the carpaine molecule in the unit cell and the remaining half of it was generated by employing computational techniques. The molecules in the unit cell adopt herringbone configuration and are stabilized by N–H…O and C–H…O intermolecular hydrogen bonds (Rajnikant *et al* 1998b).

(vi) *5N-ethyl, 8-carboxy, 9-oxo-11-methyl-pyridol[2,1-b] quinazoline*: The compound (VI) has been prepared by refluxing 2,4-dimethyl-2,3-dihydroquinazoline and diethyl ethoxy methylene malonate (Mahajan 1995). These compounds possess significant biological properties such as anti-inflammatory, anti-coagulant, analgesic (Babita 1994) etc.

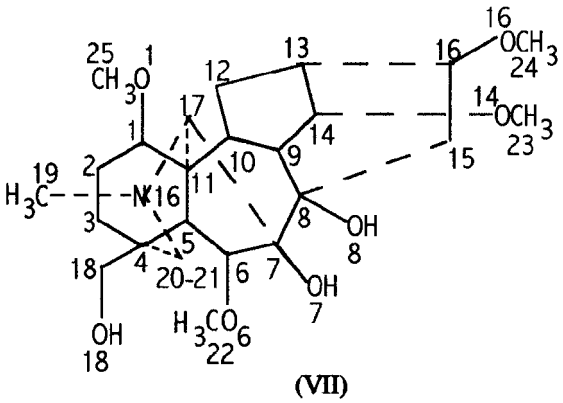


(VI)

Chemical formula: $C_{16}H_{16}N_2O_3$; cell parameters a = 9·775(1), b = 15·868(1), c = 9·799(1) Å, b = 113·50(1)°; unit cell volume: 1393·9 Å^3; crystal system/space group: monoclinic/$P2_1/c$; no. of molecules per unit cell (Z): 4; radiation used (CuKa, l): 1·5418 Å; no. of measured reflections: 2852; R-factor: 0·048.

The mean values of two C(sp^2)–N bonds i.e. N5–C13 and N5–C14, are in agreement with the standard value (Allen *et al* 1987). The length of the bond N5–C13 is close to the values obtained in E- and Z-isomers of 1-(2-amino-1-cyano-2-thioethylene) pyridinium–ylide (Fischer *et al* 1983). The C9=O3 bond length [1·255(2)Å] is greater than its theoretical value [1·199Å] and it may probably be due to the strong intramolecular O2–H17…O3 hydrogen bond. The benzene ring is perfectly planar and the pyridone ring deviates slightly from planarity [maximum deviation is – 0·023 Å for the C14 atom]. The pyrimidine ring has an 11*b*-sofa conformation with the asymmetry parameter ΔC_s[C11 = 0·87(38)]. The dihedral angle between the least-squares planes of benzene and pyridone rings is 28·61(5)°, indicating that the molecule is somewhat folded, may be due to the sofa conformation of the pyrimidine ring. The molecular packing in the unit cell is of herringbone type and molecules are stabilized by three intramolecular and three intermolecular hydrogen bonds (Rajnikant *et al* 2000).

(vii) *Royline monohydrate*: The compound (VII) is a diterpenoid alkaloid isolated from *Inula royleana*, a shrub growing in the western temperate Himalayas at an altitude of 7000–12000 ft above the sea level (Rajnikant *et al* 2001a). The plant is considered to be poisonous and is used as a disinfectant and an insecticide. It is known to be commonly used against the head louse (Chopra *et al* 1945).



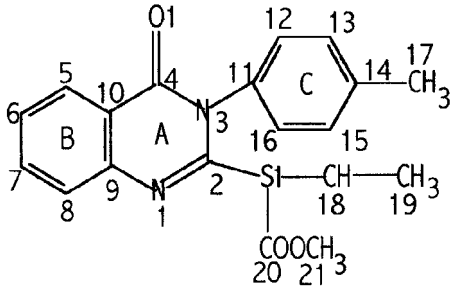
(VII)

Chemical formula: $C_{25}H_{41}NO_7.H_2O$; cell parameters: a = 10·985(1), b = 7·898(1), c = 14·956(1) Å, b = 102·96(1)°; unit cell volume: 1264·52 Å^3; crystal system/space group: monoclinic/$P2_1$; no. of molecules per unit cell (Z): 2; radiation used (MoKa, l): 0·71073 Å; no. of measured reflections: 2399; R-factor: 0·033.

The geometric parameters of the molecule, i.e. bond lengths and bond angles, are quite close to the literature values (Bhandary *et al* 1990; Joshi *et al* 1992). The central ring system of royline is formed by the fusion of four six-membered and two five-membered rings. The mean value of three C(sp^3)–N bonds [1·465(11)Å] is comparable with the corresponding values obtained in the case of Delvestine (Bhandary *et al* 1990) and Delsoline (Joshi *et al* 1992). Rings A, B and C exist in distorted chair conformations whereas ring D acquires half-boat, ring E-adopts half-chair and ring F occurs in C(14)-envelope conformations. The molecular packing of royline in the unit cell when viewed down *b*-axis makes it amply clear that the molecule is folded within itself. Molecular folding of this kind is generally observed in molecules having multiple ring structures and it is mainly attributed to the

distortions developed in individual ring systems. The crystal structure is stabilized by the O–H…O type intermolecular contacts involving the molecule of crystal water (Rajnikant *et al* 2001a).

(viii) *Methyl-3,4-dihydro-3-(p-methylphenyl)-4-oxo-2-quinazolinyl thiopropionate*: Alkaloids containing a quinazoline moiety are known for their biological properties (Babita 1994) and possess analgesic, antiallergic, anti-inflammatory, secretion inhibition, anticoagulant properties (Baker *et al* 1961; Siegfied *et al* 1992). The compound (VIII) has been synthesized by adding a solution of 3-(*p*-methylphenyl)-2-thio-quinazoline-4(1H) one, methyl-2-chloropropionate (0·1 mol) in acetone (50 ml) with potassium carbonate (1·5 g) and the reaction mixture refluxed further for 15 h in an oil bath. The solvent was removed under reduced pressure to get a solid which has been recrystallized from ethanol (Rajnikant *et al* 2001b).

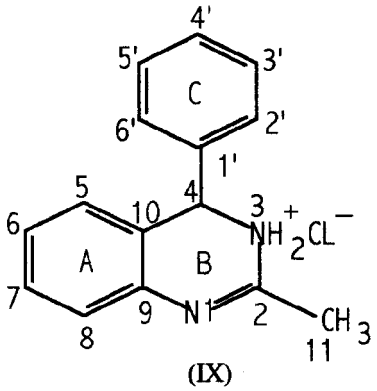


(VIII)

Chemical formula: $C_{19}H_{18}N_2O_3S$; cell parameters: a = 9·094(2), b = 9·428(3), c = 10·612(3) Å; a = 94·55(3), b = 95·44(2), g = 106·75(3)°; unit cell volume: 861·9 Å^3; crystal system/space group: triclinic/$P\bar{1}$; no. of molecules per unit cell (Z): 2; radiation used (MoKa, l): 0·71073 Å; no. of measured reflections: 3233; R-factor: 0·054.

Rings A and B of the quinazoline moiety adopt almost planar conformations with the average value of torsion angles being 1·9(3) and 1·4(4)°, respectively. The phenyl ring C also exists in planar conformation with average value of torsion angles 0·8(4)°. The ketone group located at C4 is deviated from the mean plane of ring A by 0·050(3) Å and methyl group at C14 is deviated from the mean plane of ring C by 0·036(3) Å. The conformational designations across the single bonds N1–C2–S1–C18, C2–S1–C18–C20, S1–C18–C20–O2 and O2–C20–O3–C21 of thiopropionate chain at C2 position of quinazoline are + synperiplanar, – synclinal, – synclinal and + synperiplanar (Klyne and Prelog 1996), respectively. The molecules in the unit cell are held in reversed orientations. The crystal structure is stabilized by an intermolecular interaction C7–H7…O2 (Rajnikant *et al* 2001b).

(ix) *2-methyl-4-phenyl-3,4-dihydro-quinazolinium chloride*: The compound (IX) has been synthesized by an interaction of *N*-acylated *o*-aminoacetophenone with formamide or *N*-methylformamide in 85% formic acid. The reaction mixture was refluxed for 6–7 h, cooled, diluted with water, basified with NH_4OH and extracted with chloroform. The chloroform extract was dried over anhydrous Na_2SO_4 and distilled *in vacuo*. The product obtained was crystallized from ethanol (Suri *et al* 1993; Rajnikant *et al* 2002a). It possesses important biological activities such as anti-allergic, anti-coagulant, anti-inflammatory, analgesic, secretion inhibition (Babita 1994) etc.



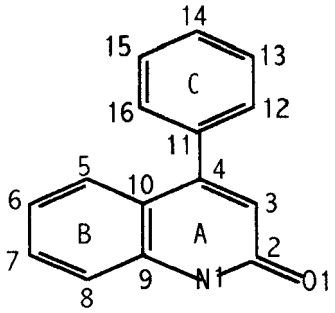
(IX)

Chemical formula: $C_{15}H_{14}N_2{\cdot}HCl$; cell parameters: a = 9·682(1), b = 10·532(1), c = 13·139(1) Å, b = 90·82(2)°; unit cell volume: 1774·32 Å^3; crystal system/space group: monoclinic/$P2_1/c$; no. of molecules per unit cell (Z): 4; radiation used (CuKa, l): 1·5418 Å; no. of measured reflections: 1364; R-factor: 0·057.

The rings A and B are planar with maximum deviation of 0·003(5) and 0·007(4) Å, respectively. The dihedral angle between these rings is 0·5(1)° confirming strict planarity of the fused ring system. In phenyl ring C which is also planar, its twist with respect to rest of the molecule as characterized by the torsion angle N3–C4–C1′–C6′ is 137·6(4)°. The twist is further confirmed by the corresponding torsion angle N3–C4–C1′–C2′ (– 43·5°). The dihedral angle between the plane of ring C and the quinazoline moiety is 79·3(1)°. In the unit cell molecules are stacked in reversed orientations along *b*-axis. An intermolecular hydrogen bond N3–H3…C11 between the chloride anion and nitrogen atom (N3) of the cation is responsible for the stability of the molecules in the unit cell (Rajnikant *et al* 2002a).

(x) *4-phenylquinolin-2(1H)-one*: Alkaloids containing a quinoline possess high antibacterial, antirrhythmic and antihypertensive activities (Jones 1977; Yates 1984; Zacharias and Glusker 1988; Hua *et al* 1997; Newell *et al* 1998). The compound (X) was synthesized by adding a mixture of aniline (0·1 mol) and benzoyl acetate (0·1 mol) in dioxane (50 ml) in a round bottomed flask, heated with reflux condenser for 3 h or 4 h in an oil bath, cooled and neutralized with sodium carbonate. The separated oil was extracted in chloroform. Removal of the

solvent under vacuum gave heavy oil, which was distilled under reduced pressure. A mixture of benzoylacetanilide (0·1 mol) and concentrated H_2SO_4 (20 ml) was heated on an oil bath with stirring at 70–80°C for 30 min and at 100°C for 1 h, then cooled and poured in ice water (500 ml) with continuous stirring. The resultant solid was filtered off and recrystallized from ethanol (Rajnikant *et al* 2002b).



(X)

Chemical formula: $C_{15}H_{11}NO$; cell parameters: a = 7·382(2), b = 21·795(3), c = 14·066(5) Å; unit cell volume: 2263·1 Å^3; crystal system/space group: orthorhombic/*Pbca*; no. of molecules per unit cell (Z): 8; radiation used (MoKa, l): 0·71073 Å; no. of measured reflections: 1987; R-factor: 0·039.

The mean bond lengths C(sp^2)–N [1·369(3)Å] are quite close to their theoretical values (Sutton 1965). Rings A and B of quinoline moiety adopt almost planar conformations with average torsion angles of 1·2(3)° and 1·0(3)°, respectively. The phenyl ring C also exists in a planar conformation with an average torsion angle of 0·6(4)° and shows a dihedral angle of 64·65(6)° with the quinoline moiety. The unit cell packing of the molecules down a-axis shows that the molecules are overlapped in paired configuration. The molecular structure is stabilized by intermolecular C–H…O and N–H…O interactions (Rajnikant *et al* 2002b).

3. Comparative crystallographic findings and the role of hydrogen bonding in alkaloids

Looking at the source of synthesis/isolation of all the ten alkaloidal molecules and, of course, the medicinal/pharmacological activity they exhibit, precise crystallographic data along with chemical structure and atomic numbering scheme, followed by the salient features of each structure, provides us first hand information about the crystal system these molecules have preference for. In the present case, alkaloids have shown their first preference to exist in monoclinic and orthorhombic crystal systems.

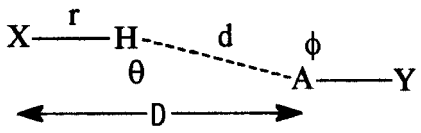
The phenomenon of multiple molecules in the asymmetric unit cell is completely ruled out but for the exception that only half molecule of carpaine exists in the unit cell (Rajnikant *et al* 1998b). This observation, however, is not true in case of some other organic molecular assemblies (Rajnikant *et al* 1995a,d; Rajnikant 2001).

In three-dimensional structure of these molecules (Rajnikant *et al* 1993, 1996, 1998a,b, 2000, 2001a,b, 2002a,b; Magotra *et al* 1996) where in some cases the geometrical parameters like bond distances and bond angles do agree with the values reported for their analogous structures while in some cases these parameters are worth comparison. The accuracy in the measurement of *hkl* reflections and their corresponding intensities is indicative of a better data resolution ($\sin q/l$) while the precision in the calculation of molecular parameters is indicative of better yield of the reliability index. In the present case the reliability index ranges from 0·033–0·069 which itself speaks about the crystal quality, data collection, structure determination and refinement. Some of the important C–N distances and C–N–C bond angles in the reported molecules are presented in table 1. The following observations can be drawn from the compared data: (i) The C–N distances as obtained in all the ten alkaloids present a wide range of values falling between 1·059 and 1·517 Å. The broad spectrum of C–N distances shows that, depending upon the nature and position of the substituent or the presence of ring system in its closer proximity, this bond is able to accommodate the torsion in and around the surrounding bonds caused due to the influence of neighbouring atoms. The C–N distance appears to be more flexible than standard C–C, C=C, C≡C distances which are quite fixed and do not vary under ordinary conditions and (ii) the magnitude of the C–N–C bond angle (i.e. all those angles in which nitrogen is held in the ring moiety) varies abnormally from 109·0–128·0°. It could be attributed to the same fact as stated above that nitrogen when substituted for a carbon atom in the ring structure adopts more flexibility in view of the torsional magnitude of the neighbouring bonds.

3.1 *Analysis of hydrogen bonding in alkaloids*

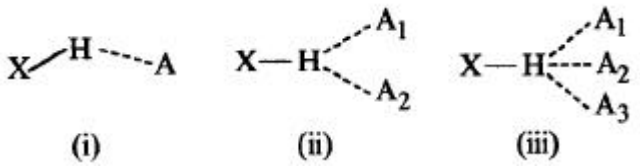
Covalently bonded atoms often produce a configuration that behaves like an electric dipole. Several such dipoles may be bonded together as a result of electrostatic attraction between them. The dipole bond in which hydrogen atom acts as the positive end of the dipole is known as hydrogen bond. Hydrogen bonding is usually formed between the most electronegative atoms like fluorine, oxygen and nitrogen because these atoms produce strong dipoles (Wahab 1999). In a hydrogen bond X–H…A, the functional group X–H is called the 'donor' (sometimes called 'proton donor') and A is called the 'acceptor'. The bond may be described in terms of the d, D, q and r and if the hydrogen bond is extended on the acceptor side as X–H…A–Y, an acceptor angle f, H…A–Y may also be

defined (Desiraju and Steiner 1999) as shown in the diagram below



(Definition of the geometrical parameters *d, D, q, r* and *f* for a hydrogen bond)

Due to the long range character of the hydrogen bond, and to a pronounced softness of the angle at H, donors may interact simultaneously with more than one acceptor.



To distinguish the different resulting configurations, (i) is called a two-centre bond because the H-atom is bonded to two atoms, X and A, and analogously (ii) is called a three-centre, and (iii) a four-centre bond. The patterns (ii) and (iii) are often called bifurcated hydrogen bond and trifurcated hydrogen bond (Steiner 1995), respectively.

Hydrogen bonds are classified into two groups viz. intramolecular and intermolecular. Intramolecular hydrogen bonding occurs within two atoms of the same molecule while in intermolecular hydrogen bonding two or more than two molecules of the same or different compounds combine to give a polymeric aggregate.

The study of interactions in organic molecules has attracted the attention of crystallographers during the past two decades (Pimentel and McClellan 1960; Jeffery and Saenger 1991; Berstein *et al* 1994). Based on the results of various workers on hydrogen bonding (Nishio and Hirota 1989; Nishio *et al* 1995, 1998; Aakeroy and Seddon 1993a,b; Aakeroy 1997), Desiraju and Steiner (1999) tried to make some empirical rules on the distance and angle cut-off criteria on mixed kind of organic molecules.

The geometry of intra- and intermolecular hydrogen bonds as obtained is presented in tables 3 and 4, respectively and each table has been followed by brief observations made on the basis of general data as presented in table 2.

Some of the properties of very strong, strong and weak hydrogen bonds as tabulated by Desiraju and Steiner in an International monogram on crystallography (1999) in case of a variety of hydrogen bonds as retrieved from Cambridge Crystal Data Centre (UK) are presented in table 2. All the parameters for e.g. bond lengths *d*(H…A) Å, D(X…A) Å etc have been compared with our own data and the following have been observed: (i) The average D(X…A) Å value i.e. 2·6 Å in the present case i.e. for the ten alkaloids, does fall within the range as suggested for "strong" hydrogen bond, (ii) the average *d*(H…A) Å value i.e. 2·4 Å in the present case also, fall under the category of "weak" hydrogen bonds, and (iii) so far as the average angular value i.e. 130·8° of C–H…O, O–H…O and C–H…N interactions is concerned, the range as suggested by Desiraju for "weak" hydrogen bonds is

Table 1. Some selected C–N (Å) bond distances and C–N–C (°) bond angles.

Molecule	C–N (Å)	C–N–C (°)
I	C11–N12 = 1·488	C13–N12–C11 = 114·3
	C14–N12 = 1·441	C14–N12–C11 = 109·0
	C13–N12 =1·467	C14–N12–C13 = 113·0
II	C6–N7 = 1·059	C6–N7–C13a = 111·8
	C8–N7 = 1·490	C6–N7–C8 = 109·3
	C3a–N7 = 1·517	C8–N7–C13a = 111·5
III	C1–N10 = 1·460	C3A–N4–C4A = 115·9
	C3A–N4 = 1·288	C3A–N10–C9 = 123·4
	C3A–N10 = 1·370	C1–N10–C9 = 123·5
	C9–N10 = 1·383	C1–N10–C3A = 113·0
	C4A–N4 = 1·401	
IV	C1–N14 = 1·512	C13–N6–C15 =122·1
	C11–N14 = 1·405	C11–N14–C13 = 122·4
	C13–N14 = 1·335	C1–N14–C13 = 120·4
	C13–N6 = 1·335	C1–N14–C11 = 117·2
	C15–N6 = 1·396	
V	C2–N1 = 1·460	C2–N1–C6 = 114·5
	C6–N1 = 1·458	
VI	C13–N5 = 1·419	C14–N5–C15 = 118·7
	C14–N5 = 1·366	C13–N5–C15 = 118·8
	C15–N5 = 1·476	C13–N5–C14 = 120·5
	C11–N10 = 1·486	C11–N10–C14 = 120·7
	C14–N10 = 1·373	C9–N10–C14 = 122·8
		C9–N10–C11 = 116·2
VII	C15–N16 = 1·463	C17–N16–C21 = 111·5
	C17–N16 = 1·469	C15–N16–C21 = 115·3
	C21–N16 = 1·462	C15–N16–C21 = 116·1
VIII	C2–N1 = 1·277	C2–N1–C9 = 117·6
	C9–N1 = 1·390	C4–N3–C11 = 117·5
	C2–N3 = 1·387	C2–N3–C11 = 121·0
	C4–N3 = 1·409	C2–N3–C4 = 121·5
	C11–N3 = 1·446	
IX	C2–N1 = 1·325	C2–N1–C9 = 121·9
	C9–N1 = 1·401	C2–N3–C4 = 128·0
	C2–N3 = 1·321	
X	C2–N1 = 1·358	C2–N1–C9 = 124·4
	C9–N1 = 1·380	

Table 2. Comparative data for different kinds of hydrogen bonds.

Properties	Very strong	Strong	Weak	Mol. I–X
D(X–H…A) range Å	2·2–2·5	2·5–3·2	3·0–4·0	2·51–3·68
d(H…A) range Å	1·2–1·5	1·5–2·2	2·0–3·0	1·56–2·81
q (X–H…A) range (°)	175–180	130–180	90–180	99–176
Effect on crystal packing	Strong	Distinctive	Variable	Variable
Utility in crystal engineering	Unknown	Useful	Partly useful	Partly

Table 3. Geometry of intramolecular C–H…O, O–H…O and C–H…N interactions.

Molecule*	X–H…A	H…A (Å)	X–A (Å)	X–H…A(°)
II	C–H…O	2·51	2·99	109
V	C–H…O	2·34	2·68	99
	C–H…O	2·54	2·96	107
VI	C–H…O	2·19	2·66	109
	C–H…O	2·81	3·29	109
	O–H…O	1·56	2·51	156
VII	O–H…O	2·25	2·73	118
	O–H…O	1·83	2·64	149
	C–H…N	2·47	2·97	110
	C–H…O	2·53	2·85	99
	C–H…O	2·58	2·97	105
	C–H…O	2·19	2·78	118
	C–H…O	2·65	2·97	100
	C–H…O	2·48	2·94	109
	C–H…O	2·49	2·93	107

(i) The overall *d*(H…A) range in case of intramolecular interactions comes out to be between 1·56 and 2·81 Å, thus making these interactions fall under the category of "strong to weak" interactions; (ii) the overall D(X…A) range in case of intramolecular interactions comes out to be between 2·51 and 3·29 Å hence making these interactions fall under the category of "strong to weak" interactions, and (iii) the *q* range i.e. 99–149° in case of intramolecular interactions fall under the category of "weak" interactions.

in conformity with the angular range we obtained in all the ten alkaloids.

4. Outlook

The quest of researchers world over is mainly to study the matter in all forms. All kinds of materials, irrespective of their application or utility to the industry or society, need to be characterized by making use of various available scientific techniques. In this paper, we have tried to provide an insight into the chemical and crystallographic aspects of alkaloids which are considered very potent especially for their use in medical science. The literature on the chemical and crystallographic aspects of alkaloids is available as isolated papers but there appears to be no documented study which could provide a detailed account of the three-dimensional structure of some alkaloids especially with emphasis on the role of hydrogen bonding in organic molecular assemblies. The main purpose of the study is to ascertain whether the results of these ten molecules are in conformity with what is available in the literature for analogous structures. It has been observed that some of the geometrical and structural parameters including the geometry of individual ring systems is in consonance with the established scheme and in some cases, few deviations in terms of C–N bond distances and C–N–C bond angles have also been observed.

Currently, research in hydrogen bonding concentrates on the weakest and the strongest species. In the field of weak hydrogen bonding, more publications now appear than ever, and progress is far more rapid than a few years ago. Therefore, it is presumed to have substantial progress in a number of important fields, such as the role on C–H…O, C–H…N etc hydrogen bonds in molecular recognition, in the self-assembly of molecules, in the design

Table 4. Geometry of intermolecular C–H…O, O–H…O and N–H…O interactions.

Molecule	X–H…A	H…A(Å)	X–A(Å)	X–H…A(°)
II	C–H…O	2·43	3·41	154
	C–H…O	2·43	3·30	142
	C–H…O	2·65	3·46	147
	C–H…O	2·56	3·41	132
III	O–H…O	1·90	2·84	170
	O–H…O	1·68	2·71	178
V	N–H…O	2·35	3·23	144
	C–H…O	2·37	3·11	131
VI	C–H…O	2·67	3·43	131
	C–H…O	2·70	3·59	159
	C–H…N	2·78	3·48	123
VIII	C–H…O	2·79	3·68	153
X	N–H…O	1·98	2·83	176·2
	C–H…O	2·57	3·41	150·4

*Only molecules II, V and VI exhibit both intra- and intermolecular.
(i) The overall *d*(H…A) range in case of intermolecular interactions comes out to be between 2·35 and 2·79 Å, thus making these interactions fall under the category of "strong to weak" interactions; (ii) the overall D(X…A) range in case of intermolecular interactions comes out to be between 2·83 and 3·68 Å hence making these interactions fall under the category of "strong to weak" interactions; and (iii) the *q* range i.e. 123–176° in case of intermolecular interactions fall under the category of "weak" interactions.

of crystal structures, in the architecture and function of biological systems. The present study has provided us a broad base to carry out further work by taking into our fold some more data. It is hoped that study of this kind might help us in bringing the role of hydrogen bonding in alkaloids to a broader end.

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References

Aakeroy C B 1997 *Acta Crystallogr*. **B53** 569
Aakeroy C B and Seddon K R 1993a *Chem. Soc. Rev.* **22** 397
Aakeroy C B and Seddon K R 1993b *Z. Naturforsch.* **b48** 1023
Allen F H, Kennard O and Watson D G 1987 *J. Chem. Soc. Perkin. Trans.* **2** SI
Anshu Sawhney 2003 *Three-dimensional structure elucidation of some nitrogen containing molecules using crystallographic and computational techniques*, Ph D Thesis, University of Jammu, Jammu Tawi
Atal C K 1980 *Chemistry and pharmacology of vasicine*: *A new oxytocic and abortifacient* (Jammu: Regional Research Laboratory)
Babita M 1994 *Chemistry of natural products* Ph D Thesis, Regional Research Laboratory, Jammu Tawi
Baker B R, Koehler R, Goodman L and De Graw J 1961 *Org. Chem*. **26** 1156
Bergman J, Brynolf A, Elman B and Vuorinen E 1986 *Tetrahedron* **42** 3697
Berg S S and Lucas J M S 1961 *Nature* **189** 64
Berstein J, Etter M C and Leiserowitz L 1994 *The role of hydrogen bonding in molecular assemblies*; *in Structure correlation* (eds) H-B Burgi and J D Dunitz (Weinheim: VCH) **2** p. 431
Bhandary K K, Ramasubbu N and Joshi B S 1990 *Acta Crystallogr. Struct. Commun*. **C46** 1704
Bruderer H, Metzger J, Brossi A and Dally J J 1976 *Helv. Chim. Acta* **59** 2793
Byke R and Vandyke C 1997 *Cocaine* (eds) R C Peterson and R C Stillman (Washington) **97**
Cameron A F, Hair N J, Greengrass C W and Romage R 1974 *Acta Crystallogr*. **B30** 282
Chopra I C, Kohli J D and Handa K L 1945 *Indian J. Med. Res*. **33** 139
Chopra R N 1958 *Chopra's indigenous drugs of India* 2nd Ed. p. 412
Choudhary B I and Panda S K 2003 *Science Reporter* **40** 57
Desiraju G J and Steiner T 1999 *The weak hydrogen bond* (New York: International Union of Crystallography)
Duax W L and Norton D A 1975 *Atlas of steroid structure* (New York: Plenum) **I**
Ebel F, Rupp W and Tranth O 1958 *Chem. Abstr*. **52** 1639
Farrugia L J 1997 *J. Appl. Cryst*. **30** 565
Fischer E, Knippel M and Wollin K M 1983 *J. Prakt. Chem*. **325** 261
Gorinsky C and Moss D S 1973 *J. Cryst. Mol. Struct*. **3** 299
Govindachari T R and Narasimhan N S 1955 *J. Chem. Soc*. 1563
Govindachari T R, Nagarajan K and Viswanathan N 1965 *Tetrahedron Letts* **24** 1907
Gupta B D and Banerjee S K 1994 Private Communication, Regional Research Laboratory, Jammu Tawi
Hua D H *et al* 1997 *J. Org. Chem*. **62** 6888
Jeffery G A and Saenger W 1991 *Hydrogen bonding in biological structures* (Berlin: Springer-Verlag)
Jones G 1977 *Chemistry of heterocyclic compounds*: *I. Quinolines* (Chichester: Wiley) **32** p. 93
Joshi B S, Desai H K, Pelletier S W and Newton M G 1992 *J. Crystallogr. Spectrosc. Res*. **22** 477
Joshi B S, Newton M G, Lee D W, Barber A D and Pelletier S W 1996 *Tetrahedron Asym.* **7** 25
Kistenmacher T J and Shigematsu T 1974 *Acta Crystallogr*. **B30** 1528
Klyne W and Prelog V 1996 *Experientia* **XVI** 521
Magotra D K, Gupta V K, Rajnikant, Goswami K N, Thappa R K and Agarwal S G 1996 *Acta Crystallogr*. **C52** 1491

Mahajan B 1995 *Chemistry of natural products* Ph D Thesis, Regional Research Laboratory, Jammu Tawi

Mclean E 1970 *Parm. Rev.* **22** 429

Mehta D R, Naravane J S and Desai R M 1963 *J. Org. Chem.* **28** 445

Moss D S and Watson F E 1984 *Acta Crystallogr.* **C40** 1960

Nardelli M 1983 *Comput. Chem.* **7** 95

Newell S W *et al* 1998 *Int. J. Oncol.* **12** 433

Nishio M and Hirota M 1989 *Tetrahedron* **45** 7201

Nishio M, Umezawa Y, Hirota M and Takeuchi Y 1995 *Tetrahedron* **51** 8665

Nishio M, Hirota M and Umezawa Y 1998 *The CH/p. Evidence, nature and consequences* (New York: Wiley) p. 4

Picorari P, Renaldi M and Antolini L 1992 *Acta Crystallogr.* **C48** 2027

Pimentel G C and McClellan A L 1960 *The hydrogen bond* (San Francisco: Freeman)

Rajnikant 1988 *Determination of crystal and molecular structure of some medicinally important compounds by X-ray crystallographic techniques*, Ph D Thesis, University of Jammu, Jammu Tawi

Rajnikant 2001 *Mol. Mater.* **14** 165

Rajnikant, Goswami K N, Yadava V S, Padmanabhan V M and Banerjee S K 1993 *Acta Crystallogr.* **C49** 505

Rajnikant, Watkin D and Tranter G 1995 *Acta Crystallogr.* **C51** 1452, 2071, 2161, 2388

Rajnikant, Gupta V K, Singh A, Lal M and Varghese B 1996 *Mol. Mater.* **6** 253

Rajnikant, Gupta V K, Singh A, Lal M, Manisekaran T and Rangari V D 1998a *Mol. Mater.* **9** 227

Rajnikant, Gupta V K, Lal M, Rangari V D, Belsare D P, Soni B S and Varghese B 1998b *Mol. Mater.* **9** 131

Rajnikant, Gupta V K and Singh A 2000 *Crystallogr. Rep.* **45** 611

Rajnikant, Gupta V K and Lal M 2001a *Crystallogr. Rep.* **46** 230

Rajnikant, Gupta V K, Deshmukh M B, Varghese B and Dinesh 2001b *Cryst. Res. Technol.* **36** 1451

Rajnikant, Gupta V K, Suri O P and Lal M 2002a *Indian J. Pure & Appl. Phys.* **40** 59

Rajnikant, Gupta V K, Deshmukh M B, Varghese B and Dinesh 2002b *Crystallogr. Rep.* **47** 449

Sharma S D 1985 *X-ray analysis of crystal structure of some organic compounds*, Ph D Thesis, University of Jammu, Jammu Tawi

Sharma S D, Gupta V K, Goswami K N and Padmanabhan V M 1993 *Cryst. Res. Technol.* **28** 1115

Sheldrick G M 1986 *SHELXS86 program for the solution of crystal structures* (Germany: University of Gottingen)

Sheldrick G M 1993 *SHELXS93 program for the refinement of crystal structures* (Germany: University of Gottingen)

Sheldrick G M 1997a *SHELXS97 program for crystal structure determination* (Germany: University of Gottingen)

Sheldrick G M 1997b *SHELXL97 program for refinement of crystal structures* (Germany: University of Gottingen)

Siegfied L, Karl D, Guenther W, Herwart A and Dieter I 1992 *Chem. Abs.* **116** 34567

Steiner T 1995 *C–H...O hydrogen bonding in crystals, Cryst. Rev. Institut fur Kristallographie, Freie Universitat Berlin, Takustrabe, D-14195 Berlin, Germany* **6**

Stout G H and Jensen L H 1968 *X-ray structure determination* (New York: Macmillan) p. 315

Stroud R M 1973 *Acta Crystallogr.* **B29** 690

Sutton L E 1965 *Tables of interatomic distances and configuration in molecules and ions* (London: The Chemical Society)

Thappa R K, Agarwal S G, Dhar K L, Gupta V K and Goswami K N 1996 *Phytochemistry* **42** 1485

Wahab M A 1999 *Solid state physics* (New Delhi: Narosa Publishing House) p. 101

Winterstein E and Trier G 1910 *Die Alkaloide, eine Monographie der naturlichen Basen, Borntrager, Berlin*

Wong-Ng W and Nyburg S C 1979 *Canadian J. Chem.* **57** 157

Yates F S 1984 *Comprehensive heterocyclic chemistry* (eds) A R Katrizky and C W Rees (New York: Pergamon) **2** p. 511

Zacharias D and Glusker J P 1988 *Acta Crystallogr. Cryst. Struct. Commun.* **C44** 1656