Acta Crystallographica Section A
Foundations of Crystallography
ISSN 0108-7673

Received 11 August 2005
Accepted 29 September 2005

Comparative crystallographic and hydrogen-bonding analysis of cholestane derivatives

Rajnikant,* Dinesh and Chand Bhavnaish

Condensed Matter Physics Group, Post-Graduate Department of Physics, University of Jammu, Jammu Tawi-180006, India. Correspondence e-mail: rkantverma@rediffmail.com

A crystallographic comparison comprised of some geometrical and structural features for a series of steroids (cholestane derivatives) is made in the present paper. Selected bond distances and bond angles of interest are discussed in detail. Conformations of individual ring systems in a series of 28 cholestane derivatives are calculated and discussed. Graphical presentations of ring conformations are made for all the five- and six-membered rings to show the frequency of their occurrence. X—H$\cdots A$ intra- and intermolecular interactions in the identified molecules are discussed with the standard distance and angle cut-off criteria. Distance–angle scatter plots for both kinds of interactions are presented for better understanding of packing interactions existing in cholestane molecules.

1. Introduction

The cholesterol molecule in steroid biochemistry and pharmacology is well known as a four-ring structure of which three are six-membered cyclohexane rings and one is a five-membered carbon ring. A representative illustration of the cholesterol molecule is presented in Fig. 1.

Removal of the hydroxyl group at the C3 position of cholesterol and reduction of the double bond between C5 and C6 converts cholesterol into a fully saturated compound called cholestane ($C_{27}H_{48,}$ with a cyclopentanoperhydrophenanthrene ring system), which is the parent compound of all C_{27} steroids. There are other important steroids that are produced from cholesterol during steroid hormone biogenesis by desmolase (or lyase) enzymes which break C—C bonds, usually in the vicinity of a tertiary C atom. Without considering the detail of the reactions or the specific compounds involved, the cholestane skeleton gives rise to parent compounds in other important steroid series (Fig. 2) (Makin, 1975).

In view of the relationship of various parent steroid hydrocarbons, *viz* cholestane, cholane, pregnane, androstane and estrane, we became interested in building up a small compendium of each of this series of steroids which will essentially have interest in their (i) medicinal activity, (ii) molecular and crystal structure, (iii) molecular geometry and conformational parameters, (iv) non-planar conformations of individual ring systems, and (v) molecular packing interactions, and this paper is part of our on-going research on steroids.

In the present paper, we identify from the literature a series of 28 derivatives of cholestane. A critical survey of the

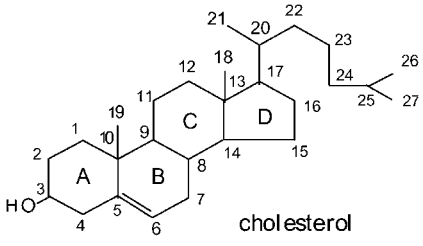

Figure 1
The cyclopentanoperhydrophenanthrene nucleus and the numbering scheme of cholesterol.

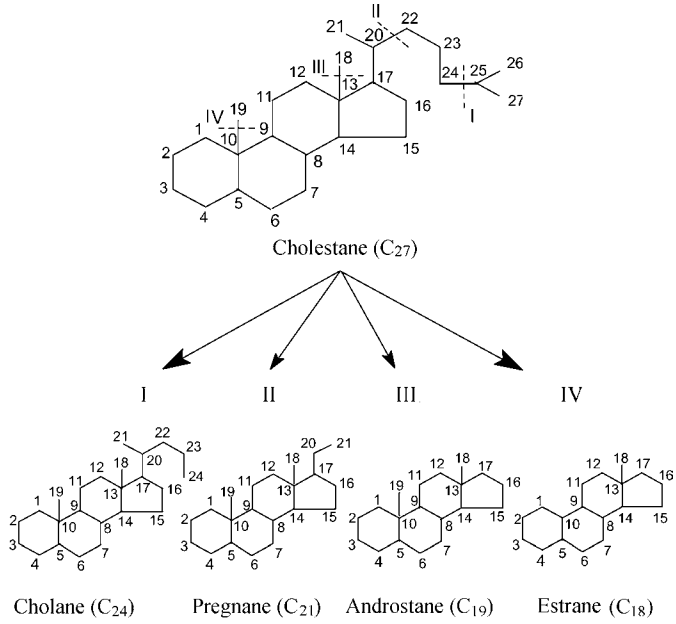

Figure 2
Relationship between various parent steroid hydrocarbons and cholestane.

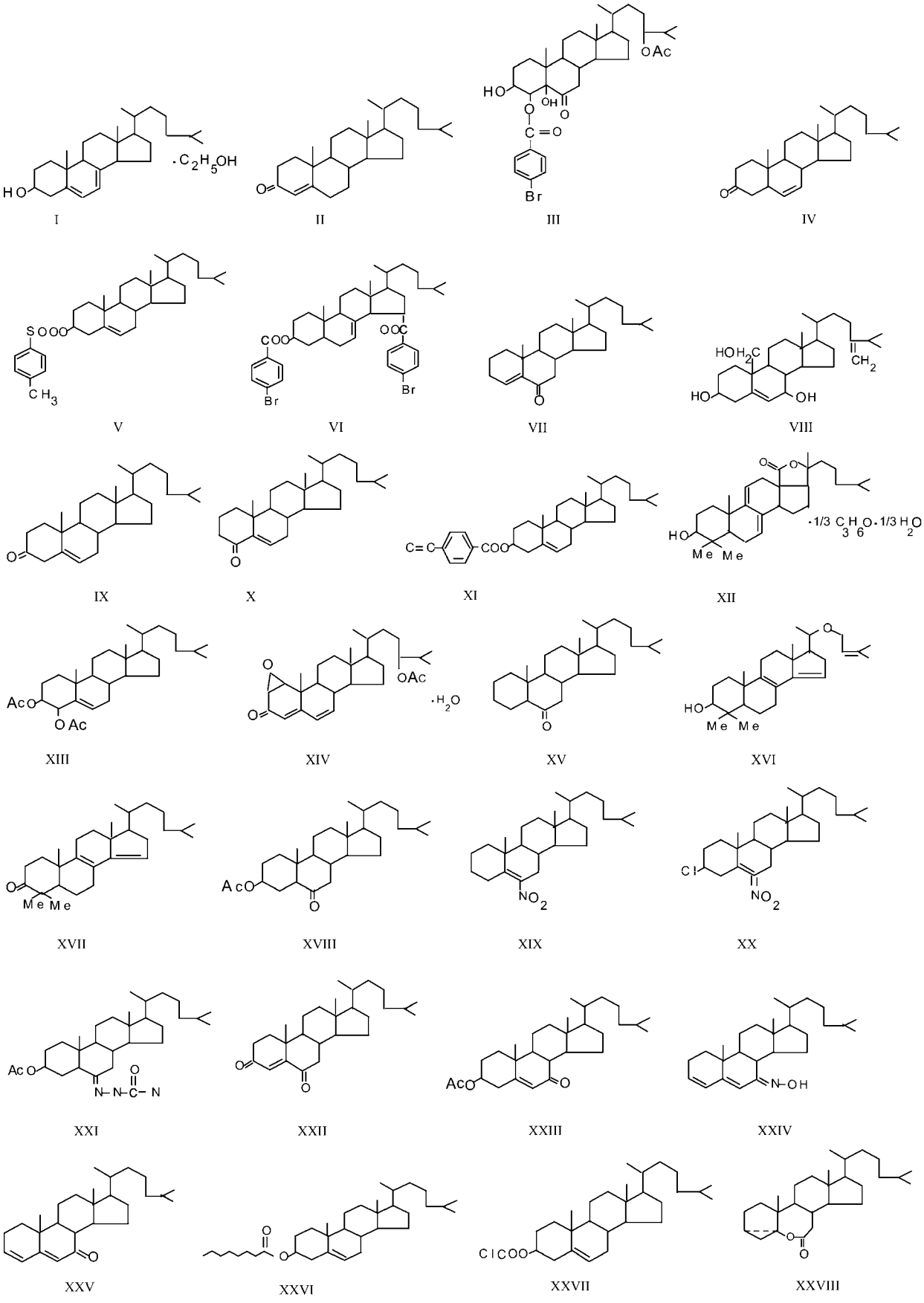

Figure 3
Chemical structures of molecules I–XXVIII.

Table 1
Chemical name, chemical formula and published reference of molecules I–XXVIII.

Molecule	Chemical name	Chemical formula	Reference
I	Lumisterol–ethanol	$C_{27}H_{44}O \cdot C_2H_5OH$	(*a*)
II	Cholest-4-en-3-one	$C_{27}H_{44}O$	(*b*)
III	Lobosterol 4-*p*-bromobenzoate	$C_{37}H_{53}O_7Br$	(*c*)
IV	Cholest-6-en-3-one	$C_{27}H_{44}O$	(*d*)
V	Cholesteryl *p*-toluenesulfonate	$C_{27}H_{45}OSO_2 \cdot C_6H_4CH_3$	(*e*)
VI	5α,14β-Cholest-7-ene-3β,15β-diol di-*p*-bromobenzoate	$C_{41}H_{52}O_4Br_2$	(*f*)
VII	Cholest-4-en-6-one	$C_{27}H_{44}O$	(*g*)
VIII	24-Methylenecholest-5-ene-3β,17β,19-triol	$C_{28}H_{46}O_3$	(*h*)
IX	Cholest-5-en-3-one	$C_{27}H_{44}O$	(*i*)
X	Cholest-5-en-4-one	$C_{27}H_{44}O$	(*j*)
XI	Cholesteryl 4-vinylbenzoate	$C_{36}H_{52}O_2$	(*k*)
XII	(20*S*)-3β-Hydroxyholosta-7,9-diene	$C_{30}H_{46}O_3 \cdot 1/3C_3H_6O \cdot 1/3H_2O$	(*l*)
XIII	Cholest-5-ene-3β,4β-diyl diacetate	$C_{31}H_{50}O_4$	(*m*)
XIV	24(*R*)-Acyloxy-1α,2α-epoxycholesta-4,6-dien-3-one hydrate	$C_{29}H_{42}O_4 \cdot H_2O$	(*n*)
XV	5α-Cholest-6-one	$C_{27}H_{46}O$	(*o*)
XVI	(20*R*)-4,4-Dimethyl-22-oxa-5α,20-cholesta-8,14,24-trien-3β-ol	$C_{28}H_{44}O_2$	(*p*)
XVII	4,4-Dimethyl-5α-cholesta-8,14-dien-3-one	$C_{29}H_{46}O$	(*p*)
XVIII	3β-Acetoxy-5α-cholestan-6-one	$C_{29}H_{48}O_3$	(*q*)
XIX	6-Nitrocholest-5-ene	$C_{27}H_{45}NO_2$	(*r*)
XX	3β-Chloro-6-nitrocholest-5-ene	$C_{27}H_{44}NO_2Cl$	(*s*)
XXI	3β-Acetoxy-5α-cholestan-6-one-semicarbazone	$C_{30}H_{51}O_3N_3$	(*t*)
XXII	Cholest-4-ene-3,6-dione	$C_{27}H_{44}O_2$	(*u*)
XXIII	3β-Acetoxycholest-5-ene-7-one	$C_{29}H_{46}O3$	(*v*)
XXIV	Cholesta-3,5-diene-7-one-oxime	$C_{27}H_{43}NO$	(*w*)
XXV	Cholesta-3,5-diene-7-one	$C_{27}H_{42}O$	(*x*)
XXVI	Cholesteryl caprylate	$C_{35}H_{60}O_2$	(*y*)
XXVII	Cholesteryl chloroformate	$C_{28}H_{45}O_2Cl$	(*z*)
XXVIII	5a-Oxa-β-homo-5α-cholestan-6-one	$C_{27}H_{44}O_2$	(*aa*)

References: (*a*) de Kok & Romers (1974); (*b*) Sheldrick *et al.* (1976); (*c*) Losman *et al.* (1976); (*d*) Guy *et al.* (1977); (*e*) Chandross & Bordner (1977); (*f*) Gilliland *et al.* (1977); (*g*) Nassimbeni *et al.* (1977); (*h*) Losman & Karlsson (1978); (*i*) Grochulski *et al.* (1991); (*j*) Wawrzak *et al.* (1991); (*k*) Socci *et al.* (1995); (*l*) Ilyin *et al.* (1998); (*m*) Kennedy *et al.* (1999); (*n*) Rajalakshmi *et al.* (2000); (*o*) Rajnikant *et al.* (2000); (*p*) Boer *et al.* (2001); (*q*) Rajnikant, Gupta, Shafi *et al.* (2001); (*r*) Rajnikant, Gupta, Firoz *et al.* (2001*a*); (*s*) Rajnikant, Gupta, Firoz *et al.* (2001*b*); (*t*) Rajnikant, Gupta, Khan *et al.* (2001*a*); (*u*) Rajnikant, Gupta, Khan *et al.* (2001*b*); (*v*) Rajnikant, Gupta, Khan, Shafi, Hashmi *et al.* (2002); (*w*) Rajnikant, Gupta, Khan, Shafi, Shafiullah & Dinesh (2002); (*x*) Rajnikant, Dinesh, Anshu Sawney *et al.* (2005); (*y*) Rajnikant, Dinesh & Bandhan Sharma (2005); (*z*) Rajnikant, Dinesh, Kewal Gupta & Sonum Lotus (2005); (*aa*) Rajnikant, Dinesh & Mousmi (2005).

Cambridge Structural Database has been made and we have considered the structural data of those compounds whose crystal data have been collected by using a computer-controlled single-crystal X-ray diffractometer. Some of the structures of the cholestane derivatives have also been reported by our research group and a comparative study has been evolved *vis-a-vis* what exists in the literature. The chemical structures of each molecule (I–XXVIII) are shown in Fig. 3. The chemical name, chemical formula and corresponding reference of the published work in respect of each molecule is presented in Table 1.[1]

2. Comparative geometrical parameters

2.1. Bond distances and angles

Most of the molecules in the present study have substituents at the C3 position. Therefore, it is of interest to investigate C2—C3 and C3—C4 bond distances and the C2—C3—C4 bond angle and these data are presented in Table 2.

The substitution at the C3 position of the steroid nucleus causes significant changes in the bond distances in ring *A*, depending upon whether C2—C3 or C3—C4 is a single or a double bond. The bond distance C2(sp^3)—C3(sp^3) lies in the range 1.484–1.540 Å (average value 1.508 Å). The bond distance C2(sp^3)—C3(sp^3) in molecules XII′′ (1.493 Å), XVIII (1.488 Å), XX (1.484 Å), XXIII′ (1.487 Å), XXVI (1.494 Å) and XXVII (1.494 Å) are shorter than the standard value of 1.533 Å (Sutton, 1965; Allen *et al.*, 1987). The bond distance C3(sp^3)—C4(sp^3) lies in the range 1.479–1.573 Å (average value 1.523 Å). This bond distance in molecules V (1.479 Å), XI (1.490 Å) and XVI (1.573 Å) shows a significant deviation from the accepted value of 1.533 Å. The deviations of bond distances C2(sp^3)—C3(sp^3) and C3(sp^3)—C4(sp^3) could be due to the effect of some functional group located at C3 which invariably is involved in C—H···O/O—H···O/O—H···N intra/intermolecular interactions. The C2(sp^3)—C3(sp^2)/C2(sp^2)—C3(sp^3) bond distance in molecules having substitutions at C3 lies in the range 1.475–1.517 Å (average value 1.490 Å), whereas the bond distance C3(sp^3)—C4(sp^2)/C3(sp^2)—C4(sp^3) lies in the range 1.479–1.521 Å (average value 1.502 Å). The bond distance C2(sp^3)—C3(sp^2)/C2(sp^2)—C3(sp^3) in molecules XIV (1.475 Å) and XXII (1.479 Å) and the bond distance C3(sp^3)—C4(sp^2)/C3(sp^2)—C4(sp^3) in molecule IV (1.479 Å) are smaller compared to the accepted value of 1.505 Å (Bartell & Bonham, 1960; Sutton, 1965). It is probably the involvement of the O atom of the keto group in C—H···O/O—H···O intra/intermolecular

[1] Supplementary data including asymmetry parameters (ΔC_2 and ΔC_s) and average values of torsion angles for different conformations of rings *A*, *B*, *C* and *D* are available from the IUCr electronic archives (Reference: XO5005). Services for accessing these data are described at the back of the journal.

Table 2
C2—C3 and C3—C4 bond distances (Å) and C2—C3—C4 bond angles (°) for molecules I–XXVIII.

	Bond distance C2—C3		Bond distance C3—C4				Bond angle C2—C3—C4	
Molecule	$(sp^3)-(sp^3)$	$(sp^3)-(sp^2)/(sp^2)-(sp^3)$	$(sp^3)-(sp^3)$	$(sp^3)-(sp^2)/(sp^2)-(sp^3)$	$(sp^2)-(sp^2)$	$(sp^2)=(sp^2)$	C3(sp^3)	C3(sp^2)
I	1.523	–	1.520	–	–	–	110.5	–
II	–	1.490	–	–	1.463	–	–	117.2
III	1.526	–	1.555	–	–	–	109.0	–
IV	–	1.484	–	1.479	–	–	–	117.0
IV′	–	1.495	–	1.495	–	–	–	118.5
V	1.496	–	1.479	–	–	–	108.2	–
VI	1.540	–	1.540	–	–	–	110.3	–
VII	1.560	–	–	1.500	–	–	107.7	–
VIII	1.520	–	1.560	–	–	–	111.0	–
VIII′	1.510	–	1.560	–	–	–	112.0	–
IX	–	1.498	–	1.510	–	–	–	113.6
X	1.540	–	–	1.497	–	–	111.9	–
XI	1.515	–	1.490	–	–	–	111.6	–
XII	1.505	–	1.504	–	–	–	115.0	–
XII′	1.526	–	1.508	–	–	–	116.1	–
XII″	1.493	–	1.538	–	–	–	113.9	–
XIII	1.516	–	1.520	–	–	–	111.9	–
XIV	–	1.475	–	–	1.465	–	–	115.9
XV	1.516	–	1.503	–	–	–	111.0	–
XVI	1.534	–	1.573	–	–	–	113.3	–
XVII	–	1.485	–	1.521	–	–	–	115.4
XVII′	–	1.517	–	1.506	–	–	–	116.7
XVIII	1.488	–	1.515	–	–	–	112.1	–
XIX	1.527	–	1.509	–	–	–	110.6	–
XIX′	1.526	–	1.520	–	–	–	110.9	–
XX	1.484	–	1.535	–	–	–	111.0	–
XXI	1.498	–	1.509	–	–	–	111.2	–
XXI′	1.519	–	1.512	–	–	–	112.1	–
XXII	–	1.479	–	–	1.469	–	–	116.8
XXIII	1.502	–	1.528	–	–	–	111.0	–
XXIII′	1.487	–	1.515	–	–	–	111.3	–
XXIV	–	1.520	–	–	–	1.331	–	123.1
XXIV′	–	1.474	–	–	–	1.327	–	122.6
XXV	–	1.576	–	–	–	1.317	–	122.5
XXVI	1.494	–	1.498	–	–	–	111.2	–
XXVII	1.494	–	1.503	–	–	–	112.3	–
XXVIII	1.481	–	1.494	–	–	–	114.8	–

– indicates the absence of a particular type of bond/angle; ′ indicates the second independent molecule; ″ indicates the third independent molecule.

interactions that causes deviation in the corresponding bond distances.

The substitution of a group at the C3 position also causes a significant change in the value of bond angle C2—C3—C4 in ring *A*, depending upon whether C3 is sp^3 or sp^2 hybridized. The bond angle C2—C3—C4 in molecules with a substituent at the C3(sp^3) position varies from 109.0 to 116.1° (average value 112.0°). The bond angle C2—C3—C4 with C3(sp^3) in molecules XII (115.0°), XII′ (116.1°), XII″ (113.9°) and XVI (113.3°) shows a significant deviation from the tetrahedral value of 109.46°. The deviation in the C2—C3—C4 bond angle in these molecules is caused by O—H···O intermolecular interactions, which are probably due to the presence of the OH group at the C3 position. The bond angle C2—C3—C4 with C3(sp^2) in molecules with a substituent at the C3 position varies from 113.6 to 118.5° (average value 117.1°). The bond angle C2—C3—C4 with C3(sp^2) in molecules IX (113.6°), XIV (115.9°), XVII (115.4°), XVII′ (116.7°) and XXII (116.8°) shows some deviation from the value of 120.0° for sp^2-type hybridization. The presence of a ketone group makes the C2—C3—C4 bond angle deviate significantly and it also results in the occurrence of C—H···O/O—H···O intra- and intermolecular interactions.

2.2. Ring conformations

The most predominant parameters that play an important role in describing the conformation of five- and six-membered moieties of steroidal molecules are asymmetry parameters (ΔC_2 and ΔC_S) (Duax & Norton, 1975). The asymmetry parameters have been calculated for the individual ring systems of all the molecules (I–XXVIII) and their detailed analysis shows the existence of different types of conformations. These conformations as obtained for individual ring systems are presented in Table 3.

The following observations can be made from the different ring conformations as adopted by individual ring systems of molecules I–XXVIII.

(i) There is hardly any observable effect of the substituents at the C3 atom or any other position on the conformation of ring *A*; but, owing to multiple bonds and quasi-*trans* ring

Table 3
Different types of conformations in the individual ring systems (molecules I–XXVIII).

Molecule	Ring *A*	Ring *B*	Ring *C*	Ring *D*
I	Normal chair	Half-chair	Twist	Envelope
II	Sofa	Normal chair	Normal chair	Intermediate between envelope & half-chair
III	Normal chair	Normal chair	Normal chair	Half-chair
IV	Normal chair	Half-chair	Normal chair	Intermediate between envelope & half-chair
IV′	Normal chair	Half-chair	Normal chair	Intermediate between envelope & half-chair
V	Normal chair	Half-chair	Normal chair	Intermediate between envelope & half-chair
VI	Normal chair	Half-chair	Twist	Half-chair
VII	Intermediate between sofa & half-chair	Distorted chair	Normal chair	Half-chair
VIII	Normal chair	Half-chair	Normal chair	Half-chair
VIII′	Normal chair	Half-chair	Normal chair	Intermediate between envelope & half-chair
IX	Normal chair	Half-chair	Normal chair	Half-chair
X	Distorted chair	Intermediate between sofa & half-chair	Normal chair	Envelope
XI	Normal chair	Half-chair	Normal chair	Intermediate between envelope & half-chair
XII	Normal chair	Sofa	Half-chair	Envelope
XII′	Normal chair	Intermediate between sofa & half-chair	Half-chair	Envelope
XII′′	Normal chair	Intermediate between sofa & half-chair	Half-chair	Envelope
XIII	Normal chair	Half-chair	Normal chair	Envelope
XIV	Sofa	Intermediate between sofa & half-chair	Normal chair	Intermediate between envelope & half-chair
XV	Normal chair	Normal chair	Normal chair	Intermediate between envelope & half-chair
XVI	Normal chair	Distorted chair	Half-chair	Envelope
XVII	Distorted chair	Twist	Intermediate between sofa & half-chair	Envelope
XVII′	Distorted chair	Twist	Half-chair	Envelope
XVIII	Normal chair	Normal chair	Normal chair	Half-chair
XIX	Normal chair	Half-chair	Normal chair	Intermediate between envelope & half-chair
XIX′	Normal chair	Half-chair	Normal chair	Intermediate between envelope & half-chair
XX	Normal chair	Half-chair	Normal chair	Intermediate between envelope & half-chair
XXI	Normal chair	Normal chair	Normal chair	Intermediate between envelope & half-chair
XXI′	Normal chair	Normal chair	Normal chair	Intermediate between envelope & half-chair
XXII	Sofa	Distorted chair	Normal chair	Half-chair
XXIII	Normal chair	Half-chair	Normal chair	Envelope
XXIII′	Normal chair	Sofa	Normal chair	Half-chair
XXIV	Intermediate between sofa & half-chair	Sofa	Normal chair	Envelope
XXIV′	Half-chair	Half-chair	Normal chair	Half-chair
XXV	Intermediate between sofa & half-chair	Sofa	Normal chair	Intermediate between envelope & half-chair
XXVI	Normal chair	Half-chair	Normal chair	Half-chair
XXVII	Normal chair	Half-chair	Normal chair	Half-chair
XXVIII	Sofa	Twist	Normal chair	Half-chair

fusions (*A*/*B*), ring *A* has different conformations. The same observations can be made for other rings.

(ii) The incidence of occurrence of a chair conformation in ring *A* is quite large (78%). The conformation of ring *A* is either sofa or intermediate between sofa and half-chair when there is a double bond in it and ring junction (*A*/*B*) is quasi-*trans*. Ring *A* in molecule XXVIII occurs in the sofa conformation ($\Delta C_2 = 37.9$, $\Delta C_S = 1.29$) although it is a saturated ring. This type of behaviour by the saturated ring may be due to the presence of an extra bond between C3 and C5.

(iii) The incidence of occurrence of a half-chair conformation in ring *B* is 46%. Ring *B* occurs in the sofa conformation when there is a double bond in it and ring fusions are quasi-*trans* (*A*/*B*) and *trans* (*B*/*C*). Ring *B* exists in the half-chair conformation if there is a double bond in it and the ring fusions are quasi-*trans*/*trans* (*A*/*B*) and *trans*/quasi-*trans* (*B*/*C*).

The conformation of saturated ring *B* is twist when ring fusion (*A*/*B*) is *trans* and there is a double bond between C8 and C9.

(iv) The incidence of occurrence of the chair conformation in ring *C* is quite large (78%). The saturated ring *C* exists in a twist conformation in the case of molecules I and VI and this is an uncommon feature for this type of ring in the steroid nucleus. The twist conformation in these molecules may be a result of the *cis* (*C*/*D*) ring junction and the presence of the double bond between C7 and C8.

(v) Ring *D* has a slight tendency towards a conformation intermediate between envelope and half-chair (38%).

2.3. Graphical presentation of ring conformations

In order to find the relative frequency of various types of conformations occurring in six-membered and five-membered rings in molecules I–XXVIII, pie charts have been drawn (Figs. 4*a*, *b*). From these charts, it is quite clear that the incidence of occurrence of the three six-membered rings in the chair conformation (normal as well as distorted-chair) is 60% followed by 21% for the half-chair. Similarly for the five-membered rings, the incidence of occurrence of the conformation intermediate between half-chair and envelope is 38% followed by half-chair and envelope conformations (32 and 30%, respectively).

3. Hydrogen bonding

During the period 1962–1980, interest in hydrogen bonding arose because of a misconception that hydrogen-bonded distances (*i.e.* *X*···*A* or H···*A*) should be less than the sum of the van der Waals radii. Some isolated examples of short C—H···O bonds in crystal structures were reported but none of these examples could revive any general interest (Palenik, 1965; Sundaralingam, 1966; Pletcher & Sax, 1972). A general survey as carried out by Taylor & Kennard (1982) for more than 100 organic crystal structures revealed the existence of a number of C—H···O, C—H···N and C—H···Cl interactions. The real turning point came from the publications of Steiner & Saenger (1992*a*,*b*), who examined the geometry of both C—H···O and O—H···O hydrogen bonds using the criteria H···O < 2.7 Å and ∠C—H···O > 90°, thereby confirming that 65% of the bonds were considered to have been formed as C—H···O hydrogen bonds.

Backed up by the recent studies that have been carried out by other workers (Steiner, 1996; Jeffery, 1997; Steiner, 1998; Desiraju & Steiner, 1999), we became interested in compiling and examining various kinds of hydrogen-bonded (C—H···O, O—H···O, O—H···N and N—H···O) interactions present in the molecules of the cholestane series of steroids (molecules I–XXVIII). We had the following aims and objectives.

(i) To find out whether intra- or intermolecular C—H···O/O—H···O/O—H···N/N—H···O bonding is dominant in this class of steroids and also if one type of interaction predominated over another.

Table 4
Geometry of C—H···O, O—H···O and O—H···N/N—H···O intra- and intermolecular interactions.

Molecule	*X*—H···*A*	*d*(H···*A*) (Å)	*D*(*X*···*A*) (Å)	θ(*X*—H···*A*) (°)
Intramolecular interactions				
XIV	C1—H1···O1	2.460	3.430	169.0
XVII	C2—H2*A*···O3	2.342	2.804	108.8
XXII	C4—H4*A*···O2	2.440	2.776	99.0
XXIII	C4—H4*A*···O3	2.670	3.150	111.0
	C15—H15*B*···O1	2.436	2.913	110.0
	C4′—H4′*B*···O3′	2.796	3.230	108.0
	C15′—H15′*B*···O1′	2.472	2.925	108.3
XXIV	O1—H1···O1′	2.670	3.190	122.9
	O1′—H1′···O1′	2.738	3.191	111.6
	C15—H15*A*···O1′	2.612	3.204	119.6
	C15′—H15′*A*···O1	2.568	3.402	144.2
	O1—H1···N1′	2.005	2.768	154.7
	O1′—H1′···N1	2.173	2.889	146.0
	O1′—H1′···N1′	2.558	3.057	112.0
XXV	C15—H15*B*···O1	2.490	2.890	104.9
XXVI	C3—H3···O2	2.210	2.590	101.9
	C30—H30*A*···O2	2.670	2.880	92.3
XXVII	C19—H19*A*···O2	2.720	3.154	108.1
Intermolecular interactions				
II	C26—H26C···O1	2.710	3.520	142.8
VIII	O1—H1O···O2	1.850	2.840	145.6
	O3—H3O···O1	1.860	2.790	141.3
	O2—H2O···O2′	1.780	2.750	150.1
	O2′—H′2O···O1	1.770	2.770	152.7
	O1′—H1O···O3′	1.810	2.790	141.8
	O3′—H3O···O3	1.750	2.730	148.4
XII	O1(*W*)—H1(*W*)···O3	1.761	2.785	147.7
	O1(Ac)—H···O3′	1.870	2.903	142.5
	O1(*W*)—H2(*W*)···O3″	1.720	2.722	151.7
	O1(Ac)—H···O1(*W*)	1.890	2.928	140.2
XIV	O1(*W*)—H1(*W*)···O4	2.150	3.085	174.0
	O1(*W*)—H2(*W*)···O1	1.780	2.799	170.0
XV	C1—H1*B*···O6	2.584	3.487	154.9
	C2—H2*B*···O6	2.720	3.572	146.9
XVI	O3—H3O···O3	2.180	2.979	165.0
XVIII	C19—H19*B*···O30(1)	2.670	3.570	157.1
	C29—H29*C*···O30(2)	2.720	3.320	120.8
XIX	C4—H4*A*···O2′	2.554	3.441	152.0
	C4′—H4′*A*···O2	2.590	3.459	149.2
	C19′—H19′C···O1	2.631	3.553	160.8
	C17′—H17′···O1	2.659	3.584	157.6
	C26′—H26′*C*···O2	2.734	3.584	148.0
	C27′—H27′*B*···O2	2.660	3.528	150.6
XX	C1—H1*A*···O1	2.630	3.503	151.0
	C3—H3···O2	2.650	3.558	175.0
XXI	N2—H1···O3′	1.936	2.872	174.2
	N3—H3*A*···O2	2.101	2.931	161.8
	N2′—H2′*A*···O3	2.046	2.843	153.5
XXII	C1—H1*A*···O2	2.570	3.274	122.0
	C27—H27*A*···O1	2.660	3.487	144.0
XXIII	C2′—H2′*B*···O3′	2.704	3.427	131.6
XXIV	C19—H19*A*···O1	2.762	3.661	156.1
	C19—H19*A*···O1′	2.765	3.697	163.7
	C1′—H1′*B*···O1	2.524	3.480	168.3
XXV	C11—H11*A*···O1	2.980	3.810	143.7
	C19—H19*A*···O1	2.650	3.600	167.9
	C27—H27*B*···O1	2.940	3.650	166.4
XXVII	C8—H8···O2	2.420	3.050	130.9
XXVIII	C2—H2*B*···O1	2.730	3.580	102.5
	C4—H4*A*···O2	2.610	3.660	147.3

(*W*) water molecule; (Ac) acetone molecule.

(ii) To examine the role of hydrogen bonding in crystal packing through solvent–solute and solvent–solvent interactions.

(iii) To make a small compendium of hydrogen bonding on a comparative graphical scale.

Comparative data of intra- and intermolecular interactions of the types C—H···O, O—H···O, O—H···N and N—H···O as observed in the steroidal molecules (I–XXVIII) are presented in Table 4.

Biochemical processes are transformations that occur in living organisms and involve a great variety of steroids, proteins, lipids, carbohydrates *etc.* and these complex substances make up some portion of the total weight of biochemical systems in which the main constituent is water (Rivelino *et al.*, 2004). All these groups are interconnected with water molecules by hydrogen bonds (Scheiner, 1997; Jeffery, 1997). The effects of solvents on the properties of organic and biological molecules have been successfully described using different and complementary theoretical models (Kollman, 1993; Cramer & Truhlar, 1999; Baldridge *et al.*, 2000). In this direction, the investigation as carried out by Allen & Tildesley (1987) on the solvation mechanism and the specific role of solute–solvent interactions could be used as a tool for supramolecular structures (Coutinho *et al.*, 2000; Canuto *et al.*, 2002).

O(*W*)—H(*W*)···O (solute) interactions have been observed in molecule XII. The three independent molecules are connected to one another through solvent–solute [O1(*W*)—H1(*W*)···O3, O1(acetone)—H(acetone)···O3′, O1(*W*)—H2(*W*)···O3′] and solvent–solvent [O1(acetone)—H(acetone)···O1(*W*)] hydrogen bonds. The solvent–solute interactions have also been observed in molecule XIV, in which the O atom of a water molecule acts as a proton donor.

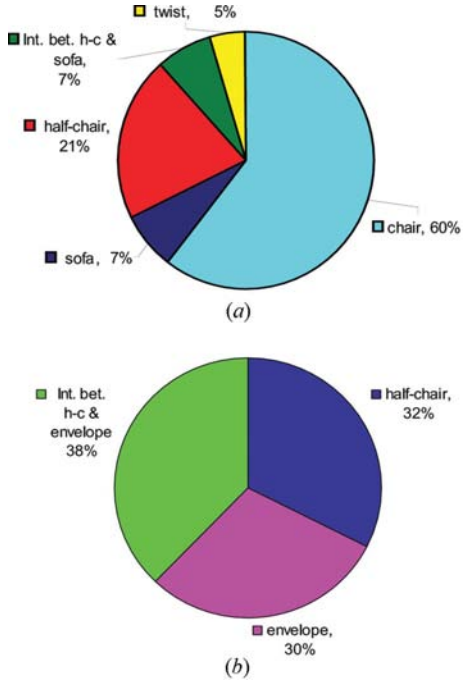

Figure 4
(*a*) Relative frequency of occurrence (in %) for various types of conformations in six-membered rings *A*, *B* and *C* (molecules I–XXVIII). (*b*) Relative frequency of occurrence (in %) for various types of conformation in five-membered ring *D* (molecules I–XXVIII).

Table 5
Range for $d(H\cdots A)$, $D(X\cdots A)$ and $\theta(X—H\cdots A)$ for C—H···O, O—H···O and O—H···N/N—H···O intra- and intermolecular hydrogen bonds.

Type of bond	$d(H\cdots A)$ range (Å)	$D(X\cdots A)$ range (Å)	$\theta(X—H\cdots A)$ range (°)
Intramolecular			
(*a*) C—H···O	2.210–2.720	2.590–3.430	92.3–169.0
(*b*) O—H···O	2.670–2.738	3.190–3.191	116.6–122.9
(*c*) O—H···N	2.005–2.558	2.768–3.057	112.0–154.7
Intermolecular			
(*a*) C—H···O	2.420–2.980	3.050–3.797	102.5–175.0
(*b*) O—H···O	1.720–2.180	2.730–3.085	140.2–174.0
(*c*) N—H···O	1.936–2.101	2.843–2.931	153.5–174.2

The solvent–solvent interactions as observed in molecule XII have been rarely found in steroids and such investigations might be important to understand the more complicated processes that occur for biomolecules in aqueous solutions (Rivelino et al., 2004).

From the available data of intramolecular interactions, it has been observed that the C atom is the most predominant hydrogen donor with frequency of occurrence 72.2% and the O atom acts as hydrogen acceptor with frequency of occurrence 83.3%. Most of the intramolecular C—H···O hydrogen bonds have been observed in molecules having a keto group. The overall $d(H\cdots A)$ range lies between 2.005 and 2.738 Å, the $D(X\cdots A)$ range is between 2.590 and 3.430 Å, and the angular range $\theta(X—H\cdots A)$ falls between 92.3 and 169.0°. The range for $d(H\cdots A)$, $D(X\cdots A)$ and angular range $\theta(X—H\cdots A)$ for C—H···O, O—H···O and O—H···N intramolecular hydrogen bonds is presented in Table 5.

In the case of intermolecular interactions, it has also been observed that that the C atom acts as the most predominant hydrogen donor with frequency of occurrence 61% and the O atom acts as hydrogen acceptor with frequency of occurrence 100%. Most of the intermolecular C—H···O hydrogen bonds are observed in molecules having a keto group. The overall range $d(H\cdots A)$ lies between 1.720 and 2.980 Å, the $D(X\cdots A)$ range is between 2.722 and 3.697 Å, and the angular range $\theta(X—H\cdots A)$ falls between 102.5 and 175.0°. The range for $d(H\cdots A)$, $D(X\cdots A)$ and angular range $\theta(X—H\cdots A)$ for C—H···O, O—H···O and N—H···O intermolecular hydrogen bonds are presented in Table 5.

On the basis of interaction data, it may be concluded that C—H···O hydrogen bonding is predominant (frequency of occurrence 64.4%) and it agrees well with the conclusions of Steiner & Saenger (1992*a*). The C—H···O hydrogen bond is observed mostly in molecules having a keto group as substituent and the O—H···O hydrogen bond is found in molecules having the OH group as substituent.

3.1. Graphical presentation of interactions

The main structural feature distinguishing the hydrogen bond from the other non-covalent interactions is the preference for linearity (Steiner, 2002). A better way to analyse

preferences is to draw d–θ and D–θ scatter plots. The plots include all contacts found in molecules I–XXVIII with d < 2.9 Å and D < 3.8 Å at any occurring angle.

The graphical projection of $d(H\cdots A)$ against $\theta(X—H\cdots A)$ and $D(X\cdots A)$ against $\theta(X—H\cdots A)$, *i.e.* d–θ and D–θ scatter plots, have been made for intramolecular interactions and are shown in Figs. 5(*a*) and 5(*b*), respectively. The d–θ and D–θ scatter plots have also been made for intermolecular interactions (Figs. 6*a* and 6*b*, respectively).

For intramolecular hydrogen bonds, the following observations can be made.

(i) In the case of the C—H···O type of hydrogen bond, density of spots [for $d(H\cdots A)$ = 2.40–2.67 Å and $D(X\cdots A)$ = 2.85–3.15 Å] is predominant in the $\theta(X—H\cdots A)$ range ~100–112°.

(ii) For the O—H···O type of hydrogen bond, the density of spots [for $d(H\cdots A)$ = 2.67–2.75 Å and $D(X\cdots A)$ = 3.18–3.19 Å] is predominant in the $\theta(X—H\cdots A)$ range ~112–122°.

(iii) The density of spots is greater in the $d(H\cdots A)$ range 2.0–2.17 Å and $D(X\cdots A)$ range 2.77–2.88 Å for $\theta(X—H\cdots A)$ in the range ~146–155° in the case of O—H···N hydrogen bonds.

(iv) The incidence of occurrence of C—H···O intramolecular hydrogen bonds is 72.2%; it is 11.1 and 16.6% for O—H···O and O—H···N hydrogen bonds, respectively.

For intermolecular hydrogen bonds, the following observations can be made.

(i) The density of spots [for $d(H\cdots A)$ = 2.55–2.75 Å and $D(X\cdots A)$ = 3.45–3.68 Å] is predominant in the $\theta(X—H\cdots A)$ range ~145–170° in the case of C—H···O hydrogen bonds.

(ii) For the O—H···O type of hydrogen bond, the density of spots is greater in the $d(H\cdots A)$ range 1.72–1.87 Å and $D(X\ldots A)$ range 2.7–2.9 Å for $\theta(X—H\cdots A)$ in the range ~140–155°.

(iii) In the case of N—H···O hydrogen bonds, the density of spots [for $d(H\cdots A)$ = 2.04–2.10 Å and $D(X\cdots A)$ = 2.85–2.93 Å] is predominant for $\theta(X—H\cdots A)$ in the range ~153–174.°

(iv) The frequency of occurrence of C—H···O, O—H···O and N—H···O intermolecular hydrogen bonds is 61, 31.7 and 7.3%, respectively.

There are densely populated clusters of data points at short distances and fairly linear angles and each point in these clusters represents a hydrogen bond. Plots analogous to these figures have been published for other kinds of hydrogen bonds, such as O—H···O, C—H···O (Steiner & Saenger, 1992*a*,*b*) and N—H···O (Olovsson & Jonsson, 1976). These plots show the same general features (preference for linearity), which indicates that the angular characteristics of all kinds of hydrogen bonds are related.

Upon comparison of the frequency of contacts from H(C) to O and N, *vis-a-vis* their crystal structures, it is observed that H(C) atoms have a statistical preference for contacts to 'O' rather than 'C' or 'N' atoms. For O and N atoms to act as

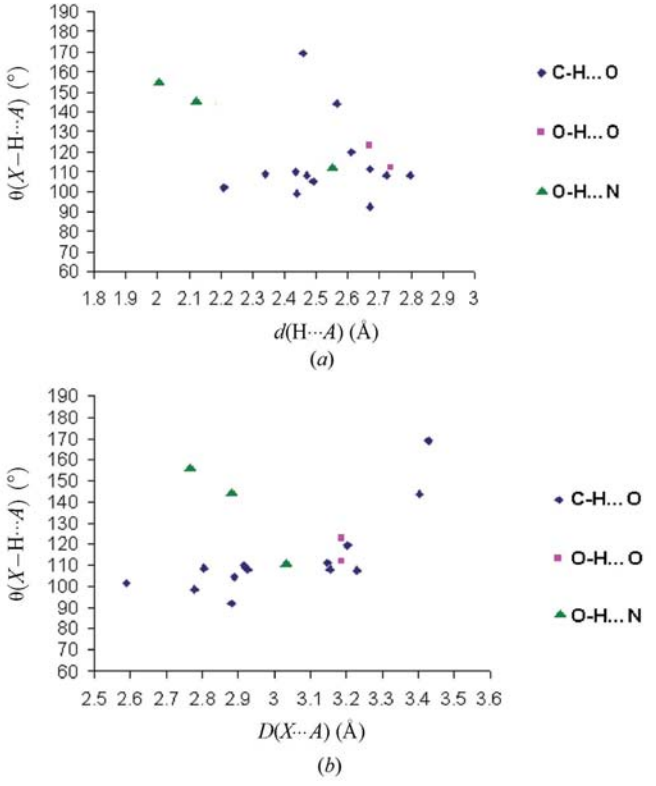

Figure 5
(*a*) d–θ scatter plot for intramolecular C—H···O, O—H···O and O—H···N hydrogen bonds. (*b*) D–θ scatter plot for intramolecular C—H···O, O—H···O and O—H···N hydrogen bonds.

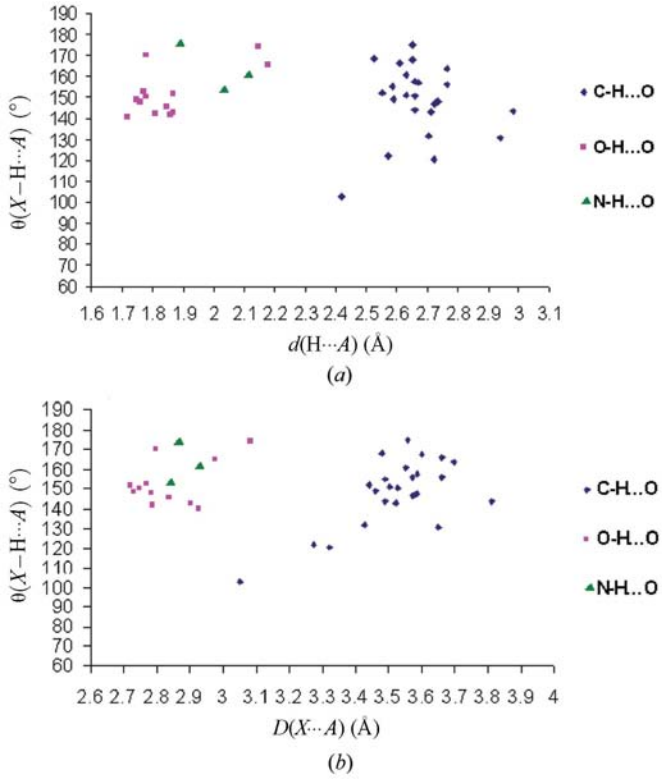

Figure 6
(*a*) d–θ scatter plot for intermolecular C—H···O, O—H···O and N—H···O hydrogen bonds. (*b*) D–θ scatter plot for intermolecular C—H···O, O—H···O and N—H···O hydrogen bonds.

acceptors, the relative frequency of their occurrence in molecules I–XXVIII is 94.9 and 5.1%, respectively. The C atoms act as donors but not as acceptors in molecules I–XXVIII. Most of the C—H···O contacts have distance d(H···O) less than 2.7 Å and, based on the criterion that the van der Waals distance should be < 2.7 Å, it was regarded as a certain indication of hydrogen bonding. The geometrical characteristics of C—H···O contacts are similar to those of O—H···O, N—H···O and O—H···N hydrogen bonds and this indicates the property of directionality on the donor as well as on the acceptor side of the contacts. It was mostly through a consideration of the effects of C—H···O and O—H···O hydrogen bonds on the crystal packing that a relaxation of the distance criteria became necessary (Desiraju, 1991; Desiraju & Steiner, 1999).

4. Concluding remarks

The research work reported in this article is another statement in the chemical-crystallographic relation that has existed between X-ray crystallography and organic chemistry throughout the last century (Dunitz, 1981). This relationship is quite friendly and may lead to unexpected and fruitful developments in both subjects. The crystallographic comparison of some geometrical and structural features for a series of cholestane derivatives shows that substituents are mostly located at the C3 position of the steroid nucleus. These substituents are linked by either intra- or intermolecular hydrogen bonds, which helps us in understanding the stacking interactions in supramolecular structures. The lengthening and shortening of bond distances C2—C3 and C3—C4 could be due to the involvement of the substituents (at the C3 position) in hydrogen-bonding interactions. The deviation of the C2—C3—C4 bond angle from its normal value could also be affected by hydrogen bonds. The bending in this bond angle typically amounts to only few degrees, which resembles the results shown by Desiraju & Steiner (1999). The importance of hybridization (single/double bond) and ring fusions (*cis*/*trans*) for the conformation of individual ring systems and stability of cholestane molecules has been studied.

Upon comparison of intra- and intermolecular hydrogen bonds, the C—H···O hydrogen bonding has been found to be predominant and the frequent contacts from H(C) atoms have a statistical preference to 'O' rather than 'C' and 'N' atoms. The presence of solvent leads to the formation of solvent–solute and solvent–solvent intermolecular interactions. The understanding of intermolecular interactions in crystal packing and utilization of such understandings in the design of new molecules/supramolecules with desired physical and chemical properties is the future intention for chemists/crystallographers.

The correspondence author (Rajnikant) is grateful to the Science and Engineering Council of the Department of Science & Technology, Government of India, for funding under a sponsored research project (No. SR/S2/CMP-47/2003). One of the co-authors (Dinesh) is grateful to Professor M. Nespolo, Faculty of Sciences, Henri Poincaré University, Nancy, France, for providing international air fare for attending the workshop.

References

Allen, F. H., Kennard, O., Watson, D. G., Bramer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
Allen, M. P. & Tildesley, D. J. (1987). *Computer Simulation of Liquid*. New York: Oxford University Press.
Baldridge, K. K., Jonas, V. & Bain, A. D. (2000). *J. Chem. Phys.* **113**, 7519–7529.
Bartell, L. S. & Bonham, R. A. J. (1960). *J. Chem. Phys.* **32**, 824–826.
Boer, D. R., Kooijman, H., Groen, M., van der Louw, J., Kelder, J. & Kroon, J. (2001). *Acta Cryst.* C**57**, 1177–1181.
Canuto, S., Coutinho, K. & Trzesniak, D. (2002). *Adv. Quantum Chem.* **41**, 161–167.
Chandross, R. J. & Bordner, J. (1977). *Acta Cryst.* B**33**, 2934–2937.
Coutinho, K., Canuto, S. & Zerner, M. C. (2000). *J. Chem. Phys.* **112**, 9874–9880.
Cramer, C. J. & Truhlar, D. G. (1999). *Chem. Rev.* **99**, 2161–2200.
Desiraju, G. R. (1991). *Acc. Chem. Res.* **24**, 270–276.
Desiraju, G. R. & Steiner, T. (1999). *The Weak Hydrogen Bond in Structural Chemistry and Biology*. IUCr/Oxford University Press.
Duax, W. L. & Norton, D. A. (1975). *Atlas of Steroid Structure*, Vol. 1, p. 18. New York: Plenum Press.
Dunitz, J. D. (1981). *Structural Studies on Molecules of Biological Interest*, pp. 47–59. Oxford: Clarendon.
Gilliland, G. L., Newcomer, M. E., Parish, E. J., Schroepfer, G. J. & Quiocho, F. A. (1977). *Acta Cryst.* B**33**, 3117–3121.
Grochulski, P., Wawrzak, Z. & Galdecki, Z. (1991). *Acta Cryst.* C**47**, 682–684.
Guy, J. J., Allen, F. H., Kennard, O. & Sheldrick, G. M. (1977). *Acta Cryst.* B**33**, 1236–1244.
Ilyin, S. G., Antonov, A. S., Stonik, V. A., Antipin, A. Y. & Elyakov, G. B. (1998). *Acta Cryst.* C**54**, 1156–1158.
Jeffery, G. A. (1997). *An Introduction to Hydrogen Bonding*, pp. 400–408. New York: Oxford University Press.
Kennedy, A. R., Pitt, A. R., Suckling, C. J., Suckling, K. E. & Thomas, M. (1999). *Acta Cryst.* C**55**, 1570–1572.
Kok, A. J. de & Romers, C. (1974). *Acta Cryst.* B**30**, 1695–1701.
Kollman, P. (1993). *Chem. Rev.* **93**, 2395–2417.
Losman, D. & Karlsson, R. (1978). *Acta Cryst.* B**34**, 2586–2589.
Losman, D., Karlsson, R., Declercq, J. P. & Germain, G. (1976). *Acta Cryst.* B**32**, 2513–2515.
Makin, H. L. J. (1975). *Biochemistry of Steroid Hormones*, pp. 4–5. Oxford: Blackwell Scientific Publications.
Nassimbeni, L. R., Russell, J. C. & Cragg, G. M. L. (1977). *Acta Cryst.* B**33**, 3755–3758.
Olovsson, I. & Jonsson, P. G. (1976). *The Hydrogen Bond. Recent Developments in Theory and Experiment*, pp. 393–456. Amsterdam: North Holland.
Palenik, G. J. (1965). *Acta Cryst.* **19**, 47–55.
Pletcher, J. & Sax, M. (1972). *J. Am. Chem. Soc.* **94**, 3998–4002.
Rajalakshmi, K., Pattabhi, V., Venkatesan, C. S., Nadamuni, G. & Srikrishna, A. (2000). *Acta Cryst.* C**56**, e307–e308.
Rajnikant, Dinesh, Anshu Sawney, Mousmi & Shafiullah (2005). *Crystallogr. Rep.* **50**, 419–422.
Rajnikant, Dinesh & Bandhan Sharma (2005). *Crystallogr. Rep.* In the press.
Rajnikant, Dinesh, Kewal Gupta & Sonum Lotus (2005). *Bull. Mater. Sci.* In the press
Rajnikant, Dinesh & Mousmi (2005). *J. Chem. Crystallogr.* In the press.
Rajnikant, Gupta, V. K., Firoz, J., Shafiullah & Gupta, R. (2000). *Crystallogr. Rep.* **45**, 785–788.

Rajnikant, Gupta, V. K., Firoz, J., Shafiullah & Gupta, R. (2001*a*). *Cryst. Res. Technol.* **36**, 471–476.
Rajnikant, Gupta, V. K., Firoz, J., Shafiullah & Gupta, R. (2001*b*). *Crystallogr. Rep.* **46**, 415–418.
Rajnikant, Gupta, V. K., Khan, E. H., Shafi, S., Hashmi, S., Shafiullah, Varghese, B. & Dinesh (2001*a*). *Cryst. Res. Technol.* **36**, 1281–1288.
Rajnikant, Gupta, V. K., Khan, E. H., Shafi, S., Hashmi, S., Shafiullah, Varghese, B. & Dinesh (2001*b*). *Crystallogr. Rep.* **46**, 963–966.
Rajnikant, Gupta, V. K., Khan, E. H., Shafi, S., Hashmi, S., Shafiullah, Varghese, B. & Dinesh (2002). *Crystallogr. Rep.* **47**, 75–79.
Rajnikant, Gupta, V. K., Khan, E. H., Shafi, S., Shafiullah & Dinesh (2002). *J. Chem. Crystallogr.* **32**, 325–329.
Rajnikant, Gupta, V. K., Shafi, S., Khan, E. H., Firoz, J., Shafiullah & Gupta, R. (2001). *Cryst. Res. Technol.* **36**, 215–221.
Rivelino, R., Canuto, S. & Cautinho, K. (2004). *Braz. J Phys.* **34**, 84–89.
Scheiner, S. (1997). *Hydrogen Bonding: a Theoretical Perspective*. New York: Oxford University Press.
Sheldrick, G. M., Oeser, E., Caira, M. R., Nassimbeni, L. R. & Pauptit, R. A. (1976). *Acta Cryst.* B**32**, 1984–1987.
Socci, E. P., Farmer, B. L., Chabinyc, M. L., Fratini, A. V., Bunning, T. J. & Adams, W. W. (1995). *Acta Cryst.* C**51**, 888–891.
Steiner, T. (1996). *Crystallogr. Rev.* **6**, 1–57.
Steiner, T. (1998). *Acta Cryst.* B**54**, 456–463.
Steiner, T. (2002). *Angew. Chem. Int. Ed. Engl.* **41**, 48–50.
Steiner, T. & Saenger, W. (1992*a*). *Acta Cryst.* B**48**, 819–827.
Steiner, T. & Saenger, W. (1992*b*). *J. Am. Chem. Soc.* **114**, 10146–10154.
Sundaralingam, M. (1966). *Acta Cryst.* **21**, 495–506.
Sutton, L. E. (1965). *Tables of Interatomic Distances and Configurations in Molecules and Ions.* Spec. Publ. No. 18. London: The Chemical Society.
Taylor, R. & Kennard, O. (1982). *J. Am. Chem. Soc.* **104**, 5063–5070.
Wawrzak, Z., Grochulski, P. & Galdecki, Z. (1991). *Acta Cryst.* C**47**, 687–689.