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HBF_4 and HBr Salts of New Chiral Cyclens

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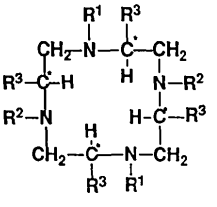
Abstract

The structures of salts of four new chiral cyclens (1,4,7,10-tetraazacyclododecane) have been determined: (2*RS*,5*RS*,8*RS*,11*SR*)-2,5,8,11-tetrabenzyl-1,4,7,10-tetraethyl-4,7,10-triaza-1-azoniacyclododecane tetrafluoroborate [$C_{44}H_{61}N_4^+.BF_4^-$, tetb = (2*RS*,5*RS*,8*RS*,11*SR*)-2,5,8,11-tetrabenzyl-1,4,7,10-tetraethylcyclen (I)], (2*R*,5*R*,8*R*,11*R*)-1,4,7,10-tetraethoxycarbonylmethyl-2,5,8,11-tetraethyl-4,10-diaza-1,7-diazoniacyclododecane bis(tetrafluoroborate) [$C_{32}H_{62}N_4O_8^{2+}.2BF_4^-$, tcte = (2*R*,5*R*,8*R*,11*R*)-1,4,7,10-tetraethoxycarbonylmethyl-2,5,8,11-tetraethylcyclen (II)], (2*R*,5*R*,8*R*,11*R*)-1,7-dibenzyl-2,5,8,11-tetraethyl-1,7-diaza-4,10-diazoniacyclododecane dibromide [$C_{30}H_{50}N_4^{2+}.2Br^-$, dbte = (2*R*,5*R*,8*R*,11*R*)-1,7-dibenzyl-2,5,8,11-tetraethyl-cyclen (III)], (2*R*,5*R*,8*R*,11*R*)-1,4,7,10-tetrabenzyl-2,5,8,11-tetraethyl-1,7-diaza-4,10-diazoniacyclododecane dibromide [$C_{44}H_{62}N_4^{2+}.2Br^-$, tbte = (2*R*,5*R*,8*R*,11*R*)-1,4,7,10-tetrabenzyl-2,5,8,11-tetraethyl-cyclen (IV)]. In forming salts, cyclen molecules are protonated. For the tetrafluoroborates of both (I) and (II), the 12-membered rings have a square conformation with the methylene C atoms occupying the corners. For the bromide of (III), the ring also has a square conformation with asymmetric C-atom occupied corners. The conformation of (IV)$H^{2+}.2Br^-$ differs significantly from that of the original molecule (IV). On protonation, the molecular symmetry changes from C_4 to C_2, and the corner atoms from N to asymmetric C.

Comment

Continuing our studies on chiral cyclens and their complexes (Tsuboyama, Tsubomaya, Higashi & Yanagita, 1970; Tsuboyama *et al.*, 1981; Kobayashi, Sakurai, Hasegawa, Tsuboyama & Tsuboyama, 1982), we report the structure determinations of four new cyclen salts. The first two compounds were obtained as cyclic tetramers from the corresponding *N*-substituted chiral aziridines, (*RS*)-1-ethyl-2-benzylaziridine and (*R*)-1-ethoxycarbonylmethyl-2-ethylaziridine, in the presence of $BF_3.Et_2O$ in benzene. Compound (III), (*RRRR*)-dbte, was obtained from the tetrabenzyl cyclen (IV), (*RRRR*)-tbte (Tsuboyama *et al.*, 1970), by symmetrical debenzylation. The HBF_4 salts were crystallized from the respective reaction mixtures. The anions are trapped so tightly in the crystals that the free bases could not be obtained by washing with alkaline solution. Few crystal structure determinations of HBF_4 salts of amines have so far been reported. Both (III) and (IV) were analyzed as their hydrobromides.



(I) tetb $R^1 = R^2 = Et$, $R^3 = CH_2Ph$
(II) tcte $R^1 = R^2 = CH_2COOEt$, $R^3 = Et$
(III) dbte $R^1 = CH_2Ph$, $R^2 = H$, $R^3 = Et$
(IV) tbte $R^1 = R^2 = CH_2Ph$, $R^3 = Et$
(V) te $R^1 = R^2 = H$, $R^3 = Et$

The analytical data were consistent with the presence of one BF_4^- species associated with (I), two with (II), and two Br ions with both (III) and (IV).

(I) HBF_4
(II) $2HBF_4$
(V) Free

(III) 2HBr
(IV) 2HBr

(IV) Free

The symmetries of these salts were identified as C_1 for (I) and C_2 for the latter three by ^1H or ^{13}C NMR spectra. In order to confirm the above assignment, and to examine the steric effects of chirality and ring substituents on ring formation, the structure determinations were carried out by X-ray analyses.

For molecule (I), the structure of the *RRRS* molecule is shown in Fig. 1(*a*). The configurations of the four chiral centers are consistent with those assigned by the spectral data. The square conformation of the 12-membered ring is a distorted cap form, similar to that of the C_1 molecule of (*RRRS* + *SSSR*)-tbte (Sakurai, Hiramatsu, Tsuboyama & Tsuboyama, 1980). The benzyl groups attached to the asymmetric *R* and *S* C atoms point in opposite directions from the ring. The H atom at N(4) was found by

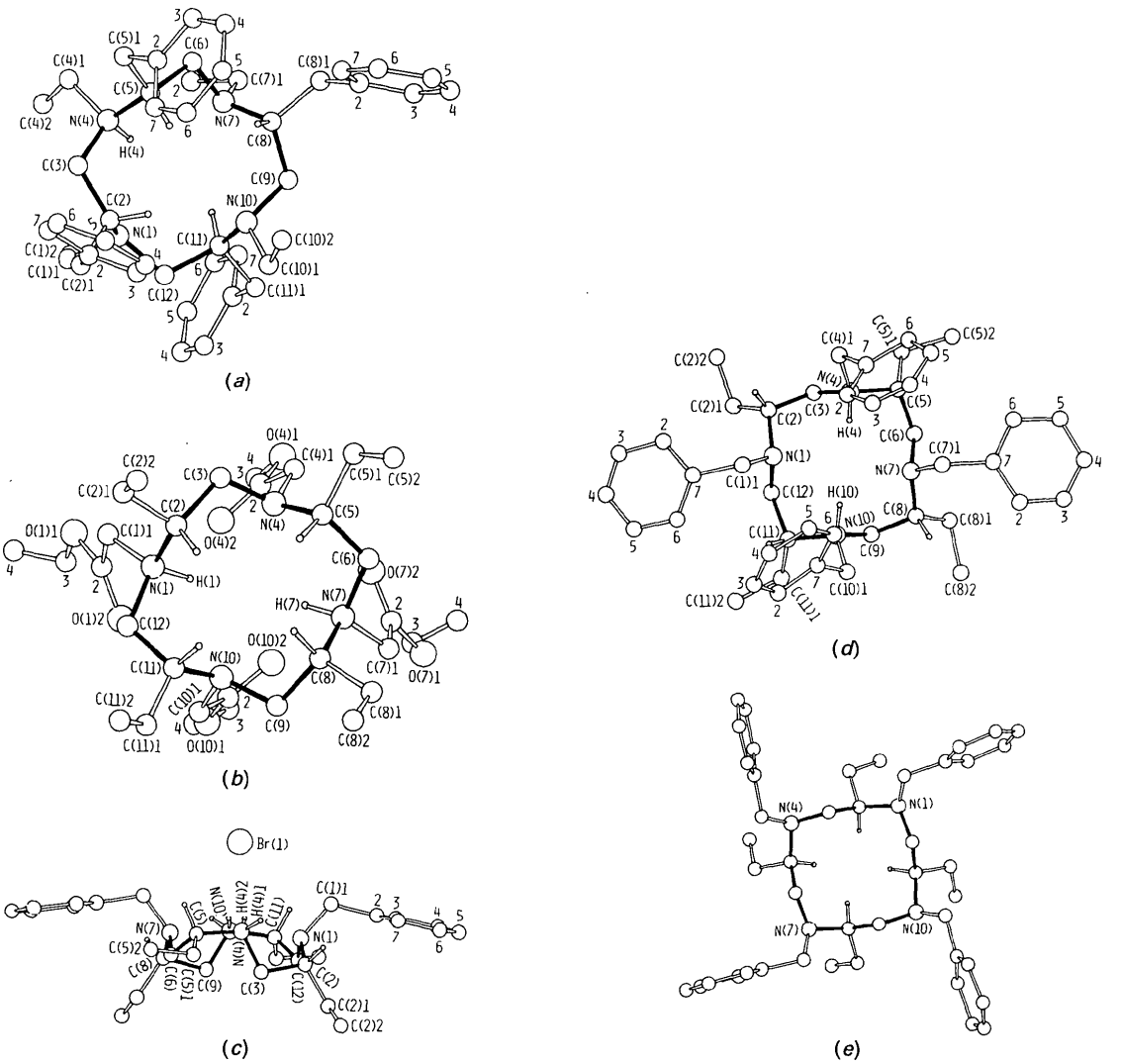


Fig. 1. The molecular structures of (*a*) (*RRRS*)-(I)H^+, (*b*) (II)H_2^{2+}, (*c*) (III)H_2^{2+} with Br(1) , (*d*) (IV)H_2^{2+} and (*e*) (*RRRR*)-(IV). For clarity, the H atoms are omitted, except for those attached to the chiral C atoms and the protonated N atoms.

difference Fourier synthesis and the bond lengths around the protonated N(4) atom are significantly longer than those of other N atoms. This N atom is situated in the least crowded region, for H atoms, of the chiral C atoms. In spite of the replacement of the substituent, the ring conformation of tetb is not significantly different from that of (*RRRS* + *SSSR*)-tbte.

For molecule (II) (Fig. 1*b*), the 12-membered ring has a square-crown shape similar to those of (*RRRR*)-te [(2*R*,5*R*,8*R*,11*R*)-2,5,8,11-tetraethylcyclen (V)] or (*RRRR*)-tbte (IV) having C_4 symmetry (Sakurai, Kobayashi, Tsuboyama & Tsuboyama, 1978*a*,*b*). In contrast with (IV), the methylene C atoms are at the corners. The torsion angles around the corner atoms are divided into two sets as shown in Table 2. Those involving C(3) and C(9) are more twisted than those involving C(6) and C(12). The form and direction of the *N*-substituents are also divided into two sets. The torsion angles C(*n*)2—O(*n*)1—C(*n*)3—C(*n*)4 (*n* = 1, 4, 7, 10) for the ethoxycarbonylmethyl groups are 138 (4), −169 (4), 107 (6) and −163 (3)°, respectively. The overall conformation of the molecule is, therefore, approximate C_2 symmetry.

Although the H atoms attached to N atoms were not identified directly owing to a high *R* value, the bond lengths around N(1) and N(7) are slightly longer than those around N(4) and N(10), as shown in Table 2. It is likely that N(1) and N(7) are protonated symmetrically. Thus, in forming the salts, the molecular symmetry of (II), C_4, has

changed to C_2 as was assigned based on the NMR spectral data. Bond parameters of the BF_4 ion for both structures show typical tetrahedral geometry.

Molecule (III) (Fig. 1*c*) has two symmetrical *N*-substituents. The 12-membered ring has a square conformation with the asymmetric C atoms at the corners. The molecule lies on a crystallographic twofold axis at (0,0,*z*), which passes through the Br(1) ion and the center of the cyclen ring; Br(2) is situated on the other twofold axis at $(0,\frac{1}{2},z)$. Atoms N(7) to C(12) are generated from N(1) to C(6) by the symmetry operation $-x$, $-y$, z. Therefore, the overall molecular shape, including Br(1), looks like the five-coordinate Cu^{II} complex of (*RRRR*)-tbte which has asymmetric C corners with a Cl ion at the apex (Sakurai, Kobayashi, Hasegawa, Tsuboyama & Tsuboyama, 1982). The deviation of Br(1) from the mean plane formed by the four N atoms is 2.964 (4) Å. A similar deviation [2.941 (6) Å] of the apical Cl ion is observed in the tbte–Cu^{II} complex. The protonation is anticipated at the secondary amino group [N(4) or N(10)] owing to its stronger basicity. The H(N4)2 atom attached to N(4) was actually found from difference Fourier synthesis. A hydrogen bond exists between the protonated N(4) and the Br(2) atoms, and this hydrogen bond produces a zigzag chain of molecules along the *a* axis [N(4)···Br(2) 3.360 (8) Å, N(4)—H(N4)1···Br(2) 177 (10)°], as shown in the crystal packing (Fig. 2). The distance between N(4) and Br(1) is 3.507 (8) Å.

There is an example of an HBr salt of a 12-membered ring, azacyclododecane (Dunitz & Weber, 1964), where the protonated N atom is situated at the corner and is hydrogen bonded to the Br ion.

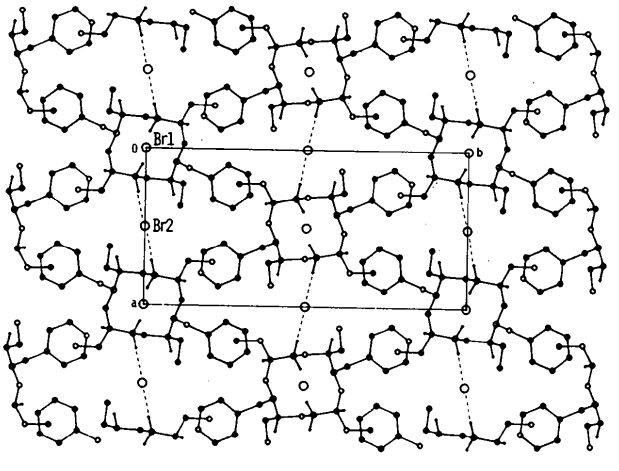


Fig. 2. The crystal structure of $(III)H_2^{2+}.2Br^-$ projected along the *c* axis. Dashed lines indicate the hydrogen bonds.

Regardless of their similar *RRRR* configurations, different corner-square rings are observed for (II).2HBF$_4$ and (III).2HBr. This may be due to the difference in bulk of the substituents. However, a question still remains as to how the original conformation differs on protonation. Comparison of the results of free molecule (IV) and its salt, $(IV)H_2^{2+}.2Br^-$ (Fig. 1*d*), gives an answer. The square structure of the original molecule (IV) (Sakurai *et al.*, 1978*b*; Sakurai *et al.*, 1983) has N-occupied corners, and four N substituents produce an 'open' conformation (Fig. 1*e*). On the other hand, the geometry for protonated (IV) drastically changes from having N corners to the asymmetric C corner structure with alternate 'open' and 'closed' conformations (Sakurai *et al.*, 1978*b*). Although the H atoms at the N atoms could not be found directly, bond lengths around N(4) and N(10) suggested the same symmetrical protonation pattern as in the cases of (II) and (III). Thus, a similar protonation pattern was assigned to N(4) and N(10) having the closed benzyl groups. As a result, the overall molecular symmetry becomes approximate C_2 with asymmetric C corners similar to $(III)H_2^{2+}.2Br^-$.

When the 12-membered chiral cyclen ring takes a square [3333] conformation (Dale, 1973), there are three different possibilities according to the kind of corner atom. For all free bases of the chiral cyclens determined so far, the methylene C atoms occupy the corners, except for (IV), which has N atoms at the corners. In the present protonated molecules, the observed ring structures are methylene C corners for $(I)H^+$ and $(II)H_2^{2+}$, and chiral C for $(III)H_2^{2+}$ and $(IV)H_2^{2+}$. Thus, all three corner forms actually appear. The results show that the ring form is controlled by a delicate balance between various factors including number of parameters, configurations, variety of C and N substituents and protonation.

Experimental

$(I)H^+.BF_4^-$

Crystal data

$C_{44}H_{61}N_4^+.BF_4^-$
M_r = 732.78
Monoclinic
$P2_1/c$
a = 23.386 (5) Å
b = 9.690 (2) Å
c = 20.367 (5) Å
β = 114.94 (2)°
V = 4185 (2) Å^3
Z = 4
D_x = 1.163 Mg m^{-3}
D_m = 1.162 Mg m^{-3}

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 20 reflections
θ = 9–11°
μ = 0.075 mm^{-1}
T = 293 K
Prismatic
0.68 × 0.55 × 0.34 mm
Colorless

Data collection

Rigaku AFC-4 diffractometer
ω and $\omega/2\theta$ (2θ>30°) scans
Absorption correction: none
9612 measured reflections
5709 independent reflections
5168 observed reflections [$|F_o| > 3\sigma(|F_o|)$]

θ_{max} = 27.5°
$h = -30 \rightarrow 30$
$k = 0 \rightarrow 12$
$l = 0 \rightarrow 26$
3 standard reflections
monitored every 100 reflections
intensity variation: −1.5%

Refinement

Refinement on F
R = 0.060
wR = 0.055
S = 1.50
5168 reflections
722 parameters
All H-atom parameters refined

$w = 1/(a|F_o|^2 + b|F_o| + c)$
$(\Delta/\sigma)_{max}$ = 0.75 [N(4); z]
$\Delta\rho_{max}$ = 0.33 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

(II)H_2^{2+}.2BF_4^-

Crystal data

$C_{32}H_{62}N_4O_8^{2+}.2BF_4^-$
M_r = 804.48
Orthorhombic
$P2_12_12_1$
a = 20.81 (1) Å
b = 15.03 (1) Å
c = 13.88 (1) Å
V = 4343 (5) Å^3
Z = 4
D_x = 1.231 Mg m^{-3}
D_m = 1.224 Mg m^{-3}

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 14 reflections
θ = 10-12°
μ = 0.102 mm^{-1}
T = 296 K
Prismatic
0.80 × 0.56 × 0.30 mm
Colorless

Data collection

Rigaku AFC-4 diffractometer
ω and $\omega/2\theta$ (2θ>30°) scans
Absorption correction: none
4898 measured reflections
2187 independent reflections
2032 observed reflections [$|F_o| > 3\sigma(|F_o|)$]

θ_{max} = 27.5°
$h = 0 \rightarrow 27$
$k = 0 \rightarrow 19$
$l = 0 \rightarrow 18$
4 standard reflections
monitored every 150 reflections
intensity variation: −0.14%

Refinement

Refinement on F
R = 0.108
wR = 0.096
S = 3.04
2001 reflections
735 parameters
All H-atom parameters refined

$w = 1/(a|F_o|^2 + b|F_o| + c)$
$(\Delta/\sigma)_{max}$ = 0.64 [F(2)2; β_{33}]
$\Delta\rho_{max}$ = 0.38 e Å^{-3}
$\Delta\rho_{min}$ = −0.30 e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

(III)H_2^{2+}.2Br^-

Crystal data

$C_{30}H_{50}N_4^{2+}.2Br^-$
M_r = 626.54

Mo $K\alpha$ radiation
λ = 0.71073 Å

Orthorhombic
$P2_12_12$
a = 9.973 (1) Å
b = 20.718 (3) Å
c = 7.541 (2) Å
V = 1558.2 (6) Å^3
Z = 2
D_x = 1.335 Mg m^{-3}
D_m = 1.338 Mg m^{-3}

Data collection

Rigaku AFC-4 diffractometer
ω and $\omega/2\theta$ (2θ>30°) scans
Absorption correction: none
1897 measured reflections
1402 independent reflections
1306 observed reflections [$|F_o| > 3\sigma(|F_o|)$]

Refinement

Refinement on F
R = 0.060
wR = 0.068
S = 2.18
1306 reflections
264 parameters
All H-atom parameters refined

(IV)H_2^{2+}.2Br^-

Crystal data

$C_{44}H_{62}N_4^{2+}.2Br^-$
M_r = 806.78
Orthorhombic
$P2_12_12_1$
a = 17.243 (3) Å
b = 17.873 (2) Å
c = 14.156 (2) Å
V = 4363 (1) Å^3
Z = 4
D_x = 1.228 Mg m^{-3}
D_m = 1.220 Mg m^{-3}

Data collection

Enraf-Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
5542 measured reflections
2560 independent reflections
2275 observed reflections [$|F_o| > 4\sigma(|F_o|)$]

Refinement

Refinement on F
R = 0.099
wR = 0.112
S = 5.83

Cell parameters from 20 reflections
θ = 10-12°
μ = 2.599 mm^{-1}
T = 293 K
Plate
0.55 × 0.35 × 0.20 mm
Colorless

θ_{max} = 27.5°
$h = 0 \rightarrow 12$
$k = 0 \rightarrow 26$
$l = 0 \rightarrow 9$
4 standard reflections
monitored every 100 reflections
intensity variation: −0.5%

$w = 1/(a|F_o|^2 + b|F_o| + c)$
$(\Delta/\sigma)_{max}$ = 0.72 [Br(1); β_{11}]
$\Delta\rho_{max}$ = 0.62 e Å^{-3}
$\Delta\rho_{min}$ = −0.50 e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 25 reflections
θ = 9-12°
μ = 1.871 mm^{-1}
T = 293 K
Plate
0.55 × 0.40 × 0.25 mm
Colorless

θ_{max} = 27.5°
$h = 0 \rightarrow 22$
$k = 0 \rightarrow 22$
$l = 0 \rightarrow 18$
3 standard reflections
frequency: 120 min
intensity variation: −10.0%

$w = 1/(a|F_o|^2 + b|F_o| + c)$
$(\Delta/\sigma)_{max}$ = 0.48 [C(10)3; β_{13}]
$\Delta\rho_{max}$ = 1.08 e Å^{-3}
$\Delta\rho_{min}$ = −0.63 e Å^{-3}

2275 reflections
699 parameters
All H-atom parameters refined

Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$B_{eq} = (4/3)\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}
(I)$H^+.BF_4^-$				
N(1)	0.3175 (1)	0.3593 (2)	0.4543 (1)	2.9 (1)
N(4)	0.3238 (1)	0.1226 (2)	0.5422 (1)	2.6 (1)
N(7)	0.3066 (1)	−0.0604 (2)	0.4196 (1)	3.2 (1)
N(10)	0.2326 (1)	0.1692 (2)	0.3182 (1)	3.5 (1)
C(2)	0.2671 (1)	0.3343 (3)	0.4784 (2)	2.9 (1)
C(3)	0.2946 (2)	0.2568 (3)	0.5497 (2)	3.1 (2)
C(5)	0.2745 (1)	0.0090 (3)	0.5148 (1)	2.7 (1)
C(6)	0.2988 (2)	−0.1079 (3)	0.4835 (2)	3.1 (2)
C(8)	0.2466 (1)	−0.0787 (3)	0.3540 (2)	3.2 (2)
C(9)	0.2402 (2)	0.0278 (3)	0.2962 (2)	3.9 (2)
C(11)	0.2879 (1)	0.2558 (3)	0.3303 (1)	3.1 (2)
C(12)	0.2921 (2)	0.3845 (2)	0.3759 (2)	3.3 (2)
C(1)1	0.3605 (2)	0.4726 (4)	0.4947 (2)	3.8 (2)
C(1)2	0.4233 (2)	0.4663 (6)	0.4892 (3)	5.4 (2)
C(4)1	0.3810 (2)	0.0851 (4)	0.6108 (2)	3.7 (2)
C(4)2	0.4375 (2)	0.1714 (6)	0.6210 (3)	5.4 (2)
C(7)1	0.3610 (2)	−0.1224 (4)	0.4121 (2)	4.5 (2)
C(7)2	0.4225 (2)	−0.0593 (8)	0.4621 (3)	7.2 (3)
C(10)1	0.1723 (2)	0.2303 (4)	0.2690 (2)	5.3 (2)
C(10)2	0.1164 (2)	0.1600 (7)	0.2741 (4)	7.7 (3)
C(2)1	0.2323 (2)	0.4639 (3)	0.4862 (2)	3.5 (2)
C(2)2	0.1699 (1)	0.4310 (3)	0.4882 (2)	3.7 (2)
C(2)3	0.1175 (2)	0.4058 (4)	0.4242 (2)	4.9 (2)
C(2)4	0.0594 (2)	0.3773 (4)	0.4244 (4)	6.6 (3)
C(2)5	0.0531 (3)	0.3754 (4)	0.4878 (4)	7.5 (3)
C(2)6	0.1042 (3)	0.3994 (5)	0.5513 (4)	7.0 (3)
C(2)7	0.1631 (2)	0.4275 (4)	0.5525 (2)	4.9 (2)
C(5)1	0.2519 (1)	−0.0386 (3)	0.5718 (2)	3.3 (2)
C(5)2	0.1824 (1)	−0.0739 (3)	0.5357 (2)	3.3 (2)
C(5)3	0.1613 (2)	−0.2087 (3)	0.5234 (2)	4.3 (2)
C(5)4	0.0979 (2)	−0.2386 (4)	0.4862 (3)	5.4 (2)
C(5)5	0.0543 (2)	−0.1357 (4)	0.4619 (2)	5.3 (2)
C(5)6	0.0742 (2)	−0.0006 (4)	0.4749 (3)	6.1 (3)
C(5)7	0.1374 (2)	0.0291 (4)	0.5107 (2)	5.0 (2)
C(8)1	0.2382 (2)	−0.2273 (3)	0.3242 (2)	3.7 (2)
C(8)2	0.1710 (2)	−0.2741 (3)	0.2819 (2)	3.9 (2)
C(8)3	0.1502 (2)	−0.3198 (5)	0.2119 (2)	6.3 (3)
C(8)4	0.0900 (3)	−0.3734 (6)	0.1755 (3)	8.7 (3)
C(8)5	0.0502 (3)	−0.3799 (6)	0.2082 (3)	8.3 (3)
C(8)6	0.0694 (2)	−0.3323 (6)	0.2774 (3)	7.1 (3)
C(8)7	0.1298 (2)	−0.2806 (5)	0.3142 (2)	5.5 (2)
C(11)1	0.2937 (2)	0.3004 (4)	0.2601 (2)	3.9 (2)
C(11)2	0.3590 (2)	0.3508 (3)	0.2758 (2)	3.8 (2)
C(11)3	0.3726 (2)	0.4910 (4)	0.2761 (2)	4.4 (2)
C(11)4	0.4336 (2)	0.5355 (5)	0.2935 (2)	5.6 (2)
C(11)5	0.4812 (2)	0.4433 (6)	0.3100 (2)	6.2 (3)
C(11)6	0.4693 (2)	0.3037 (5)	0.3102 (2)	6.1 (3)
C(11)7	0.4081 (2)	0.2582 (4)	0.2927 (2)	4.8 (2)
B	0.3485 (2)	−0.1230 (4)	0.1886 (2)	4.8 (3)
F(1)	0.3929 (1)	−0.1245 (3)	0.2580 (1)	9.0 (2)
F(2)	0.3650 (1)	−0.2010 (3)	0.1440 (2)	8.6 (2)
F(3)	0.2949 (1)	−0.1779 (4)	0.1878 (2)	11.1 (2)
F(4)	0.3394 (2)	0.0077 (3)	0.1665 (2)	12.5 (2)
(II)$H_2^{2+}.2BF_4^-$				
N(1)	0.026 (1)	0.217 (1)	0.105 (1)	5.6 (5)
N(4)	0.074 (1)	0.366 (1)	−0.024 (1)	5.5 (4)
N(7)	0.209 (1)	0.317 (1)	−0.008 (1)	5.9 (5)
N(10)	0.160 (1)	0.172 (1)	0.124 (1)	5.3 (4)
C(2)	0.020 (1)	0.320 (1)	0.131 (1)	6.3 (6)
C(3)	0.016 (1)	0.371 (1)	0.034 (1)	6.7 (7)
C(5)	0.123 (1)	0.432 (1)	0.002 (2)	7.1 (7)
C(6)	0.189 (1)	0.410 (1)	−0.032 (2)	6.6 (7)
C(8)	0.226 (1)	0.309 (1)	0.101 (1)	6.0 (5)
C(9)	0.225 (1)	0.210 (1)	0.129 (1)	6.0 (6)
C(11)	0.121 (1)	0.188 (1)	0.215 (1)	5.4 (7)
C(12)	0.053 (1)	0.171 (1)	0.195 (1)	6.4 (6)
C(2)1	−0.042 (1)	0.337 (1)	0.188 (2)	7.6 (8)
C(2)2	−0.034 (2)	0.415 (3)	0.252 (4)	18.0 (13)
C(5)1	0.105 (1)	0.529 (1)	−0.034 (2)	10.1 (9)
C(5)2	0.143 (2)	0.601 (2)	0.003 (3)	14.0 (14)
C(8)1	0.294 (1)	0.351 (2)	0.130 (2)	8.9 (7)
C(8)2	0.305 (1)	0.359 (2)	0.227 (3)	11.3 (9)
C(11)1	0.143 (1)	0.139 (1)	0.304 (2)	8.3 (10)
C(11)2	0.125 (2)	0.177 (4)	0.396 (2)	18.3 (15)
C(1)1	−0.035 (1)	0.176 (1)	0.070 (1)	5.7 (5)
C(1)2	−0.022 (1)	0.090 (1)	0.020 (1)	6.9 (8)
C(1)3	−0.062 (2)	−0.022 (2)	−0.082 (4)	16.5 (15)
C(1)4	−0.112 (4)	−0.070 (2)	−0.076 (5)	26.8 (8)
C(4)1	0.060 (1)	0.366 (1)	−0.125 (1)	6.4 (7)
C(4)2	0.040 (1)	0.276 (1)	−0.161 (2)	9.3 (10)
C(4)3	0.022 (3)	0.181 (3)	−0.298 (2)	17.0 (12)
C(4)4	0.024 (4)	0.183 (4)	−0.381 (4)	22.7 (8)
C(7)1	0.263 (1)	0.288 (1)	−0.071 (1)	7.0 (7)
C(7)2	0.240 (1)	0.261 (2)	−0.167 (2)	10.3 (10)
C(7)3	0.261 (3)	0.154 (3)	−0.314 (4)	18.1 (13)
C(7)4	0.279 (5)	0.205 (5)	−0.367 (5)	36.8 (8)
C(10)1	0.163 (1)	0.079 (1)	0.098 (2)	6.4 (6)
C(10)2	0.169 (1)	0.064 (1)	−0.003 (2)	7.2 (7)
C(10)3	0.168 (2)	−0.040 (2)	−0.127 (3)	12.0 (10)
C(10)4	0.148 (3)	−0.121 (3)	−0.151 (4)	15.8 (8)
O(1)1	−0.071 (1)	0.062 (1)	−0.031 (1)	10.2 (5)
O(1)2	0.029 (1)	0.050 (1)	0.025 (1)	8.0 (5)
O(4)1	0.032 (1)	0.275 (1)	−0.254 (1)	11.4 (7)
O(4)2	0.035 (1)	0.211 (1)	−0.114 (1)	10.0 (5)
O(7)1	0.285 (1)	0.222 (2)	−0.218 (1)	15.1 (8)
O(7)2	0.187 (1)	0.279 (1)	−0.198 (1)	10.4 (6)
O(10)1	0.166 (1)	−0.017 (1)	−0.032 (1)	7.8 (4)
O(10)2	0.177 (1)	0.123 (1)	−0.065 (1)	10.2 (6)
B(1)	0.365 (2)	0.062 (4)	0.063 (5)	17 (3)
F(1)1	0.372 (1)	0.142 (1)	0.061 (1)	13.9 (5)
F(1)2	0.315 (1)	0.027 (1)	0.112 (2)	15.6 (5)
F(1)3	0.415 (1)	0.017 (2)	0.089 (3)	24.1 (9)
F(1)4	0.359 (2)	0.037 (3)	−0.028 (2)	29.6 (11)
B(2)	−0.145 (3)	0.013 (3)	0.222 (4)	14 (2)
F(2)1	−0.101 (1)	0.065 (1)	0.239 (2)	16.7 (6)
F(2)2	−0.175 (1)	0.021 (2)	0.136 (2)	18.3 (7)
F(2)3	−0.134 (1)	−0.074 (1)	0.231 (1)	14.9 (5)
F(2)4	−0.197 (1)	0.026 (1)	0.284 (2)	16.0 (5)
(III)$H_2^{2+}.2Br^-$				
Br(1)	0	0	0.1453 (2)	3.70 (6)
Br(2)	1/2	0	−0.1024 (2)	5.31 (8)
N(1)	0.089 (1)	0.0938 (4)	−0.257 (1)	2.3 (2)
C(2)	0.206 (1)	0.0767 (4)	−0.367 (1)	2.6 (3)
C(3)	0.196 (1)	0.003 (1)	−0.407 (1)	2.7 (3)
N(4)	0.186 (1)	−0.0326 (4)	−0.239 (1)	2.4 (3)
C(5)	0.160 (1)	−0.1048 (4)	−0.257 (1)	2.3 (3)
C(6)	0.030 (1)	−0.1177 (4)	−0.352 (1)	2.1 (3)
C(1)1	0.127 (1)	0.135 (1)	−0.103 (1)	2.9 (3)
C(1)2	0.187 (1)	0.2021 (5)	−0.144 (1)	2.9 (3)
C(1)3	0.105 (1)	0.255 (1)	−0.151 (1)	3.4 (4)
C(1)4	0.161 (1)	0.316 (1)	−0.179 (1)	4.1 (4)
C(1)5	0.293 (1)	0.324 (1)	−0.198 (1)	3.8 (4)
C(1)6	0.376 (1)	0.271 (1)	−0.193 (2)	4.6 (5)
C(1)7	0.323 (1)	0.209 (1)	−0.161 (2)	4.2 (4)
C(2)1	0.227 (1)	0.1162 (5)	−0.538 (1)	3.2 (3)
C(2)2	0.366 (2)	0.108 (1)	−0.619 (3)	7.0 (6)
C(5)1	0.280 (1)	−0.1366 (4)	−0.346 (2)	3.0 (4)
C(5)2	0.276 (2)	−0.210 (1)	−0.333 (2)	4.2 (4)
(IV)$H_2^{2+}.2Br^-$				
Br(1)	−0.0356 (2)	0.6981 (1)	0.2615 (2)	5.93 (8)
Br(2)	0.0349 (2)	0.5911 (2)	−0.3017 (2)	8.59 (12)
N(1)	0.081 (1)	0.569 (1)	0.013 (1)	3.0 (4)
C(2)	0.030 (1)	0.626 (1)	−0.030 (1)	2.7 (4)
C(3)	−0.050 (2)	0.620 (1)	0.011 (2)	3.8 (5)
N(4)	−0.087 (1)	0.544 (1)	−0.001 (1)	3.7 (4)
C(5)	−0.155 (1)	0.529 (1)	0.063 (1)	3.5 (5)
C(6)	−0.130 (1)	0.511 (1)	0.162 (2)	3.4 (5)
N(7)	−0.074 (1)	0.446 (1)	0.165 (1)	3.2 (4)
C(8)	−0.035 (1)	0.439 (1)	0.254 (1)	3.9 (5)

C(9)	0.037 (1)	0.487 (1)	0.257 (1)	3.4 (5)
N(10)	0.091 (1)	0.468 (1)	0.178 (1)	3.4 (4)
C(11)	0.151 (1)	0.528 (1)	0.159 (2)	3.4 (5)
C(12)	0.115 (1)	0.592 (1)	0.103 (1)	2.6 (4)
C(2)1	0.057 (1)	0.710 (1)	−0.016 (2)	3.3 (5)
C(2)2	0.022 (1)	0.759 (1)	−0.092 (2)	3.7 (5)
C(5)1	−0.212 (1)	0.596 (1)	0.063 (2)	4.1 (5)
C(5)2	−0.293 (2)	0.572 (2)	0.100 (3)	7.4 (8)
C(8)1	−0.082 (2)	0.460 (2)	0.342 (2)	5.7 (7)
C(8)2	−0.040 (4)	0.431 (3)	0.436 (3)	11.1 (11)
C(11)1	0.194 (1)	0.553 (1)	0.247 (2)	4.5 (6)
C(11)2	0.277 (2)	0.576 (2)	0.233 (2)	5.5 (5)
C(1)7	0.209 (1)	0.588 (1)	−0.073 (1)	4.0 (5)
C(1)2	0.204 (1)	0.650 (1)	−0.130 (2)	3.5 (5)
C(1)3	0.269 (2)	0.698 (2)	−0.139 (2)	5.5 (7)
C(1)4	0.331 (2)	0.689 (2)	−0.090 (2)	4.9 (9)
C(1)5	0.338 (2)	0.629 (2)	−0.033 (2)	6.6 (8)
C(1)6	0.277 (1)	0.580 (1)	−0.023 (2)	3.8 (6)
C(1)1	0.139 (1)	0.539 (1)	−0.054 (1)	2.4 (4)
C(4)7	−0.117 (2)	0.445 (1)	−0.123 (2)	6.0 (7)
C(4)2	−0.051 (3)	0.404 (2)	−0.138 (2)	7.8 (8)
C(4)3	−0.063 (3)	0.327 (3)	−0.152 (4)	11.5 (12)
C(4)4	−0.128 (4)	0.298 (3)	−0.151 (3)	10.3 (10)
C(4)5	−0.197 (3)	0.333 (3)	−0.141 (2)	10.0 (10)
C(4)6	−0.194 (3)	0.414 (3)	−0.126 (2)	9.5 (12)
C(4)1	−0.105 (2)	0.529 (1)	−0.106 (1)	4.5 (6)
C(7)7	−0.179 (1)	0.344 (1)	0.193 (2)	4.8 (6)
C(7)2	−0.167 (2)	0.299 (1)	0.274 (2)	6.0 (7)
C(7)3	−0.228 (2)	0.278 (1)	0.326 (2)	6.1 (8)
C(7)4	−0.300 (2)	0.296 (2)	0.303 (2)	6.1 (7)
C(7)5	−0.316 (1)	0.342 (1)	0.224 (2)	5.0 (6)
C(7)6	−0.255 (2)	0.367 (1)	0.168 (2)	5.1 (7)
C(7)1	−0.110 (1)	0.373 (1)	0.135 (2)	4.3 (5)
C(10)7	0.169 (2)	0.366 (1)	0.102 (2)	4.7 (7)
C(10)2	0.250 (2)	0.373 (1)	0.093 (2)	5.5 (6)
C(10)3	0.281 (3)	0.348 (2)	0.010 (3)	9.3 (10)
C(10)4	0.237 (4)	0.310 (2)	−0.060 (3)	10.9 (11)
C(10)5	0.157 (3)	0.306 (2)	−0.042 (2)	8.7 (7)
C(10)6	0.123 (2)	0.328 (1)	0.034 (2)	6.7 (7)
C(10)1	0.129 (2)	0.390 (1)	0.191 (2)	4.0 (5)

Table 2. *Selected bond lengths* (Å), *bond angles* (°) *and torsion angles* (°) *for* (*a*) $(I)H^+.BF_4^-$, (*b*) $(II)H_2^{2+}.2BF_4^-$, (*c*) $(III)H_2^{2+}.2Br^-$ *and* (*d*) $(IV)H_2^{2+}.2Br^-$

	(*a*)	(*b*)	(*c*)	(*d*)
N(1)—C(2)	1.477 (5)	1.60 (2)	1.48 (1)	1.48 (2)
C(2)—C(3)	1.517 (4)	1.56 (3)	1.55 (2)	1.50 (3)
C(3)—N(4)	1.505 (4)	1.44 (2)	1.48 (1)	1.51 (2)
N(4)—C(5)	1.519 (3)	1.48 (2)	1.52 (1)	1.50 (3)
C(5)—C(6)	1.522 (5)	1.48 (3)	1.50 (1)	1.50 (3)
C(6)—N(7)	1.463 (5)	1.50 (2)	1.47 (1)	1.50 (3)
N(7)—C(8)	1.484 (3)	1.57 (2)		1.44 (3)
C(8)—C(9)	1.525 (5)	1.54 (2)		1.50 (3)
C(9)—N(10)	1.476 (4)	1.48 (2)		1.50 (3)
N(10)—C(11)	1.474 (4)	1.52 (2)		1.51 (3)
C(11)—C(12)	1.533 (4)	1.48 (2)		1.53 (3)
C(12)—N(1)	1.471 (4)	1.53 (2)		1.46 (3)
N(1)—C(1)1	1.481 (4)	1.50 (2)	1.49 (1)	1.48 (2)
C(2)—C(2)1	1.541 (5)	1.53 (3)	1.54 (1)	1.60 (2)
N(4)—C(4)1	1.517 (3)	1.43 (2)		1.54 (3)
C(5)—C(5)1	1.536 (5)	1.58 (3)	1.52 (1)	1.54 (3)
N(7)—C(7)1	1.473 (5)	1.50 (2)		1.51 (3)
C(8)—C(8)1	1.543 (4)	1.60 (3)		1.53 (4)
N(10)—C(10)1	1.466 (4)	1.45 (2)		1.55 (3)
C(11)—C(11)1	1.552 (5)	1.51 (3)		1.52 (3)
C(12)—N(1)—C(2)	111.9 (2)	107 (1)	116.6 (7)	114 (1)
N(1)—C(2)—C(3)	108.8 (2)	107 (1)	107.1 (7)	111 (1)
C(2)—C(3)—N(4)	111.0 (3)	115 (1)	109.2 (7)	114 (2)
C(3)—N(4)—C(5)	110.9 (2)	114 (1)	115.3 (8)	115 (2)
N(4)—C(5)—C(6)	109.5 (3)	114 (1)	111.6 (7)	112 (2)
C(5)—C(6)—N(7)	110.3 (2)	114 (1)	113.9 (8)	112 (2)
C(6)—N(7)—C(8)	109.7 (3)	110 (1)		112 (2)
N(7)—C(8)—C(9)	111.2 (3)	108 (1)		111 (2)
C(8)—C(9)—N(10)	112.3 (3)	112 (1)		112 (2)
C(9)—N(10)—C(11)	111.7 (3)	113 (1)		114 (2)
N(10)—C(11)—C(12)	113.0 (3)	109 (1)		110 (2)
C(11)—C(12)—N(1)	114.6 (2)	114 (1)		113 (2)
C(11)—C(12)—N(1)—C(2)	−93.9 (3)	−73 (2)	152.5 (8)	165 (2)
C(12)—N(1)—C(2)—C(3)	158.3 (3)	161 (1)	−93.4 (9)	−84 (2)
N(1)—C(2)—C(3)—N(4)	−58.1 (3)	−65 (2)	−55.6 (9)	−57 (2)
C(2)—C(3)—N(4)—C(5)	−85.3 (3)	−85 (2)	173.4 (7)	162 (2)
C(3)—N(4)—C(5)—C(6)	160.7 (2)	161 (2)	−60.3 (10)	−77 (2)
N(4)—C(5)—C(6)—N(7)	−64.8 (3)	−49 (2)	−63.0 (9)	−55 (2)
C(5)—C(6)—N(7)—C(8)	−88.0 (3)	−75 (2)		166 (2)
C(6)—N(7)—C(8)—C(9)	151.3 (3)	162 (1)		−87 (2)
N(7)—C(8)—C(9)—N(10)	−67.4 (3)	−66 (2)		−56 (2)
C(8)—C(9)—N(10)—C(11)	112.1 (3)	−84 (2)		163 (2)
C(9)—N(10)—C(11)—C(12)	−161.2 (3)	165 (1)		−78 (1)
N(10)—C(11)—C(12)—N(1)	79.6 (3)	−50 (2)		−58 (2)

The title compounds were obtained as single crystals by a previously described method (Tsuboyama *et al.*, 1970) and were recrystallized from acetonitrile/benzene, ethyl acetate, ethanol and acetonitrile/benzene, respectively. The intensity data for $(I)H^+.BF_4^-$ and $(IV)H_2^{2+}.2Br^-$ were corrected for deterioration. The structures were solved by direct methods using *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). All the H atoms of $(I)H^+.BF_4^-$ and $(III)H_2^{2+}.2Br^-$ were located from difference Fourier syntheses, and the positions of those of $(II)H_2^{2+}.2BF_4^-$ and $(IV)H_2^{2+}.2Br^-$ were calculated assuming ideal geometry. Refinement was carried out by full-matrix least-squares methods with anisotropic displacement parameters for all non-H atoms and isotropic displacement parameters for H atoms. For the weighting schemes, *a*, *b* and *c* were automatically calculated. The absolute configurations were assigned from the known configurations of the ligand as an internal reference (Tsuboyama *et al.*, 1970). Calculations were performed using the *UNICS*-III program system (Sakurai & Kobayashi, 1979) on a FACOM M-1800 computer.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and interatomic distances have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71471 (65 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: OH1033]

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17α-Benzyl-3β,17β-dihydroxy-5-androstene

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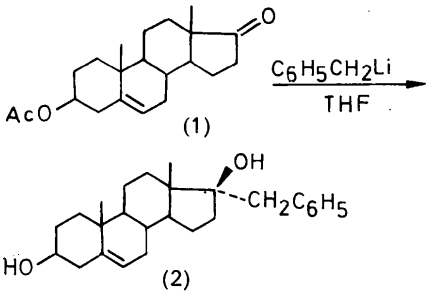
Abstract

The asymmetric unit of the title compound, 17α-benzyl-5-androst-5-ene-3β,17β-diol, $C_{26}H_{36}O_2$, contains two molecules, which differ slightly in the conformation of the *D* ring. Of the four OH groups in the two symmetry-independent molecules, *A* and *B*, three participate in O—H···O hydrogen bonding. Crystal packing involves molecules of *A* forming helix-like chains along the *b* axis, with hydrophobic loops occupied by one part of the *B* molecules; their other parts are involved in hydrogen-bonded bridges to the neighbouring chains.

Comment

Our previous reports (Miljković & Gaši, 1982; Miljković, Gaši, Kindjer, Stanković, Ribar & Argay, 1985) describe synthetic procedures for 3β,17β-dihydroxy-17α-picolyl-5-androstene and its 5α-analogues as intermediates in multistep syntheses of 21,27-hisnorsolanidine and 21,27-hisnordemissidine. Now, as a part of a broader project aiming at the synthesis of novel antiandrogenic compounds, the synthesis of 17α-benzyl-3β,17β-dihydroxy-5-androstene was performed in a way analogous to the previously described synthesis of 3β,17β-dihydroxy-17α-picolyl-5-androstene. Stereospecific addition of benzyllithium to the 17-carbonyl group of dehydroepiandrosterone acetate (1) afforded a satisfactory yield (61.20%) of the title compound (2). Its structure was deduced on the basis of chemical and spectroscopic evidence.



In this paper the detailed structure of compound (2) is described, as the final proof of the proposed stereochemistry at C(17). The structure was solved by the use of direct methods. Since the starting material was synthesized from natural estrone, the absolute stereochemistry of which is known (Fieser & Fieser, 1967), for the purposes of the X-ray structure refinement it was assumed that the same enantiomer occurs in the crystalline state.

A perspective view of the two symmetry-independent molecules *A* and *B*, computed from the final atomic coordinates listed in Table 1, is shown in Fig. 1. Selected bond lengths, bond angles and torsion angles, given in Table 2, show that there is no significant difference between the two symmetry-independent molecules, including their conformations (shown in Fig. 2). Ring-puckering parameters (Cremer & Pople, 1975) and asymmetry parameters (Duax, Weeks & Rohrer, 1976), listed in Table 3, define the conformation of the rings. Rings *A* and *C* have chair conformations in both molecules; ring *B* is in an 8β,9α-half-chair conformation [the distances of C(8) and C(9) from the best plane of the remaining four atoms are −0.313 (6) and 0.420 (6) Å, respectively, for molecule *A*, and −0.393 (7) and 0.313 (7) Å, respectively, for molecule *B*]. Ring *D* in molecule *A* exhibits a 13β-envelope conformation [the distance of C(13) from the best plane of the remaining four atoms is −0.676 (7) Å], while in molecule *B* it adopts a transition form between a 13β-envelope [distance of C(13) is −0.666 (1) Å] and a 13β,14α-half-chair conformation [distances of C(13) and C(14) are −0.514 (1) and 0.191 (7) Å, respectively]. The non-bonded torsion angle C(19)—C(10)···C(13)—C(18) is 10.6 (6)° in molecule *A* and 12.2 (5)° in molecule *B*. The non-bonded O(1)···O(2) distances are 11.176 (6) and