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STEROIDAL ANALOGUES OF UNNATURAL CONFIGURATION—18[1]

CONFORMATIONAL ANALYSIS OF 17β - HYDROXY - 4,4,9 - TRIMETHYL-9β,10α - ESTR - 5 - EN - 3 - ONE AND THE DERIVED 2α - AND 2β - BROMO-COMPOUNDS

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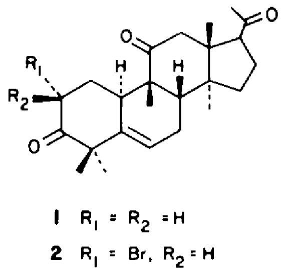
Abstract—A comparative study is presented, in which the results of force-field calculations for 17β-hydroxy 4,4,9-trimethyl-9β,10α-estr-5-en-3-one **4** and the derived 2α- and 2β-bromo-compounds **5** and **6** are considered in relation to conclusions drawn from X-ray crystallographic and spectroscopic data. It is demonstrated that, whereas rings A of the compounds **4**–**6** adopt chair conformations in the solid state, those of the parent ketone **4** and the 2α-bromo-compound **5** display properties consonant with conformational equilibria between chair and boat-like forms in solution.

In an earlier study,[2] the 2α- and 2β-bromo-compounds **2** and **3** derived from 4,4,14 - trimethyl - 19(10→9β)*abeo* - 10α - pregn - 5 - ene - 3,11,20 - trione (**1**) were differentiated with the aid of their spectroscopic properties, and through equilibration resulting in conversion of the less into the more stable isomer (**2**→**3**). Lanthanoid-induced shift NMR spectroscopy led to the further conclusion that ring A of the equatorial isomer **3** adopts a chair conformation. However, it was not possible to deduce the ring A conformation of the 2α - bromo - compound **2** from the available data, although CD spectroscopy supported an inference that the severe steric interaction between the 2α-Br and 4α-CH_3 groups would favour the adoption of a non-chair conformation.

A possible solution to the problem of identifying spectroscopic properties ascribable only to ring A functionality in the triketones **1**–**3** may be envisaged through the use of 17β - hydroxy - 4,4,9 - trimethyl-9β,10α - estr - 5 - en - 3 - one (**4**)[3] as a model substrate; the immediate environment of ring A in **4** is identical to that of **1**, and it was not expected that differences in the more remote structural features would prejudice a meaningful comparison of data between the appropriate substances in the respective series. In addition to the intrinsic interest in thus establishing whether conformational aberrations are indeed present in ring A, it was considered that the model system **4** would be more amenable to a comparative analysis of data derived from molecular mechanics, spectroscopy, and X-ray diffraction. Such comparisons have been invaluable in ascertaining the scope and limitations of predictive methods for conformational analysis,[4] and α-bromoketones of the type represented by **5** and **6** offer a challenging extension of the more general problems encountered in 4,4-dimethyl steroids.[5-7]



1 $R_1 = R_2 = H$
2 $R_1 = Br, R_2 = H$
3 $R_1 = H, R_2 = Br$

In the first instance, force-field calculations were carried out upon structures **4**–**6** using the MM-2 programme,[8] in order to identify feasible conformers in each case, and to ascertain their respective steric energies. In each case, the input parameters comprised the all-chair geometry and those of the four different ring A twist-boats which could be constructed with the aid of Dreiding models. The close proximity of two highly polar groups (C=O and C–Br) in **5** and **6** required[9] the utilisation of the charge interaction option of MM-2. The charges used as input for MM-2 were calculated using CNDO (see Experimental). The calculated puckering parameters[10] and steric energies are given in Table 1, and reflect only the ring A chair and that boat-like conformation of lowest steric energy for each structure. Ring A puckering parameters derived from single crystal X-ray analysis (*vide infra*) are included in Table 1 for comparison.

These results predict that the parent ketone **4** should display a slight preference for a ring A chair over the non-chair conformation which may be represented as the hybrid conformation [$0.51\ {}^1T_3 + 0.27\ B_{3,10} + 0.22\ E_{10}$] (see footnote d, Table 1). The same applies to the 2 - bromo - derivatives **5** and **6**, but with an increasing tendency to the chair form. Rings B, C and D appear to be insensitive to variations in the substitution pattern and conformation of ring A, and are not discussed further. Figure 1 indicates the equilibria expected for **4**–**6** according to the Boltzman distribution.

These predictions are not inconsistent with earlier spectroscopic data for **1**, **2** and **3** respectively,[2] but

Table 1. Calculated steric energies and ring A conformations of **4**, **5** and **6**

Compound	E[a]	Puckering Parameters[b,c] θ	φ	Q	Hybrid Conformational Notation[d,e]
Ketone 4					
chair	43.43	10	353	0.53	${}^1C_4(77) + {}^1E(15) + {}^1H_2(8)$
boat	43.76	83	43	0.71	${}^1T_3(51) + B_{3,10}(27) + E_{10}(22)$
X-ray	-	13	42	0.51	${}^1C_4(69) + {}^1H_{10}(18) + E_{10}(13)$
2α-Br-3-one 5					
chair	43.56	16	20	0.50	${}^1C_4(64) + {}^1H_{10}(22) + {}^1E(15)$
boat	44.21	83	40	0.72	${}^1T_3(60) + E_{10}(21) + B_{2,10}(19)$
X-Ray (I)[f]	-	33	34	0.45	${}^1H_{10}(53) + {}^1C_4(33) + E_{10}(14)$
(II)	-	34	48	0.50	$E_{10}(37) + {}^1C_4(34) + {}^1H_{10}(29)$
2β-Br-3-one 6					
chair	42.98	11	343	0.54	${}^1C_4(73) + {}^1H_2(15) + {}^1E(12)$
boat	43.98	81	39	0.71	${}^1T_3(62) + E_{10}(25) + B_{3,10}(13)$
X-Ray (I)[f,g]	-	9	352	0.56	${}^1C_4(79) + {}^1E(13) + {}^1H_2(8)$
(II)	-	15	319	0.57	${}^1C_4(65) + {}^1H_2(21) + E_2(14)$

a. Steric energy [Kcal/mol] as calculated by MM-2.

b. Puckering parameters given only for ring A; rings B(~E_8), C(~${}^8C_{12}$) and D(~${}^{13}T_{14}$) were essentially unchanged throughout.

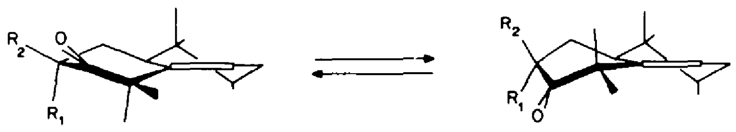
c. θ and φ in degrees [°]; Q in Angstrom [Å].

d. The hybrid conformational notation describes a ring conformation as a linear combination of the three closest salient conformations[11] on the puckering parameter sphere. The numbers in brackets indicate the relative weight of that conformation. The algorithm for calculating the linear combination from the puckering parameters θ and φ will be published soon.

e. Steroid numbering used for ring atoms.

f. This crystal contained two molecules per asymmetric unit.

g. X-ray done on the 17β-t-butoxy derivative **9**.



4a	64 : 36	4b
5a	75 : 25	5b
6a	84 : 16	6b

Fig. 1. Predicted conformational equilibria for **4**, **5** and **6**.

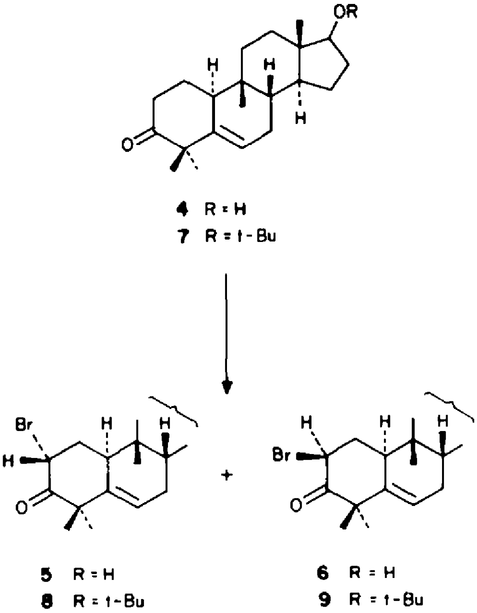
neither do they provide an unequivocal definition of conformational preferences in ring A, owing to the small energy differences calculated for the respective pairs of conformers. Accordingly, the model compound **4** was brominated in order to examine and compare the X-ray crystallographic and spectroscopic properties of the products.

Treatment of **4** in chloroform at 25° with pyridinium hydrobromide perbromide afforded a readily-separable mixture of **5** (66%) and **6** (27%). Equilibration of each of the isomers was carried out in acetonitrile containing a trace of hydrogen bromide at 25°, and the progress of the reactions was monitored through measurement of the rotations. After 26 h no further change occurred, and the measured value of the rotation revealed that the ratio **5** : **6** was 18 : 82 in each case. A comparison of the calculated steric energies of the conformers of **5** and **6** (Table 1) yields an equilibrium ratio ca 27 : 73 for **5** : **6** at 25°, a result whose close correspondence with the experimental finding lends credence to the force-field prediction.

The details of the X-ray crystallographic investigation may be found in the Experimental. Since no suitable crystal of the 2β - bromo - compound **6** could be grown, its 17 - t-butoxy - derivative **9** was used instead. Each of the brominated compounds **5** and **9** contain two molecules per asymmetric unit, which differ slightly in conformation. Table 1 includes the ring-A conformations of **4**, **5** and **9** as determined by X-ray.

It is apparent from the hybrid conformational notation (Table 1) and from the Ortep representations of **4**, **5** (I), and **9** (I), (Fig. 2) that rings-A of these molecules in the solid state adopt essentially the $^1C_4$ chair conformation, with that of the 2α - bromo - derivative (**5**) undergoing flattening due to severe steric interaction of the 2α- and 4α-substituents.

However, spectroscopic evidence supported the molecular mechanics prediction of conformational equilibria for **4** and **5**, rather than the X-ray finding of chairlike conformations. Thus, the NMR spectrum of the 2α - bromo - compound **5** in deuteriochloroform showed a signal for the 2β-proton (triplet at δ 4.59, J 6 Hz), suggestive of an axial 2-substituent in a ring A chair, whereas infrared absorption for the carbonyl group displayed solvent-dependent behaviour (Fig. 3) which may be ascribed to a conformational equilibrium between the $^1C_4$ and $[B_{3,10} + {}^1T_3]$ forms (**5a**$\rightleftarrows$**5b**, Fig. 1). The increasing contribution of the higher frequency component of



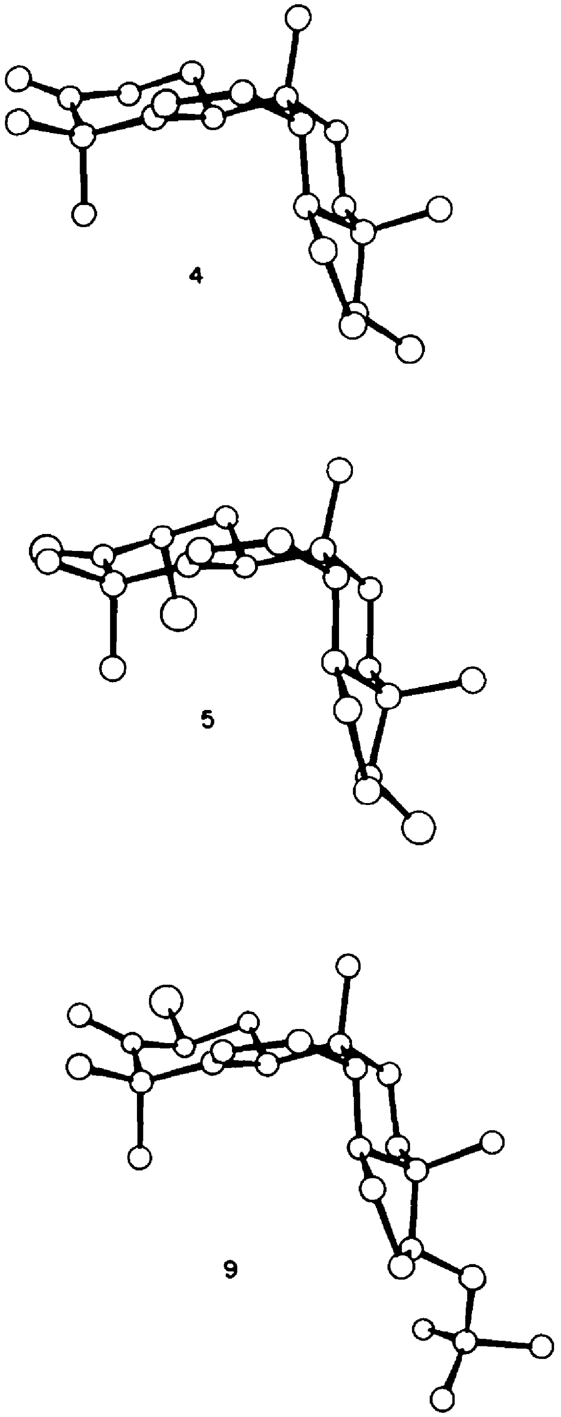
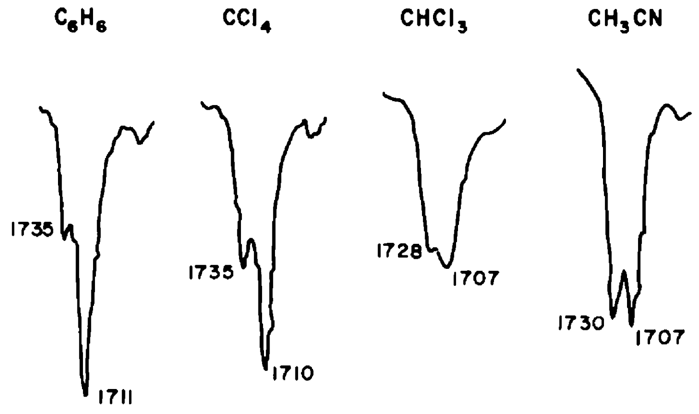


Fig. 2. Perspective drawing of **4**, **5**(I) and **9**(I).



2α-bromo-3-ketone **5**

2β-bromo-3-ketone **6**

Fig. 3. Solvent dependent carbonyl absorption of **5** and **6**.

the carbonyl absorption in the more polar solvents (Fig. 3) is consonant with an increasing population of the boat-like conformer **5b** in which the substituents at C(2) and C(3) approach coplanarity.

By contrast, the NMR signal for the 2α-proton of **6** (quartet at δ 5.06, *J* 13.5 and 6 Hz) showed that the bromo-group is equatorial, and this was further borne out by IR absorption for the carbonyl group at 1732 cm^{-1}, the frequency of which was insensitive to polarity of the solvent used (Fig. 3). These results accord with those obtained[1] for the 2β - bromo - 3,11,20 - triketone **3**, and clearly demonstrate that ring A of **6** adopts a chair conformation in solution.

A similar solvent dependence was observed in CD spectroscopy (Fig. 4). Thus, although the Cotton effects of the 3-ketone **4** and the 2β - bromo compound **9** are relatively insensitive to solvent polarity, that of the 2α-bromo - compound **8** undergoes a blue shift and decrease in magnitude in the more polar media. The spectrum in cyclohexane accords with a substantial contribution by an axial α - bromo - group ($^1C_4$ conformer, **5a**), whereas that in acetonitrile may be ascribed to a conformer population containing a significant proportion of a pseudo-equatorial α-bromo-group ($B_{3,10}$ + $^1T_3$ conformer, **5b**).

Further experimental evidence for this phenomenon was sought in variable-temperature NMR studies; however, spectra of **4**–**5** recorded in the range − 75 to 95° showed insignificant changes. It was concluded that such conformational equilibria as do exist in this temperature range experience a very low barrier to interconversion, since there was no chemical shift or splitting pattern disturbance which could be ascribed to conformer differentiation.

The solvent dependence of the conformational equilibrium in the case of **5**, and the relative non-dependence in the case of **6**, result from the local dipole moments of the competing conformers in the ring A region. These will be greater for those conformers with nearly coplanar carbonyl and bromine groups, i.e. **5b** > **5a** and **6a** > **6b**. The transition from non-polar to polar solvent will stabilise that conformer which has the greatest dipole moment. In the case of **5** this stabilisation is noticeable since the equilibrium is shifted from *ca* 75 : 25 (**5a** : **5b** as calculated by MM-2), to a point where **5b** predominates. In contrast, the conformer **6a** already pre-

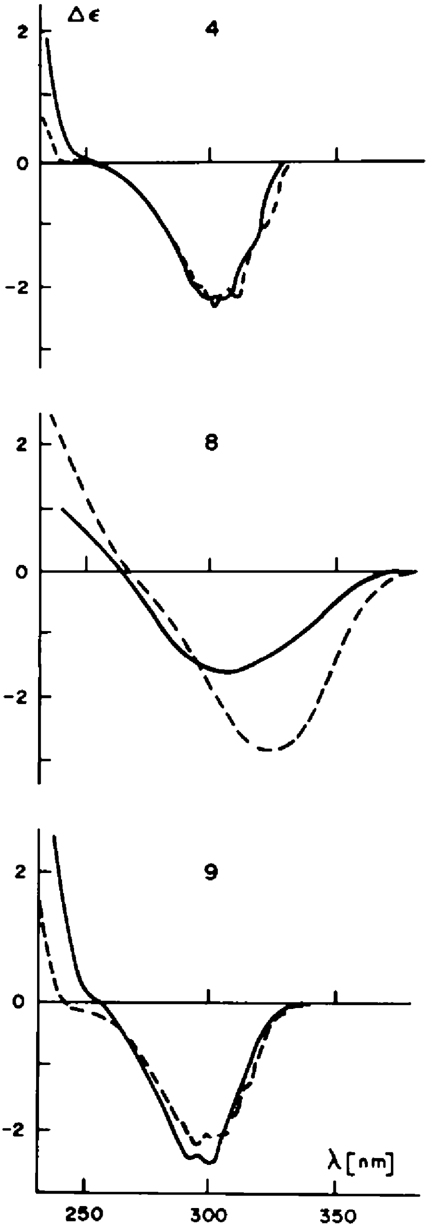


Fig. 4. Solvent dependent CD spectra of 4, 8 and 9 (—— acetonitrile; - - -cyclohexane).

dominates in the non-polar solvent, and a further stabilisation by increasing solvent polarity will not be readily discerned spectroscopically. Unfortunately it is not yet feasible to quantify solvation effects in the MM-2 programme.

In an attempt to determine the solution state conformation of the non-brominated compound **4**, as well as to verify the findings for **5** and **6**, a series of lanthanoid-induced shift (LIS) NMR experiments was conducted on the 17β-t-butyloxy-derivatives **7–9**. These were routinely prepared from **4**, and identified by spectroscopic comparisons with the respective 17β-hydroxy-compounds **4–6**. The t-butyl group has been shown[12] to be effective in blocking hydroxy-groups toward lanthanoid complexation; in this way, it was possible to treat **7–9** as monofunctional systems with respect to lanthanoid complexation, an essential precondition for a meaningful statistical evaluation of the LIS data.[13]

The slopes of the LIS plots for the identifiable protons are given in the Experimental (Table 3). These data, used in conjunction with the geometries derived from force-field calculations for the corresponding parent compounds **4–6**, were evaluated with the aid of a computer programme (see Experimental). Calculated agreement factors (AF) were plotted against the percentages of the extreme conformations (Fig. 5).

A pronounced minimum in the plot of the parent ketone **7** is seen at the position corresponding to ca 40% $^{1}C_{4}$ and 60% $[^{1}T_{3} + B_{3,10} + E_{10}]$, thus implying a conformational equilibrium slightly favouring the boat-like form. This result accords reasonably well with the force-field prediction (64 : 36) and, in the absence of other supporting spectroscopic data, provides the only independent experimental evidence for such an equilibrium (**4a**⇌**4b**) in solution.

The AF plot for the 2β-bromo-compound **9** reveals a preference for the $^{1}C_{4}$ conformer, in agreement with all the other spectroscopic data for **9** and the corresponding 17β-hydroxy-compound **6**. In the case of the 2α-bromo-compound **8**, the AF plot is insensitive to conformational change in ring A, and no conclusion can be drawn from these data.

It should be noted that the low energy barrier to conformational interconversion suggested by the variable-temperature NMR study on **5**, indicates that the finding of $^{1}C_{4}$ conformations for rings A in **4** and **5** in the crystalline state, does not detract from the conclusions regarding conformational equilibria of **4** and **5** in solution.

It is concluded that the force field predictions present a plausible interpretation of the conformational behaviour of compounds **4–9** in solution.

EXPERIMENTAL

General directions (Ref. 14)

Bromination of 17β-*hydroxy*-4,4,9-*trimethyl*-9β,10α-*estr*-5-*en*-3-*one* (**4**). The ketone (**4**)[3] (268 mg) was treated with pyridinium hydrobromide perbromide (330 mg) in chloroform (50 ml) at 25° for 12 h. The reaction mixture was taken up in benzene, washed with sat $NaHCO_3$ aq and water,

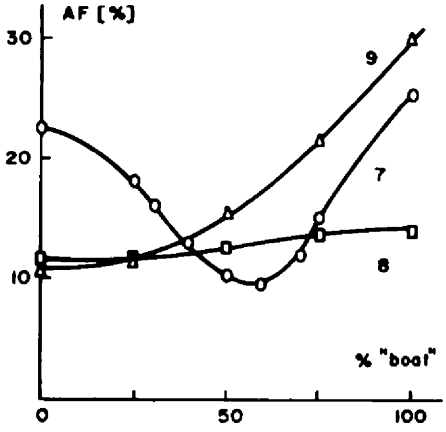


Fig. 5. LIS derived agreement factors for varying proportions of the "boat" form in the equilibria "chair"⇌"boat".

dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed on silica gel (30 g) with hexane–EtOAc (1 : 1) to give 2α - bromo - 17β - hydroxy-4,4,9 - trimethyl - 9β,10α - estr - 5 - en - 3 - one (5) (221 mg), m.p. 116–118° (from CH_2Cl_2–hexane), $[\alpha]_D$ − 97.6°(*c* 0.9, CH_3CN), δ0.81, 0.9 (9β- and 13β-Me), 1.28, 1.39 (4,4-Me_2), 3.0 br (1H, *W*17 Hz, 10α-H), 3.7 (1H, t, *J*8 Hz, 17α-H), 4.59 (1H, t, *J* 6Hz, 2β-H), and 5.6 (1H, dt, *J* 5.5 and 2 Hz, 6-H). Found: C, 63.8; H, 7.95: Br, 20.3; M^+, 394.396. $C_{21}H_{31}BrO_2$ requires C, 63.8; H, 7.9; Br, 20.2%; *M* 394.396, and 2β - bromo - 17β - hydroxy - 4,4,9 - trimethyl - 9β, 10α - estr - 5 - en - 3 - one (6) (91 mg), m.p. 173–184° dec (from CH_2Cl–hexane), $[\alpha]_D$-23.9° (*c*0.8, CH_3CN), δ 0.83, 0.87 (9β- and 13β-Me), 1.31, 1.36 (4,4-Me_2), 3.69 (1H, t, *J* 8 Hz, 17α-H), 5.06 (1H, dd, *J* 13.5 and 6 Hz, 2α-H), and 5.6 (1H, dt, *J* 6 and 2 Hz, 6-H). Found: C, 63.8; H, 8.1; Br, 20.45%; M^+, 394.396.

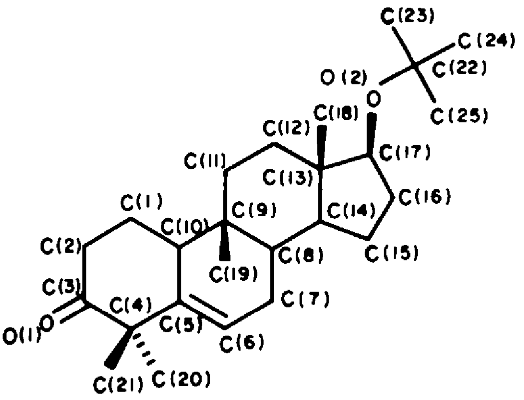
17β - *t* - *Butoxy* - 4,4,9 - *trimethyl* - 9β,10α - *estr* - 5 - *en* - 3 - *one* (7). Freshly distilled isobutene (40 ml) was added to the hydroxyketone (4) (170 mg) in CH_2Cl_2 (3 ml), contained in a pre-cooled (−30°) Parr hydrogenation flask. An open sample tube containing H_3PO_4 (100%, 53 mg) and $BF_3 \cdot Et_2O$ (freshly distilled, 63 μl) was dropped into the mixture, and a portion of the isobutene was evaporated to displace any oxygen present in the flask. The vessel was sealed and shaken for 18 h at 22°, then cooled to −30° and opened. The contents were poured into sat $NaHCO_3$ aq and the mixture was extracted with benzene. The extract was washed with water (× 3) dried ($MgSO_4$), and evaporated *in vacuo*. The residue was adsorbed on silica gel (20 g). Elution with hexane–EtOAc (9 : 1) gave the t-butyl ether (7) (170 mg), m.p. 120–122° (from EtOH), $[\alpha]_D$ 20.7° (*c* 0.9), ν_{max} 1706 cm^{-1}, δ0.8 (13β-Me), 0.86 (9β-Me), 1.15 (t-Bu), 1.26, 1.28 (4,4-Me_2), 3.33 (1H, t, *J*7.5 Hz, 17α-H), 5.47 (1H, dt, *J* 5.5 and 2 Hz, 6–H). Found: C, 80.75; H, 10.8%, M^+, 372. $C_{25}H_{40}O_2$ requires C, 80.6; H, 10.8%; *M*, 372.

Bromination of the t-butoxy-compound (7)

The compound (7) (300 mg) was brominated as described in a previous experiment. Chromatography of the product on silica gel (30 g) with hexane–EtOAc (49 : 1) gave three fractions (75, 170, and 83 mg). The middle fraction comprised a 1 : 1 mixture, whereas the first and last were considerably enriched in the respective isomers. Repeated fractional crystallization of the first fraction from hexane afforded 2α-bromo - 17 - t - butoxy - 4,4,9 - trimethyl - 9β,10α - *estr* - 5 - *en* - 3 - *one* (8), m.p. 134–136°, δ 0.81 (13β-Me), 0.93 (9β-Me), 1.15 (t-Bu), 1.32 1.43 (4,4-Me_2), 299br (1H, *W* 15 Hrz, 10α-H), 3.42 (1H, t, *J*8 Hz, 17α-H), 4.63 (1H, t, *J*6 Hz, 2β-H), and 5.62br (1H, *W* 14 Hz, 6-H). Found: M^+, 452.211, $C_{25}H_{39}{}^{81}BrO_2$ requires *M*, 452.211. Similar treatment of the third fraction afforded 2β - bromo - 17β - t - butoxy - 4,4,9 - trimethyl - 9β,10α - estr - 5 - en - 3 - one (9), m.p. 176–179°, $[\alpha]_D$-15.4° (*c* 1.0), δ0.8 (13β-Me), 0.86 (9β-Me), 1.15 (t-Bu), 1.33, 1.37 (4,4-Me_2), 3.38 (1H, t, *J* 8 Hz, 17α-H), 5.05 (1H, dd, *J* 13 and 6 Hz, 2α-H), and 5.6br (1H, *W*11 Hz, 6-H). Found: C, 66.2; H, 8.8; Br, 18.2; M^+, 450.452. $C_{25}H_{39}BrO_2$ requires C, 66.5; H, 8.7; Br, 17.7%; *M*, 450.452.

Molecular mechanics calculations

The standard MM-2 programme[8] was used with the charge interaction option and the associated changed torsional constant $[V_3(O{=}C{-}C{-}Br) = -2.0]$[15] being employed for **5a**, **5b**, **6a** and **6b**. The charge distribution input data were generated as follows: Approximate geometries of the four conformers were calculated using MM-2 in the standard (dipole interaction) mode. These geometries were incorporated into CNDO[16] calculations of the model compound 2 - bromo - 5 - ethylene - 4,6,6 - trimethyl - cyclohexanone. The resulting charge distributions for the four conformers were very similar and therefore the mean values were used as input for all four steroid calculations. Table 2 gives those values derived from CNDO which were used as input for MM-2.



LIS data

LIS data were obtained through incremental addition of $Eu(fod)_3$ (up to ca 0.6 equiv.) to a solution of the compound (ca 0.1 mmol) in $CDCl_3$. Shifts showed linear responses in the range examined.

Evaluation of LIS data

LIS data of compounds 7–9 were evaluated using a computer programme based upon a described general procedure,[17] but incorporating the following modifications:

(a) if a conformational equilibrium is suspected, the two extreme geometries (A and B) are entered as input to the programme; these geometries are derived from the force-field calculations,

(b) various proportions of conformational mixing of A and B are tested sequentially; for a certain assumed equilibrium ratio [x%A, (100-x)%B], the geometric factor of proton i then takes the form:

$$GF_i = \frac{x}{100}\left(3\cos^2\theta_{i,A} - 1\right)r_{i,A}^{-3} + \frac{100-x}{100}\left(3\cos^2\theta_{i,B} - 1\right)_{i,B}^{-3}$$

(c) the scaling factor and the agreement factor are then calculated as if only one geometry had been entered,

Table 2. Charge distribution input data for MM-2 calculation of **5a**, **5b**, **6a**, and **6b**

Atom[a]	Net Charge[b,c]	SD[d]
C1	0.037	0.003
C2	0.003	0.001
C3	0.256	0.002
C4	0.008	0.001
C5	0.016	0.002
C6	-0.020	0.001
C10	0.037	0.001
O1	-0.264	0.005
Br	-0.117	0.006
C2-H	0.038	0.004

a) Steroid numbering.

b) Decimal fractions of the electronic charge e.

c) Mean value of 4 CNDO calculations using geometries **5a**, **5b**, **6a**, **6b** .

d) Standard deviation from the 4 calculations.

Table 3. Slopes of LIS plots for compounds **7**–**9**[a]

Proton(s)	Ketone **7**	2α-Br-3-one **8**	2β-Br-3-one **9**
1α-H	2.010[b]	0.994	1.031
1β-H	2.156[b]	0.994	1.345
2α-H	7.070	-	2.204
2β-H	7.070	2.446	-
6-H	2.070	0.637	0.517
7α-H	0.926	0.349	0.252
7β-H	0.939	0.241	-[c]
10β-H	2.603	1.072	0.903
17α-H	0.681	0.333	0.282
13β-Me	0.539	0.345	0.325
9β-Me	0.930	0.341	0.353
4α-Me	4.698	1.100	1.198
4β-Me	3.743	1.625	0.960
t -Bu	0.227	0.187	0.171

a [Δδ/mol.Eu] the slopes were derived by linear regression of the experimentally determined plots of δ vs [Eu] for the $Eu(fod)_3$ spectra.

b Identified with the aid of the LIS spectra of the 2α-^{2}H,2β-^{2}H derivative of **7** .

c Unambiguous assignment not possible.

Table 4. Crystal data and refinement parameters for **4**, **5** and **9**

Parameter	**4**	**5**	**9**
Mol. formula	$C_{21}H_{32}O_2$	$C_{21}H_{31}O_2Br$	$C_{25}H_{39}O_2Br$
a Å	14.67	23.35	14.08
b Å	14.67	23.35	12.9
c Å	7.43	7.52	14.54
β/γ °	120.0(γ)	90.0	98.96(β)
V Å^3	1 385	4 100	2 444
Dc gcm^{-3}	1.14	1.28	1.23
Z	3	8	4
Space group	$P3_1$	$P4_3$	$P2_1$
μ cm^{-1}	0.38(Mo-Kα)	26.03(Cu-Kα)	22.34(Cu-Kα)
Scan rate ° s^{-1}	0.04	0.03	0.03
Scan width °	1.20	2.4	2.0
Scan range °	$3<\theta<22.5$	$2<\theta<55$	$2<\theta<55$
Measured intensities	1 379	2 948	3 608
Unobserved intensities (I 2σI)	150	334	147
Number of parameters	206	433	511
$R=\Sigma\|\Delta F\|/\Sigma\|Fo\|$	0.052	0.084	0.087

(d) the agreement factors are plotted against conformational proportions in order to indicate the true conformational equilibrium.

The relative observed slopes of all the identified protons of **7**–**9** are listed in Table 3. With the aid of these values and the calculated geometries (all-chair and boat-chair-chair local minima for each compound), the agreement factors (AF) were calculated and are depicted in Fig. 5. These results are based upon consideration of reasonable Eu positions only, viz. those determined according to the following constraints: $d = 3.0 \pm 0.6$ Å; $\rho = 90$–$180°$; $\phi = 0 \pm 30°$ or $180 \pm 30°$ where; $d =$ O—Eu distance, $\rho = C_3$–O—Eu bond angle, and $\phi = C_2$–C_3–O—Eu torsion angle.

Crystallographic analysis

Diffraction quality crystals of **4** and **5** were obtained from CH_2Cl_2 + n-hexane and those of **9** from n-hexane only. After preliminary Weissenberg examination the crystals were transferred to a four circle diffractometer for data collection. Crystal data and details of the crystallographic analyses are given in Table 4. Data have been deposited with the Cambridge Crystallographic Data Centre.

The program SHELX[18] was used for all crystallographic computations, and these structures were solved by standard methods. Unit weight refinement were used and, in all cases, anisotropic thermal parameters were refined for the non-hydrogen atoms. All the hydrogen atoms of compound **4** could be located with the aid of difference-Fourier methods, and were included in the refinement with a common isotropic thermal parameter that converged to a value of 0.057(3) Å^2. No hydrogen atoms were calculated for the other two structures.

Both bromo-conpounds **5** and **9** crystallized with two non-identical molecules in the asymmetric unit. There is an intermolecular hydrogen bond between the two O–17 oxygen atoms in **5**, with an interoxygen distance of 2.86 Å and a peak in the final difference Fourier map at a distance of 1.11 Å and 1.72 Å from the two oxygen atoms.

REFERENCES

[1] Part 17, J. R. Bull, D. C. Levendis and A. Tuinman, *Tetrahedron* **38**, 347 (1982).
[2] J. R. Bull and A. J. Hodgkinson, *Tetrahedron* **28**, 3969 (1972).
[3] J. R. Bull, J. Floor and A. Tuinman, *J. Chem. Soc.* Perkin Trans. I 1537 (1978).
[4] N. L. Allinger, *Adv. Phys. Org. Chem.* **13**, 1 (1976) and refs cited.
[5] N. L. Allinger, U. Burkert and W. H. de Camp, *Tetrahedron* **33**, 1891 (1977).
[6] U. Burkert and N. L. Allinger, *Tetrahedron* **34**, 807 (1978).
[7] D. A. Dougherty, K. Mislow, J. W. Hoffman and J. Jacobus, *J. Org. Chem.* **44**, 1585 (1979).
[8] N. L. Allinger, *QCPE* **13**, 395 (1981).
[9] N. L. Allinger and M. T. Wuesthoff, *Tetrahedron* **33**, 3 (1977).
[10] D. Cremer and J. A. Pople, *J. Am. Chem. Soc.* **97**, 1354 (1975).
[11] J. C. A. Boeyens, *J. Cryst. Mol. Struct.* **8**, 317 (1978).
[12] J. R. Bull and A. Tuinman, *Tetrahedron* **29**, 1101 (1973).
[13] O. Hofer, *Topics Stereochem.* **9**, 111 (1976).
[14] J. C. A. Boeyens, J. R. Bull, J. Floor and A. Tuinman, *J. Chem. Soc.* Perkin Trans. I. 808 (1978).
[15] L. Došen-Mićovic and N. L. Allinger, *Tetrahedron* **34**, 3385 (1978).
[16] H. L. Hase and A. Schweig, *QCPE* **6**, 261 (1974).
[17] Ref. 11, pp. 122–131.
[18] G. M. Sheldrick, *Computing in Crystallography*. (Edited by H. Schenk, R. Olthof-Hazenkamp, H. van Koningsveld and G. C. Bassi). Delft University Press (1978).