organic compounds

The α- and β-epoxides of 3β-acetoxy-5α-lanost-9(11)-en-7-one

Masood Parvez,[a]* Oliver E. Edwards[b] and Zdzisław Paryzek[c]

[a]Department of Chemistry, The University of Calgary, 2500 University Drive NW, Calgary, Alberta, Canada T2N 1N4, [b]678 Portage Avenue, Ottawa, Ontario, Canada K1G 1T4, and [c]Faculty of Chemistry, A. Mickiewicz University, 60-780 Poznań, Poland
Correspondence e-mail: parvez@ucalgary.ca

The structures of 3β-acetoxy-9α,11α-epoxy-5α-lanost-9(11)-en-7-one and 3β-acetoxy-9β,11β-epoxy-5α-lanost-9(11)-en-7-one, $C_{32}H_{52}O_4$, differ in their respective substituted cyclohexanone rings but adopt similar conformations in the other three rings. In both of the crystal structures, weak intermolecular C—H···O interactions are present.

Comment

In experiments directed at transforming the lanostane skeleton into that of curcurbitane (by migration of the angular methyl group at C-10 to C-9), two epoxides were prepared by the *m*-chloroperoxybenzoic acid oxidation of 3β-acetoxy-lanosta-9(11)-en-7-one (Paryzek, 1976, 1978). One of these was originally assigned the α-configuration, (I), and the other, the β-configuration, (II), on the basis of the chemical shifts attributed to H-11, as well as circular dichroism evidence. The BF₃-induced rearrangement of the β-isomer (II) in acetic anhydride yielded 3β,11β-diacetoxy-10α-curcurbit-5-en-7-one and 3β,11β-diacetoxy-10α-curcurbit-1(10)-en-7-one (Paryzek, 1976, 1979). Under the same conditions, the α-epoxide (I) yielded 3β-acetoxy-18(13→12β)-*abeo*-lanosta-8,13(17)-dien-7-one as the major product (Baddeley *et al.*, 1979), though subsequent reinvestigation of the reaction additionally revealed the presence of minor amounts of curcurbitenes in which the angular methyl group (C-19) at C-10 had migrated to C-9 (Paryzek *et al.*, 1983; Paryzek & Wydra, 1985). Similar conclusions about the chemistry and stereochemistry of the two epoxides were reported (Baddeley *et al.*, 1979).

Although the assignments of configuration to (I) and (II) seemed secure, the 19-methyl migration accompanying the rearrangement of the β-epoxide (II) was remarkable in view of expectations for antiperiplanar shift relative to the C—O bond being ruptured. In addition, migration of C-18 and C-19 methyl groups reported for the α-epoxide (I) in acetic anhydride (see above) gave us concern. Hence, in the hope of

confirming the assigned stereochemistry and understanding the above phenomena we sought structural data on the crystalline epoxides (I) and (II). The results reported here support the previous conclusions about their configurations and provide information on their conformations that contributes to our understanding of their chemistry.
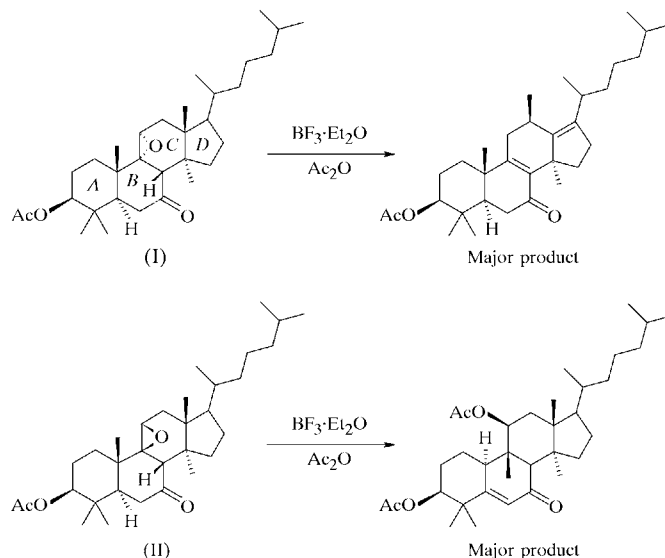
In rearrangements of epoxides, migration of the methyl group *trans*–antiperiplanar to the C—O bond being ruptured has been postulated to be preferred on stereoelectronic grounds. However, migration of methyl groups originally in a *cis* relationship to the breaking epoxide bond has also been observed (Blunt *et al.*, 1968). The observed methyl migration in the reaction of the epoxide (II) is in accordance with the statement of Hartshorn & Kirk (1965) that 'axial cleavage' of epoxides should follow a reaction pathway having lower
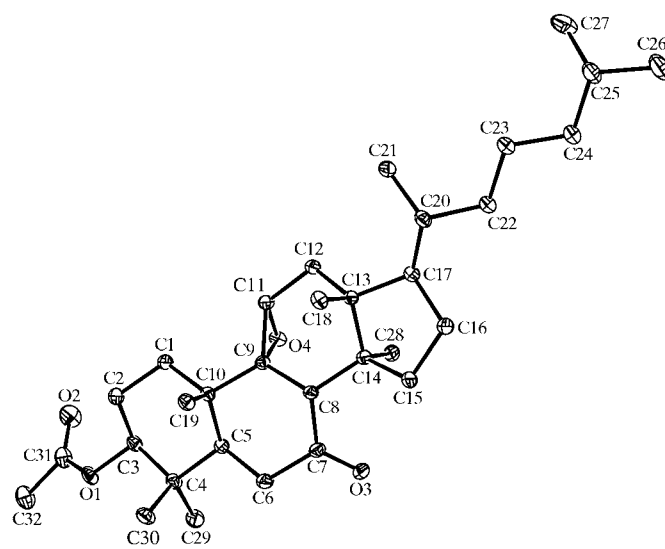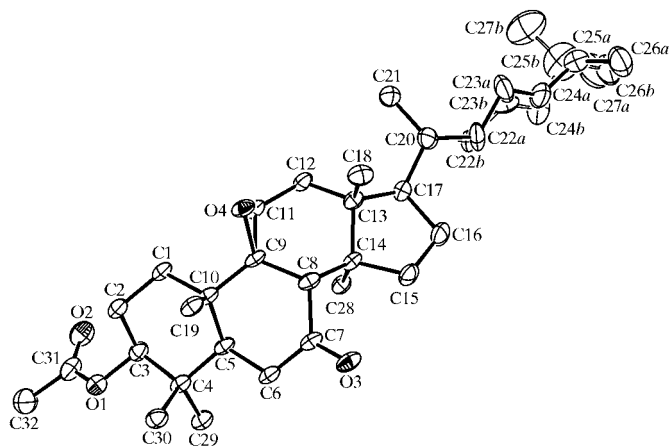

Figure 1
An *ORTEPII* (Johnson, 1976) drawing of α-epoxide (I), with displacement ellipsoids plotted at the 30% probability level. H atoms have been excluded for clarity.

organic compounds

Figure 2

An *ORTEPII* (Johnson, 1976) drawing of β-epoxide (II), with displacement ellipsoids plotted at the 25% probability level. H atoms have been excluded for clarity and hollow bonds have been used to distinguish between the disordered side-chain atoms C22a–C27a and C22b–C27b.

energy requirements than the 'equatorial' case. The 'axial cleavage' also involves less change in atomic positions than the 'equatorial' case, in accordance with the principle of least nuclear motion (Hine, 1977).

The structures of (I) and (II) (Figs. 1 and 2, respectively) are composed of a typical steroidal skeleton with a five-membered and three six-membered rings, as well as an epoxide group with α and β orientations (see scheme). Ring A in both structures adopts a classical chair conformation, with puckering parameters (Cremer & Pople, 1975) $Q = 0.561$ (3) and 0.567 (5) Å, $\theta = 7.2$ (2) and 9.1 (4)°, and $\varphi = 57.6$ (18) and 72 (3)°, respectively, in (I) and (II). Ring B in (I) is in a slightly distorted chair conformation, with puckering parameters $Q = 0.566$ (2) Å, $\theta = 15.3$ (2)° and $\varphi = 314.0$ (8)°. In (II), the corresponding ring is in a half-chair conformation, with C5 0.624 (7) Å out of the plane formed by the other five atoms (C6–C10) in the ring; the maximum deviation of any atom from the least-squares plane of these atoms is 0.162 (4) Å (for C6). The torsion angles reveal further evidence of conformational differences (Tables 1 and 2). Rings C of (I) and (II) adopt half-chair conformations with atoms C13 and C14 lying 0.665 (3) and 0.718 (6) Å out of the planes formed by the remaining ring atoms; the maximum deviations of atoms from these least-squares planes are 0.152 (2) Å for atom C8 and 0.086 (3) Å for atom C12 in (I) and (II), respectively. These significant conformational differences may be attributed to the epoxide orientation. The five-membered rings in both structures exhibit envelope conformations, with atom C14 lying 0.680 (3) and 0.672 (8) Å out of the planes of the remaining atoms of the corresponding rings.

The C20/C22–C25 side chains are fully extended in both structures. A search of the Cambridge Structural Database (2006 Release, Version 5.28; Allen, 2002) for structures containing a steroidal skeleton with a carbonyl function at C7 showed only two structures [refcodes GEBJIG (Sakamaki *et al.*, 1988) and PEFSOI (Mungarulire *et al.*, 1993)]. Ring B in

the former adopts a conformation similar to that observed in (II), while the coordinates for the second structure are not included. In (I) and (II), both structures are devoid of classical hydrogen bonds; however, non-conventional interactions of the type C—H···O are present in the two structures.

Experimental

The syntheses of epoxides (I) and (II) have been reported (Paryzek, 1978). The crystals of (I) [m.p. 446 (2) K] were grown from a solution of CH_3OH by slow evaporation at room temperature, while those of (II) [m.p. 489 (2) K] were grown from a mixture of CH_3OH and CH_3COCH_3 (10:1).

Epoxide (I)

Crystal data

$C_{32}H_{52}O_4$	$V = 1469.9$ (9) Å^3
$M_r = 500.74$	$Z = 2$
Monoclinic, $P2_1$	Mo $K\alpha$ radiation
$a = 11.483$ (4) Å	$\mu = 0.07$ mm^{-1}
$b = 7.612$ (3) Å	$T = 173$ (2) K
$c = 16.903$ (6) Å	$0.14 \times 0.12 \times 0.10$ mm
$\beta = 95.79$ (3)°	

Data collection

Nonius KappaCCD diffractometer	5281 measured reflections
Absorption correction: multi-scan (*SORTAV*; Blessing, 1997)	3578 independent reflections
	3157 reflections with $I > 2\sigma(I)$
$T_{min} = 0.990$, $T_{max} = 0.993$	$R_{int} = 0.020$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.039$	334 parameters
$wR(F^2) = 0.098$	H-atom parameters constrained
$S = 1.05$	$\Delta\rho_{max} = 0.22$ e Å^{-3}
3578 reflections	$\Delta\rho_{min} = -0.15$ e Å^{-3}

Table 1
Selected torsion angles (°) for (I).

C10—C5—C6—C7	−56.7 (3)	C7—C8—C9—C10	51.7 (2)
C5—C6—C7—C8	46.1 (3)	C8—C9—C10—C5	−61.0 (2)
C6—C7—C8—C9	−42.0 (2)	C6—C5—C10—C9	61.5 (2)

Epoxide (II)

Crystal data

$C_{32}H_{52}O_4$	$V = 1506$ (3) Å^3
$M_r = 500.74$	$Z = 2$
Monoclinic, $P2_1$	Mo $K\alpha$ radiation
$a = 13.356$ (6) Å	$\mu = 0.07$ mm^{-1}
$b = 6.233$ (13) Å	$T = 173$ (2) K
$c = 18.104$ (16) Å	$0.26 \times 0.08 \times 0.03$ mm
$\beta = 92.14$ (7)°	

Data collection

Nonius KappaCCD diffractometer	2892 measured reflections
Absorption correction: multi-scan (*SORTAV*; Blessing, 1997)	2892 independent reflections
	2108 reflections with $I > 2\sigma(I)$
$T_{min} = 0.982$, $T_{max} = 0.998$	$R_{int} = 0.000$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.056$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.154$	
$S = 1.10$	
2892 reflections	$\Delta\rho_{max} = 0.35$ e Å^{-3}
419 parameters	$\Delta\rho_{min} = -0.20$ e Å^{-3}

Table 2
Selected torsion angles (°) for (II).

C10—C5—C6—C7	−37.6 (5)	C7—C8—C9—C10	11.7 (5)
C5—C6—C7—C8	−2.1 (6)	C8—C9—C10—C5	−49.5 (5)
C6—C7—C8—C9	15.8 (6)	C6—C5—C10—C9	62.1 (4)

The absolute structures could not be established in these analyses owing to the absence of significant anomalous effects and the Friedel pairs were thus merged prior to refinement. In the structure of (II), the side chain was disordered and soft restraints were applied to the bond lengths and angles for two orientations, *a* and *b*, of atoms C22–C27. In both structures, most of the H atoms were located in difference Fourier syntheses and, for (I), all H atoms were included in the refinements at geometrically idealized positions, with C—H distances of 0.98–1.00 Å and isotropic displacement parameters of 1.2 (non-methyl) or 1.5 (methyl) times the equivalent isotropic displacement parameters of the atoms to which they were bonded. In (II), all atoms were treated as riding atoms, but the non-disordered H atoms were allowed isotropic displacement parameters. A calculation of potential solvent volume using *PLATON* (Spek, 2007) indicated eight voids in the unit cell of (II), with a total volume of 70 Å^3, bearing no significance. The final difference maps were free of any chemically significant features.

For both epoxides, data collection: *COLLECT* (Hooft, 1998); cell refinement: *DENZO* (Otwinowski & Minor, 1997); data reduction: *SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SAPI91* (Fan, 1991); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97* (Sheldrick, 1997).

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Baddeley, G. V., Samaan, H. J., Simes, J. J. H. & Ai, T. H. (1979). *J. Chem. Soc. Perkin Trans. 1*, pp. 7–14.
Blessing, R. H. (1997). *J. Appl. Cryst.* **30**, 421–426.
Blunt, J. W., Hartshorn, M. P. & Kirk, D. N. (1968). *J. Chem. Soc. C*, pp. 635–640.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Fan, H.-F. (1991). *SAPI91*. Rigaku Corporation, Tokyo, Japan.
Hartshorn, M. P. & Kirk, D. N. (1965). *Tetrahedron*, **21**, 1547–1558.
Hine, J. (1977). *Adv. Phys. Org. Chem.* **15**, 1–61.
Hooft, R. (1998). *COLLECT*. Nonius BV, Delft, The Netherlands.
Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Mungarulire, J., Munabu, R. M., Murasaki, C., Eguchi, T., Fujimoto, Y., Kakinuma, K., Kobayashi, K., Uramoto, M. & Ikekawa, N. (1993). *Chem. Pharm. Bull.* **41**, 411–413.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Paryzek, Z. (1976). *Tetrahedron Lett.* pp. 4761–4762.
Paryzek, Z. (1978). *J. Chem. Soc. Perkin Trans. 1*, pp. 329–336.
Paryzek, Z. (1979). *J. Chem. Soc. Perkin Trans. 1*, pp. 1222–1227.
Paryzek, Z. & Wydra, R. (1985). *Can. J. Chem.* **63**, 1280–1286.
Paryzek, Z., Wydra, R. & Błaszczyk, K. (1983). *Chem. Lett.* pp. 1171–1172.
Sakamaki, H., Take, M.-A., Matsumoto, T., Iwadare, T. & Ichinohe, Y. (1988). *J. Org. Chem.* **53**, 2622–2624.
Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.
Spek, A. L. (2007). *PLATON*. Version 30107. Utrecht University, The Netherlands.