Crystal data

$C_{31}H_{26}N_2O$
$M_r = 442.54$
Monoclinic
$P2_1/n$
$a = 10.58\,(1)$ Å
$b = 16.10\,(2)$ Å
$c = 13.954\,(10)$ Å
$\beta = 100.97\,(1)°$
$V = 2334\,(4)$ Å^3
$Z = 4$
$D_x = 1.259$ Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
$\lambda = 1.54178$ Å
Cell parameters from 15 reflections
$\theta = 2\text{–}28°$
$\mu = 0.592$ mm^{-1}
$T = 293\,(2)$ K
Rectangular
0.25 × 0.20 × 0.15 mm
Yellow

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
4382 measured reflections
4159 independent reflections
3081 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.028$
$\theta_{\rm max} = 69.88°$
$h = 0 \rightarrow 12$
$k = 0 \rightarrow 19$
$l = -16 \rightarrow 16$
3 standard reflections every 200 reflections intensity decay: 1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.063$
$wR(F^2) = 0.165$
$S = 1.099$
4159 reflections
309 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.038P)^2 + 3.2P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\rm max} = 0.030$
$\Delta\rho_{\rm max} = 0.236$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.213$ e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 1997)
Extinction coefficient: 0.0037 (3)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

	(I)^a	(II)^b	(III)^c
N1—N2	1.385 (4)	1.311 (3)	1.234 (8)
N2—C19	1.288 (4)	1.443 (3)	1.461 (8)
N1—C2	1.475 (4)	1.490 (3)	1.516 (5)
C19—C11	1.516 (4)	1.491 (4)	1.535 (9)
C11—C2	1.579 (4)	1.308 (4)	1.507 (7)
N1—N2—C19	109.2 (3)	109.5 (2)	112.3 (5)
N2—C19—C11	113.5 (3)	108.2 (2)	105.7 (6)
C2—C11—C19	99.5 (2)	111.4 (2)	100.5 (4)
N1—C2—C11	100.6 (3)	100.4 (2)	104.5 (4)
N2—N1—C2	111.0 (2)	110.5 (2)	111.3 (4)

Notes: (*a*) present study; (*b*) 3,5,5-trimethyl-3-pyrazoline *N*,*N'*-dioxide; (*c*) a pyrazoline derivative of eunicin acetate.

H atoms were positioned geometrically using a riding model with C—H = 0.93, 0.96, 0.97 and 0.98 Å, but they were not refined.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *SDP* (Frenz, 1978). Program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997). Molecular graphics: *ZORTEP* (Zsolnai, 1997). Software used to prepare material for publication: *SHELXL97* and *PARST* (Nardelli, 1983, 1995).

RK thanks UGC for a fellowship and DV thanks UGC (India) for providing funding under the UGC Career Award scheme.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1522). Services for accessing these data are described at the back of the journal.

References

Ankhiwala, M. D. & Hathi, M. V. (1996). *Indian J. Heterocycl. Chem.* **5**, 229–230.

Beher, L. C., Fusco, R. & Jufbose, C. H. (1967). *The Chemistry of Heterocyclic Compounds.* Vol 22, *Pyrazoles, Pyrazolidines, Indazoles and Condensed Rings.* Chichester: Wiley Interscience.

Enraf–Nonius (1989). *CAD-4 Software.* Version 5.0. Enraf–Nonius, Delft, The Netherlands.

Frenz, B. A. (1978). *The Enraf–Nonius CAD-4 SDP – a Real-Time System for Concurrent X-ray Data Collection and Crystal Structure Solution. Computing in Crystallography*, edited by H. Schenk, R. Olthof-Hazekamp, H. van Koningsveld & G. C. Bassi, pp. 64–71. Delft University Press.

Gusar, N. I., Gulko, L. I., Gorodetskova, N. R. & Klebanov, B. M. (1995). *Chem. Abstr.* **122**, 290766f.

Jorgensen, P., Koksbang, R. & Lindhardt, P. (1986). *Acta Cryst.* C**42**, 1273–1274.

Khalil, S., Hossain, M. B. van der Helm, D., Alam, M. & Sanduja, R. (1996). *Acta Cryst.* C**52**, 1272–1274.

Nardelli, M. (1983). *Comput. Chem.* **7**, 95–98.

Nardelli, M. (1995). *J. Appl. Cryst.* **28**, 659.

Sharma, S. M., Osha, A. C. & Manohar, R. (1993). *Indian J. Biochem.* **2**, 63–65.

Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, pp 467–473.

Sheldrick, G. M. (1997). *SHELXL97. Program for the Refinement of Crystal Structures.* University of Göttingen, Germany.

Zsolnai, L. (1997). *ZORTEP. An Interactive ORTEP Program for Structure Illustration.* University of Heidelberg, Germany.

Acta Cryst. (1999). C**55**, 1677–1680

(+)-23,24-Dinor-3α,9α-epoxy-11-oxo-5β-cholan-22-oic acid: mutual carboxyl-to-ether dimeric hydrogen bonding in a steroidal carboxy–keto ether

Hugh W. Thompson, Andrew P. J. Brunskill and Roger A. Lalancette*

Carl A. Olson Memorial Laboratories, Department of Chemistry, Rutgers University, Newark, NJ 07102, USA. E-mail: lalancette@hades.rutgers.edu

(*Received 8 February 1999; accepted 6 May 1999*)

Abstract

The title steroidal carboxy–keto ether, $C_{22}H_{32}O_4$, forms non-centrosymmetric dimers involving two distinct carboxyl-to-ether hydrogen bonds [O···O = 2.718 (3)

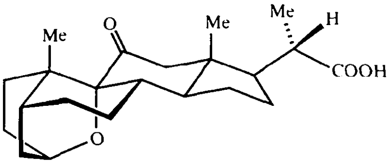
Acta Crystallographica Section C
ISSN 0108-2701 © 1999

and 2.701 (3) Å], in which the ketone does not participate. The asymmetric unit is the dimer, whose two molecules are conformationally distinct. The principal conformational difference between the two molecules lies in the carboxyl-group rotation which differs by 28.2 (5)°. The C=O oxygen of one of the carboxyl groups shows unusual anisotropy, attributed to thermal motion associated with a packing cavity surrounding that carboxyl group but absent in the other. Several C—H···O close contacts are present.

Comment

Supplementing a carboxylic acid with other functional groups expands the repertoire of available hydrogen-bonding modes. For keto acids, the five solid-state motifs known, in order of diminishing prevalence, are: acid dimerization (Thompson *et al.*, 1998), carboxyl-to-ketone catemerization (Zewge *et al.*, 1998), intramolecular hydrogen-bond formation (Thompson *et al.*, 1996), carboxyl-to-ketone dimerization (Kosela *et al.*, 1995) and acid-to-acid catemerization (Lalancette *et al.*, 1998). Several cases also exist of hydrates with more complex hydrogen-bonding patterns (Lalancette *et al.*, 1997, 1998).

In nonracemic polycyclic keto acids (*e.g.* terpenoids), the above hydrogen-bonding preferences shift away from acid dimers, apparently due to the unavailability of centrosymmetric arrangements, combined with conformational restrictions imposed by the ring systems (Brunskill *et al.*, 1999). We have investigated the hydrogen-bonding behavior of the steroidal carboxy–keto ether (I), present as a single enantiomer. Although the category of ε-keto acids into which (I) falls contains examples of catemers as well as dimers (Zewge *et al.*, 1998), neither of these hydrogen-bonding modes is adopted. Instead, the asymmetric unit consists of a pair of molecules, (I) and (I′), dimerized by hydrogen bonding between the acid and ether functions, and shown with the steroid numbering in Fig. 1.



(I)

Because of the rigidity of the polycyclic skeleton, the most significant conformational options lie in the branched chain attached at C17. Here, the substituents at C20, which has the *S* configuration, are staggered with respect to those at C17, with the methyl (C21) *anti* to C16 and the torsional angles C16—C17—C20—C21 [−177.4 (3)°] and C16′—C17′—C20′—C21′ [−173.1 (3)°] differing by 4.3 (4)° for the two molecules. The principal conformational difference between (I) and (I′), however, lies in the rotation of the carboxyl group about C20—C22. Although the carboxyl C=O is aimed toward the *β* face of the molecule in both species, the torsional angle C17—C20—C22—O3 is 56.0 (4)°, while the same angle in (I′) is 84.2 (3)°, a difference of 28.2 (5)°. The entire configurational and general conformational arrangement of the side-chain at C17 resembles that for (+)-3-oxo-23,24-dinor-5α-cholan-22-oic acid and its monohydrate (Lalancette *et al.*, 1998), whose hydrogen-bonding arrangements, however, involve an acid-to-acid catemer and acid-to-water-to-acid patterns.

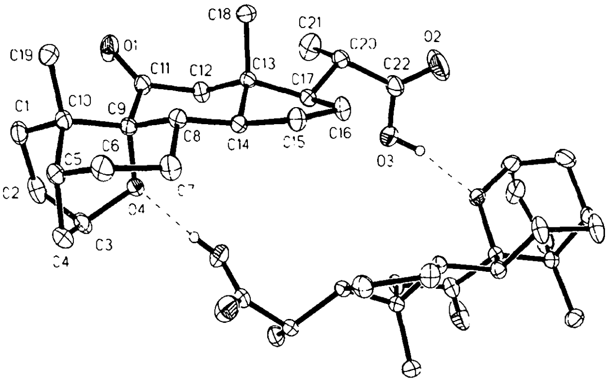


Fig. 1. The asymmetric unit for compound (I) showing the dimeric carboxyl-to-ether hydrogen bonding. The steroidal numbering is shown for only the unprimed molecule. All non-carboxyl H atoms have been excluded for clarity. Displacement ellipsoids are set at the 20% probability level.

As is well recognized, bicyclo[2.2.2]octane systems are not entirely rigid, with the nominally parallel bonds often significantly skewed, presumably to relieve eclipsing strain in their ethylene bridges (Deutsch, 1972; Blackstock *et al.*, 1987; Zimmerman *et al.*, 1992). In (I), this bridged, ether-containing portion of the molecule displays a packing-induced conformational difference for (I) *versus* (I′), described by the C8—C9—O4—C3 torsional angle, which is found to differ for (I) and (I′) by 3.4 (4)°.

Complete or partial averaging of C—O bond lengths and C—C—O angles by disorder is frequent in acid-to-acid dimers (Leiserowitz, 1976). However, the geometry of acids that are not dimerically hydrogen bonded precludes any of the usual disordering processes, and typically these are highly ordered. The bond lengths in (I) are 1.170 (5) and 1.309 (4) Å, with angles of 126.3 (4) and 112.9 (3)°; in (I′) the bond lengths are 1.202 (4) and 1.334 (4) Å, with angles of 126.3 (3) and 111.5 (3)°. Our own survey of 56 keto acid structures which are not acid dimers gives average values of 1.20 (1) and 1.32 (2) Å, and 124.5 (14) and 112.7 (17)° for these lengths and angles, while values cited as typical for highly ordered dimeric carboxyls are 1.21 and 1.31Å, and 123 and 112° (Borthwick, 1980).

The O atom of the C═O carboxyl group in molecule (I) exhibits an unusual degree of anisotropy, which we attribute to thermal motion permitted by a surrounding cavity. Assessment of van der Waals interactions near this oxygen (O2) in the packed structure reveals such a cavity in (I), which is absent in (I′). For (I), the nearest H atom is H21*F* of a translationally related neighbor in the *a* direction, at a distance of 3.05 Å. For (I′) the nearest intermolecular hydrogen is H19*D* in a screw-related neighbor in the *b* direction (2.55 Å).

The hydrogen bonding present is entirely mutual carboxyl-to-ether hydrogen bonding within the dimerized asymmetric unit [O3···O4′ = 2.718 (3) Å and O3′···O4 = 2.701 (3) Å]. Cases of carboxyl-to-ketone dimerization are among the rarest modes of hydrogen bonding in keto acids (Peeters *et al.*, 1983; Abell *et al.*, 1991; Kosela *et al.*, 1995), but in this instance the ketone takes no part in the hydrogen bonding. A contributing factor in this hydrogen-bonding mode may be the greater basicity of ethers compared to ketones and acids. Typical pK_a values cited for these three functional groups (protonated) are −3.5, −7 and −6, respectively (March, 1985; Searles & Tamres, 1967), suggesting that hydrogen bonding to an ether might be significantly favored in such a case. In other cases where carboxyl-to-ether hydrogen bonding is the only such interaction present the bonding motif is seen to be catemeric, usually following a screw axis (Funk *et al.*, 1988; Vencato *et al.*, 1986; Semmelhack & Zhang, 1989; Mravik *et al.*, 1996; Loyola *et al.*, 1991; Brown *et al.*, 1994; Cambie *et al.*, 1998).

The cell contains four asymmetric units ($Z = 8$). Four attractive intermolecular C—H···O close contacts are found: C14′—H14*B*···O3^{i} (2.65 Å), C8—H8*A*···O1′^{ii} (2.61 Å), C19′—H19*D*···O2′^{iii} (2.55 Å) and C14—H14*A*···O3′^{i} (2.65 Å) [symmetry codes: (i) x, y, z; (ii) $x, y+1, z$; (iii) $2-x, -\frac{1}{2}+y, \frac{1}{2}-z$]. All of the above contacts probably represent polar attractions contributing materially to the packing forces (Jönsson, 1972; Leiserowitz, 1976; Berkovitch-Yellin & Leiserowitz, 1982).

The solid-state (KBr) infrared spectrum of (I) displays normal ketone absorption at 1710 cm^{-1}, plus a band at 1736 cm^{-1}, conforming to known shifts due to removal of hydrogen bonding from carboxyl C═O. In $CHCl_3$ solution, where dimers predominate, the peaks coalesce to a single absorption at 1708 cm^{-1}, with a typical carboxyl-dilution shoulder at *ca* 1740 cm^{-1}.

Experimental

Compound (I) was purchased as the (+)-enantiomer, of known absolute configuration, from Steraloids Inc., Newport, RI, USA. Crystals (m.p. 467 K) were obtained from a 1:1:1 mixture of acetone, acetonitrile and water.

Crystal data

$C_{22}H_{32}O_4$
$M_r = 360.48$
Orthorhombic
$P2_12_12_1$
$a = 10.588\ (1)$ Å
$b = 12.547\ (1)$ Å
$c = 28.989\ (2)$ Å
$V = 3851.1\ (5)$ Å^3
$Z = 8$
$D_x = 1.243$ Mg m^{-3}
D_m not measured

Cu *Kα* radiation
$\lambda = 1.54180$ Å
Cell parameters from 25 reflections
$\theta = 5.6$–29.6°
$\mu = 0.668$ mm^{-1}
$T = 293\ (2)$ K
Irregular block
0.76 × 0.40 × 0.16 mm
Colorless

Data collection

Siemens *P*4 diffractometer
$2\theta/\theta$ scans
Absorption correction: numerical (Sheldrick, 1997)
$T_{min} = 0.673$, $T_{max} = 0.817$
6440 measured reflections
3597 independent reflections (plus 2108 Friedel-related reflections)

4819 reflections with $I > 2\sigma(I)$
$R_{int} = 0.031$
$\theta_{max} = 67.5°$
$h = -12 \rightarrow 12$
$k = 0 \rightarrow 14$
$l = 0 \rightarrow 34$
3 standard reflections every 97 reflections intensity variation: <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.051$
$wR(F^2) = 0.133$
$S = 1.03$
5705 reflections
479 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0655P)^2 + 0.7672P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.17$ e Å^{-3}

Extinction correction: *SHELXL*97 (Sheldrick, 1997*a*)
Extinction coefficient: 0.0048 (3)
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = −0.1 (3)

Table 1. *Selected geometric parameters (Å, °)*

O1—C11	1.209 (4)	O1′—C11′	1.206 (4)
O2—C22	1.170 (5)	O2′—C22′	1.202 (4)
O3—C22	1.309 (4)	O3′—C22′	1.334 (4)
O4—C3	1.458 (4)	O4′—C3′	1.453 (4)
O4—C9	1.466 (4)	O4′—C9′	1.464 (4)
O2—C22—C20	126.3 (4)	O2′—C22′—C20′	126.3 (3)
O3—C22—C20	112.9 (3)	O3′—C22′—C20′	111.5 (3)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H3···O4′	0.82	1.92	2.718 (3)	164
O3′—H3′···O4	0.82	1.90	2.701 (3)	167
C14′—H14*B*···O3	0.98	2.65	3.589 (4)	161
C8—H8*A*···O1′^{i}	0.98	2.61	3.366 (4)	134
C19′—H19*D*···O2′^{ii}	0.96	2.55	3.433 (5)	152
C14—H14*A*···O3′	0.98	2.65	3.601 (4)	165

Symmetry codes: (i) $x, 1+y, z$; (ii) $2-x, y-\frac{1}{2}, \frac{1}{2}-z$.

Data collection: *XSCANS* (Siemens, 1996). Cell refinement: *XSCANS*. Data reduction: *XSCANS*. Program(s) used to solve structure: *PATSEE* in *SHELXS*97 (Sheldrick, 1997*b*). Program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997*a*). Molecular graphics: *SHELXL*97. Software used to prepare material for publication: *SHELXL*97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1199). Services for accessing these data are described at the back of the journal.

References

Abell, A. D., Trent, J. O. & Robinson, W. T. (1991). *J. Chem. Soc. Chem. Commun.* pp. 362–363.

Berkovitch-Yellin, Z. & Leiserowitz, L. (1982). *J. Am. Chem. Soc.* **104**, 4052–4064.

Blackstock, S. C., Lorand, J. P. & Kochi, J. K. (1987). *J. Org. Chem.* **52**, 1451–1460.

Borthwick, P. W. (1980). *Acta Cryst.* B**36**, 628–632.

Brown, A., Grigg, R., Ravishankar, T. & Thornton-Pett, M. (1994). *Tetrahedron Lett.* **35**, 2753–2756.

Brunskill, A. P. J., Thompson, H. W. & Lalancette, R. A. (1999). *Acta Cryst.* C**55**, 566–568.

Cambie, R. C., Mitchell, L. H., Rickard, C. E. F. & Rutledge, P. S. (1998). *Acta Cryst.* C**54**, 1672–1673.

Deutsch, E. (1972). *J. Org. Chem.* **37**, 3481–3486.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Funk, R. L., Daily, W. J. & Parvez, M. (1988). *J. Org. Chem.* **53**, 4141–4143.

Jönsson, P.-G. (1972). *Acta Chem. Scand.* **26**, 1599–1619.

Kosela, S., Yulizar, Y., Chairul, Tori, M. & Asakawa, Y. (1995). *Phytochemistry*, **38**, 691–694.

Lalancette, R. A., Brunskill, A. P. J. & Thompson, H. W. (1997). *Acta Cryst.* C**53**, 1838–1842.

Lalancette, R. A., Thompson, H. W. & Brunskill, A. P. J. (1998). *Acta Cryst.* C**54**, 421–424.

Leiserowitz, L. (1976). *Acta Cryst.* B**32**, 775–802.

Loyola, L. A., Morales, G., Rodriguez, B., Jimenez-Barbero, J., Pedreros, S., de la Torre, M. C. & Perales, A. (1991). *J. Nat. Prod.* **54**, 1404–1408.

March, J. (1985). *Advanced Organic Chemistry*, 3rd ed., p. 220. New York: Wiley.

Mravik, A., Bocskei, Z., Keszei, S., Elekes, F. & Fogassy, E. (1996). *Tetrahedron Asymmetry*, **7**, 1477–1484.

Peeters, O. M., Blaton, N. M. & de Ranter, C. J. (1983). *Bull. Soc. Chim. Belg.* **92**, 191–192.

Searles, S. Jr & Tamres, M. (1967). *The Chemistry of the Ether Linkage*, edited by S. Patai, pp. 260–262. New York: Wiley.

Semmelhack, M. F. & Zhang, N. (1989). *J. Org. Chem.* **54**, 4483–4485.

Sheldrick, G. M. (1997*a*). *SHELXL97. Program for the Refinement of Crystal Structures.* University of Göttingen, Germany.

Sheldrick, G. M. (1997*b*). *SHELXS97. Program for the Solution of Crystal Structures.* University of Göttingen, Germany.

Siemens (1996). *XSCANS User's Manual.* Version 2.2. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Thompson, H. W., Lalancette, R. A. & Brunskill, A. P. J. (1998). *Acta Cryst.* C**54**, 1180–1182.

Thompson, H. W., Lalancette, R. A. & Coté, M. L. (1996). *Acta Cryst.* C**52**, 2372–2376.

Vencato, I., Mascarenhas, Y. P., Souza, M. P., Matos, M. E. O., Machado, M. I. L. & Filho, R. B. (1986). *Ann. Acad. Bras. Cienc.* **58**, 525–529.

Zewge, D., Brunskill, A. P. J., Lalancette, R. A. & Thompson, H. W. (1998). *Acta Cryst.* C**54**, 1651–1653.

Zimmerman, H. E., King, R. K. & Meinhardt, M. B. (1992). *J. Org. Chem.* **57**, 5484–5492.

Acta Cryst. (1999). C**55**, 1680–1682

(+)-3-Oxoandrosta-1,4-diene-17β-carboxylic acid: catemeric hydrogen bonding in a steroidal keto acid

Hugh W. Thompson, Roger A. Lalancette* and Andrew P. J. Brunskill

Carl A. Olson Memorial Laboratories, Department of Chemistry, Rutgers University, Newark, NJ 07102, USA. E-mail: lalancette@hades.rutgers.edu

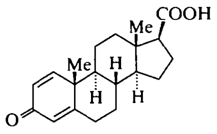
(*Received 14 April 1999; accepted 3 June 1999*)

Abstract

The title keto acid, $C_{20}H_{26}O_3$, forms translational carboxyl–ketone hydrogen-bonding catemers [$O\cdots O = 2.665\,(3)$ Å]. The cell contains two molecules screw-related in **b**, with opposite end-to-end orientation, yielding two parallel, counterdirectional screw-related hydrogen-bonding chains. Intermolecular $C—H\cdots O{=}C$ close contacts to the carboxyl group were found, involving three different neighboring molecules.

Comment

Our interest in the crystal structures of keto carboxylic acids centers on the molecular characteristics that control their five known solid-state hydrogen-bonding patterns. In achiral and racemic keto acids, the most common motif is acid dimerization, in which the ketone is not involved (Thompson *et al.*, 1991; Coté *et al.*, 1995). However in nonracemates with significant conformational restrictions (*e.g.* polycyclics), the prevalence of acid-to-ketone catemers rises dramatically (Brunskill *et al.*, 1999). We have consequently sought keto acids with terpenoid origins as subject materials, and now report the crystal structure and hydrogen-bonding behavior of the title steroid, (I).



(I)

Fig. 1 shows the asymmetric unit with its steroid numbering. The only significant conformational option is rotation of the carboxyl group, which is turned so that the C16—C17 bond lies near the carboxyl plane, with the C=O turned toward C16 [C16—C17—C20—O2 = −14.2 (5)°]. In the 1,2-dihydro analog of this compound, (II), whose structure we have previously reported (Brunskill *et al.*, 1997), this angle was −10.3 (4)°. The two