by C(2), C(3), C(4), C(5), C(6)] is 0·004 (11) Å. N(1), N(2), C(1), C(2), C(3) are roughly planar and coplanar with the benzene ring. The torsion angles along bonds of the hydrazone part are very close to 180° (Table 3). The best least-squares plane defined by all these atoms gave displacements of the atoms from 0·005 (9) [for C(1')] to 0·078 (9) Å [for C(3')]. The dihedral angle between planes defined by N(1), N(2), C(2), C(3) and C(3), C(4), C(5), C(6) is 88·2 (8)°. The sugar conformation is stabilized by an intramolecular hydrogen bond between the hydrazone moiety and a nitro group [N(1)—H···O(1') 2·613 (7); N(1)—H(N1) 0·81; H(N1)···O(1') 2·10 Å; $\angle$120°] (Fig. 2).

References

BJÅMER, K., FURBERG, S. & PETERSEN, C. S. (1964). *Acta Chem. Scand.* **18**, 587–595.
CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A24, 321–324.
DUKEFOS, T. & MOSTAD, A. (1965). *Acta Chem. Scand.* **19**, 685–696.
FURBERG, S. & PETERSEN, C. S. (1962). *Acta Chem. Scand.* **16**, 1539–1548.
FURBERG, S. & SOLBAKK, J. (1969). *Acta Chem. Scand.* **23**, 3248–3256.
FUSKA, J., LINEK, K. & BUZINKAY, Š. (1974). *Neoplasma*, **21**, 561–568.
KETTNER, M., MAČIČKOVÁ, T. & LINEK, K. (1983). *Experientia.* In the press.
LINEK, K. & NOVOTNÁ, Z. (1980). Czechoslovak Patent 208 807.
MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J. P. & WOOLFSON, M. M. (1980). *MULTAN*80. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.
STEWART, J. M., MACHIN, P. A., DICKINSON, C. W., AMMON, H. L., HECK, H. & FLACK, H. (1976). The XRAY76 system. Tech. Rep. TR-446. Computer Science Center, Univ. of Maryland, College Park, Maryland.
STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
TAKEDA, Y. (1979). *Carbohydr. Res.* **77**, 9–23.
ZEMEK, J. & LINEK, K. (1977). *Folia Microbiol. (Prague)*, **22**, 237–238.

Structures of 3β-Hydroxy-5β-bufa-14,20,22-trienolide, C24H32O3, and 3β-Acetoxy-15α-(o-nitrobenzoyloxy)-7-oxo-5β,14β-bufa-8,20,22-trienolide, C33H35NO9[*]

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Abstract. $C_{24}H_{32}O_3$ (I), $M_r = 368\cdot5$, orthorhombic, $P2_12_12_1$, $a = 8\cdot461$ (4), $b = 12\cdot725$ (6), $c = 19\cdot12$ (1) Å, $V = 2058$ (2) Å^3, $D_x = 1\cdot19$ Mg m^{-3}, $Z = 4$, μ(Mo $K\alpha$) = 0·042 mm^{-1}, $F(000) = 800$, final $R = 0\cdot073$ for 2160 reflections; $C_{33}H_{35}NO_9$ (II), $M_r = 589\cdot6$, monoclinic, $P2_1$, $a = 11\cdot301$ (6), $b = 39\cdot53$ (2), $c = 7\cdot650$ (4) Å, $\beta = 103\cdot92$ (2)°, $V = 3317$ (3) Å^3, $D_x = 1\cdot18$ Mg m^{-3}, $Z = 4$, μ(Mo $K\alpha$) = 0·052 mm^{-1}, $F(000) = 1248$, final $R = 0\cdot128$ for 3184 reflections; graphite-monochromated Mo $K\alpha$ radiation ($\lambda = 0\cdot7107$ Å) used in both determinations. A conformational analysis of the lactone ring with respect to the remainder of the molecule has been performed for both bufatrienolides. The crystallographically determined conformations correspond well with theoretically predicted energy minima.

Introduction. Medicinal preparations derived from plants of the genus *Scilla* (Lilliaceae family) and toads of the genus *Bufo* (Bufonidae family) have been used

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from antiquity for heart failure (*e.g.* congestive) and a variety of other purposes. The active constituents have been shown to be steroids bearing a 5-substituted 2-pyrone ring at the 17β position known as bufadienolides (Ode, Pettit & Kamano, 1975). Biosynthetic products of this type continue to be of interest in areas ranging from cancer (Kamano, Pettit, Inoue, Tozawa & Komeichi, 1977) and cardiology (Stache, Radscheit, Haede & Fritsch, 1982) to firefly defensive substances (Meinwald, Wiemer & Eisner, 1979). The present crystal structure determinations of two bufadienolide derivatives were required as part of total synthetic and stereochemical studies of naturally occurring bufadienolides.

Experimental. Preliminary photography of single crystals of (I) and (II) established their space groups as $P2_12_12_1$ and $P2_1$ respectively. In each case accurate cell constants were obtained by least squares from the settings of 25 reflections measured on a Philips PW 1100 four-circle diffractometer; intensities were collected by the ω–2θ scan technique and the intensities of three reference reflections were monitored periodically to ascertain stability of the crystals. Experimental details of the data collection are listed in Table 1.

Both (I) and (II) were solved by direct methods using the random-start tangent-refinement method (Yao Jia-xing, 1981) as incorporated by G. M. Sheldrick into the *SHELXTL* program. For (I), the ensuing E map yielded the positions of all non-hydrogen atoms and this was confirmed by subsequent weighted difference syntheses. The final full-matrix least-squares refinement was carried out using the *SHELX*76 system (Sheldrick, 1978) with all non-hydrogen atoms treated anisotropically. H atoms in the methyl groups were refined as rigid units and remaining H atoms were placed at $1\cdot00$ Å from their parent carbons. The H positions were dictated by the geometry of the molecule except for the hydroxyl H in the 3β position which was placed in a site calculated according to hydrogen-bonding considerations (see *Discussion*) and constrained to ride at $1\cdot00$ (1) Å from the parent oxygen. For (II), the initial E maps yielded 77 of the non-hydrogen atoms, and the remainder were located in subsequent weighted difference syntheses. Owing to the large number of independent atoms, final refinements were carried out using the *SHELX*76 system (Sheldrick, 1978) with the blocked-matrix technique, all atoms being treated isotropically; H atoms were placed at $1\cdot00$ Å from their parent carbons, their positions being dictated by the geometry of the molecules, with the methyl H atoms refined as rigid groups. In both structures care was employed in the determination of O(21) *vs* C(23). This was achieved by omitting those atoms from a structure factor calculation and analysing the appropriate peaks in the subsequent difference electron density map. Details of the final refinements (function minimized $\sum w||F_o| - |F_c||^2$) for both (I) and (II) are shown in

Table 1. The weighting schemes were refined to give the smallest systematic variation of $w\Delta^2$ with the magnitude of F_o, as shown by analyses of variance computed after the final cycles. In the final cycles for each structure the mean e.s.d. in the parameters of the non-hydrogen atoms was >10 times the average parameter shift, while final difference maps were smooth showing in both structures maximum residual electron density of the order of $0\cdot5$ e Å^{-3}. Complex neutral-atom scattering factors were taken from Cromer & Mann (1968) for C, N, O, and from Stewart, Davidson & Simpson (1965) for H, with dispersion corrections from Cromer & Liberman (1970).

Discussion. Table 2 lists the final fractional coordinates.*

Perspective views of (I) and (II) [a single illustration representative of both molecules A and B for (II)] are shown in Fig. 1. Bond lengths, angles and selected torsion angles are shown in Figs. 2 to 4. Both determinations were undertaken to establish unequivocally the atomic and molecular configurations

* Lists of structure factors, hydrogen-atom coordinates and anisotropic temperature factors have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38420 (41 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.
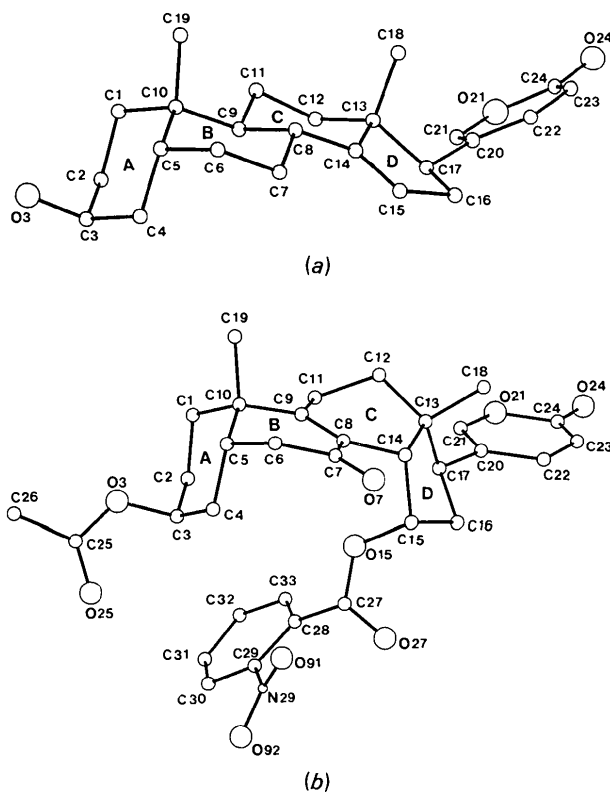

(a)

(b)

Fig. 1. Perspective views of structures (a) (I) and (b) (II) [single representative for molecules A and B for (II)].

required for projected circular-dichroism studies and for the purpose of eventually developing a useful synthetic approach to certain 11-oxygenated bufadienolides (Pettit, Kamano, Inoue, Komeichi, Nassimbeni & Niven, 1982). An earlier assignment for bufatrienolide (II) based upon other techniques has now been verified.

Table 1. *Experimental and refinement parameters*

Compound	(I)	(II)
Crystal dimensions (mm)	$0.55 \times 0.34 \times 0.40$	$0.50 \times 0.28 \times 0.28$
Scan mode	$\omega-2\theta$	$\omega-2\theta$
Scan width ($°\theta$)	1·1	0·3
Scan speed ($°\theta s^{-1}$)	0·04	0·01
Range scanned (2θ) (°)	6–48	6–46
Stability of standard reflections (%)	1·07	2·35
Number of reflections collected	3513	4716
Number of 'observed' reflections (with $I_{rel} > 2\sigma I_{rel}$)	2160	3184
Number of variables	256	355
R	0·073	0·128
$R_w(=\sum w^{1/2}\|F_o\|-\|F_c\|\|/\sum w^{1/2}\|F_o\|)$	0·086	0·141
Weighting scheme w	$(\sigma^2 F + 0.009953 F^2)$	$(\sigma^2 F + 0.010678 F^2)$
U (methyl H) (Å^2)	0·072 (8)	0·12 (2)
U (aromatic, methylene and methine H) (Å^2)	0·074 (4)	0·07 (1)
U (hydroxyl) (Å^2)	0·20 (6)	—

Table 2. *Fractional atomic coordinates* ($\times 10^4$) *and temperature factors* ($\text{Å}^2 \times 10^3$) *for non-hydrogen atoms*

$U_{eq} = \frac{1}{3}$ (trace of the orthogonalized U_{ij} matrix).

Compound (I)

	x	y	z	U_{eq}
C(1)	2072 (8)	3328 (4)	1508 (3)	48 (3)
C(2)	2224 (8)	3028 (5)	738 (3)	51 (3)
C(3)	3862 (8)	2674 (5)	560 (4)	57 (3)
C(4)	5066 (7)	3542 (5)	756 (3)	50 (3)
C(5)	4943 (7)	3887 (4)	1528 (3)	48 (3)
C(6)	6145 (8)	4716 (5)	1690 (4)	64 (4)
C(7)	5743 (7)	5794 (5)	1362 (4)	54 (3)
C(8)	4073 (7)	6130 (4)	1568 (3)	44 (3)
C(9)	2828 (6)	5288 (4)	1402 (3)	43 (3)
C(10)	3246 (7)	4205 (5)	1738 (3)	45 (3)
C(11)	1167 (7)	5688 (5)	1563 (3)	53 (3)
C(12)	752 (7)	6682 (4)	1176 (4)	53 (3)
C(13)	1911 (7)	7586 (4)	1325 (3)	40 (3)
C(14)	3609 (7)	7195 (4)	1248 (3)	43 (3)
C(15)	4500 (7)	7871 (5)	913 (3)	48 (3)
C(16)	3620 (8)	8820 (5)	711 (4)	63 (4)
C(17)	1889 (7)	8451 (4)	773 (3)	44 (3)
C(18)	1687 (9)	8009 (5)	2063 (3)	57 (3)
C(19)	3139 (9)	4275 (5)	2544 (3)	62 (4)
C(20)	631 (7)	9322 (4)	881 (3)	46 (3)
C(21)	−889 (7)	9139 (5)	649 (3)	60 (4)
C(22)	927 (7)	10251 (4)	1187 (3)	48 (3)
C(23)	−181 (5)	10961 (4)	1304 (3)	36 (3)
C(24)	−1704 (10)	10813 (5)	1130 (4)	60 (4)
O(3)	4144 (6)	1709 (3)	904 (3)	71 (3)
O(21)	−2041 (7)	9871 (5)	765 (3)	90 (4)
O(24)	−2686 (6)	11485 (4)	1275 (3)	83 (3)

Table 2 (cont.)

Compound (II)

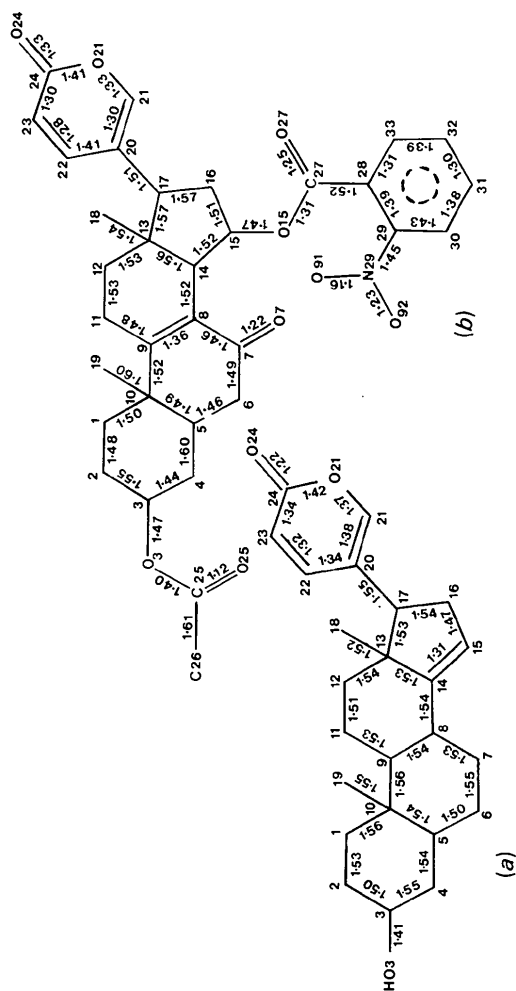|	Molecule *A*					Molecule *B*			
	x	y	z	U_{iso}		x	y	z	U_{iso}
C(1)	4492 (15)	9966 (5)	1280 (22)	75 (4)	C(1)	9783 (14)	6683 (4)	5937 (21)	68 (4)
C(2)	3208 (15)	9974 (5)	232 (23)	77 (5)	C(2)	8651 (16)	6673 (5)	4514 (22)	77 (5)
C(3)	2355 (17)	10096 (4)	1417 (23)	76 (5)	C(3)	8895 (16)	6513 (5)	2790 (23)	75 (4)
C(4)	2504 (16)	9911 (5)	3076 (24)	81 (5)	C(4)	9934 (14)	6704 (4)	2243 (21)	69 (4)
C(5)	3895 (13)	9856 (4)	4126 (19)	62 (4)	C(5)	11046 (14)	6752 (4)	3708 (20)	67 (4)
C(6)	3907 (17)	9641 (4)	5686 (22)	75 (5)	C(6)	11891 (16)	6983 (4)	2984 (25)	79 (5)
C(7)	3606 (12)	9285 (3)	5126 (18)	52 (3)	C(7)	11411 (14)	7350 (4)	2653 (22)	72 (4)
C(8)	3945 (12)	9164 (3)	3515 (17)	51 (3)	C(8)	10701 (11)	7467 (3)	3884 (17)	47 (3)
C(9)	4454 (10)	9371 (3)	2473 (15)	38 (3)	C(9)	10416 (12)	7279 (3)	5177 (17)	50 (3)
C(10)	4674 (13)	9745 (4)	2913 (19)	55 (4)	C(10)	10776 (14)	6907 (4)	5421 (20)	64 (4)
C(11)	4813 (14)	9231 (4)	876 (19)	59 (4)	C(11)	9786 (12)	7435 (4)	6483 (18)	52 (3)
C(12)	5293 (14)	8869 (4)	1276 (21)	64 (4)	C(12)	10213 (13)	7815 (4)	6868 (19)	60 (4)
C(13)	4365 (10)	8626 (3)	1738 (15)	38 (3)	C(13)	10000 (11)	8024 (3)	5204 (16)	40 (3)
C(14)	3612 (11)	8800 (3)	2954 (17)	45 (3)	C(14)	10290 (11)	7828 (3)	3557 (16)	44 (3)
C(15)	2275 (12)	8740 (3)	2085 (18)	52 (3)	C(15)	9148 (11)	7869 (3)	2031 (17)	44 (3)
C(16)	2260 (13)	8434 (4)	893 (18)	55 (3)	C(16)	8446 (13)	8176 (4)	2471 (18)	53 (3)
C(17)	3369 (11)	8506 (3)	44 (16)	44 (3)	C(17)	8631 (10)	8128 (3)	4480 (15)	40 (3)
C(18)	5049 (13)	8317 (4)	2716 (19)	56 (4)	C(18)	10805 (13)	8334 (4)	5645 (20)	60 (4)
C(19)	6072 (16)	9788 (5)	3941 (24)	80 (5)	C(19)	11934 (15)	6890 (5)	6930 (23)	75 (4)
C(20)	3749 (11)	8210 (3)	−942 (16)	39 (3)	C(20)	8187 (11)	8412 (3)	5471 (16)	43 (3)
C(21)	4161 (14)	8274 (4)	−2359 (20)	63 (4)	C(21)	7655 (13)	8356 (4)	6774 (19)	62 (4)
C(22)	3564 (13)	7868 (4)	−566 (20)	59 (4)	C(22)	8269 (13)	8748 (4)	5013 (19)	56 (4)
C(23)	3900 (13)	7642 (4)	−1545 (19)	59 (4)	C(23)	7739 (12)	8998 (4)	5800 (18)	52 (3)
C(24)	4332 (19)	7713 (5)	−2933 (28)	96 (6)	C(24)	7197 (16)	8937 (5)	7093 (23)	74 (5)
C(25)	1714 (29)	10675 (7)	1654 (38)	131 (8)	C(25)	8533 (23)	5916 (6)	3041 (30)	107 (6)
C(26)	2330 (35)	11042 (8)	2074 (48)	171 (13)	C(26)	9253 (30)	5584 (8)	3673 (45)	146 (10)
C(27)	632 (16)	9077 (5)	524 (23)	75 (5)	C(27)	7431 (14)	7515 (4)	623 (21)	66 (4)
C(28)	248 (11)	9352 (3)	−884 (17)	44 (3)	C(28)	6597 (12)	7244 (4)	921 (18)	51 (3)
C(29)	−649 (15)	9587 (4)	−812 (21)	67 (4)	C(29)	6240 (12)	6981 (3)	−256 (18)	49 (3)
C(30)	−1013 (17)	9823 (5)	−2269 (23)	82 (5)	C(30)	5358 (14)	6754 (4)	55 (21)	67 (4)
C(31)	−468 (18)	9785 (5)	−3686 (28)	89 (5)	C(31)	4916 (16)	6790 (5)	1520 (22)	75 (4)
C(32)	387 (18)	9567 (5)	−3733 (23)	77 (5)	C(32)	5250 (15)	7056 (4)	2656 (23)	73 (4)
C(33)	725 (14)	9347 (4)	−2287 (19)	62 (4)	C(33)	6094 (12)	7284 (4)	2326 (18)	53 (3)
O(3)	2693 (13)	10450 (4)	1812 (19)	99 (4)	O(3)	9349 (12)	6169 (4)	3212 (17)	95 (4)
O(7)	3143 (9)	9097 (3)	6047 (14)	71 (3)	O(7)	11585 (11)	7507 (3)	1399 (16)	89 (3)
O(15)	1818 (8)	9041 (2)	997 (11)	52 (2)	O(15)	8365 (7)	7567 (2)	1994 (11)	48 (2)
O(21)	4497 (12)	8049 (3)	−3436 (17)	92 (4)	O(21)	7116 (11)	8598 (3)	7615 (16)	85 (3)
O(24)	4641 (17)	7506 (5)	−4123 (26)	142 (6)	O(24)	6740 (14)	9142 (4)	7847 (20)	112 (4)
O(25)	734 (32)	10595 (9)	1364 (43)	217 (11)	O(25)	7477 (21)	5986 (6)	2574 (27)	157 (7)
O(27)	−111 (18)	8879 (5)	968 (25)	140 (6)	O(27)	7236 (12)	7692 (3)	−779 (17)	91 (4)
O(291)	−475 (21)	9545 (6)	2140 (33)	164 (7)	O(291)	7764 (14)	7010 (4)	−1623 (20)	108 (4)
O(292)	−2142 (18)	9748 (5)	588 (25)	136 (6)	O(292)	6183 (12)	6781 (4)	−3091 (18)	98 (4)
N(29)	−1140 (21)	9611 (5)	768 (29)	116 (6)	N(29)	6754 (14)	6919 (4)	−1663 (20)	79 (4)

Fig. 2. Bond lengths (Å) for (a) structure (I), (b) structure (II), molecule A, (c) structure (II), molecule B; for (a) 0·008 Å ≤σ≤ 0·01 Å, for (b) and (c) 0·01 Å ≤σ≤ 0·05 Å.
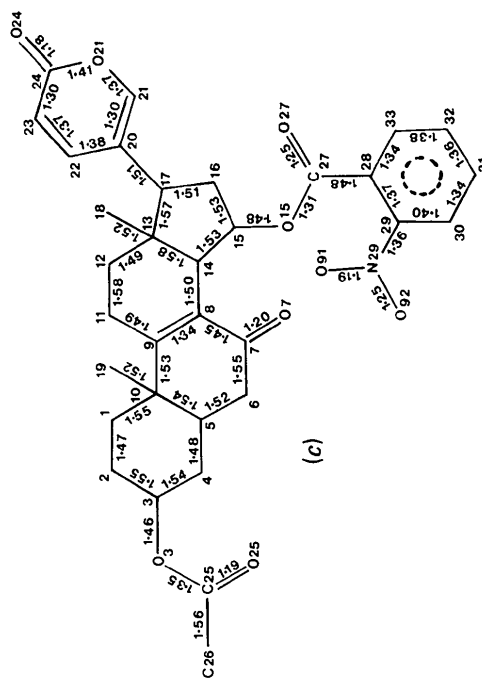
Fig. 2 (cont.) (c)

Table 3. Ring conformations of the steroid skeletons

| | | Asymmetry parameters* | | | | Pucker parameters† | | |
| | | (I) | (II) | | | (I) | (II) | |
			A	B			A	B
Ring A	$\Delta C_{2(2)}$	$\Delta C_{s(1)}$	$\Delta C_{s(1)}$	Q(Å)	0·554	0·518	0·569
	1·4	1·8	1·7	φ(°)	280	354	357
				θ(°)	3	9	8
					$^1C_4$	$^1C_4$	$^1C_4$
Ring B	$\Delta C_{s(7)}$	$\Delta C_{s(5)}$	$\Delta C_{s(5)}$	Q(Å)	0·550	0·416	0·457
	0·6	7·8	7·1	φ(°)	282	170	170
				θ(°)	179	127	126
					$^4C_1$	E_1	E_1
Ring C	$\Delta C_{s(11)}$	$\Delta C_{2(8,14)}$	$\Delta C_{2(8,14)}$	Q(Å)	0·513	0·539	0·518
	1·0	4·5	7·5	φ(°)	116	333	335
				θ(°)	10	108	110
					$^1C_4$	$^1T_3$	$^1T_3$
Ring D	$\Delta C_{s(17)}$	$\Delta C_{s(16)}$	$\Delta C_{s(16)}$	Q(Å)	0·286	0·448	0·420
	1·0	7·0	7·6	θ(°)	36	63	63
					E_2	$^3H_2/^3E$	$^3H_2/^3E$
						1:1	1:1

* In each case, only the parameter of lowest magnitude has been reported.

† The total degree of pucker is described by the radial coordinate Q, and the angular coordinates φ and θ (six-membered rings), or θ (five-membered rings) describe the shape of the ring. For the conformational nomenclature, the atoms in each ring are considered in a clockwise order starting with the lowest number in the ring.

For (I), the C(14)—C(15) bond length of 1·31 (1) Å as compared with the range 1·51 (1)—1·55 (1) Å for the remainder of the steroid skeleton establishes the existence of a double bond at C(14)—C(15). Of particular note with (II) is the definitive evidence that allylic oxidation of 3β-acetoxy-15α-(o-nitrobenzoyl-oxy)-5β,14β-bufa-8,20,22-trienolide (Nassimbeni et al., 1982) yields the 7-one and not the 11-one. The latter would have been a particularly useful gamabufotalin-type precursor.

With respect to molecular packing, in (I), a close contact between O(3) and O(24)(x + 1, y − 1, z), of 2·79 (1) Å, implies that there is a weak hydrogen bond. The initial positioning of a hydrogen at 1·00 (1) Å from O(3), such that the angle O(3)—H(33)···O(24) was 180°, refined to yield an angle O(3)—H(33)···O(24) of 106°; this fact, together with the high temperature factor of H(33), implies that little credence can be attached to its final location. For (II) the packing of the molecules is unremarkable, there being no inter-molecular close contacts less than 3·0 Å.

The molecular conformations of the individual steroid rings are presented in Table 3 in terms of asymmetry parameters (Duax & Norton, 1975) and parameters of pucker (Boeyens, 1978). Results indicate noteworthy conformational similarity to the related 3β-acetoxy-15α-(o-nitrobenzoyloxy)-5β,14β-bufa-
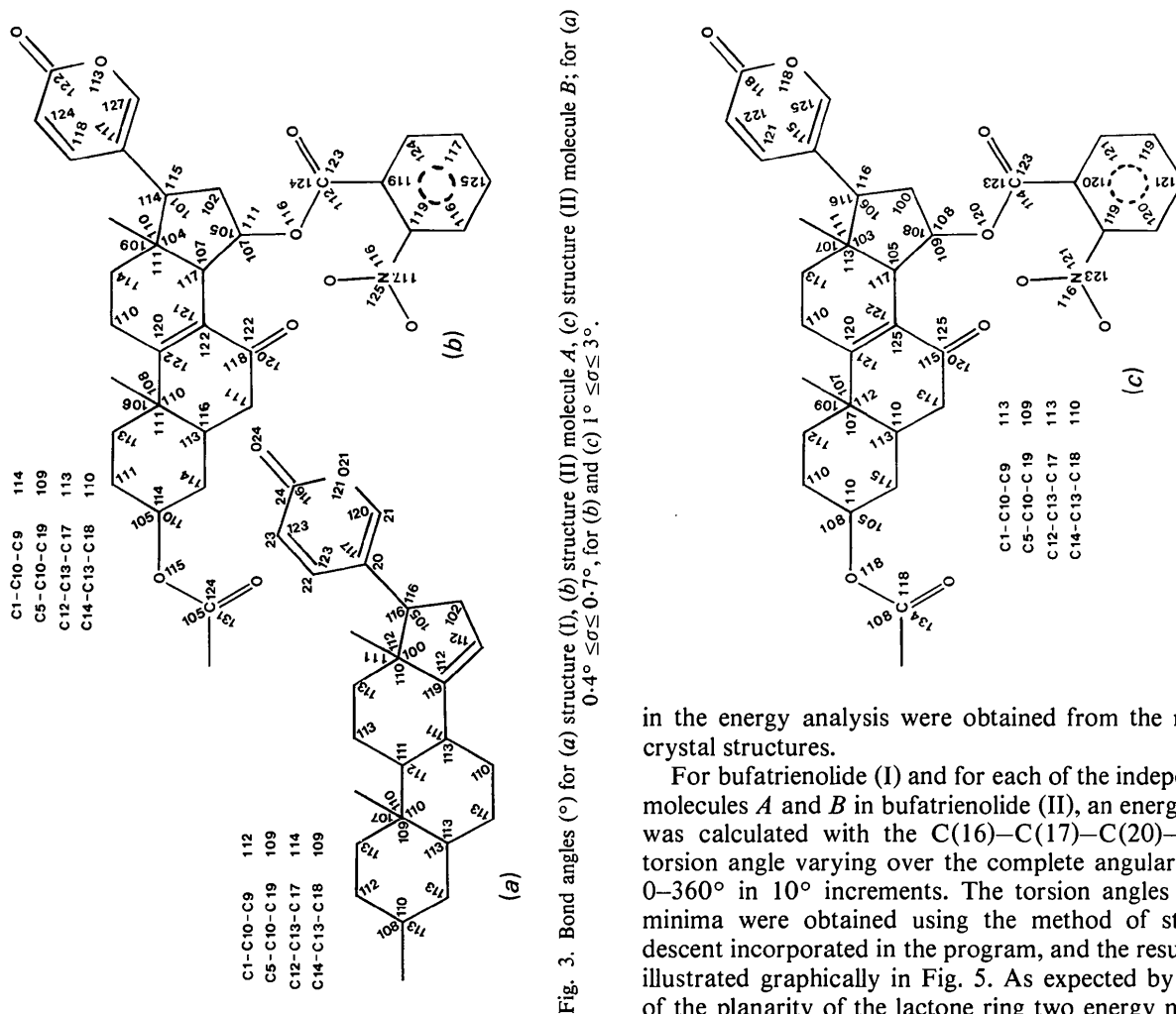
Fig. 3. Bond angles (°) for (a) structure (I), (b) structure (II) molecule A, (c) structure (II) molecule B; for (a) 0·4° ⩽ σ ⩽ 0·7°, for (b) and (c) 1° ⩽ σ ⩽ 3°.

Fig. 3 (cont.) (c)

8,20,22-trienolide (Nassimbeni et al., 1982). Attention has been focused on the lactone ring at C(17) which is believed to be essential for the cell-growth inhibition (KB system) displayed by such bufadienolides. A conformational analysis of the torsion angle C(16)–C(17)–C(20)–C(21) was completed by calculating the van der Waals energy using empirical atom-pair potentials. This method of evaluating molecular energies is well established and has been reviewed by Kitaigorodsky (1978) and Mirsky (1978). The coefficients of the atom–atom potentials are of the form $U(r) = a\exp(-br)/r^d - c/r^6$ where r is the distance between any pair of atoms and the coefficients a, b, c, d are those given by Giglio (1969) such that $U(r)$ is evaluated in kcal ($\equiv 4\cdot184$ kJ) where r is in Å. No account was taken of possible torsional potentials for the σ bonds, partial atomic charges or dipole interactions. The program EENY (Motherwell, 1974) calculates molecular coordinates as defined by the appropriate torsion angles and sums the energy for all non-bonded pairs of atoms whose separation is dependent upon the torsion angles. Atomic coordinates used

in the energy analysis were obtained from the refined crystal structures.

For bufatrienolide (I) and for each of the independent molecules A and B in bufatrienolide (II), an energy map was calculated with the C(16)–C(17)–C(20)–C(21) torsion angle varying over the complete angular range 0–360° in 10° increments. The torsion angles at the minima were obtained using the method of steepest descent incorporated in the program, and the results are illustrated graphically in Fig. 5. As expected by virtue of the planarity of the lactone ring two energy minima were obtained at torsion angles differing by the order of 180°. In each example the two energy minima differed by a small amount, presumably due to the asymmetry of the lactone ring, with the lower of the two energies corresponding to the O(21) trans to C(16). In addition the lowest energies obtained corresponded closely to those observed in the crystal structures. For bufatrienolide (I), calculated $U_{min} = -0\cdot38$ kJ mol^{-1} corresponds to a torsion angle value of 159° [τ observed in crystal, 152·7 (6)°]. For bufatrienolide (II) molecule A, calculated $U_{min} = 2\cdot38$ kJ mol^{-1} corresponds to a torsion angle value of 158° [τ observed in crystal, 146 (1)°], and molecule B, calculated $U_{min} = 0\cdot50$ kJ mol^{-1} corresponds to a torsion angle value of 146° [τ observed in crystal, 141 (1)°]. Analogous calculations using a previously studied bufadienolide (Nassimbeni et al., 1982) gave comparable results; calculated $U_{min} = 1\cdot46$ kJ mol^{-1} corresponds to a torsion angle value of 151° [τ observed in crystal, 142 (1)°]. These results imply that the conformation of the lactone ring is mainly a result of intra- and not intermolecular interaction with packing forces contributing minimally as evidenced by the small difference in

τ for molecules *A* and *B* in bufatrienolide (II). Interestingly, the conflict between X-ray data and force-field calculations as reported for the conformation of a progesterone side chain (Duax, Griffin & Rohrer, 1981) was not observed here.
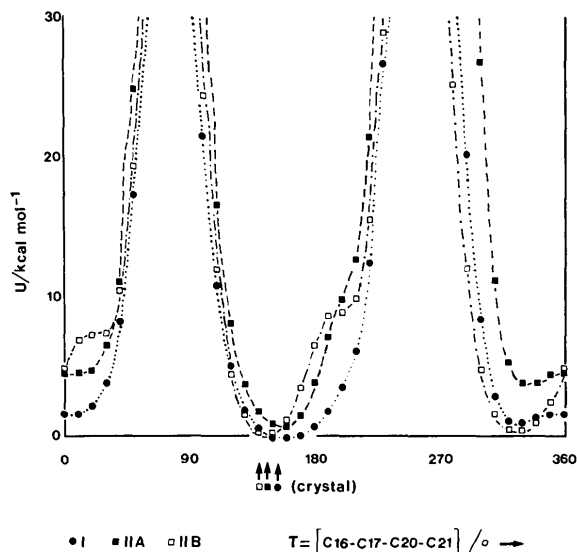
Fig. 5. Graphical representation of energy changes on variation of torsion angle C(16)—C(17)—C(20)—C(21) for (I), (II)*A*, and (II)*B*. (1 k cal $\equiv$ 4·184 k J.)

References

BOEYENS, J. C. A. (1978). *J. Cryst. Mol. Struct.* **8** (6), 317–320.
CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.
CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A**24**, 321–324.
DUAX, W. L., GRIFFIN, J. F. & ROHRER, D. C. (1981). *J. Am. Chem. Soc.* **103**, 6705–6712.
DUAX, W. L. & NORTON, D. A. (1975). *Atlas of Steroid Structure*, Vol. 1, p. 16. New York: IFI/Plenum Data Company.
GIGLIO, E. (1969). *Nature, London*, **222**, 339–341.
KAMANO, Y., PETTIT, G. R., INOUE, M., TOZAWA, M. & KOMEICHI, Y. (1977). *J. Chem. Res.* (*M*), pp. 837–845.
KITAIGORODSKY, A. I. (1978). *Chem. Soc. Rev.* **7**, 133–163.
MEINWALD, J., WIEMER, D. F. & EISNER, T. (1979). *J. Am. Chem. Soc.* **101**, 3055–3060.
MIRSKY, K. (1978). *Computing in Crystallography*, edited by H. SCHENK, R. OLTHOF-HAZEKAMP, H. VAN KONINGSVELD & G. C. BASSI, pp. 169–182. Delft Univ. Press.
MOTHERWELL, W. D. S. (1974). *Potential Energy Program*, Cambridge Univ. (unpublished).
NASSIMBENI, L. R., NIVEN, M. L., PETTIT, G. R., KAMANO, Y., INOUE, M. & EINCK, J. (1982). *Acta Cryst.* B**38**, 2163–2166.
ODE, R., PETTIT, G. R. & KAMANO, Y. (1975). *Cardenolides and Bufadienolides* in *International Review of Science, Organic Chemistry Series Two*, edited by W. F. JOHNS, Vol. 8, ch. 6, pp. 145–171. London: Butterworths.
PETTIT, G. R., KAMANO, Y., INOUE, M., KOMEICHI, Y., NASSIMBENI, L. R. & NIVEN, M. L. (1982). *J. Org. Chem.* **47**, 1503–1506.
SHELDRICK, G. M. (1978). *SHELX* in *Computing in Crystallography*, edited by H. SCHENK, R. OLTHOF-HAZEKAMP, H. VAN KONINGSVELD & G. C. BASSI, pp. 34–42. Delft Univ. Press.
STACHE, U., RADSCHEIT, K., HAEDE, W. & FRITSCH, W. (1982). *Liebigs Ann. Chem.* pp. 342–354.
STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
YAO JIA-XING (1981). *Acta Cryst.* A**37**, 642–644.

Fig. 4. Selected torsion angles (°) for (*a*) structure (I), (*b*) structure (II) molecule *A*, (*c*) structure (II) molecule *B*. σ as for Fig. 3.