References

Akama, Y., Nakai, T. & Kawamura, F. (1976). *Bunseki Kagaku*, **25**, 496–500.

Akama, Y., Nakai, T. & Kawamura, F. (1981). *Analyst* (*London*), **106**, 250–253.

Akama, Y., Saito, H., Hayashi, A., Sato, K., Tanaka, S. & Kanno, H. (1993). *Bunseki Kagaku*, **42**, 115–118.

Akama, Y., Tong, A., Ishima, S. & Kajitani, M. (1992). *Anal. Sci.* **8**, 41–44.

Beurskens, P. T., Admiraal, G., Beurskens, G., Bosman, W. P., Garcia-Granda, S., Gould, R. O., Smits, J. M. M. & Smykalla, C. (1992). *The DIRDIF Program System*. Technical Report. Crystallography Laboratory, Univ. of Nijmegen, The Netherlands.

Jensen, B. S. (1959). *Acta Chem. Scand.* **13**, 1668–1670.

Maquestiau, A., Van Haverbeke, Y. & Muller, R. N. (1975). *J. Heterocycl. Chem.* **12**, 85–90.

Miao, F., Liu, X. & Li, Y. (1991). *J. Inorg. Chem.* (*Chin.*), **7**, 129–132.

Molecular Structure Corporation (1989). *TEXSAN. Single Crystal Structure Analysis Software*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.

O'Connell, M. J., Ramsay, C. G. & Steel, P. J. (1985). *Aust. J. Chem.* **38**, 401–409.

Sheldrick, G. M. (1985). *SHELXS86*. *Crystallographic Computing* 3, edited by G. M. Sheldrick, C. Krüger & R. Goddard, pp. 175–189. Oxford Univ. Press.

Umetani, S., Sasayama, K. & Matsui, M. (1982). *Anal. Chim. Acta*, **134**, 327–331.

Wamhoff, H., Schramm, D. & Korte, F. (1971). *Synthesis*, pp. 216–217.

Zeigan, D., Engelhardt, G. & Uhlemann, E. (1981). *Z. Chem.* **21**, 187–188.

Acta Cryst. (1995). C**51**, 1314–1319

Three Lactone Fused Perhydroisoxazolo[2,3-*a*]pyridines: a Conformational Study

Angel Alvarez-Larena and Juan F. Piniella

Unidad de Cristalografía, Universidad Autónoma de Barcelona, 08193 Bellaterra, Spain

Pau Cid, Pedro de March, Marta Figueredo,
Josep Font, Sergio Milán and Angeles Soria

Departamento de Química, Universidad Autónoma de Barcelona, 08193 Bellaterra, Spain

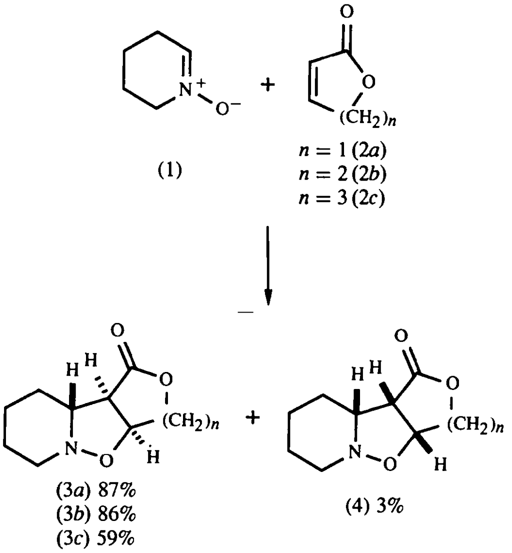
(*Received* 19 *September* 1994; *accepted* 24 *November* 1994)

Abstract

(3a*RS*,9a*SR*,9b*SR*)-Octahydro-1*H*-furo[3′,4′:4,5]isoxazolo[2,3-*a*]pyridin-1-one ($C_9H_{13}NO_3$), (4a*RS*,10a*RS*,10b*RS*)-octahydro-1*H*,3*H*-pyrano[3′,4′:4,5]isoxazolo[2,3-*a*]pyridin-1-one ($C_{10}H_{15}NO_3$), and (5a*RS*,11a*RS*,11b*RS*)-decahydro-1*H*-oxepino[3′,4′:4,5]isoxazolo[2,3-*a*]pyridin-1-one ($C_{11}H_{17}NO_3$), *exo* products of the reaction between 3,4,5,6-tetrahydropyridine 1-oxide and five-, six- and seven-membered α,β-unsaturated lactones, adopt, in the solid state, the preponderant conformation observed in chloroform or acetone solution. The perhydroisoxazolo[2,3-*a*]pyridine substructure presents a *cis* fusion when the lactone ring is five-membered and a *trans* fusion when it is six- or seven-membered. In the three compounds, the piperidine ring exhibits a more or less distorted chair conformation depending on the product. The lactone ring conformation involves a local pseudo twofold axis running through the carbonyl C atom (five-membered lactone) or through the midpoint of the C—C bond that joins the carbonyl group to the ring junction (six- and seven-membered lactones). On the other hand, the isoxazolidine ring shows an envelope conformation when the lactone ring is six- or seven-membered, whereas an intermediate conformation between the envelope and the half-chair is observed when the lactone is five-membered.

Comment

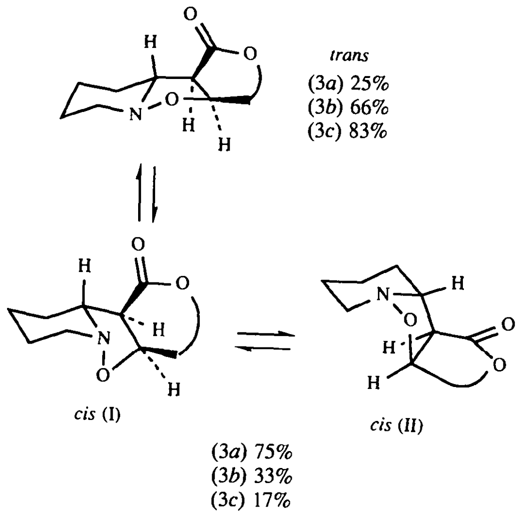
The 1,3-dipolar cycloaddition of nitrones to alkenes has proved to be a powerful synthetic tool for the preparation of nitrogen-containing natural products (for recent reviews, see Tufariello, 1984; Torssell, 1988; Annunziata, Cinquini, Cozzi & Raimondi, 1989). Electron-deficient unsymmetrically 1,2-disubstituted olefins add regiospecifically to nitrones affording only isoxazolidines with the electron-withdrawing group attached to the 4-position. In this context, the reactions between the nitrone (1) and α,β-unsaturated lactones (2*a*)–(2*c*) have been studied (Cid *et al.*, 1993). In this cycloaddition, *exo* adducts have been obtained as major or exclusive products.



The cycloadducts formed contain the perhydroisoxazolo[2,3-*a*]pyridine substructure which may exist in solution as a mixture of one rigid *trans* and two flexi-

Acta Crystallographica Section C
ISSN 0108-2701 ©1995

ble *cis* conformers due to both N and six-membered ring inversion processes. A conformational analysis has been carried out by NMR methods (Cid *et al.*, 1990, 1993).



Important differences in the conformational behaviour in solution have been found as a function of the lactone ring size. In the *exo* adducts, the preference for the *trans*-fused invertomer increases with the size of the lactone ring; moreover, of the two possible chair conformers of the *cis* invertomer, compounds (3*b*) and (3*c*) prefer the one depicted in (II), whereas (3*a*) shows a clear predominance of (I). An X-ray crystal structure determination has been undertaken on compounds (3*a*)–(3*c*) in order to complete the NMR conformational analysis mentioned above, and to provide further structural data of these new heterocyclic systems.

All the bond lengths and angles have values that are within normal limits. Views of the compounds with the atomic numbering schemes are shown in Figs. 1–3. The perhydroisoxazolo[2,3-*a*]pyridine substructure presents a *cis* conformation in (3*a*), whereas in (3*b*) and (3*c*) it adopts the *trans* conformation. Moreover, only the form (I) is observed in the *cis* invertomer of (3*a*). In the three compounds, the conformer present in the crystal is that predominantly observed in chloroform or acetone solution.

Considering the conformation of each moiety forming the tricyclic compounds, the piperidine ring has a distorted chair conformation in the three compounds, as can be seen in Fig. 4. The smallest distortion is observed in (3*b*) (Table 7). Greater conformational differences are present in the isoxazolidine ring. In (3*b*) the ring clearly adopts an envelope conformation, the N atom occupying the flap position. For product (3*c*) a similar, although more distorted, conformation is observed (Table 7). Finally, in cycloadduct (3*a*) the isoxazolidine ring shows an intermediate conformation between an envelope with the N atom in the flap position and a half-chair with the

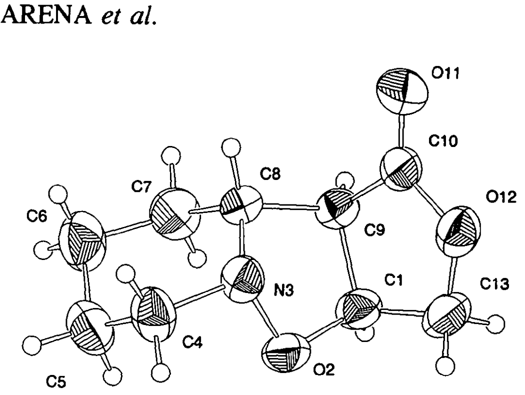


Fig. 1. View of (3*a*) showing the numbering scheme. Displacement ellipsoids are drawn at 50% probability.

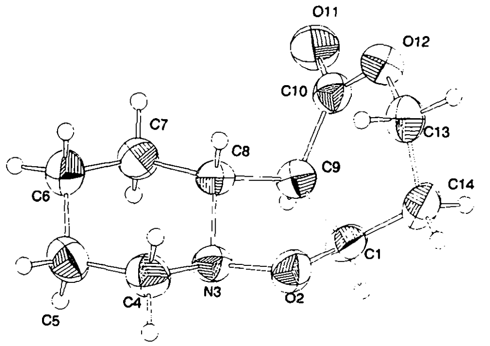


Fig. 2. View of (3*b*) showing the numbering scheme. Displacement ellipsoids are drawn at 50% probability.

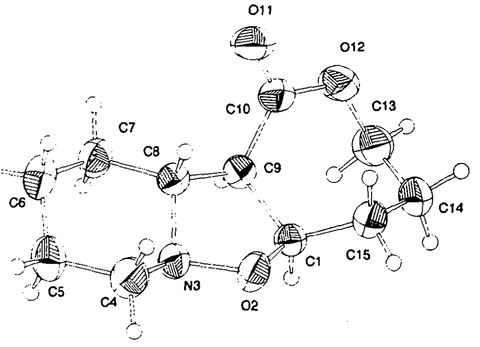


Fig. 3. View of (3*c*) showing the numbering scheme. Displacement ellipsoids are drawn at 50% probability.

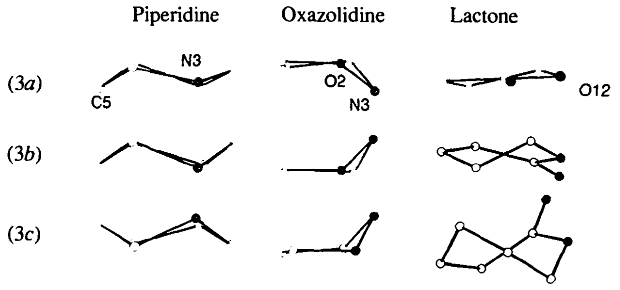


Fig. 4. Ring conformations for the three moieties forming (3*a*)–(3*c*) (*PLUTON*93; Spek, 1993).

twofold axis through C1. According to the asymmetry parameters this conformation is closer to the half-chair than to the envelope (Table 7).

This kind of conformation can be found in other isoxazolidines. In the Cambridge Structure Database (Allen *et al.*, 1991), about one hundred structures are described containing non-fused isoxazolidine rings or forming part of a polycyclic system. The envelope is the more usual conformation adopted by this heterocycle and in most cases the N atom is in the flap position. Some examples can be cited: JECVOC, $\Delta C_S^{\rm N} = 0.3$ (Inouye, Kohno & Kakisawa, 1990); DASKAJ, $\Delta C_S^{\rm N} = 1.2$ (Doepp, Krüger, Makedakis & Nour-el-Din, 1985); JEBXIX, $\Delta C_S^{\rm O} = 0.4$ (Denmark, Young-Choon Moon & Senanayake, 1990); VAWFEE, $\Delta C_S^{\rm C} = 0.3°$ (Obodovskaya, Starikova, Pokrovskaya & Eliseeva, 1988). The half-chair conformation is also observed, the twofold axis usually being placed through a C atom. For example: BUWXUM, $\Delta C_2^{\rm C} = 2.3$ (Ferrier *et al.*, 1983); FOJNAT, $\Delta C_2^{\rm C} = 1.5$ (Wada, Takamoto, Tsubotani & Kamiya, 1987); MIXTCA, $\Delta C_2^{\rm C} = 2.1$ (Rudchenko *et al.*, 1978); WASTOZ, $\Delta C_2^{\rm O} = 0.5$ (Tinant *et al.*, 1992); PYBZNO10, $\Delta C_2^{\rm N} = 1.7°$ (Murray-Rust & Murray-Rust, 1975). A conformation between the envelope and the half-chair can be observed in, for example: DIRYEI, $\Delta C_2^{\rm C} = 10.6$, $\Delta C_S^{\rm C} = 8.4$ (Wovkulich & Uskokovic, 1985); JIZPAJ, $\Delta C_2^{\rm C} = 9.8$, $\Delta C_S^{\rm N} = 9.4$ (Peters, Peters, von Schnering, Adams & Bottle, 1991); SPZXAN, $\Delta C_2^{\rm C} = 8.7$, $\Delta C_S^{\rm O} = 5.7°$ (Colombi *et al.*, 1978). It is interesting to point out that some compounds exhibit two different kinds of conformation in the solid state, for example: VAGWUV, envelope $\Delta C_S^{\rm N} = 0.4$ and intermediate conformation $\Delta C_2^{\rm C} = 5.1$, $\Delta C_S^{\rm O} = 5.8°$ (van Eijk, Verboom, van Veggel, Reinhoudt & Harkema, 1988); CUVZUO, envelope $\Delta C_S^{\rm C} = 1.2$ and intermediate conformation $\Delta C_2^{\rm O} = 11.4$, $\Delta C_S^{\rm C} = 9.1°$ (Aurich, Baum, Massa & Mogendorf, 1985).

The last cycle of the title compounds, the lactone, presents a local pseudo twofold axis in all three cases. In (3*a*), the conformation of the five-membered lactone ring is half-chair with the twofold axis running through C10. In (3*b*), the conformation of the six-membered lactone ring is also half-chair, and in (3*c*) the seven-membered lactone conformation can be described as a twist-boat. In both (3*b*) and (3*c*), the twofold axis runs through the midpoint of the C9—C10 bond adjacent to the carbonyl group. In the cycloaddition, equimolar amounts of the two enantiomers of (3*a*)–(3*c*) are obtained. The crystals of (3*a*) and (3*c*) are racemic. On the contrary, the two enantiomers of (3*b*) crystallize separately.

Experimental

Colourless prismatic crystals were grown by vapour diffusion of pentane into a methylene chloride solution of (3*a*), by vapour diffusion of pentane into a chloroform solution of (3*b*), and from evaporation of an ether solution of (3*c*) at room temperature.

Compound (3*a*)

Crystal data

$C_9H_{13}NO_3$
$M_r = 183.20$
Orthorhombic
Pbca
$a = 8.653\,(1)$ Å
$b = 11.418\,(5)$ Å
$c = 18.018\,(2)$ Å
$V = 1780.2\,(8)$ Å^3
$Z = 8$
$D_x = 1.367$ Mg m^{-3}

Mo $K\alpha$ radiation
$\lambda = 0.71069$ Å
Cell parameters from 25 reflections
$\theta = 10.19\text{–}13.91°$
$\mu = 0.103$ mm^{-1}
$T = 293\,(2)$ K
Prism
0.7 × 0.2 × 0.2 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
1562 measured reflections
1562 independent reflections
1087 observed reflections [$I > 2\sigma(I)$]

$\theta_{\rm max} = 24.89°$
$h = 0 \rightarrow 10$
$k = 0 \rightarrow 13$
$l = 0 \rightarrow 21$
3 standard reflections
frequency: 120 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0378$
$wR(F^2) = 0.0968$
$S = 1.073$
1562 reflections
120 parameters
Only H-atom U's refined
$w = 1/[\sigma^2(F_o^2) + (0.0479P)^2 + 0.6770P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} = 0.057$

$\Delta\rho_{\rm max} = 0.192$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.137$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.014 (2)
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2) *for* (3*a*)

$$U_{\rm eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$U_{\rm eq}$
C1	0.0400 (2)	0.5197 (2)	0.19147 (12)	0.0475 (6)
O2	0.1574 (2)	0.54123 (12)	0.13788 (9)	0.0621 (5)
N3	0.2580 (2)	0.4360 (2)	0.14051 (9)	0.0466 (5)
C4	0.3465 (3)	0.4390 (2)	0.07098 (12)	0.0588 (6)
C5	0.2542 (3)	0.4210 (2)	0.00074 (13)	0.0643 (7)
C6	0.1614 (3)	0.3093 (2)	0.00593 (14)	0.0731 (8)
C7	0.0550 (3)	0.3165 (2)	0.07301 (12)	0.0591 (6)
C8	0.1433 (2)	0.3409 (2)	0.14379 (11)	0.0391 (5)
C9	0.0398 (2)	0.3874 (2)	0.20494 (11)	0.0391 (5)
C10	0.1111 (2)	0.3731 (2)	0.28018 (12)	0.0433 (5)
O11	0.1479 (2)	0.28292 (14)	0.31043 (9)	0.0619 (5)
O12	0.1378 (2)	0.47724 (13)	0.31223 (8)	0.0543 (5)
C13	0.0754 (3)	0.5704 (2)	0.26696 (14)	0.0597 (7)

Table 2. *Selected geometric parameters* (Å, °) *for* (3*a*)

C1—O2	1.423 (2)	C6—C7	1.522 (3)
C1—C13	1.510 (3)	C7—C8	1.513 (3)
C1—C9	1.530 (3)	C8—C9	1.516 (3)

O2—N3	1.484 (2)	C9—C10	1.498 (3)
N3—C4	1.469 (3)	C10—O11	1.208 (2)
N3—C8	1.473 (3)	C10—O12	1.342 (3)
C4—C5	1.511 (3)	O12—C13	1.445 (3)
C5—C6	1.510 (3)		
O2—C1—C13	113.6 (2)	N3—C8—C7	116.3 (2)
O2—C1—C9	106.2 (2)	N3—C8—C9	99.7 (2)
C13—C1—C9	103.6 (2)	C7—C8—C9	112.3 (2)
C1—O2—N3	104.9 (1)	C10—C9—C8	112.1 (2)
C4—N3—C8	113.8 (2)	C10—C9—C1	104.5 (2)
C4—N3—O2	105.1 (2)	C8—C9—C1	103.3 (2)
C8—N3—O2	101.7 (1)	O11—C10—O12	121.1 (2)
N3—C4—C5	115.8 (2)	O11—C10—C9	127.6 (2)
C6—C5—C4	110.1 (2)	O12—C10—C9	111.3 (2)
C5—C6—C7	109.0 (2)	C10—O12—C13	110.2 (2)
C8—C7—C6	112.0 (2)	O12—C13—C1	107.6 (2)

Compound (3*b*)

Crystal data

$C_{10}H_{15}NO_3$
$M_r = 197.23$
Orthorhombic
$P2_12_12_1$
$a = 6.765$ (3) Å
$b = 8.930$ (2) Å
$c = 16.166$ (5) Å
$V = 976.6$ (6) Å^3
$Z = 4$
$D_x = 1.341$ Mg m^{-3}

Mo $K\alpha$ radiation
$\lambda = 0.71069$ Å
Cell parameters from 25 reflections
$\theta = 9.94$–$20.10°$
$\mu = 0.099$ mm^{-1}
$T = 293$ (2) K
Prism
0.6 × 0.3 × 0.2 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
1023 measured reflections
1023 independent reflections
889 observed reflections [$I > 2\sigma(I)$]

$\theta_{\max} = 24.95°$
$h = 0 \rightarrow 8$
$k = 0 \rightarrow 10$
$l = -1 \rightarrow 19$
3 standard reflections frequency: 60 min intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0281$
$wR(F^2) = 0.0719$
$S = 1.089$
1023 reflections
129 parameters
Only H-atom U's refined
$w = 1/[\sigma^2(F_o^2) + (0.0392P)^2 + 0.1142P]$ where $P = (F_o^2 + 2(F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.117$

$\Delta\rho_{\max} = 0.116$ e Å^{-3}
$\Delta\rho_{\min} = -0.092$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.038 (4)
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 3. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2) *for* (3*b*)

$$U_{eq} = (1/3)\Sigma_i\Sigma_jU_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
C1	1.0217 (3)	0.4251 (3)	0.69251 (14)	0.0456 (5)
O2	0.9926 (2)	0.3477 (2)	0.77030 (9)	0.0505 (4)
N3	1.1418 (3)	0.4166 (2)	0.82334 (10)	0.0423 (4)
C4	1.1550 (4)	0.3327 (3)	0.90031 (13)	0.0518 (6)
C5	1.3242 (4)	0.3996 (3)	0.94871 (13)	0.0548 (6)
C6	1.5166 (4)	0.3932 (3)	0.90044 (14)	0.0568 (6)
C7	1.4916 (3)	0.4673 (3)	0.81588 (14)	0.0511 (6)
C8	1.3179 (3)	0.3972 (2)	0.77246 (12)	0.0388 (5)
C9	1.2452 (3)	0.4642 (2)	0.69079 (13)	0.0411 (5)
C10	1.3622 (3)	0.4068 (3)	0.61850 (12)	0.0445 (5)
O11	1.5132 (2)	0.4656 (2)	0.59598 (11)	0.0630 (5)
O12	1.3015 (3)	0.2834 (2)	0.57936 (9)	0.0519 (4)
C13	1.1174 (4)	0.2108 (3)	0.60451 (14)	0.0517 (6)
C14	0.9605 (4)	0.3245 (3)	0.62289 (15)	0.0527 (6)

Table 4. *Selected geometric parameters* (Å, °) *for* (3*b*)

C1—O2	1.448 (3)	C6—C7	1.528 (3)
C1—C14	1.498 (3)	C7—C8	1.505 (3)
C1—C9	1.552 (3)	C8—C9	1.531 (3)
O2—N3	1.460 (2)	C9—C10	1.502 (3)
N3—C4	1.456 (3)	C10—O11	1.205 (3)
N3—C8	1.458 (3)	C10—O12	1.336 (3)
C4—C5	1.510 (3)	O12—C13	1.462 (3)
C5—C6	1.519 (3)	C13—C14	1.499 (4)
O2—C1—C14	109.2 (2)	N3—C8—C9	100.2 (2)
O2—C1—C9	104.8 (2)	C7—C8—C9	119.4 (2)
C14—C1—C9	113.0 (2)	C10—C9—C8	111.6 (2)
C1—O2—N3	102.4 (1)	C10—C9—C1	116.8 (2)
C4—N3—C8	111.7 (2)	C8—C9—C1	102.1 (2)
C4—N3—O2	109.1 (2)	O11—C10—O12	118.5 (2)
C8—N3—O2	100.6 (1)	O11—C10—C9	122.2 (2)
N3—C4—C5	106.6 (2)	O12—C10—C9	119.2 (2)
C4—C5—C6	111.6 (2)	C10—O12—C13	119.8 (2)
C5—C6—C7	110.4 (2)	O12—C13—C14	111.0 (2)
C8—C7—C6	108.9 (2)	C1—C14—C13	111.1 (2)
N3—C8—C7	109.0 (2)		

Compound (3*c*)

Crystal data

$C_{11}H_{17}NO_3$
$M_r = 211.26$
Monoclinic
$P2_1/n$
$a = 6.0456$ (7) Å
$b = 16.735$ (3) Å
$c = 10.786$ (2) Å
$\beta = 98.84$ (1)°
$V = 1078.3$ (3) Å^3
$Z = 4$
$D_x = 1.301$ Mg m^{-3}

Mo $K\alpha$ radiation
$\lambda = 0.71069$ Å
Cell parameters from 25 reflections
$\theta = 10.00$–$15.20°$
$\mu = 0.094$ mm^{-1}
$T = 293$ (2) K
Prism
0.4 × 0.4 × 0.3 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
1893 measured reflections
1893 independent reflections
1493 observed reflections [$I > 2\sigma(I)$]

$\theta_{\max} = 24.91°$
$h = -7 \rightarrow 7$
$k = 0 \rightarrow 19$
$l = 0 \rightarrow 12$
3 standard reflections frequency: 120 min intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0367$
$wR(F^2) = 0.0879$
$S = 1.092$
1890 reflections
138 parameters
Only H-atom U's refined

$\Delta\rho_{\max} = 0.171$ e Å^{-3}
$\Delta\rho_{\min} = -0.144$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.058 (3)

$w = 1/[\sigma^2(F_o^2) + (0.0345P)^2 + 0.3628P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = -0.050$

Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 5. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2) *for* (3*c*)

$$U_{\rm eq} = (1/3)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$U_{\rm eq}$
C1	0.2531 (3)	0.08231 (9)	0.51460 (14)	0.0364 (4)
O2	0.1079 (2)	0.06517 (8)	0.40013 (10)	0.0477 (3)
N3	0.2673 (2)	0.05636 (8)	0.31134 (12)	0.0394 (4)
C4	0.1403 (3)	0.05405 (13)	0.1847 (2)	0.0524 (5)
C5	0.3110 (3)	0.05316 (12)	0.0948 (2)	0.0551 (5)
C6	0.4692 (3)	0.12361 (12)	0.1149 (2)	0.0537 (5)
C7	0.5732 (3)	0.13198 (12)	0.2523 (2)	0.0480 (5)
C8	0.3874 (3)	0.13228 (9)	0.33126 (14)	0.0346 (4)
C9	0.4449 (3)	0.13353 (9)	0.47375 (14)	0.0360 (4)
C10	0.4638 (3)	0.21730 (11)	0.5258 (2)	0.0465 (4)
O11	0.4534 (3)	0.27652 (8)	0.46210 (13)	0.0666 (4)
O12	0.5001 (3)	0.22624 (8)	0.65122 (11)	0.0623 (4)
C13	0.4938 (4)	0.15686 (12)	0.7310 (2)	0.0591 (5)
C14	0.2574 (3)	0.13021 (12)	0.7343 (2)	0.0545 (5)
C15	0.1198 (3)	0.12239 (11)	0.6038 (2)	0.0462 (4)

Table 6. *Selected geometric parameters* (Å, °) *for* (3*c*)

C1—O2	1.430 (2)	C7—C8	1.510 (2)
C1—C15	1.504 (2)	C8—C9	1.523 (2)
C1—C9	1.559 (2)	C9—C10	1.508 (2)
O2—N3	1.467 (2)	C10—O11	1.202 (2)
N3—C4	1.461 (2)	C10—O12	1.345 (2)
N3—C8	1.463 (2)	O12—C13	1.449 (2)
C4—C5	1.521 (3)	C13—C14	1.503 (3)
C5—C6	1.513 (3)	C14—C15	1.527 (2)
C6—C7	1.525 (2)		
O2—C1—C15	108.9 (1)	N3—C8—C9	101.0 (1)
O2—C1—C9	104.5 (1)	C7—C8—C9	119.7 (1)
C15—C1—C9	115.5 (1)	C10—C9—C8	112.4 (1)
C1—O2—N3	101.9 (1)	C10—C9—C1	115.0 (1)
C4—N3—C8	109.8 (1)	C8—C9—C1	102.3 (1)
C4—N3—O2	108.0 (1)	O11—C10—O12	118.0 (2)
C8—N3—O2	100.3 (1)	O11—C10—C9	124.0 (2)
N3—C4—C5	106.6 (1)	O12—C10—C9	118.0 (2)
C6—C5—C4	112.1 (2)	C10—O12—C13	119.5 (1)
C5—C6—C7	111.6 (2)	O12—C13—C14	111.3 (2)
C8—C7—C6	108.5 (1)	C13—C14—C15	112.9 (1)
N3—C8—C7	108.0 (1)	C1—C15—C14	111.0 (1)

Table 7. *Asymmetry parameters* (°)* *and total puckering amplitude*† *for the three rings forming* (3*a*)–(3*c*)

Piperidine ring:

	$\Delta C_s^{\rm N3}$	$\Delta C_s^{\rm C4}$	$\Delta C_s^{\rm C5}$	$\Delta C_2^{\rm N3-C4}$	$\Delta C_2^{\rm C4-C5}$	$\Delta C_2^{\rm C5-C6}$	Q
(3*a*)	4.6	13.2	8.7	12.6	15.5	3.0	0.514
(3*b*)	1.3	8.2	7.9	6.5	11.3	5.2	0.601
(3*c*)	3.5	13.4	10.3	11.9	16.7	4.9	0.612

Remaining asymmetry parameters are greater than 100°

Isoxazolidine ring:

	$\Delta C_s^{\rm N3}$	$\Delta C_2^{\rm C1}$	q_2
(3*a*)	12.4	8.0	0.466
(3*b*)	1.0	25.6	0.508
(3*c*)	6.4	34.1	0.507

Remaining asymmetry parameters between 19 and 76°

Lactone ring:

(3*a*) $\Delta C_2^{\rm C10} = 0.9$ $q_2 = 0.160$
Remaining asymmetry parameters between 6 and 26°

(3*b*) $\Delta C_2^{\rm C9-C10} = 2.5$ $Q = 0.543$
Remaining asymmetry parameters between 29 and 66°

(3*c*) $\Delta C_2^{\rm C14} = 5.1$ $Q = 1.145$
Remaining asymmetry parameters between 27 and 109°

* Duax, Weeks & Rohrer (1976).
† Cremer & Pople (1975).

For all compounds, data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; program(s) used to solve structures: *SHELXS*86 (Sheldrick, 1985); program(s) used to refine structures: *SHELXL*93 (Sheldrick, 1993); molecular graphics: *ZORTEP* (Zsolnai, 1994).

The X-ray measurements have been carried out at the Servei de Difracció de Raigs-X de la Universitat Autònoma de Barcelona.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: NA1129). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Allen, F. H., Davies, J. E., Galloy, J. J., Johnson, O., Kennard, O., Macrae, C. F., Mitchell, E. M., Mitchell, G. F., Smith, J. M. & Watson, D. G. (1991). *J. Chem. Inf. Comput. Sci.* **31**, 187–204.

Annunziata, R., Cinquini, M., Cozzi, F. & Raimondi, L. (1989). *Gazz. Chim. Ital.* **119**, 253–269.

Aurich, H. G., Baum, G., Massa, W. & Mogendorf, K.-D. (1985). *Acta Cryst.* **C41**, 573–576.

Cid, P., de March, P., Figueredo, M., Font, J., Milán, S., Soria, A. & Virgili, A. (1993). *Tetrahedron*, **49**, 3857–3870.

Cid, P., Figueredo, M., Font, J., Jaime, C., de March, P. & Virgili, A. (1990). *Magn. Reson. Chem.* **28**, 947–951.

Colombi, S., Vecchio, G., Gottarelli, G., Samori, B., Lanfredi, A. M. M. & Tiripicchio, A. (1978). *Tetrahedron*, **34**, 2967–2976.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

Denmark, S. E., Young-Choon Moon & Senanayake, C. B. W. (1990). *J. Am. Chem. Soc.* **112**, 311–315.

Doepp, D., Krüger, C., Makedakis, G. & Nour-el-Din, A. M. (1985). *Chem. Ber.* **118**, 510–525.

Duax, W. L., Weeks, C. M. & Rohrer, D. C. (1976). *Top. Stereochem.* **9**, 271–383.

Eijk, P. J. S. S. van, Verboom, W., van Veggel, F. C. J. M., Reinhoudt, D. N. & Harkema, S. (1988). *Recl Trav. Chim. Pays-Bas*, **107**, 142–151.

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

Ferrier, R. J., Furneaux, R. H., Prasit, P., Tyler, P. C., Brown, K. L., Gainsford, G. J. & Diehl, J. W. (1983). *J. Chem. Soc. Perkin Trans.* 1, pp. 1621–1628.

Inouye, Y., Kohno, Y. & Kakisawa, H. (1990). *Acta Cryst.* **C46**, 640–643.

Murray-Rust, J. & Murray-Rust, P. (1975). *Acta Cryst.* **B31**, 589–592.

Obodovskaya, A. E., Starikova, Z. A., Pokrovskaya, I. E. & Eliseeva, L. N. (1988). *Zh. Strukt. Khim.* **29**, 183–187.

Peters, K., Peters, E.-M., von Schnering, H. G., Adams, W. & Bottle, S. E. (1991). *Z. Kristallogr.* **197**, 309–311.

Rudchenko, V. F., D'yachenko, O. A., Chervin, I. I., Zolotoi, A. B., Atovmyan, L. O. & Kostyanovskii, R. G. (1978). *Izv. Akad. Nauk SSSR Ser. Khim.* pp. 850–859.
Sheldrick, G. M. (1985). *SHELXS86. Crystallographic Computing* 3, edited by G. M. Sheldrick, C. Krüger & R. Goddard, pp. 175–189. Oxford Univ. Press.
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures.* Univ. of Göttingen, Germany.
Spek, A. L. (1993). *PLUTON93. Program for the Display and Analysis of Crystal and Molecular Structures.* Univ. of Utrecht, The Netherlands.
Tinant, B., Declercq, J.-P., Lorenc, L. J., Rajkovic, M., Milovanovic, A. & Mihailovic, M. L. J. (1992). *Bull. Soc. Chim. Belg.* **101**, 953–958.
Torssell, K. B. G. (1988). *Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis.* Weinheim: VCH Verlagsgesellschaft.
Tufariello, J. J. (1984). *1,3-Dipolar Cycloaddition Chemistry*, Vol. 2, ch. 9. New York: John Wiley.
Wada, Y., Takamoto, M., Tsubotani, S. & Kamiya, K. (1987). *Acta Cryst.* C**43**, 1786–1788.
Wovkulich, P. M. & Uskokovic, M. R. (1985). *Tetrahedron*, **41**, 3455–3462.
Zsolnai, L. (1994). *ZORTEP.* Heidelberg Univ., Germany.

Acta Cryst. (1995). C**51**, 1319–1322

On the Isostructural Molecular Compound Formation of a Steroid with α- and β-Naphthols

ZSOLT BÖCSKEI AND KÁLMÁN SIMON

Department of Chemical Research, Chinoin Pharmaceuticals, POB 110, 1325 Budapest, Hungary

GÁBOR AMBRUS AND ÉVA ILKÖY

Institute for Drug Research, POB 82, 1325 Budapest, Hungary

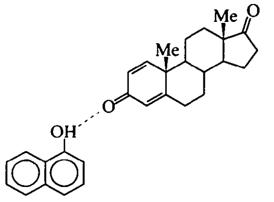
(*Received* 11 *July* 1994; *accepted* 22 *November* 1994)

Abstract

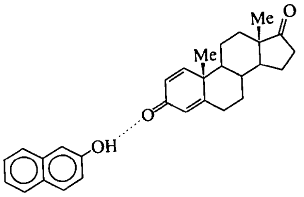
The crystal structures of the molecular compounds androsta-1,4-diene-3,17-dione–1-naphthol (1/1) and androsta-1,4-diene-3,17-dione–2-naphthol (1/1), two isomers of $C_{19}H_{24}O_2.C_{10}H_8O$, are described. The degree of isostructurality is characterized and an explanation for the preservation of a mutual crystal structure is established. Correlation is made between the chemical properties and the properties found in the crystals.

Comment

Since the late 1950's androsta-1,4-diene-3,17-dione, (I), has been used as a key intermediate in the synthesis of estrone (Dryden, Webber & Wieczorek, 1964). Industrial production of (I) by microbial transformation of progesterone with *Fusarium* species (Fried, Thoma & Klingsberg, 1953) and by microbial side-chain cleavage of natural sterols with *Arthrobacter simplex* (Nagasawa, Bae, Tamura & Arima, 1969) and *Mycobacteria* (Wix, Büki, Tömörkény & Ambrus, 1968) as well as the mutants of the latter (Marsheck, Kraychy & Muir, 1972) has been developed. In the course of experiments on the isolation of (I) from the fermentation broth it was found that β-naphthol (m.p. 395–396 K) and (I) form a 1:1 molecular compound, BENA, in several solvents (m.p. 442–443 K) (Pauncz, Wix, Rados & Alföldi, 1961). A similar molecular compound, ALNA (m.p. 436–438 K), was obtained with α-naphthol (m.p. 369 K) and (I). Since the solubilities of the molecular compounds are considerably different from those of the starting materials and the by-products of fermentation [*e.g.* androst-4-ene-3,17-dione, (II)], the formation of the molecular compound with β-naphthol proved to be useful in the purification of (I). In this study we report the crystal structures of the compounds ALNA and BENA and try to explain their properties on a crystallographic basis.



ALNA



BENA

It was established that the two crystals are highly isostructural (see Tables 1, 2, 3 and 4, and Figs. 3 and 4), although the hydrogen-bond data given below show that the complex formed between β-naphthol and the steroid is clearly stronger than that formed by α-naphthol. It is also worth mentioning that the more stable molecular compound is easier to prepare in the form of good quality single crystals, a fact which is also reflected by the quality of our data and results.

The only important difference between the two crystal structures is in the position of the naphthol OH group, which is linearly hydrogen-bonded to the conjugated carbonyl group in position 3 of a neighbouring steroid molecule in both compounds [ALNA: O1N—H1ON 0.95, H1ON···O1 1.87, O1N···O1 2.76(2) Å, O1N—H1ON···O1 156°; BENA: O1N—H1ON 1.14, H1ON···O1 1.58, O1N···O1 2.684(6) Å, O1N—H1ON···O1 161°]. To characterize the degree of isostructurality between the two compounds we calculated the unit-cell similarity (Π) as well as the isostructurality indices [$I_i(n)$ and $I_i(n^*)$] as defined by Kálmán, Párkányi & Argay (1993). All point to a very high degree of isostructurality, with $\Pi = 4.94 \times 10^{-4}$, $I_i(31) = 92\%$ and $I_i(31^*) = 93\%$. In addition, this particular case seems to add a new subclass, or at least an

Acta Crystallographica Section C
ISSN 0108-2701 ©1995