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Note

Crystal and molecular structure of (2E,4S,10R)-4-hydroxy-2-undecen-10-olide (nor-patulolide C), $C_{11}H_{18}O_3$

G. Admiraal,[1] J. M. M. Smits,[1] Paul T. Beurskens,[1]* F. M. C. Leemhuis,[2] L. Thijs,[2] and B. Zwanenburg[2]

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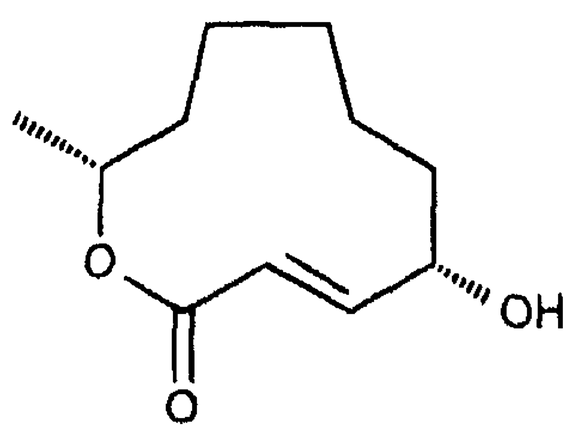
The stereogeometry and absolute configuration of the title compound has been proved by an X-ray diffraction analysis. Crystal data: monoclinic, $P2_1$, $a = 7.7976(2)$, $b = 7.8288(2)$, $c = 8.9791(4)$ Å, $\beta = 90.331(4)°$, $Z = 2$. The crystal structure has been solved by vector search methods and refined to $R = 0.042$ for 1798 observed reflections.

KEY WORDS: Crystal structure; undecen-olid; nor-patulolide.

Introduction

In conjunction with the total synthesis of naturally occurring patulolide C, a 12-membered ring lactone, a non-natural analogue with one ring carbon atom less was synthesized with the aim to compare its physical and biological properties with that of the natural product. The synthesis of this nor-patulolide C, **1**, was



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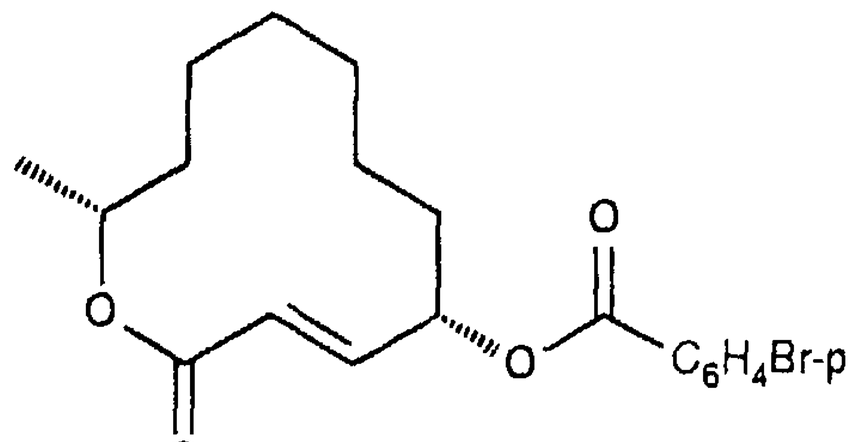
performed essentially in the same manner as described for patulolide C[1] and is published elsewhere.[2] The spectral characteristics, particularly the ^{1}H-NMR spectra of nor-patulolide C showed a distinctly different pattern in the region of the olefinic protons. Therefore, an X-ray diffraction analysis was undertaken to ascertain its structure in an unambiguous fashion and also to confirm the absolute configuration of both chiral centers. Furthermore, a comparison with the structure of the p-bromobenzoate of natural patulolide C,[3] **2** is



2

of interest from a conformational point of view. **1** has a m.p. of 126–128°C and a $[\alpha]_D^{20} = -3.25$ (c 0.4, EtOH).

Experimental

The crystal data and a summary of the data collection and the structure solution and refinement are given

[1] Crystallography Laboratory, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands.
[2] Department of Organic Chemistry, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands.
* To whom correspondence should be addressed.

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Table 1. Crystal data and summary of intensity data collection and structure solution and refinement.

Compound	$C_{11}H_{18}O_3$
Crystallization	from hexane
Formula weight	198.25
Space group	$P2_1$
Temperature, K	293
Cell constants[a]	
a, Å	7.7976(2)
b, Å	7.8288(2)
c, Å	8.9791(4)
β, °	90.331(4)
Cell volume, Å^3	548.13(3)
Formula units/unit cell	2
D_{calc}, g cm^{-3}	1.201
μ_{calc}, cm^{-1}	6.63
Diffractometer/scan	Enraf-Nonius CAD-4/ω-2θ
Radiation, graphite monochromator	Cu*K*α (λ = 1.54184 Å)
Crystal dimensions, mm	0.26 × 0.22 × 0.16
Scan width, °	1.5
Standard reflections	3
Decay of standards	10.3%
Reflections measured	4089
θ-range, °	5–70
Range of *h*, *k*, *l*	$0 \le h \le 9$ $-9 \le k \le 9$ $-10 \le l \le 10$
Corrections:	
Lorentz-polarization	
EMPABS[4] correction	0.98–1.02
Computer programs[b]	local programs
Structure solution[6–7]	vector search methods
Computer programs[b]	DIRDIF[8]
Unique reflections	2079
observed:$F_o > 4\sigma(F_o)$	1798
Structure refinement	isotropic: H-atoms anisotropic: remaining atoms
Computer programs[b]	SHELXL-93[9]
Treatment of hydrogen atoms: see experimental	
No. of parameters	146
No. of restraints	1
Weights	$1/[\sigma^2(F_o^2) + (0.0723\ P)^2 + 0.05\ P]$, where $P = [\mathrm{Max}(0,F_o^2) + 2F_c^2]/3$
Shift/esd	less than −0.08
GOOF	1.052
$R = \Sigma\|\|F_o\| - \|F_c\|\|/\Sigma\|F_o\|$	0.042
wR_2	0.122
Residual el.dens., e.Å^{-3}	0.28

[a] Least-squares refinement for 25 reflections 26° < θ < 48°.
[b] using neutral scattering factors and anomalous dispersion corrections.[5]

in Table 1. Hydrogen atoms are included on calculated positions and refined in riding mode with free isotropic temperature factors, except for the methyl group which was allowed to rotate around the C–C bond, and for H(40) which was found from a difference Fourier map and refined being constrained to O(4) with a bond length of 0.88 Å. All nonhydrogen atoms were refined with anisotropic temperature factors. The Bijvoet coefficient calculated by the program BIJVOET[10] is 0.35(4) for 200 Friedel pairs, and the Flack parameter calculated by SHELXL-93[9] is −0.08(30), both confirming the absolute configuration of the molecule. The atomic positional and vibrational parameters are given in Table 2.

Discussion

Selected bond lengths and angles are given in Table 3. The structure of nor-patulolide C is presented in Fig. 1.[11] No unusual bond lengths and bond angles are present in the molecule. The Bijvoet coefficient and the Flack parameter confirm the expected absolute configuration of the respective chiral centers, viz. 4S, 10R. These configurations are the same as in **2**, (4S,11R).[3]

The torsion angle, O(1)=C(1)–C(2)=C(3), in the alkene ester part is unusually large (48.2(4)°) and indicates a considerable deviation from planarity of the C(3)=C(2)–C(1)=O(1) unit, caused by ring strain in the macrocycle. In **2** this angle is −29.4°. These results

Table 2. Atomic coordinates (×10^3) and equivalent isotropic displacement parameters (Å^2 × 1,000).[a]

Atom	*x*	*y*	*z*	*U*(eq)[a]
C(1)	−14(3)	1356(3)	−1654(3)	55(1)
C(2)	159(3)	−519(3)	−1471(3)	56(1)
C(3)	−550(3)	−1600(3)	−2415(3)	57(1)
C(4)	−123(3)	−3466(3)	−2434(3)	59(1)
C(5)	916(3)	−3914(3)	−3798(3)	66(1)
C(6)	2330(3)	−2632(4)	−4250(3)	70(1)
C(7)	3681(3)	−2229(3)	−3094(3)	64(1)
C(8)	4628(3)	−533(4)	−3369(4)	76(1)
C(9)	3542(3)	1062(3)	−3188(3)	67(1)
C(10)	3125(3)	1521(3)	−1589(3)	61(1)
C(11)	4300(4)	2845(5)	−903(5)	93(1)
O(1)	−1362(2)	2071(2)	−1891(2)	71(1)
O(10)	1402(2)	2307(2)	−1543(2)	62(1)
O(4)	−1709(2)	−4369(2)	−2396(3)	83(1)

[a] *U*(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

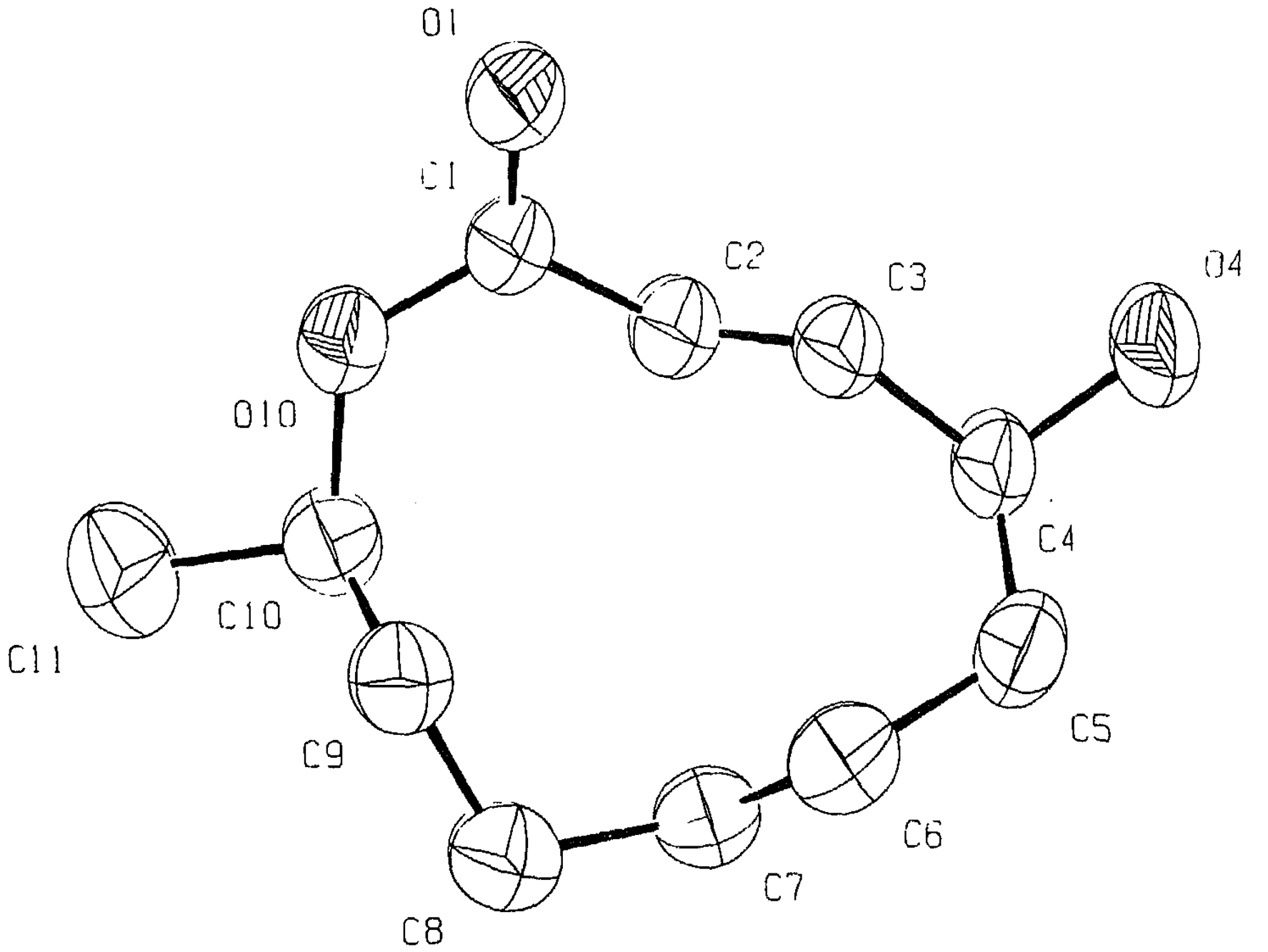

Fig. 1. Plot with thermal motion ellipsoids, and crystallographic numbering scheme.

Table 3. Selected bond lengths (Å) and angles (°).

C(1)–O(1)	1.208(3)
C(1)–O(10)	1.335(2)
C(1)–C(2)	1.484(3)
C(2)–C(3)	1.317(3)
C(3)–C(4)	1.499(3)
C(4)–O(4)	1.425(3)
C(4)–C(5)	1.513(4)
C(10)–O(10)	1.479(3)
O(1)–C(1)–O(10)	118.2(2)
O(1)–C(1)–C(2)	123.8(2)
O(10)–C(1)–C(2)	118.0(2)
C(3)–C(2)–C(1)	121.8(2)
C(2)–C(3)–C(4)	122.8(2)
O(4)–C(4)–C(3)	106.9(2)
O(4)–C(4)–C(5)	111.9(2)
C(3)–C(4)–C(5)	110.8(2)
C(1)–O(10)–C(10)	121.1(2)

Table 4. Comparison of the planarity of the alkene ester part in **1** and **2**.[a]

	C(4)	C(3)	C(2)	C(1)	O(1)	O(10)
1	−0.067	−0.190	0.397	0.056	−0.014	−0.181
2	−0.165	−0.029	0.376	0.060	−0.040	−0.202

[a] Deviations (Å) from the least-squares plane through the six atoms.

indicate that this effect of nonplanarity is most striking in the present compound. The deviations from planarity of the alkene ester parts of the present compound and **2** are compared in Table 4. The conformational differences of these patulolides are also reflected in their spectral features. A consequence of the non-planarity of the alkene ester unit is that the chemical shift of the olefinic protons are no longer influenced by conjugation and therefore have almost the same value, their difference being only 0.12 ppm. The loss of conjugation is also visible in the UV spectrum.[2]

Figure 1 is a stereo view of the packing as viewed down the *c*-axis. Intermolecular hydrogen bonds O(4)–H(40)---O(1) exist between molecules related by a translation period along b. O(4)---O(1) = 2.836(3)Å, O(4)–H(40)---O(1) = 159(4)°. The only intermolecular distance less than 3.50Å (excluding hydrogen atoms) is O(10)---C(2) at 3.426(3)Å.

References

1. Thijs, L; Egenberger, D.M.; Zwanenburg, B. *Tetrahedron Lett.* **1989**, *30*, 2153.
2. Thijs, L.; Zwanenburg, B. *J. Org. Chem.* **1993**, *58*, 7170.
3. Beurskens, G.; Smits, J.M.M.; Beurskens, P. T.; Thijs, L; Egenberger, D. M.; Zwanenburg, B. *J. Crystallogr. Spectrosc. Res.* **1989**, *19*, 919.

4. North, A.C.T.; Philips, D.C.; Mathews, F. S. *Acta Crystallogr.* **1968**, *24*, 351.
5. *International Tables for X-ray Crystallography*, Vol. IV; Kynoch Press: Birmingham, 1974.
6. Beurskens, P.T.: Beurskens, G.; Strumpel, M.; Nordman, C.E., Glusker, J.P.; Patterson B.K.; Rossi, M. *Patterson and Pattersons;* Oxford University Press: Oxford, 1987; p 356.
7. Beurskens, P.T.; Gould, R.O.; Bruins Slot; H.J.; Bosman, W.P. *Z. Kristallogr.* **1987**, *179*, 127.
8. Beurskens, P.T.; Admiraal, G.; Beurskens, G.; Bosman, W.P.; Garcia-Granda, S.; Gould, R.O.; Smits, J.M.M.; Smykalla, C. *DIRDIF 1992;* Technical Report of the Crystallography Laboratory, University of Nijmegen: Nijmegen, The Netherlands.
9. Sheldrick, G.M. *SHELXL-93 1993: A Program for Crystal Structure Determination;* University Chemical Laboratory: Cambridge, England.
10. Beurskens, G.; Beurskens, P.T. *Z. Kristallogr.* **1992**, *Supp. 6*, 213.
11. Spek, A.L. *PLATON-93 1993;* Bijvoet Center for Biomolecular Research, Utrecht University: Utrecht, the Netherlands.

SUPPLEMENTARY MATERIAL. Crystallographic data for the structure reported in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1003/5022. Copies of available material can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: teched@chemcrys.cam.ac.uk).

Table 1. Anisotropic displacement parameters (A¬2 × 10¬3).[a]

Atom	*U*11	*U*22	*U*33	*U*23	*U*13	*U*12
C(1)	51(1)	39(1)	75(1)	−3(1)	3(1)	0(1)
C(2)	53(1)	39(1)	75(1)	4(1)	3(1)	0(1)
C(3)	47(1)	38(1)	85(2)	5(1)	0(1)	−1(1)
C(4)	54(1)	37(1)	86(2)	1(1)	−4(1)	−3(1)
C(5)	68(1)	46(1)	83(2)	−11(1)	−8(1)	2(1)
C(6)	69(1)	60(1)	80(2)	−2(1)	2(1)	7(1)
C(7)	51(1)	53(1)	89(2)	−1(1)	−1(1)	9(1)
C(8)	56(1)	68(2)	105(2)	−1(2)	5(1)	2(1)
C(9)	63(1)	52(1)	84(2)	4(1)	9(1)	−4(1)
C(10)	51(1)	50(1)	81(2)	1(1)	−5(1)	−2(1)
C(11)	67(2)	89(2)	123(3)	−17(2)	−16(2)	−16(2)
O(1)	56(1)	44(1)	114(1)	−1(1)	0(1)	5(1)
O(10)	54(1)	40(1)	92(1)	−7(1)	−2(1)	−2(1)
O(4)	63(1)	41(1)	146(2)	1(1)	1(1)	−9(1)

[a] The anisotropic displacement factor exponent takes the form: $-2\,\mathrm{pi}^{\neg 2}\,[h^{\neg 2}\,a^{\neg 2}\,U11 + \cdots + 2\,h\,k\,a\,b\,U12]$.

Table 2. Hydrogen coordinates (×10¬4) and isotropic displacement parameters (A¬2 × 10¬3).

Atom	*x*	*y*	*z*	*U*(eq)
H(2)	786(3)	−944(3)	−668(3)	72(8)
H(3)	−1349(3)	−1187(3)	−3098(3)	78(9)
H(4)	545(3)	−3747(3)	−1539(3)	66(7)
H(51)	132(3)	−4042(3)	−4633(3)	84(9)
H(52)	1452(3)	−5016(3)	−3629(3)	120(14)
H(61)	2901(3)	−3077(4)	−5125(3)	90(10)
H(62)	1779(3)	−1570(4)	−4537(3)	102(11)
H(71)	4513(3)	−3149(3)	−3073(3)	125(14)
H(72)	3143(3)	−2182(3)	−2123(3)	63(7)
H(81)	5593(3)	−464(4)	−2685(4)	102(11)
H(82)	5085(3)	−549(4)	−4372(4)	110(12)
H(91)	4140(3)	2016(3)	−3639(3)	79(8)
H(92)	2475(3)	904(3)	−3732(3)	111(12)
H(10)	3137(3)	485(3)	−976(3)	71(8)
H(111)	5459(7)	2432(16)	−914(30)	140
H(112)	3960(24)	3057(28)	106(11)	140
H(113)	4226(28)	3885(12)	−1465(19)	140
H(40)	−1320(48)	−5406(66)	−2239(45)	118(13)