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(1*SR*,3*RS*,5*SR*)-3-Hydroxy-3-(2-hydroxyethyl)-*N*-phenyl-5-(*p*-tolyl)pyrrolidin-2-one

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The title compound, $C_{19}H_{21}NO_3$, is a new functionalized γ-lactam obtained in the cycloaddition reaction of *C*-(4-methylphenyl)-*N*-phenylnitrone with tulipalin A. Molecules are connected by O—H···O hydrogen bonds, forming two crossing chain motifs, $C(6)$ and $C(7)$, and generate layers parallel to the (001) plane.

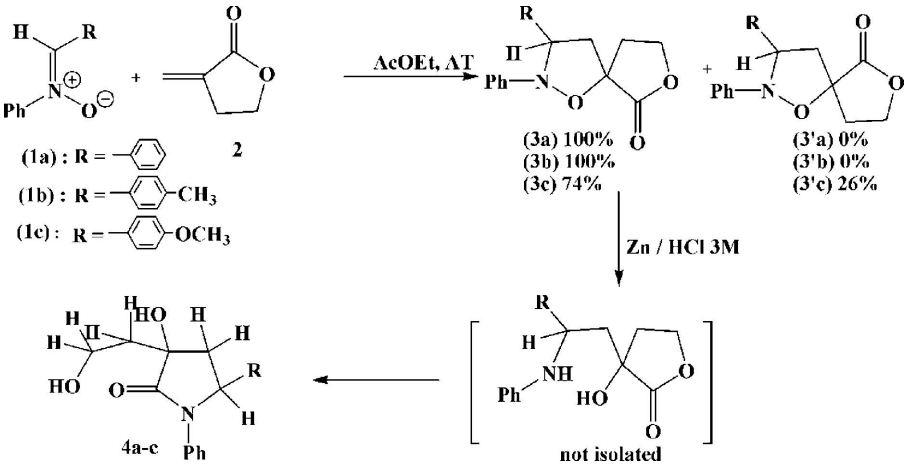
Key indicators

Single-crystal X-ray study
T = 180 K
Mean σ(C–C) = 0.004 Å
R factor = 0.055
wR factor = 0.170
Data-to-parameter ratio = 15.6

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Comment

The 1,3-dipolar cycloaddition of nitrones to olefins is one of the best procedures available for the preparation of isoxazolidines (Tufariello, 1984; Torssell, 1988). The reduction of the nitrogen–oxygen bond of the heterocycle leads to the corresponding open-chain 3-aminoalcohols.



Usually, when the resulting aminoalcohol has an electrophilic carbon at a suitable distance, nucleophilic addition of the amino group results in the formation of a new ring in the reaction product (Alibès *et al.*, 1998). This reduction–cyclization process has been successfully applied for the preparation of biologically active compounds (Goti *et al.*, 1997; Padwa *et al.*, 1981; Jung & Vu, 1996). As part of our research on bicyclic spiro compounds and their rearrangements, we previously reported that 1,3-dipolar cycloaddition of methylene-γ-butyrolactone with several nitrones afforded a mixture of diastereoisomers (Roussel *et al.*, 2003; Daran *et al.*, 2006). The cycloaddition of *C*,*N*-diphenylnitrone, (1*a*), to tulipalin A, (2) (see scheme), afforded two diastereoisomeric 5-spiro-substituted isoxazolidines at reflux in benzene or toluene (Cacciarini *et al.*, 2000). We applied the same reaction to *C*-aryl-*N*-phenylnitrones (1*a*)–(1*c*) but the reaction was carried out in ethyl acetate at room temperature (see scheme). The major isoxazolidines obtained, (3*a*)–(3*c*), were then treated

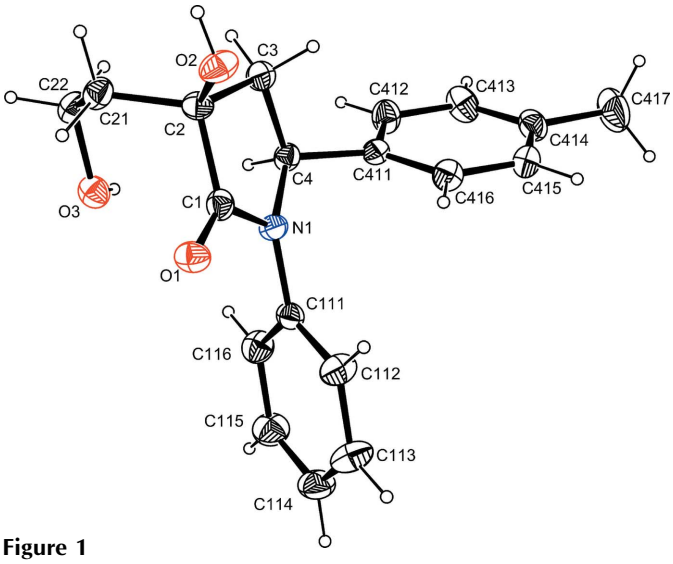


Figure 1
Molecular structure of compound (4*b*) with the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

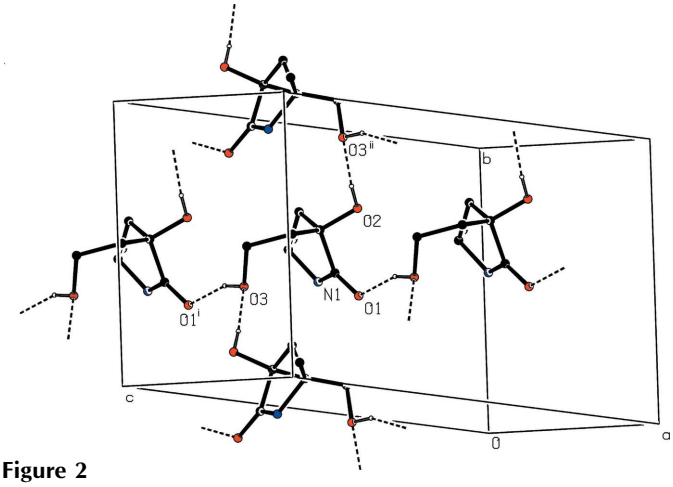


Figure 2
Crystal packing of (4*b*) showing the hydrogen bond chain motifs *C*(6) and *C*(7). The phenyl and tolyl rings as well as H atoms not involved in hydrogen bonding have been omitted for clarity. [Symmetry codes: (i) $x-1, y, z$; (ii) $1-x, \frac{1}{2}+y, \frac{3}{2}-z$.]

with Zn/3*M* HCl in order to reduce the N—O bond. The reaction did not stop at the formation of aminoalcohol but was followed by nucleophilic addition of the amino to the carbonyl group, leading in each case to a new functionalized γ-lactam, (4*a*)–(4*c*). A crystal of (4*b*) was subjected to X-ray structural analysis to determine the stereochemistry of the products (4*a*)–(4*c*) because the ^{1}H and ^{13}C NMR studies did not provide unambiguous information.

The pyrrolidine ring of (4*b*) is slightly distorted (Fig. 1) and the puckering parameters show that its conformation is close to that of an envelope: the total puckering amplitude Q and θ angle (Cremer & Pople, 1975) calculated for the atom sequence N1—C1—C2—C3—C4 are 0.230 (2) Å and 63.4 (6)°, respectively. However, this pyrrolidine ring, which may be also regarded as roughly planar with the largest deviation from the mean plane being 0.142 (2) Å at C3, makes dihedral angles of 62.5 (1) and 68.7 (1)° with the phenyl and tolyl rings, respectively.

Molecules of (4*b*) are connected by O—H···O hydrogen bonds (Table 1, Fig. 2), generating two crossing chain motifs, *C*(6) [H2···O3—C22—C21—C2—O2] and *C*(7) [H3···O1—C1—C2—C21—C22—O3] (Etter *et al.*, 1990) (Fig. 2). These hydrogen bonds assemble molecules into layers parallel to the (001) plane.

Experimental

Tulipalin A (2), and *C*-aryl-*N*-phenyl nitrones, (1*a*)–(1*c*), were synthesized according to literature procedures (Ksander *et al.*, 1977; Brüning *et al.*, 1973).

Synthesis of spiroheterocycles (3*a*)–(3*c*): a solution of (1*a*)–(1*c*) (10 mmol) and (2) (10 mmol) in ethyl acetate (40 ml), was stirred at room temperature for 24 h. The solvent was then evaporated under reduced pressure. The residue was crystallized from ethanol.

Synthesis of lactams (4*a*)–(4*c*): to a solution of cycloadduct (0.64 mmol) in the minimum volume of acetone (3–5 ml) was added activated zinc dust (61.18 mmol). To the resulting suspension was added slowly 3 *M* HCl (52.5 ml). The mixture was then stirred for 2 h at room temperature. The zinc was filtered off and rinsed with 3 *M* HCl, water and $CHCl_3$. To this mixture, while vigorously stirring, solid K_2CO_3 was slowly added until pH = 7. After stirring for two additional hours, the organic layer was separated, dried with Na_2SO_4, filtered and concentrated to give the lactam as a solid, which was subsequently recrystallized from CH_2Cl_2.

Crystal data

$C_{19}H_{21}NO_3$
M_r = 311.37
Monoclinic, $P2_1/c$
a = 5.7403 (9) Å
b = 9.0806 (11) Å
c = 30.836 (4) Å
β = 92.980 (11)°
V = 1605.2 (4) Å^3
Z = 4
D_x = 1.288 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 180 (2) K
Needle, colourless
0.59 × 0.08 × 0.08 mm

Data collection

Oxford Diffraction Xcalibur diffractometer
ω and φ scans
Absorption correction: none
12229 measured reflections
3291 independent reflections
2044 reflections with $I > 2\sigma(I)$
R_{int} = 0.060
θ_{max} = 26.3°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.055
$wR(F^2)$ = 0.170
S = 1.11
3291 reflections
211 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0768P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.30 e Å^{-3}
$\Delta\rho_{min}$ = −0.31 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O1^{i}	0.84	2.01	2.804 (3)	159
O2—H2···O3^{ii}	0.84	1.84	2.682 (3)	175

Symmetry codes: (i) $x-1, y, z$; (ii) $-x+1, y+\frac{1}{2}, -z+\frac{3}{2}$.

All H atoms were positioned geometrically and treated as riding on their parent atoms with C—H = 0.95 ($C_{aromatic}$), 0.98 (C_{methyl}), 0.99 (CH_2) and 1.00 Å (CH) and O—H = 0.84 Å, and with $U_{iso}(H) = 1.5U_{eq}(C_{methy},O)$ and $1.2U_{eq}$(other C).

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2003); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2003); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997) and *PLATON* (Spek, 2003); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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