

The conversion of a pyrrole trimer derivative into a 4,5,6,7-tetrahydro-4-(pyrrol-2-yl)indol-7-yltosylaminoindole

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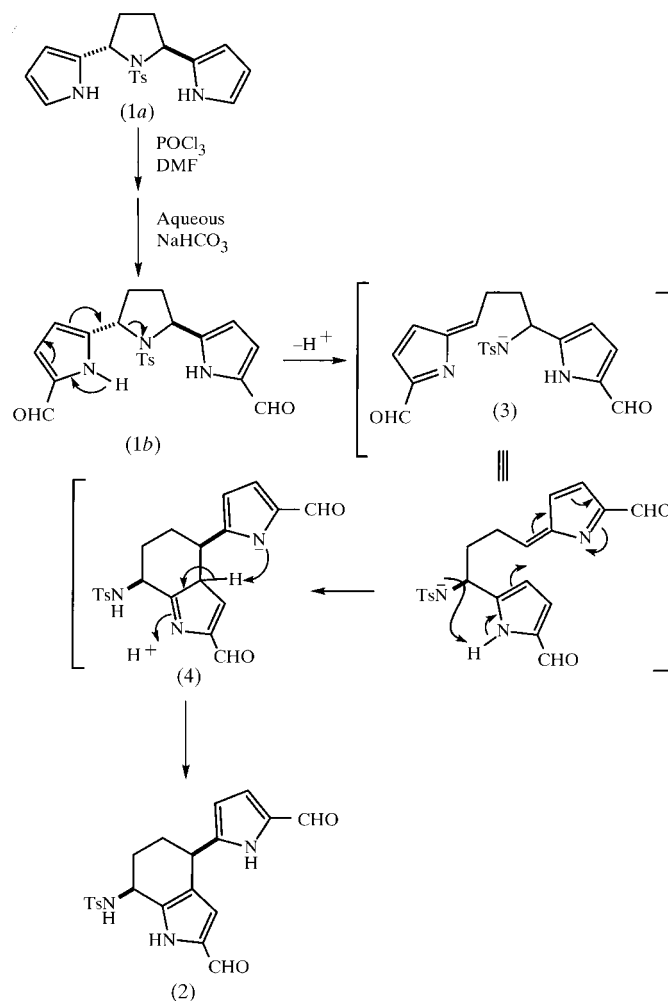
Vilsmeier formylation of *trans*-1-(4-methylphenylsulfonyl)-2,5-bis(pyrrol-2-yl)pyrrolidine leads to cleavage of the central ring then a reclosure resulting in the formation of *trans*-*N*-[2-formyl-4-(5-formylpyrrol-2-yl)-4,5,6,7-tetrahydroindol-7-yl]-toluenesulfonamide, C₂₁H₂₁N₃O₄S.

Comment

We have described (Zhao *et al.*, 1999) the Vilsmeier formylation of various derivatives of pyrrole trimer 2,5-bis(pyrrol-2-yl)pyrrolidine, which is produced as a mixture of *cis* and *trans* isomers (Zhao *et al.*, 1997), easily and simply, in moderate but usable yield, by the brief treatment of pyrrole with 20% aqueous hydrochloric acid at 273 K. Mono-tosylation of the pyrrole trimer gives a separable mixture of *cis* and *trans* tosylamides. When the *trans* isomer, (1a), was treated with the Vilsmeier reagent formed from phosphoryl chloride and dimethylformamide, followed by aqueous sodium hydrogen carbonate, two products were obtained. One was the anticipated diformyl derivative, (1b) (28%). The second (27%) was also a dialdehyde, but evidently did not have a comparable ring skeleton. An X-ray crystallographic analysis showed the product to have structure (2). We envisage the conversion of the dialdehyde (1b) into (2) as involving a sequence initiated by N-deprotonation (the aldehyde group appreciably increases the acidity of the pyrrole proton) leading to fission of the benzylic C—NTs bond with N-anion stabilization in (3) by the arylsulfonyl group (see Scheme). Next, an intramolecular alkylation of the second pyrrole ring, perhaps with proton transfer to the side-chain N atom [arrows on (3)] in such a way as to minimize steric interactions, would lead to (4) and thence (2) (Fig. 1) having the stereochemistry observed in the crystal structure determination.

The structure analysis reveals several interesting features. The *cis* relationship of the tosylamino substituents at C7 of the tetrahydroindole unit and the 5-formylpyrrol-2-yl substituent at C4, which is predicted by the mechanism proposed above, is clear – the *cis* relationship and the location of these groups

four C atoms apart demands that one of the groups be pseudo-axial and the other pseudo-equatorial on the six-membered ring – it is the tosylamino group which adopts a pseudo-axial orientation.



There are no intramolecular hydrogen bonds. However, in the lattice, two molecules are held closely together by three hydrogen bonds between the H atoms on N1 and N3, both hydrogen bonding to the aldehyde O3 atom of the second molecule, and between the H atom on N2 of the second molecule and one of the sulfonyl O atoms, O1, of the first (Table 1).

Also of interest is the orientation of the two pyrrole aldehyde functional groups. In each case, the aldehyde unit is almost completely coplanar with its attached heterocycle, the dihedral angles O—C—C—N being 1.8 (8) and 1.2 (6)°. Additionally, it is worth noting that both of the carbonyl groups are oriented with the O atom *syn* to the ring N—H bond.

Finally, we wish to draw attention to the orientation of the sulfonamide unit in this structure. We have previously noted in most arylsulfonamides a typical orientation (Zhao *et al.*, 1997, 1999; Beddoes *et al.*, 1986, 1987). In the present case, that typical orientation is extensively distorted. Thus, although the N atom is essentially planar, allowing the plane including the

N atom p orbital and the N–S bond to bisect the O–S–O angle, as usual, the relationship between the sulfonyl group and the benzene ring is non-standard – one of the O=S bonds approaches coplanarity with the benzene ring [dihedral angle -16.2 (3°)] and the other approaches being orthogonal to the ring [dihedral angle 112.6 (3°)].

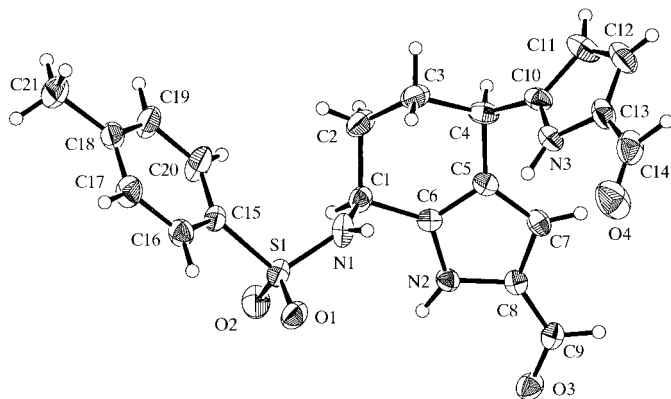


Figure 1
ORTEP (Johnson, 1965) plot of the molecule of (2), showing the atom-numbering scheme of the non-H atoms. Displacement ellipsoids are drawn at the 30% probability level.

Experimental

trans-1-(4-Methylphenylsulfonyl)-2,5-bis(pyrrol-2-yl)pyrrolidine (Zhao *et al.*, 1997) was reacted with a combination of phosphoryl chloride and dimethylformamide and then with aqueous sodium hydrogen carbonate to produce *trans*-*N*-[2-formyl-4-(5-formylpyrrol-2-yl)-4,5,6,7-tetrahydroindol-7-yl]toluenesulfonamide, $C_{21}H_{21}N_3O_4S$, in 27% yield, together with the anticipated dialdehyde, 1-(4-methylphenylsulfonyl)-2,5-bis(5-formylpyrrol-2-yl)pyrrolidine. A sample of (2) crystallized from ethanol was suitable for crystallographic examination.

Crystal data

$C_{21}H_{21}N_3O_4S$
 $M_r = 411.47$
Orthorhombic, $Pna2_1$
 $a = 11.788$ (2) Å
 $b = 6.6204$ (16) Å
 $c = 25.057$ (3) Å
 $V = 1955.5$ (6) Å³
 $Z = 4$
 $D_x = 1.398$ Mg m⁻³

Data collection

Rigaku AFC-5R diffractometer
 ω -2 θ scans
Absorption correction: ψ scans
(North *et al.*, 1968)
 $T_{min} = 0.544$, $T_{max} = 0.768$
2102 measured reflections
2102 independent reflections
1919 reflections with $I > 2\sigma(I)$

Cu $K\alpha$ radiation
Cell parameters from 17 reflections
 $\theta = 38.5$ – 39.8°
 $\mu = 1.761$ mm⁻¹
 $T = 293$ (2) K
Tabular, pink
 $0.50 \times 0.40 \times 0.15$ mm

$\theta_{max} = 79.07^\circ$
 $h = 0 \rightarrow 14$
 $k = 0 \rightarrow 8$
 $l = -31 \rightarrow 0$
3 standard reflections
every 150 reflections
intensity decay: 1.18%

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

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
$N1-H1 \cdots O3^i$	0.86	2.14	2.966 (4)	161
$N2-H2 \cdots O1^{ii}$	0.86	2.25	2.934 (4)	137
$N3-H3 \cdots O3^i$	0.86	2.16	2.989 (4)	161

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

Refinement

Refinement on F^2
 $R(F) = 0.038$
 $wR(F^2) = 0.107$
 $S = 1.066$
2102 reflections
264 parameters
H-atom parameters constrained

$$w = 1/[\sigma^2(F_o^2) + (0.0650P)^2 + 0.3269P]$$

where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{max} = 0.001$
 $\Delta\rho_{max} = 0.22$ e Å⁻³
 $\Delta\rho_{min} = -0.20$ e Å⁻³

H atoms were treated as riding with C–H 0.93–0.98, N–H 0.86 Å.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1993); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1995); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1993); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); software used to prepare material for publication: *TEXSAN*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD1093). Services for accessing these data are described at the back of the journal.

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