X-Ray crystallographic structure determination of some unique chiral sultam derivatives

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X-Ray diffraction analyses of the novel structures of chiral sultams 1–3 reveal that the nitrogen atom in the *N*-sulfonamido sultam 1 is planar, whereas the N–H bond in the *N*-unsubstituted sultam 2 and the N–F bond in the *N*-fluoro sultam 3 are nonplanar on the side of the smaller alkyl substituent, contrary to expectation.

In the course of developing new reagents for stereoselective fluorination,[1] we prepared several structurally interesting chiral sultam derivatives. Among those, we chose three representative sultams for X-ray analysis, *N*-sulfonamido sultam 1, *N*-unsubstituted sultam 2 and its *N*-fluoro analogue 3. Compounds 1 and 2 are synthetic intermediates for the potential fluorinating reagent 3. In addition to the orientation of the N–F bond in 3, the determination of the complete molecular structure is crucial for elucidation of the steric course of the asymmetric fluorination employing this reagent.

The molecular structures of compounds 1, 2 and 3 are shown in Figs. 1, 2 and 3, respectively.† The sums of the bond angles around the nitrogen atom in these compounds are 359.4, 336.6 and 315.0°, respectively. Therefore, the configuration at the nitrogen atom in 1 is almost planar, while it is pyramidal in 2 and 3.

The bond lengths N(2)–S(3) and N(2)–S(20) in 1 are 1,684(5) and 1.654(5) Å, respectively (Fig. 1). The latter is shorter than the former owing to the tendency of the nitrogen atom to donate its lone pair to the 3d orbital of S(20). Therefore, the presence of the exocyclic sulfonamido substituent contributes to the planarity of the nitrogen atom. Configurationally stable, pyramidal nitrogen atoms were observed when they are part of a three- to five-membered ring and when attached to electronegative substituents.[2] It is, however, not the case if the exocyclic
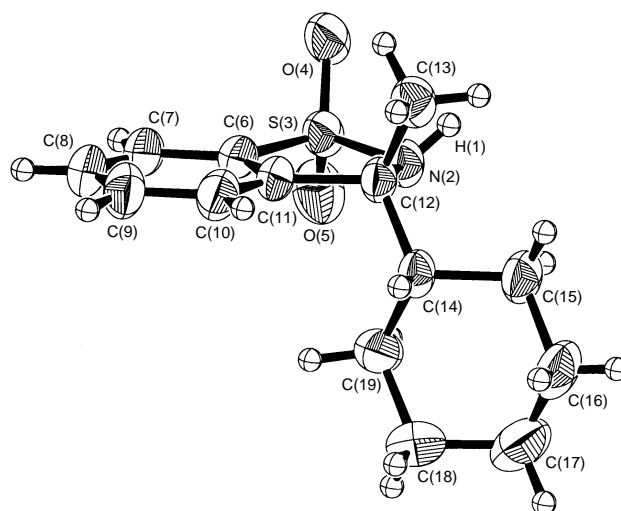

Fig. 2 ORTEP diagram of 2 with 50% thermal ellipsoids. Selected bond distances (Å) and angles (°): N(2)–S(3) 1.620(2), N(2)–C(12) 1.487(4); S(3)–N(2)–C(12) 115.6(2), S(3)–N(2)–H(1) 108(2), C(12)–N(2)–H(1) 113(2).
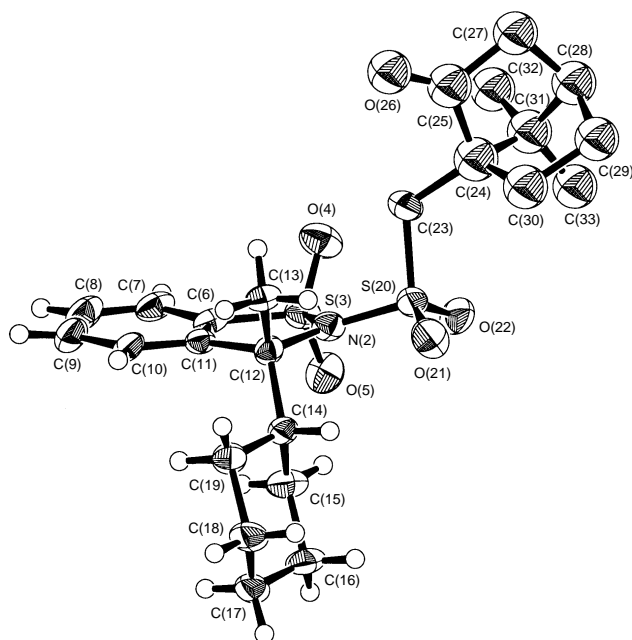
Fig. 1 ORTEP diagram of 1 with 50% thermal ellipsoids. Two of minor disordered contributions of camphor moiety are omitted for clarity. Selected bond distances (Å) and angles (°): N(2)–S(3) 1.684(5), N(2)–S(20) 1.654(5), N(2)–C(12) 1.523(8); S(3)–N(2)–S(20) 117.6(3), S(3)–N(2)–C(12) 115.6(4), C(12)–N(2)–S(20) 126.2(4).
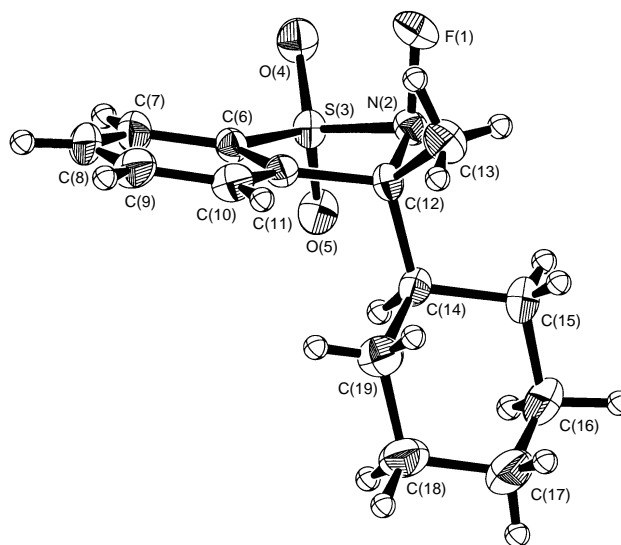
Fig. 3 ORTEP diagram of 3 with 50% thermal ellipsoids. Selected bond distances (Å) and angles (°): N(2)–F(1) 1.435(3), N(2)–S(3) 1.738(2), N(2)–C(12) 1.523(4); F(1)–N(2)–S(3) 102.3(2), F(1)–N(2)–C(12) 105.7(2), S(3)–N(2)–C(12) 107.0(2).

1 R =

2 R = H
3 R = F
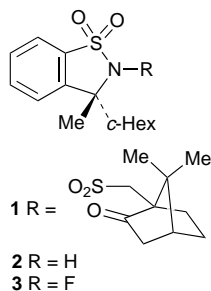
substituent has an atom that interacts with the nitrogen lone pair, such as the sulfur atom of the sulfonyl in **1**.

The nitrogen atom in compound **2** (Fig. 2) apparently has sp³ character based on the bond angles. The orientation of the amide proton is *syn* to the methyl group, namely, the lone pair of the nitrogen takes a position on the side of the larger alkyl substituent. Thus, the nitrogen pyramid is tilted in the opposite direction compared to a previous report,[2] although the reason is as yet unclear. The absence of the electronegative and rather bulky *N*-substituent such as a camphorsulfonyl group results in shortening the N(2)–S(3) distance [1.620(2) Å] and the N(2)–C(12) distance [1.487(4) Å] in **2**.

The structure of **3** was determined at 152 K (Fig. 3) since the thermal motion of the cyclohexyl group was high at room temperature. The nitrogen atom in **3** was found to be highly pyramidalized. The N(2)–S(3) bond [1.738(2) Å] is much longer than that in **1** and **2**, presumably owing to the highly electronegative character of the fluorine atom. The N(2)–F(1) bond [1.435(3) Å] is slightly elongated [*cf.*[3] 1.406(16) Å for F–NR¹R²]. The dihedral angles F(1)–N(2)–C(12)–C(14) and F(1)–N(2)–C(12)–C(13) are −161.8(2) and −40.9(3)°, respectively. Therefore, the fluorine is antiperiplanar with the cyclohexyl group. The dihedral angles F(1)–N(2)–S(3)–O(4) and F(1)–N(2)–S(3)–O(5) are 30.5(2) and 159.4(2)°, respectively. Consequently, the nitrogen lone pair seems to bisect the O(4)–S(3)–O(5) angle, probably due to optimal orbital overlap with the d-orbital of the sulfur atom. The nitrogen atom is at a distance of 0.449 Å from the least-squares plane defined by S(3), C(6), C(11), C(12) and the five-membered ring has an envelope conformation. As a result, the N–F bond of **3** is nearly perpendicular to the least-squares plane (85.8°).

Footnotes

† *Crystal data* for **1**: $C_{24}H_{33}NO_5S_2$, $M = 479.65$, orthorhombic, $a = 14.344(2)$, $b = 22.415(2)$, $c = 7.608(3)$ Å, $U = 2446(1)$ Å³, $T = 163$ K, space group $P2_12_12$ (no. 18), filtered Cu-Kα radiation, $\lambda = 1.54178$ Å, $Z = 4$, $D_c = 1.302$ Mg m⁻³, $F(000) = 1024$, colourless prism, dimensions $0.35 \times 0.20 \times 0.10$ mm, μ(Cu-Kα) = 2.259 mm⁻¹, Rigaku AFC7R diffractometer, ω–2θ scan, $4.0 < 2\theta < 130.0°$, 2420 reflections measured, 1960 reflections observed [$I > 3\sigma(I)$]. The structure was solved by direct methods (SIR92[4]) and expanded using Fourier techniques (DIRDIF94[5]).

The camphor moiety [C(24)–C(33), O(26)] was disordered over three positions with a 43 : 29 : 28 distribution. All non-hydrogen atoms were refined anisotropically except those of the disordered group that were refined as a rigid group isotropically. For this reason, the *R* value was slightly high. Hydrogen atoms were included but not refined, except those located with the disordered group and the C(23) atom attached to the disordered group, which were ignored. Isotropic temperature factors of the H atoms were set equal to U_{eq} of the bonded C atom. The final cycle of full-matrix least-squares refinement (for 221 parameters) was converged with $R_w = 0.099$, $R = 0.067$ (gof = 1.32). For **2**: $C_{14}H_{19}NO_2S$, $M = 265.37$, tetragonal, $a = 8.963(1)$, $c = 34.080(2)$ Å, $U = 2737.7(8)$ Å³, $T = 296$ K, space group $P4_32_12$ (no. 96), filtered Cu-Kα radiation, $\lambda = 1.54178$ Å, $Z = 8$, $D_c = 1.288$ mg m⁻³, $F(000) = 1136$, colourless prism with dimensions $0.40 \times 0.40 \times 0.10$ mm, μ(Cu-Kα) = 2.052 mm⁻¹, an empirical absorption correction based on azimuthal scans of several reflections, transmission factors 0.6093–0.9952; Rigaku AFC7R diffractomer, ω–2θ scan, $4.0 < 2\theta < 120.0°$, 1314 reflections measured, 1137 reflections observed [$I > 3\sigma(I)$]. The structure was solved by direct methods (SIR92) and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. The final cycle of full-matrix least-squares refinement (for 240 parameters) was converged with $R_w = 0.051$, $R = 0.040$ (gof = 0.96). S(3)–O(4) distance [1.431(3) Å] is slightly longer than S(3)–O(5) [1.420(3) Å], which can be ascribed to the intermolecular hydrogen bonding between NH and O(4) [N(2)···O(4) 2.955(3) Å]. For **3**: $C_{14}H_{18}FNO_2S$, $M = 283.36$, orthorhombic, $a = 12.704(3)$, $b = 13.518(4)$, $c = 8.263(4)$ Å, $U = 1419.0(6)$ Å³, $T = 152$ K, space group $P2_12_12_1$ (no. 19), graphite monochromated Mo-Kα radiation, $\lambda = 0.71069$ Å, $Z = 4$, $D_c = 1.326$ mg m⁻³, $F(000) = 600$, colourless prism with dimensions $0.32 \times 0.23 \times 0.17$ mm, μ(Mo-Kα) = 0.237 mm⁻¹, Rigaku AFC7R diffractometer, ω–2θ scan, $4.0 < 2\theta < 55.0°$, 1900 reflections measured, 1502 reflections observed [$I > 3\sigma(I)$]. The structure was solved by direct methods (SHELXS86[6]) and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. The final cycle of full-matrix least-squares refinement (for 244 parameters) was converged with $R_w = 0.045$, $R = 0.034$ (gof = 1.12). Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/313.

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