# Preparation, Isolation and X-Ray Crystallographic Structure Determination of a Stable, Crystalline Carbonic Anhydride of an *N*-Protected α-Amino Acid

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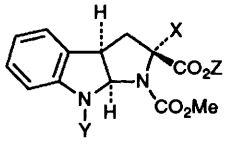
The reaction of methyl (2*S*,3a*R*,8a*S*)-2-carboxy-8-phenylsulfonyl-1,2,3,3a,8,8a-hexahydropyrrolo-[2,3-*b*]indole-1-carboxylate and isobutyl chloroformate in tetrahydrofuran at −15 °C in the presence of trimethylamine results in the formation of the corresponding mixed carboxylic–carbonic anhydride. This unusually stable mixed anhydride was isolated in the form of an analytically pure crystalline solid and its structure verified crystallographically.

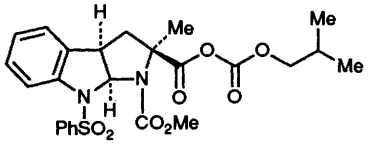
Mixed carboxylic–carbonic anhydrides are frequently the intermediates of choice for the creation of peptide bonds owing to their ease of preparation, good reactivity and relative insensitivity towards racemisation.[1,2,3] Standard procedures for peptide synthesis *via* the mixed anhydride route call for their preparation *in situ* usually below 0 °C to minimise the possibility of decomposition and racemisation.[3] Recently however, Benoiton has reported that such mixed anhydrides can be isolated from dichloromethane solution in good yield and are mostly stable over a period of days at room temperature in dichloromethane solution.[4] We report here on the isolation and X-ray crystal structure of a highly stable carboxylic–carbonic mixed anhydride isolated in the course of our studies on the enantiospecific synthesis of the so-called nonproteinogenic amino acids from (*S*)-tryptophan.[5]

The hexahydropyrroloindole **1** prepared from (*S*)-tryptophan, as discussed previously,[5,6] was treated with benzenesulfonyl chloride to provide the sulfonamide **2** in good yield as a white crystalline solid. The highly crystalline nature of this derivative renders it preferable to the analogous toluene-*p*-sulfonamide used in our original studies[5] which was somewhat reluctant to crystallise. Deprotonation of **2** with lithium diisopropylamide in tetrahydrofuran (THF) at −78 °C followed by quenching with methyl iodide gave the α-methylated derivative **3** with retention of configuration as indicated by the characteristic upfield shift of the *endo*-ester methyl group in the $^1$H NMR spectrum (δ 3.05) which is the result of shielding by the aromatic nucleus of the pyrroloindole system. Saponification of **3** with Claisen's alkali gave the corresponding acid **4**. This acid was allowed to react in dry THF, under nitrogen at −15 °C, for 80 min with an excess of isobutyl chloroformate and triethylamine. Filtration of the amine hydrochloride and chromatography of the remaining solution on silica gel gave the mixed anhydride **5** as a white crystalline solid in 88% yield. This mixed anhydride is remarkably stable showing essentially no decomposition in over a year at ambient temperature‡ and is even characterised by the presence of a molecular ion at *m*/*z* 516 in its 70 eV electron impact mass spectrum.

We were sufficiently intrigued by the stability of **5** to prepare a similar derivative of α-methylproline. Thus *N*-benzyloxycarbonylproline methyl ester was treated sequentially with lithium diisopropylamide and methyl iodide to give the derivative **6** which on saponification gave the corresponding acid **7**. Treatment of this acid with isobutyl chloroformate and aqueous work up gave the desired mixed anhydride **8** in almost pure form in 86% yield. However, unlike the case of **5**, repeated attempts at purification of **8** by chromatography on silica gel resulted only in extensive decomposition. Evidently, the stability of **5** is not simply a function of steric hindrance of the carboxy carbonyl group.

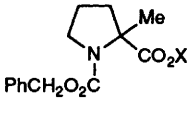
Crystals of **5** suitable for X-ray analysis were obtained from ethyl acetate–light petroleum (b.p. 40–60 °C) and the structure solved by direct methods using the SHELXTL PLUS program package.[7] The molecular structure of **5** is presented in Figs. 1 and 2. The conformation of the hexahydropyrroloindole system is grossly similar to that of the related compound **9**[8] and that of the calabar bean alkaloid Physostigmine **10**[9] and is characterised by puckering of C-3, in the terminal 5-membered ring, out away from the *endo*-surface of the molecule. This puckering has the effect of forcing the C-2 substituent in towards the *endo* surface. We now have strong NMR spectroscopic and computational evidence that the whole gamut of derivatives of **2** prepared in this laboratory adopt this same conformation in deuteriochloroform solution and hence that it is not an artifact

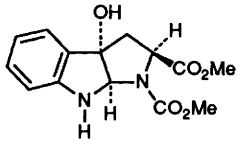




**1** X = Y = H, Z = Me
**2** X = H, Y = $PhSO_2$, Z = Me
**3** X = Me, Y = $PhSO_2$, Z = Me
**4** X = Me, Y = $PhSO_2$, Z = H

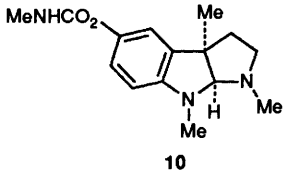
**5**





**6** X = Me
**7** X = H
**8** X = $CO_2CH_2CHMe_2$

**9**



**10**

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‡ Including a 10 week road and sea journey from London to Chicago at the height of summer.

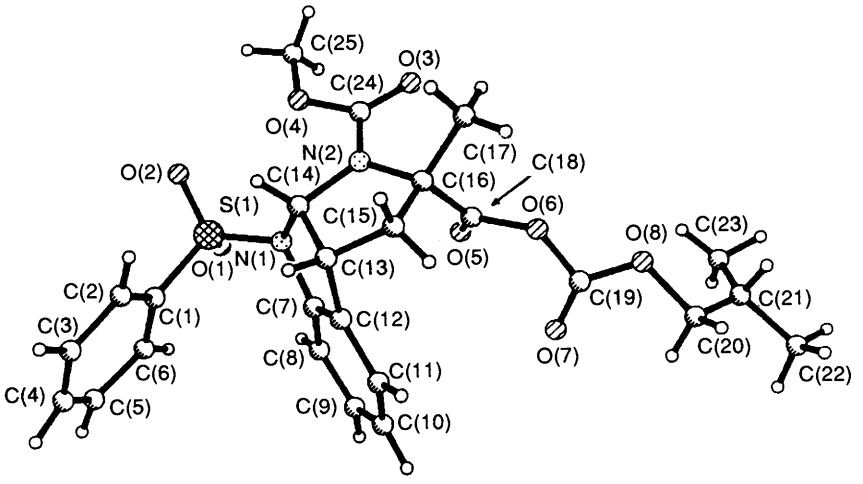


**Fig. 1** Molecular structure of **5** showing the crystallographic numbering scheme adopted

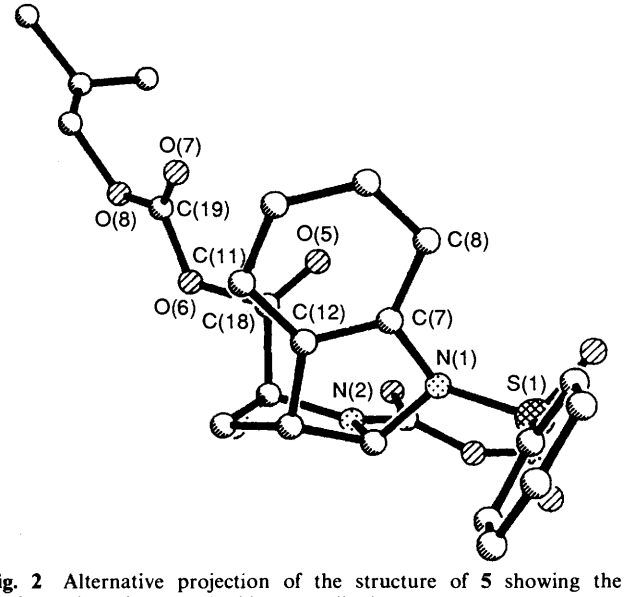


**Fig. 2** Alternative projection of the structure of **5** showing the conformation of the terminal heterocyclic ring

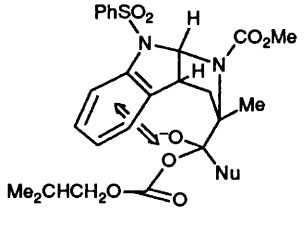


**Fig. 3**

**Table 1** Intramolecular close contacts (crystallographic numbering scheme)

| Close Contact | Distance (Å) | Close Contact | Distance (Å) |
|---|---|---|---|
| O(5)–C(7) | 3.27 | C(11)–C(18) | 3.74 |
| O(5)–C(8) | 3.79 | C(12)–C(18) | 3.22 |
| O(5)–C(9) | 4.19 | O(6)–C(11) | 4.20 |
| O(5)–C(10) | 4.19 | O(7)–C(9) | 4.46 |
| O(5)–C(11) | 3.79 | O(7)–C(10) | 3.82 |
| O(5)–C(12) | 3.27 | O(7)–C(11) | 3.64 |

of crystal packing. The most ready indicator of this conformational preference, in **2**, is the chemical shift of the methyl ester group ($\delta$ 3.05) alluded to above.

The unusual stability of **5** is intriguing particularly in the light of the more typical instability of **8**. With the obvious steric argument excluded, we consider that two alternative hypotheses may now be advanced for the stability of **5**: (i) the mixed anhydride is stabilised by a non-bonding interaction with the *endo* surface of the aromatic system, and (ii) attack of nucleophiles on the mixed anhydride system of **5** would lead to formation of an unfavoured tetrahedral intermediate (Fig. 3) in which two oxygen atoms would be forced into uncomfortably close contact with the aromatic system. Intramolecular contact distances between the pyrroloindole aromatic ring and the mixed anhydride system are given in Table 1. The planes of the aromatic ring (C-7,C-8,C-9,C-10,C-11,C-12) and the carboxylate group of the mixed anhydride (C-16,C-18,O-5,O-6) diverge at an angle of 39.3°. In the mixed anhydride system the torsion angle between the planes of the two carbonyl groups is 51.3°. The possibility of the existence of non-bonding interactions between the ester group and the aromatic system in **2**, and its derivatives, is the subject of an ongoing investigation in these laboratories which will be reported on in due course.

## Experimental

*General.*—M.p.s are uncorrected and were determined with a Kofler hot stage microscope. Optical rotations were measured with an Optical Activity AA-10 polarimeter, $[\alpha]_D$ values are given in units of $10^{-1}$ deg cm$^2$ g$^{-1}$. IR spectra were recorded as chloroform solutions with a Perkin-Elmer 983 spectrophotometer. $^1$H NMR spectra were obtained at 200, or 400 MHz as deuteriochloroform solutions, unless otherwise stated, with Varian XL 200, and Varian VXR 400 instruments respectively. Chemical shifts ($\delta$) are in ppm downfield from tetramethylsilane as internal standard, $J$ values are given in Hz. 70 eV EIMS were recorded with a VG 7070H mass spectrometer. All solvents were dried and distilled by standard techniques. Tetrahydrofuran (THF) was distilled under nitrogen from sodium benzophenone ketyl immediately prior to use. Ether refers to diethyl ether and light petroleum to the fraction boiling in the range 40–60 °C.

*Dimethyl* (2S,3aR,8aS)-8-*Phenylsulfonyl*-1,2,3,3a,8,8a-*hexahydropyrrolo*[2,3-b]*indole*-1,2-*dicarboxylate* **2**.—The hexahydropyrroloindole **1** (24.47 g; 88.6 mmol) was dissolved in pyridine (50 cm$^3$) and treated at room temperature with benzenesulfonyl chloride (18.43 g, 105 mmol). After 5 h diethyl ether was added causing crude **2** to precipitate out of solution. After filtration, the precipitate was redissolved in chloroform, washed with water, dried ($MgSO_4$) and evaporated. Crystallis-

ation of the so obtained solid from ether–dichloromethane gave the title compound in 62% yield as a white solid with m.p. 165–167 °C; $[\alpha]_D^{30}$ +91 (*c* 1, $CH_2Cl_2$); $\delta_H$(200 MHz), 2.5 (2 H, m, 3-H), 3.11 (3 H, s, $CO_2Me$), 3.6 (4 H, m, 3a-H + $NCO_2Me$), 4.56 (1 H, bd, 2-H), 6.23 (1 H, d, *J* 7, 8a-H) and 6.9–8.0 (9 H, m) (Found: C, 57.35; H, 4.7; N, 6.85; S, 7.7. $C_{20}H_{20}N_2O_6S$ requires C, 57.68; H, 4.84; N, 6.73; S, 7.70%).

*Dimethyl* (2S,3aR,8aS)-2-*Methyl*-8-*phenylsulfonyl*-1,2,3,3a,-8,8a-*hexahydropyrrolo*[2,3-b]*indole*-1,2-*dicarboxylate* **3**.—Pyrroloindole **2** (2.573 g, 6.18 mmol) was dissolved in THF (30 $cm^3$) and cooled under a nitrogen atmosphere to −78 °C and then treated with a solution of lithium disopropylamide (8.7 mmol) in THF (10 $cm^3$) and hexane (4 $cm^3$). After stirring for 20 min at −78 °C methyl iodide (2.38 g, 16.8 mmol) was added and the mixture allowed to warm to −60 °C with stirring over 1 h before being poured onto ethyl acetate (10 $cm^3$) and water (10 $cm^3$). This mixture was acidified with dilute hydrochloric acid and extracted with further ethyl acetate. The combined organic phases were washed with water and dried ($MgSO_4$) and concentrated to give the crude product (2.69 g). Crystallisation of the crude from methanol gave the title product (1.11 g, 41%). Filtration of the mother liquors on silica gel [eluent ethyl acetate–light petroleum (1:1)] and further crystallisation gave a further 21% of the title compound. The product was characterised by m.p. 144–145 °C; $[\alpha]_D$ +95 (*c* 0.72, $CH_2Cl_2$); $\delta_H$(400 MHz) 1.67 (3 H, s, 2-Me), 2.18 (1 H, dd, *J* 13.4, 7.4, 3-H), 2.74 (1 H, d, *J* 13.4, 3-H), 3.05 (3 H, s, $CO_2Me$), 3.40 (1 H, t, *J* 6.7, 3a-H), 3.59 (3 H, s, $NCO_2Me$), 6.28 (1 H, d, *J* 6.4, 8a-H) and 6.9–7.8 (9 H, m) (Found: C, 58.55; H, 5.05; N, 6.65; S, 7.65. $C_{21}H_{22}N_2O_6S$ requires C, 58.59; H, 5.15; N, 6.51; S, 7.45%).

2-*Carboxy*-2-*methyl*-8-*phenylsulfonyl*-1,2,3,3a,8,8a-*hexahydropyrrolo*[2,3-b]*indole*-1-*carboxylate* **4**.—The ester **3** (1.779 g, 4.133 mmol) was dissolved in methanol (30 $cm^3$) and treated with a solution of potassium hydroxide (21 g) in water (15 $cm^3$) and stirred at room temperature for 1 h after which all starting material had been consumed. After acidification with 2 mol $dm^{-3}$ HCl the reaction mixture was extracted with ethyl acetate. Evaporation of the extracts and crystallisation from dichloromethane–light petroleum gave the title acid (1.235 g) 72% as a white crystalline solid with m.p. 138–139 °C; $[\alpha]_D$ +99 (*c* 1, $CH_2Cl_2$); $\delta_H$(400 MHz) 1.62 (3 H, s, 2-Me), 2.07 (1 H, dd, *J* 13.4, 7.35, 3-H), 3.02 (1 H, bd, 13.4, 3-H), 3.24 (1 H, t, *J* 6.6, 3a-H), 3.82 (3 H, s, $NCO_2Me$), 6.12 (1 H, d, *J* 6.2, 8a-H) and 7.0–7.7 (9 H, m).

*The Mixed Anhydride* **5**.—The above acid **4** (204.6 mg, 0.491 mmol) was dissolved in THF (3 $cm^3$) and treated with triethylamine (64 mg, 64 mmol) and cooled under nitrogen with stirring to −15 °C before a solution of isobutyl chloroformate (83.4 mg, 61 mmol) in THF (2 $cm^3$) was added. After stirring for 80 min at this temperature the amine hydrochloride was filtered off and the solvent removed under vacuum. The residue was chromatographed on silica gel [eluent light petroleum–ethyl acetate (2:1)] to yield the mixed carboxylic–carbonic anhydride (0.223 g) 88% as a white solid with m.p. 107–109 °C; $\delta_H$(400 MHz) 0.87 (6 H, d, *J* 6.75 Hz, isobutyl $Me_2$), 1.71 (3 H, s, 2-Me), 1.88 (1 H, m, $CH_2CHMe_2$), 2.27 (1 H, dd, *J* 13.6, 7.5, 3-H), 2.77 (1 H, d, *J* 13.6), 3.47 (1 H, t, *J* 6.8, 3a-H), 3.54 (3 H, s, $NCO_2Me$), 3.82 (2 H, m, $CH_2CHMe_2$), 6.26 (1 H, d, *J* 6.45, 8a-H) and 6.9–7.8 (9 H, m) (Found: C, 57.9; H, 5.45; N, 5.35. $C_{25}H_{28}N_2O_8S$ requires C, 58.13; H, 5.46; N, 5.42%).

(±)-1-*Benzyl* 2-*methyl* 2-*methylpyrrolidine*-1,2-*dicarboxylate* **6**.—Lithium diisopropylamide (3.2 mmol) in THF (2 $cm^3$) and hexane (2.5 $cm^3$) was added at −78 °C to a stirred solution of *N*-benzyloxycarbonylproline methyl ester (760 mg, 2.89 mmol) in THF (2 $cm^3$) under a nitrogen atmosphere. After 15 min methyl iodide (1.65 g, 11.6 mmol) was added and the reaction stirred at −78 °C for a further 4 h before being poured into 2 mol $dm^{-3}$ hydrochloric acid and extracted with ethyl acetate. Chromatography of the extracts on silica gel [eluent light petroleum–ethyl acetate (2:1)] gave the title acid (375 mg) 47% as a viscous oil with $\delta_H$(200 MHz, 2 rotomers) 1.40 and 1.46 (3 H, 2s, 2-Me), 1.70–2.10 (4 H, m), 3.28 and 3.54 (3 H, 2s, $CO_2Me$), 3.44 (2 H, m, 5-H), 4.96 (2 H, m, $CH_2Ph$) and 7.0–7.4 (5 H, m); *m/z* 277.1340 (Calc. for $C_{15}H_{19}NO_4$: *M*, 277.1314).

*Benzyl* (±)-2-*Methylproline*-1-*carboxylate* **7**.—The ester **6** (257 mg) dissolved in methanol (0.5 $cm^3$) was treated at room temperature with potassium hydroxide (2.5 g) in water (2 $cm^3$) and methanol (1 $cm^3$) for 16 h then diluted with ethyl acetate and washed with 2 mol $dm^{-3}$ HCl. Concentration of the organic phase and crystallisation of the crude product from dichloromethane–light petroleum gave the title acid (237 mg) 97% as a white solid with m.p. 121 °C; $\delta_H$(200 MHz, 2 rotomers) 1.52 and 1.62 (3 H, 2-Me), 1.8–2.3 (4 H, m), 3.58 (2 H, m, 5-H), 5.09 and 5.14 (2 H, m, $CH_2Ph$) and 7.2–7.5 (5 H, m) (Found: C, 63.35; H, 6.15; N, 5.2. $C_{14}H_{17}NO_4$ requires C, 63.87; H, 6.51; N, 5.32%).

*The Mixed Anhydride* **8**.—The acid **7** (93 mg, 0.353 mmol) was dissolved in THF (1 $cm^3$) and treated with a solution of triethylamine (44 mg, 0.438 mmol) in THF (1 $cm^3$) and then cooled to −40 °C under a nitrogen atmosphere before treatment with isobutyl chloroformate (58 mg, 0.422 mmol) in THF (2 $cm^3$). The reaction was then allowed to warm to −5 °C over 90 min and then diluted with ethyl acetate (30 $cm^3$) and washed with 2 mol $dm^{-3}$ HCl (5 $cm^3$) and water (5 $cm^3$), dried ($MgSO_4$) and evaporated under reduced pressure to give the mixed anhydride (111 mg) 86% in essentially pure form as estimated by $^1H$ NMR spectroscopy. This viscous oil had $\delta_H$(200 MHz, 2 rotomers) 0.92 (3 H, d, *J* 4.51, $CH_2CHMe_2$), 0.95 (3 H, d, *J* 4.51, $CH_2CHMe_2$), 1.54 and 1.64 (3 H, 2s, 2-Me), 1.96 (4 H, m), 2.33 (1 H, m, $CH_2CHMe_2$), 3.60 (2 H, m, 5-H), 3.99 and 4.03 (2 H, 2d, *J* 5.6, $CH_2CHMe_2$), 5.12 (2 H, m, $CH_2Ph$) and 7.2–7.5 (5 H, m). Repeated chromatography on silica gel resulted in the recovery of increasingly smaller quantities of **8** having essentially the same $^1H$ NMR spectrum as that of the crude extract. No attempts to obtain microanalytical data on this evidently unstable material were made.

*X-Ray Crystallographic Structure Determination*.—Crystals were grown from ethyl acetate–light petroleum.

*Crystal data*. $C_{25}H_{28}N_2O_8S$, *M* = 516.61, Monoclinic, *a* = 9.510(4), *b* = 11.193(3), *c* = 12.050(4) Å, α = 90.00(0), β = 96.08(3), γ = 90.00(0)°, *V* = 1275.58 Å (by least squares refinement on diffractometer angles for 27 automatically centre reflections λ = 0.710 73 Å), space group $P2_1$, *Z* = 2, $D_{calc}$ = 1.34 g $cm^{-3}$. Irregular colourless crystals of approximate dimensions 0.2 × 0.3 × 0.6 mm, μ(Mo-Kα) = 1.7 $cm^{-1}$.

*Data collection and processing*. Nicolet R3m/V diffractometer, ω/2θ mode, graphite monochromated Mo-Kα radiation ($5 \leq 2\theta \leq 50°$), 2631 unique data giving 1242 with $I \geq 3\sigma(I)$.

*Structure analysis and refinement*. The structure was solved by direct methods and refined by full matrix least-squares methods. Due to the shortage of data (only 47% of the measured reflections were considered to be observed) only the sulfur atom was refined anisotropically, other non-hydrogens were isotropically modelled, and hydrogen atoms were placed in calculated positions (C–H 0.96 Å), and assigned a common fixed isotropic thermal parameter ($U$ = 0.08 $Å^2$). The carbon atoms of the isobutyl group (C-20, C-21, C-22 and C-24) exhibit a large thermal parameter due to a disorder which we have not been able to successfully refine. The least-squares refinement included 149 parameters for 1242 variables, gave $R$ = 0.0974,

**Table 2** Fractional atomic coordinates ( × $10^4$) for **5**

| | *x* | *y* | *z* |
|---|---|---|---|
| S(1) | −4486(4) | −1171 | −238(3) |
| N(1) | −3685(11) | −333(11) | −1087(9) |
| N(2) | −4523(12) | 932(12) | −2676(10) |
| O(1) | −4168(12) | −2353(12) | −453(10) |
| O(2) | −5937(12) | −792(12) | −334(10) |
| O(3) | −5584(12) | 153(12) | −4286(10) |
| O(4) | −6272(12) | −326(11) | −2626(9) |
| O(5) | −2243(13) | 67(13) | −3648(10) |
| O(6) | −1696(14) | 1832(14) | −4306(11) |
| O(7) | 406(20) | 1104(19) | −3860(16) |
| O(8) | −153(15) | 2025(14) | −5431(11) |
| C(1) | −3752(14) | −841(12) | 1111(11) |
| C(2) | −4080(18) | 171(18) | 1623(14) |
| C(3) | −3508(26) | 328(27) | 2756(20) |
| C(4) | −2645(25) | −476(23) | 3251(22) |
| C(5) | −2355(23) | −1453(21) | 2804(18) |
| C(6) | −2856(18) | −1664(18) | 1652(15) |
| C(7) | −2146(13) | −238(13) | −935(10) |
| C(8) | −1201(15) | −1217(18) | −765(12) |
| C(9) | 211(18) | −941(17) | −701(13) |
| C(10) | 652(18) | 239(16) | −772(13) |
| C(11) | −267(17) | 1167(16) | −936(13) |
| C(12) | −1744(14) | 901(14) | −1027(11) |
| C(13) | −3005(15) | 1695(14) | −1217(12) |
| C(14) | −4212(14) | 848(13) | −1450(10) |
| C(15) | −3027(19) | 2515(17) | −2224(14) |
| C(16) | −3607(16) | 1753(15) | −3181(13) |
| C(17) | −4413(20) | 2511(20) | −4119(16) |
| C(18) | −2479(17) | 1051(17) | −3701(13) |
| C(19) | −324(23) | 1587(20) | −4498(19) |
| C(20) | 1321(25) | 2061(24) | −5690(19) |
| C(21) | 1424(29) | 1622(28) | −6673(24) |
| C(22) | 2912(30) | 1731(32) | −7004(27) |
| C(23) | 702(52) | 689(47) | −7008(40) |
| C(24) | −5475(17) | 231(17) | −3272(14) |
| C(25) | −7291(20) | −1145(21) | −3133(16) |

**Table 3** Bond lengths (Å) for **5**

| | | | |
|---|---|---|---|
| S(1)–N(1) | 1.635(12) | S(1)–O(1) | 1.387(13) |
| S(1)–O(2) | 1.436(12) | S(1)–C(1) | 1.739(13) |
| N(1)–C(7) | 1.459(17) | N(1)–C(14) | 1.465(19) |
| N(2)–C(14) | 1.479(17) | N(2)–C(16) | 1.444(21) |
| N(2)–C(24) | 1.347(20) | O(3)–C(24) | 1.218(20) |
| O(4)–C(24) | 1.302(21) | O(4)–C(25) | 1.423(24) |
| O(5)–C(18) | 1.124(24) | O(6)–C(18) | 1.402(23) |
| O(6)–C(19) | 1.377(27) | O(7)–C(19) | 1.119(29) |
| O(8)–C(19) | 1.253(27) | O(8)–C(20) | 1.469(28) |
| C(1)–C(2) | 1.343(24) | C(1)–C(6) | 1.371(23) |
| C(2)–C(3) | 1.425(29) | C(3)–C(4) | 1.317(36) |
| C(4)–C(5) | 1.263(35) | C(5)–C(6) | 1.439(28) |
| C(7)–C(8) | 1.418(23) | C(7)–C(12) | 1.339(21) |
| C(8)–C(9) | 1.372(23) | C(9)–C(10) | 1.391(26) |
| C(10)–C(11) | 1.358(25) | C(11)–C(12) | 1.428(21) |
| C(12)–C(13) | 1.491(20) | C(13)–C(14) | 1.492(20) |
| C(13)–C(15) | 1.520(23) | C(15)–C(16) | 1.493(23) |
| C(16)–C(17) | 1.550(25) | C(16)–C(18) | 1.518(24) |
| C(20)–C(21) | 1.295(37) | C(21)–C(22) | 1.515(42) |
| C(21)–C(23) | 1.291(29) | | |

$R_w$ = 0.1048 (weighting scheme $w^{-1} = \sigma^2(F) + 0.001\,335F^2$) and did not shift any parameter by more than 0.01 times its estimated standard deviation. The final difference-Fourier map was featureless with the largest peak 0.46 e Å$^2$.

Fractional atomic coordinates, bond lengths and bond angles are given in Tables 2–4 respectively; isotropic thermal parameters have been deposited at the CCDC.*

**Table 4** Bond angles (°) for **5**

| | | | |
|---|---|---|---|
| N(1)–S(1)–O(1) | 107.7(7) | N(1)–S(1)–O(2) | 106.7(6) |
| O(1)–S(1)–O(2) | 119.6(7) | N(1)–S(1)–C(1) | 107.2(6)- |
| O(1)–S(1)–C(1) | 107.7(7) | O(2)–S(1)–C(1) | 107.5(7) |
| S(1)–N(1)–C(7) | 119.4(9) | S(1)–N(1)–C(14) | 122.5(9) |
| C(7)–N(1)–C(14) | 106.2(11) | C(14)–N(2)–C(16) | 113.3(11) |
| C(14)–N(2)–C(24) | 123.2(13) | C(16)–N(2)–C(24) | 123.2(13) |
| C(24)–O(4)–C(25) | 117.7(13) | C(18)–O(6)–C(19) | 121.9(16) |
| C(19)–O(8)–C(20) | 114.8(17) | S(1)–C(1)–C(2) | 121.2(11) |
| S(1)–C(1)–C(6) | 118.0(12) | C(2)–C(1)–C(6) | 120.7(14) |
| C(1)–C(2)–C(3) | 117.4(18) | C(2)–C(3)–C(4) | 120.4(25) |
| C(3)–C(4)–C(5) | 123.5(25) | C(4)–C(5)–C(6) | 119.2(21) |
| C(1)–C(6)–C(5) | 118.3(18) | N(1)–C(7)–C(8) | 125.0(13) |
| N(1)–C(7)–C(12) | 110.5(12) | C(8)–C(7)–C(12) | 124.4(13) |
| C(7)–C(8)–C(9) | 115.8(17) | C(8)–C(9)–C(10) | 120.7(17) |
| C(9)–C(10)–C(11) | 122.7(16) | C(10)–C(11)–C(12) | 117.7(16) |
| C(7)–C(12)–C(11) | 118.6(14) | C(7)–C(12)–C(13) | 110.4(12) |
| C(11)–C(12)–C(13) | 131.0(15) | C(12)–C(13)–C(14) | 103.9(13) |
| C(12)–C(13)–C(15) | 115.2(13) | C(14)–C(13)–C(15) | 106.7(12) |
| N(1)–C(14)–N(2) | 112.4(11) | N(1)–C(14)–C(13) | 106.6(11) |
| N(2)–C(14)–C(13) | 102.5(11) | C(13)–C(15)–C(16) | 104.2(14) |
| N(2)–C(16)–C(15) | 103.2(13) | N(2)–C(16)–C(17) | 112.5(13) |
| C(15)–C(16)–C(17) | 111.3(15) | N(2)–C(16)–C(18) | 109.2(14) |
| C(15)–C(16)–C(18) | 113.3(13) | C(17)–C(16)–C(18) | 107.4(14) |
| O(5)–C(18)–O(6) | 121.8(17) | O(5)–C(18)–C(16) | 129.0(17) |
| O(6)–C(18)–C(16) | 109.2(15) | O(6)–C(19)–O(7) | 120.7(22) |
| O(6)–C(19)–O(8) | 106.8(17) | O(7)–C(19)–O(8) | 132.5(24) |
| O(8)–C(20)–C(21) | 110.5(20) | C(20)–C(21)–C(22) | 111.9(25) |
| C(20)–C(21)–C(23) | 120.3(34) | C(22)–C(21)–C(23) | 117.6(34) |
| N(2)–C(24)–O(3) | 123.9(16) | N(2)–C(24)–O(4) | 111.2(14) |
| O(3)–C(24)–O(4) | 124.9(15) | | |

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* For full details of the Cambridge Crystallographic Data Centre deposition scheme see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1992, Issue 1.

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