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A concise synthesis of a highly substituted 6-(1*H*-benzimidazol-1-yl)-5-nitrosopyrimidin-2-amine: synthetic sequence and the molecular and supramolecular structures of one product and two intermediates

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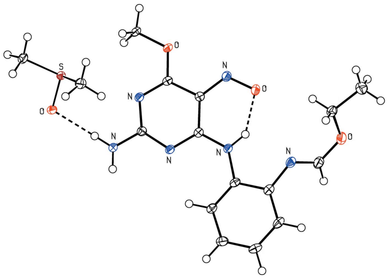
A concise and efficient synthesis of 6-benzimidazolyl-5-nitrosopyrimidines has been developed using Schiff base-type intermediates derived from N^4-(2-aminophenyl)-6-methoxy-5-nitrosopyrimidine-2,4-diamine. 6-Methoxy-N^4-{2-[(4-methylbenzylidene)amino]phenyl}-5-nitrosopyrimidine-2,4-diamine, (I), and N^4-{2-[(ethoxymethylidene)amino]phenyl}-6-methoxy-5-nitrosopyrimidine-2,4-diamine, (III), both crystallize from dimethyl sulfoxide solution as the 1:1 solvates $C_{19}H_{18}N_6O_2\cdot C_2H_6OS$, (I*a*), and $C_{14}H_{16}N_6O_3\cdot C_2H_6OS$, (III*a*), respectively. The interatomic distances in these intermediates indicate significant electronic polarization within the substituted pyrimidine system. In each of (I*a*) and (III*a*), intermolecular N—H···O hydrogen bonds generate centrosymmetric four-molecule aggregates. Oxidative ring closure of intermediate (I), effected using ammonium hexanitratocerate(IV), produced 4-methoxy-6-[2-(4-methylphenyl-1*H*-benzimidazol-1-yl]-5-nitrosopyrimidin-2-amine, $C_{19}H_{16}N_6O_2$, (II) [Cobo *et al.* (2018). Private communication (CCDC 1830889). CCDC, Cambridge, England], where the extent of electronic polarization is much less than in (I*a*) and (III*a*). A combination of N—H···N and C—H···O hydrogen bonds links the molecules of (II) into complex sheets.

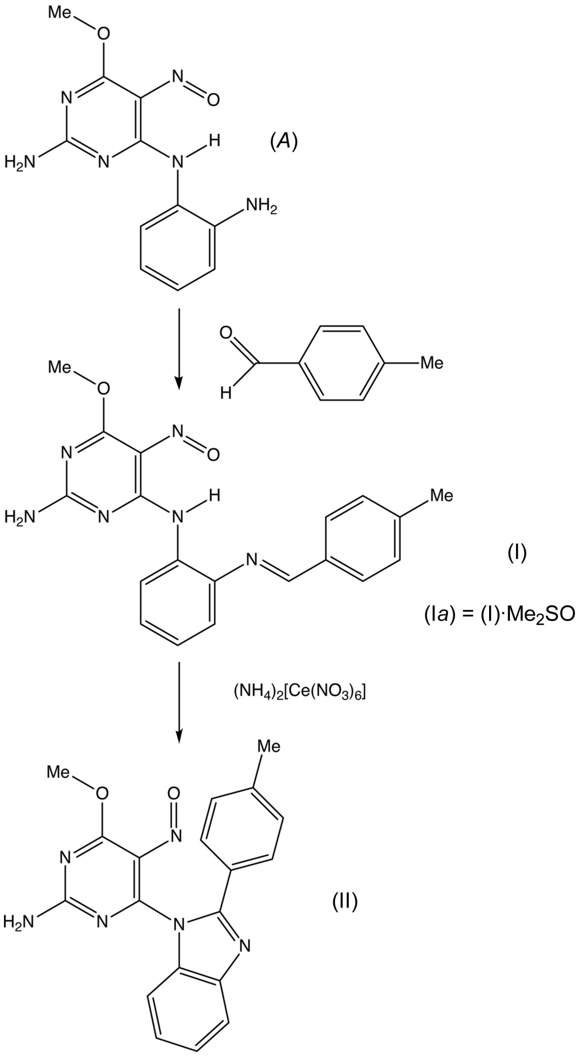
1. Introduction

Nitrosopyrimidines are an important group of heterocyclic compounds because of their value as excellent building blocks for the synthesis of novel compounds having interesting biological activities, including antibacterial (Olivella *et al.*, 2015), antifungal (Olivella *et al.*, 2012), anti-HIV (Al-Masoudi *et al.*, 2016) and antiproliferative activity (Illán-Cabeza *et al.*, 2013), as well as enzyme inhibition, *e.g.* O^6-alkylguanine-DNA alkyltransferase (AGT) inhibition (Roy *et al.*, 1996). The benzimidazole unit is also an important heterocyclic fragment present in many compounds with a very wide range of biological activities, including analgesic, antibacterial, anticonvulsant, antidepressant, antidiabetic, antifungal, anti-inflammatory, antioxidant, antitumour and antiviral properties (George *et al.*, 2017). Accordingly, this pharmacophoric motif has been widely used in drug development in the search for new uses and applications (Wang *et al.*, 2015).

We report here a short synthetic approach to new compounds containing both a pyrimidine and a benzimidazole unit as part of an exploration of possible synergies between



these two pharmacophores, and we discuss the crystal and molecular structures of one such product (Cobo *et al.*, 2018), as well as reporting those of two immediate precursors.

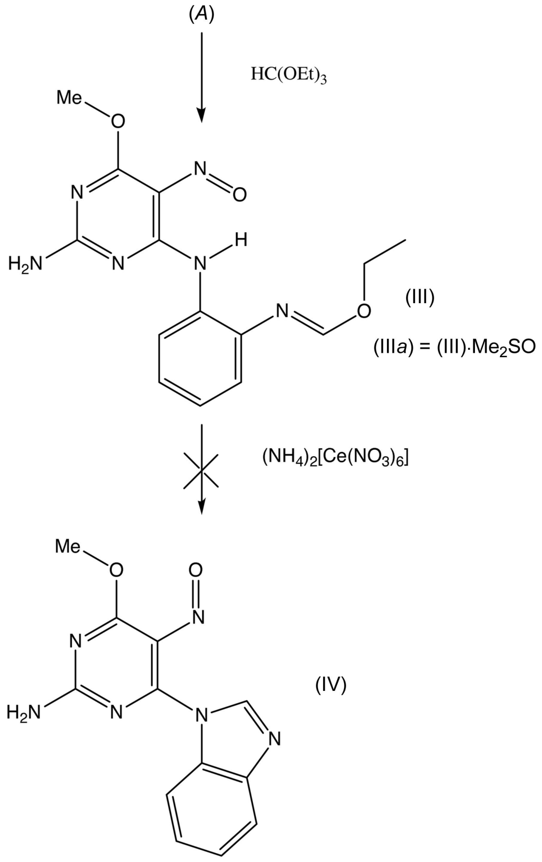


Scheme 1

The synthetic strategy employs commercially available 2-amino-4,6-dimethoxypyrimidine as the starting reagent which can be readily converted into 2,4-diamino-6-methoxy-5-nitrosopyrimidines by the use of two sequential steps, namely nitrosation using isoamyl nitrite in dimethyl sulfoxide solution followed by aminolysis, as reported previously (Marchal *et al.*, 2002); the use of 1,2-diaminobenzene in the aminolysis step generates the key intermediate N^4-(2-aminophenyl)-6-methoxy-5-nitrosopyrimidine-2,4-diamine (*A*) (see Scheme 1).

The reaction of (*A*) with 4-methylbenzaldehyde in acetic acid as solvent gave the corresponding imine derivative 6-methoxy-N^4-{2-[(4-methylbenzylidene)amino]phenyl}-5-nitrosopyrimidine-2,4-diamine, (I), in 87% yield. The final step consists of an intramolecular oxidative cyclization (Rodríguez *et al.*, 2017) of compound (I) to give 4-methoxy-6-[2-(4-methylphenyl)-1*H*-benzimidazol-1-yl]-5-nitrosopyrimidin-2-amine, (II), in 42% yield, using ammonium hexanitratocerate(IV), (NH$_4$)$_2$[Ce(NO$_3$)$_6$], as the oxidant in acetonitrile as solvent (Scheme 1).

The analogous N^4-{2-[(ethoxymethylidene)amino]phenyl}-6-methoxy-5-nitrosopyrimidine-2,4-diamine, (III), was obtained in 92% yield from the reaction of intermediate (*A*) with an excess of triethyl orthoformate, assisted by microwave radiation under solvent-free conditions; however, all attempts to form the corresponding benzimidazole derivative (IV) resulted in complete decomposition, with no detectable formation of the expected product (IV) (Scheme 2).



Scheme 2

2. Experimental

2.1. Synthesis and crystallization

2.1.1. Synthesis of intermediate (*A*). For the synthesis of intermediate (*A*), 1,2-diaminobenzene (148 mg, 1 mmol) was added to a suspension of 2-amino-4,6-dimethoxy-5-nitrosopyrimidine (108 mg, 1 mmol), which had been prepared as reported previously (Marchal *et al.*, 2002), in water (10 ml). This mixture was stirred at ambient temperature for 24 h, after which time thin-layer chromatography (TLC) monitoring showed that no starting materials were present. The resulting solid product was collected by filtration, washed with water and dried in air at 323 K. Brown solid, yield 87%, m.p. 466 K (decomposition), R_F (dichloromethane–methanol, 9:1 *v*/*v*) = 0.43. IR (ATR, cm^{-1}): 3404, 3153, 1645, 1578, 1526, 1377, 1309, 1124, 1063, 748. NMR (DMSO-d_6): δ(^{1}H) 12.95 (*s*, 1H, Ar—NH—Ar′), 8.20 and 8.10 (2 × *s*, 2H, 2-NH$_2$), 7.51 (*d*, *J* = 7.4 Hz, 1H, 6′-H), 6.96 (*t*, *J* = 7.6 Hz, 1H, 4′-H), 6.80 (*d*, *J* = 7.1 Hz, 1H, 3′-H), 6.60 (*t*, *J* = 7.1 Hz, 1H, 5′-H), 4.93 (*s*, 2H, Ar′—NH$_2$), 4.09 (*s*, 3H, O—CH$_3$); δ(^{13}C) 171.0 (C4), 163.6 (C6), 149.36 (C2), 142.2 (C2′), 138.7 (C5), 126.7 (C4′-H), 126.3 (C6′-H), 122.2 (C1′), 116.6 (C5′-H), 116.1 (C3′-H), 54.3 (O—CH$_3$). MS (EI, 70 eV) *m*/*z* (%): 260 (33) [*M*]$^+$, 144 (13), 159 (28), 198 (20), 214 (36), 215 (24), 229 (100), 230 (31), 243 (26); HRMS (ESI–QTOF) found 261.1095, $C_{11}H_{12}N_6O_2$ requires for (*M* + H)$^+$ 261.1094.

2.1.2. Synthesis of compound (I). For the synthesis of compound (I), a solution of intermediate (*A*) (1.43 g, 5.5 mmol) and 4-methylbenzaldehyde (1.00 g, 8.3 mmol) in acetic acid (15 ml) was stirred for 2 h at ambient temperature. The resulting product was collected by filtration, washed firstly with water and finally with a saturated aqueous solution of sodium carbonate, and then oven-dried at 323 K. Green solid, yield 87%, m.p. 477 K (decomposition); R_F (ethyl acetate–hexane, 3:2 *v*/*v*) = 0.30. IR (ATR, cm^{-1}): 3644, 3478, 3272, 1682, 1641, 1424, 1390, 1253, 1216, 770, 721. NMR (DMSO-*d*$_6$): δ(^{1}H) 13.91 (*s*, 1H, 6-NH), 9.00 (*dd*, *J* = 8.2, 1.3 Hz, 1H, 2′H), 8.80 (*s*, 1H, N═CH—Ar), 8.44 (*d*, *J* = 8.1 Hz, 2H, 2′′-H and 6′-H), 8.32 (*br s*, 1H, 2-NH$_2$), 7.45 (*d*, *J* = 1.5 Hz, 2H, 5′-H), 7.43 (*d*, *J* = 8.1 Hz, 2H, 3′′-H and 5′′-H), 7.25 (*td*, *J* = 8.0, 1.5 Hz, 1H, 3′-H), 7.19 (*td*, *J* = 7.6, 1.5 Hz, 1H, 4′-H), 4.10 (*s*, 3H, O—CH$_3$), 2.42 (*s*, 3H, Ar—CH$_3$); δ(^{13}C) 171.3 (C4), 163.5 (C6), 160.3 (Ar—N═CH—Ar), 146.5 (C2), 142.0 (C4′′), 139.6 (C6′), 138.9 (C1′), 133.7 (C1′′), 133.3 (C5), 129.6 (C2′′-H), 129.5 (C3′′-H and C5′′-H), 126.9 (C3′-H), 124.7 (C4′-H), 123.2 (C2′-H), 117.1 (C5′-H), 54.4 (O—CH$_3$), 21.2 (Ar—CH$_3$). MS (EI, 70 eV) *m*/*z* (%): 362.01 (100) [*M*]$^+$, 118.94 (37), 209.01 (50), 242.99 (31), 244.00 (21), 316.01 (18), 330.02 (26), 345.04 (41), 363.07 (22); HRMS (ESI–QTOF) found 363.1563, $C_{19}H_{18}N_6O_2$ requires for (*M* + H)$^+$ 363.1564. Crystals of (I*a*) suitable for single-crystal X-ray diffraction were grown by slow evaporation of a solution in dimethyl sulfoxide at ambient temperature and in the presence of air.

2.1.3. Synthesis of compound (II). For the synthesis of compound (II), ammonium hexanitratocerate(IV) (0.85 g, 1.6 mmol) was added to a stirred solution of (I) (0.29 g, 0.8 mmol) in acetonitrile (15 ml) and the resulting mixture was stirred for 5 min. A saturated aqueous solution of sodium carbonate (15 ml) was then added, after which the solvent was removed under reduced pressure to dryness. The resulting product was purified by column chromatography on silica gel 60 (0.040–0.063 mm) (ethyl acetate–hexane, 3:2 *v*/*v*). Green solid, yield 42%, m.p. 449 K (decomposition); R_F (ethyl acetate–hexane, 3:2 *v*/*v*) = 0.31. IR (ATR, cm^{-1}): 3236, 2815, 1689, 1604, 1546, 1363, 1249, 1057, 884, 770. NMR (DMSO-*d*$_6$): δ(^{1}H) 8.84 (*s*, 1H, NH), 8.81 (*s*, 1H, NH), 7.77 (*d*, *J* = 7.4 Hz, 1H, 7′-H), 7.52–7.47 (*m*, 3H, 2′′-H, 6′′-H and 4′-H), 7.32 (*td*, *J* = 7.6, 1.3 Hz, 1H, 6′-H), 7.27 (*td*, *J* = 7.7, 1.3 Hz, 1H. 5′-H), 7.18 (*d*, *J* = 8.0 Hz, 2H, 3′′-H and 5′′-H), 3.93 (*s*, 3H, O—CH$_3$), 2.28 (*s*, 3H, Ar—CH$_3$); δ(^{13}C) 163.4 (C2), 161.5 (C4), 157.5 (C6), 153.2 (C2′), 144.2 (C5), 142.7 (C3a′), 139.5 (C4′′), 136.5 (C8a′), 129.2 (C3′′-H and C5′′-H), 128.2 (C2′′-H and C6′′-H), 127.1 (C1′′), 123.5 (C6′-H), 123.3 (C5′-H), 119.2 (C7′-H), 111.7 (C4′-H), 54.5 (6-OCH$_3$), 20.9 (Ar—CH$_3$). MS (EI, 70 eV) *m*/*z* (%): 360.04 (16) [*M*]$^+$, 298.03 (15), 299.02 (13), 315.03 (60), 316.04 (13), 330.05 (100), 331.07 (23), 343.02 (22); HRMS (ESI–QTOF) found 361.1406, $C_{19}H_{16}N_6O_2$ requires for (*M* + H)$^+$ 361.1408. Crystals of (II) suitable for single-crystal X-ray diffraction were grown by slow evaporation of a solution in dimethyl sulfoxide, at ambient temperature and in the presence of air.

2.1.4. Synthesis of compound (III). For the synthesis of compound (III), a mixture of intermediate (*A*) (104 mg, 0.4 mmol) and triethyl orthoformate (0.5 ml, 0.45 g, 3.0 mmol) was subjected to microwave irradiation in a CEM monomode microwave reactor (maximum power 200 EW), using a standard mode at 373 K for 2 min. Brown solid, yield 92%, m.p. 446 K (decomposition); R_F (ethyl acetate–hexane, 3:2 *v*/*v*) = 0.27. IR (ATR, cm^{-1}): 3427, 3311, 2980, 1641, 1579, 1447, 1403, 1377, 1186, 755. NMR (DMSO-*d*$_6$): δ(^{1}H) 13.50 (*s*, 1H, 6-NH), 8.89 (*dd*, *J* = 8.2, 1.6 Hz, 1H, 2′-H), 8.31 (*s*, 1H, 2-NH), 8.24 (*s*, 1H, 2-NH), 8.15 (*s*, 1H, N═CH—OEt), 7.16–7.05 (*m*, 3H, 3′-H, 4′-H and 5′-H), 4.93 (*q*, *J* = 6.6 Hz, 2H, O—CH$_2$–), 4.09 (*s*, 3H, O—CH$_3$), 1.45 (*q*, *J* = 7.1 Hz, 3H, *C*—CH$_3$); δ(^{13}C) 171.3 (C4), 163.5 (C6), 156.9 (N═CH), 146.6 (C2), 138.7 (C5), 137.2 (C6′), 131.8 (C1′), 124.7 (C4′-H), 124.6 (C3′-H), 122.8 (C2′-H), 119.0 (C5′-H), 62.6 (O—CH$_2$), 54.4 (O—CH$_3$), 14.2 (C—CH$_3$). MS (EI, 70 eV) *m*/*z* (%): 315.96 (100) [*M*]$^+$, 133.94 (25), 143.94 (26), 168.95 (29), 213.96 (34). 227.97 (69), 228.97 (62), 243.96 (83), 252.94 (38), 256.00 (28), 256.98 (84), 270.99 (36); HRMS (ESI–QTOF) found 317.1717, $C_{14}H_{16}N_6O_3$ requires for (*M* + H)$^+$ 317.1721. Crystals of (III*a*) suitable for single-crystal X-ray diffraction were grown by slow evaporation of a solution in dimethyl sulfoxide, at ambient temperature and in the presence of air.

2.2. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1. All H atoms were located in difference maps. H atoms bonded to C atoms were then treated as riding atoms in geometrically idealized positions, with C—H = 0.95 (aromatic and alkenyl), 0.98 (CH$_3$) or 0.99 Å (CH$_2$), and with $U_{\rm iso}$(H) = $kU_{\rm eq}$(C), where k = 1.5 for the methyl groups, which were permitted to rotate but not to tilt, and 1.2 for all other H atoms bonded to C atoms. For H atoms bonded to N atoms, the atomic coordinates were refined with $U_{\rm iso}$(H) = 1.2$U_{\rm eq}$(N), giving the N—H distances shown in Table 3. In the final analysis of variance for (I*a*), there was a large value, 2.708, of $K = [{\rm mean}(F_o^2)/{\rm mean}(F_c^2)]$ for the group of 507 very weak reflections having F_c/F_c(max) in the range 0.000 < F_c/F_c(max) < 0.009, and for (III*a*) there was a large value, 2.469, for the group of 475 very weak reflections having F_c/F_c(max) in the range 0.000 < F_c/F_c(max) < 0.011. These values may well be statistical artefacts (Sheldrick, 1997).

3. Results and discussion

The constitutions of compounds (I)–(III) were fully established from their IR, ^{1}H and ^{13}C NMR spectroscopy, and mass spectra, as well as by the crystal structure analyses. Compounds (I) and (III) both crystallize from dimethyl sulfoxide solution as 1:1 solvates, denoted (I*a*) and (III*a*),

Table 1
Experimental details.

	(I*a*)	(III*a*)
Crystal data		
Chemical formula	$C_{19}H_{18}N_6O_2{\cdot}C_2H_6OS$	$C_{14}H_{16}N_6O_3{\cdot}C_2H_6OS$
M_r	440.52	394.46
Crystal system, space group	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$
Temperature (K)	100	100
a, b, c (Å)	10.801 (5), 17.301 (8), 11.777 (7)	10.8498 (11), 17.2238 (15), 11.3806 (11)
β (°)	104.28 (2)	115.351 (3)
V (Å^3)	2132.7 (19)	1921.9 (3)
Z	4	4
Radiation type	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.19	0.20
Crystal size (mm)	0.22 × 0.22 × 0.17	0.20 × 0.17 × 0.13
Data collection		
Diffractometer	Bruker D8 Venture	Bruker D8 Venture
Absorption correction	Multi-scan (*SADABS*; Bruker, 2016)	Multi-scan (*SADABS*; Bruker, 2016)
T_{min}, T_{max}	0.818, 0.969	0.935, 0.974
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	20005, 4914, 3658	51879, 4606, 3808
R_{int}	0.066	0.066
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.652	0.659
Refinement		
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.043, 0.099, 1.04	0.037, 0.088, 1.05
No. of reflections	4914	4606
No. of parameters	293	257
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.44, −0.41	0.35, −0.38

Computer programs: *APEX3* (Bruker, 2016), *SAINT* (Bruker, 2016), *SIR92* (Altomare *et al.*, 1994), *SHELXL2014* (Sheldrick, 2015) and *PLATON* (Spek, 2009).

respectively (Figs. 1 and 2). Despite their different constitutions, compounds (I*a*) and (III*a*) crystallize in the same space group, with unit-cell dimensions which are fairly similar (Table 1). The atomic coordinates of the corresponding pairs of atoms in these two compounds are all similar: most striking, the coordinates of atoms N62, C77, C71, C72 and C73 in (I*a*) are very similar to those of atoms N62, C67, O67, C68 and C69 in (III*a*), as are the coordinates of the atoms in the dimethyl sulfoxide components (*cf.* Figs. 1 and 2), while the corresponding pairs of torsion angles involving the atom sequences noted above are also very similar (Table 2). The overall constitution of the pyrimidine component in each compound confirms that the expected course of the synthesis has been followed.

The interatomic distances (Table 2) in the pyrimidine components in solvates (I*a*) and (III*a*) exhibit some interesting features. The parameter Δ, representing the difference between the C—N and N—O distances in the C-nitroso fragment, which are formally single and double bonds, respectively, provides a convenient measure of the extent of the electronic polarization: highly polarized structures exhibit small values of Δ, while unpolarized structures exhibit large values of Δ, indicative of strong bond fixation (Quesada *et al.*, 2002; Melguizo *et al.*, 2003). It has been noted previously that highly polarized electronic structures occur in a wide variety of amino-substituted nitrosopyrimidines (*e.g.* Quesada *et al.*, 2002, 2004; Melguizo *et al.*, 2003; García *et al.*, 2009; Yépes *et al.*, 2012) and that this polarization is associated with extensive charge-assisted (Gilli *et al.*, 1994) hydrogen bonding, leading to a wide variety of supramolecular aggregation, ranging from finite aggregates to three-dimensional framework structures.

Thus, in (I*a*) and (III*a*), the parameter Δ has values less than 0.01 Å, despite the formal single- and double-bond nature of the C5—N51 and N51—O51 bonds; in addition, the distances N1—C2, N1—C6, C2—N21 and C6—N61 are all very similar, although the exocyclic C—N bonds are formally single bonds, while the C—N bonds within the ring are formally delocalized with aromatic character; finally, the

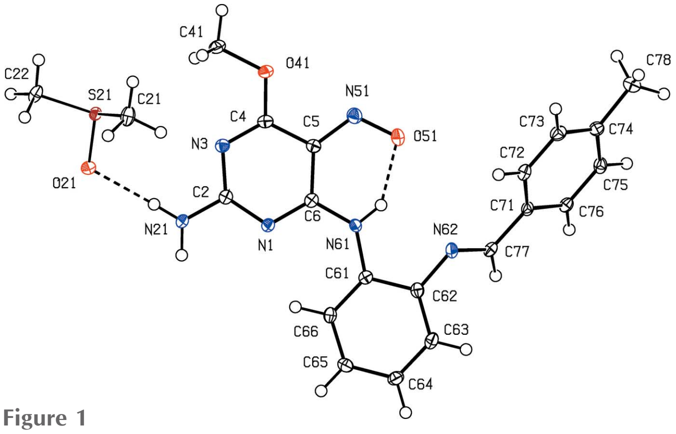
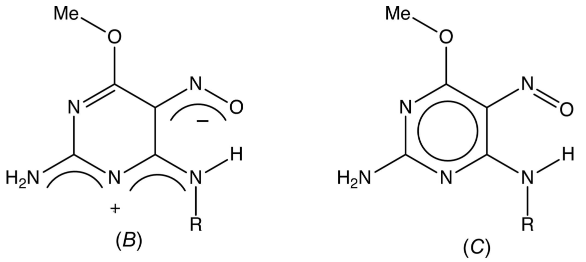


Figure 1
The independent molecular components in solvate (I*a*), showing the atom-labelling scheme and the two N—H⋯O hydrogen bonds within the selected asymmetric unit. Displacement ellipsoids are drawn at the 50% probability level.

N3—C4 bond is, in both compounds, significantly shorter than any other C—N bond associated with the pyrimidine ring. These observations indicate a significant contribution to the overall electronic structure of polarized form (*B*) (see Scheme 3), in addition to classically delocalized form (*C*).



Scheme 3

For compound (II), the structure (Fig. 3) confirms that the expected ring closure has occurred to form a benzimidazole derivative. However, the structure of the pyrimidine portion of the molecule exhibits some significant differences from those in (I*a*) and (III*a*). Firstly, although the nitroso group is still effectively coplanar with the adjacent ring, its orientation is opposite to that found in (I*a*) and (III*a*), possibly because there is now no possibility of its participation in an intramolecular N—H···O hydrogen bond. Secondly, the extent of electronic polarization in the pyrimidine fragment is much less than in (I*a*) and (III*a*), as the value of Δ readily indicates (Table 2).

The patterns of supramolecular assembly in solvates (I*a*) and (III*a*) are very similar. In each case, the molecular components are linked into centrosymmetric four-molecule aggregates characterized by an $R_4^2(8)$ (Bernstein *et al.*, 1995) motif, in which the amino group in the pyrimidine component provides the donors and atom O21 of the dimethyl sulfoxide component acts as a double acceptor (Table 3 and Fig. 4). The overall shape of these aggregates emphasis the marked conformational similarity between the two pyrimidine components. There are no direction-specific interactions between adjacent aggregates: in particular, C—H···O, C—H···N and C—H···π hydrogen bonds, and π–π stacking interactions are all absent.

Table 2
Selected geometric parameters (Å, °) for compounds (I)–(III).

Δ = [*d*(C5—N51) – *d*(N51—O51)].

Parameter	(I)	(II)	(III)
N1—C2	1.349 (2)	1.372 (3)	1.3476 (18)
C2—N3	1.368 (2)	1.353 (3)	1.3762 (18)
N3—C4	1.309 (2)	1.310 (3)	1.3034 (19)
C4—C5	1.439 (2)	1.436 (3)	1.4434 (19)
C5—C6	1.445 (2)	1.404 (3)	1.4506 (19)
C6—N1	1.328 (2)	1.322 (3)	1.3324 (18)
C2—N21	1.323 (2)	1.320 (3)	1.3240 (19)
C5—N51	1.353 (2)	1.401 (3)	1.3437 (19)
N51—O51	1.286 (2)	1.215 (3)	1.2909 (16)
C6—N61	1.345 (2)	1.417 (3)	1.3429 (18)
N61—C61	1.406 (2)		1.4087 (18)
C62—N62	1.407 (2)		1.414 (2)
N62—C67			1.261 (2)
N62—C77	1.279 (2)		
Δ	0.067	0.186	0.0528
C4—C5—N51—O51	178.94 (15)	0.1 (3)	178.58 (13)
C6—N61—C61—C62	−174.29 (16)		−173.40 (13)
C61—C62—N62—C67			−133.18 (15)
C62—N62—C67—O67			−176.57 (13)
N62—C67—O67—C68			0.6 (2)
C67—O67—C68—C69			174.70 (13)
C61—C62—N62—C77	−131.38 (17)		
C62—N62—C77—C71	178.98 (14)		
N62—C77—C71—C72	6.9 (2)		
C77—C71—C72—C73	−177.96 (15)		

The supramolecular assembly of the benzimidazole product (II) is more complex than that of compounds (I) and (III): N—H···O hydrogen bonds are absent, but a combination of two N—H···N and one C—H···O hydrogen bond (Table 3) links the molecules into complex sheets, whose formation can

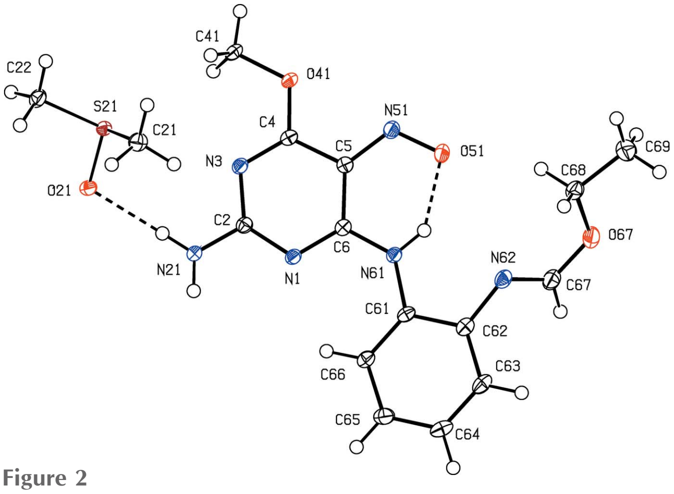


Figure 2
The independent molecular components in solvate (III*a*), showing the atom-labelling scheme and the two N—H···O hydrogen bonds within the selected asymmetric unit. Displacement ellipsoids are drawn at the 50% probability level.

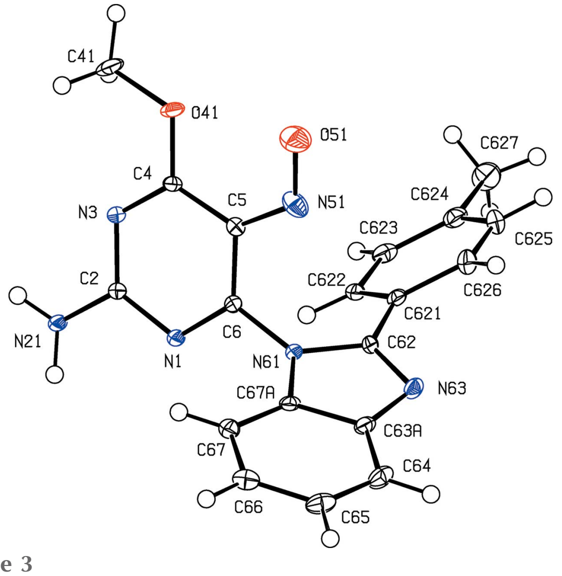
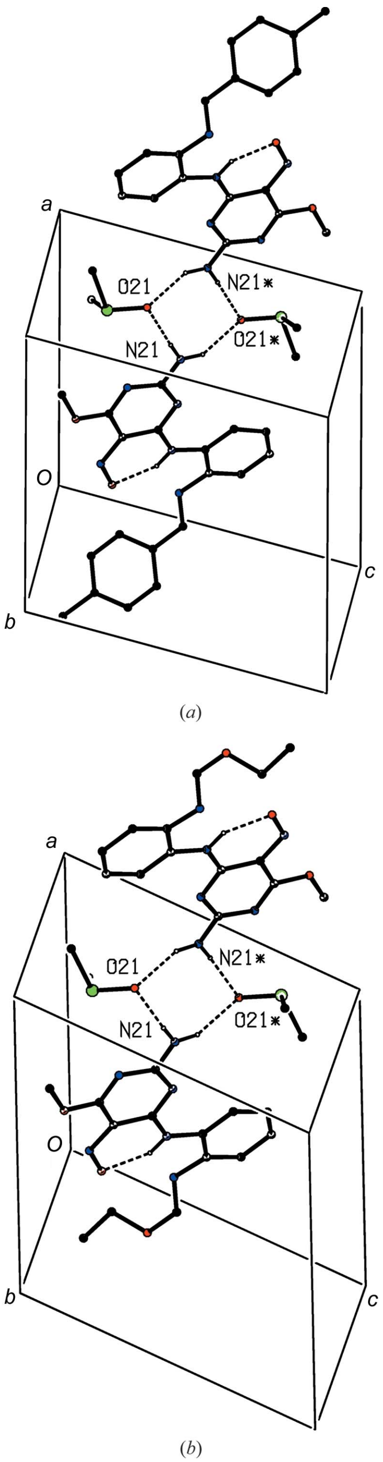


Figure 3
The molecular structure of compound (II) (Cobo *et al.*, 2018), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.



(*a*)

(*b*)

Figure 4
Part of the crystal structures of (*a*) solvate (I*a*) and (*b*) solvate (III*a*), showing the formation of the centrosymmetric four-molecule aggregates. Hydrogen bonds are drawn as dashed lines and, for the sake of clarity, H atoms bonded to C atoms have been omitted. Atoms marked with as asterisk (*) are at the symmetry position ($-x + 2$, $-y + 1$, $-z + 1$).

readily be analysed in terms of two one-dimensional substructures (Ferguson *et al.*, 1998*a*,*b*; Gregson *et al.*, 2000). The N—H···N hydrogen bond having the pyrimidine ring N1 atom as the acceptor links inversion-related pairs of molecules into a centrosymmetric $R_2^2(8)$ dimer, and this dimer can be regarded as the basic building block in the supramolecular structure. In one substructure, dimers of this type are linked by the second N—H···N hydrogen bond to form a ribbon running parallel to the [010] direction in which $R_2^2(8)$ rings centred at ($\frac{1}{2}$, $\frac{1}{2} + n$, $\frac{1}{2}$) alternate with $R_4^4(16)$ rings centred at ($\frac{1}{2}$, n, $\frac{1}{2}$) where n represents an integer (Fig. 5). In the second substructure, $R_2^2(8)$ dimers are linked by C—H···O hydrogen bonds to form a second ribbon, this time running parallel to the [01$\overline{1}$] direction and in which $R_2^2(8)$ rings centred at ($\frac{1}{2}$, $\frac{1}{2} + n$, $\frac{1}{2} - n$) alternate with $R_2^2(20)$ rings centred at ($\frac{1}{2}$, n, $1 - n$), where n again represents an integer (Fig. 6). The combination of the ribbons parallel to [010] and [01$\overline{1}$] generates a sheet lying parallel to (100), but there are no direction-specific interactions between adjacent sheets.

Table 3
Hydrogen-bond parameters (Å, °) for compounds (I)–(III).

	D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
(I)	N21—H21*A*···O21	0.87 (2)	2.05 (2)	2.922 (3)	173.7 (19)
	N21—H21*B*···O21^{i}	0.88 (2)	2.08 (2)	2.885 (3)	152.1 (19)
	N61—H61···O51	0.85 (2)	1.88 (2)	2.601 (3)	142.4 (19)
(II)	N21—H21*A*···N1^{ii}	0.91 (3)	2.24 (2)	3.145 (4)	176 (2)
	N21—H21*B*···N63^{iii}	0.88 (3)	2.08 (3)	2.936 (4)	166 (2)
	C625—H625···O51^{iv}	0.95	2.59	3.485 (5)	157
(III)	N21—H21*A*···O21	0.86 (2)	2.05 (2)	2.8916 (19)	168.7 (18)
	N21—H21*B*···O21^{i}	0.86 (2)	2.05 (2)	2.8737 (18)	157 (2)
	N61—H61···O51	0.88 (2)	1.841 (18)	2.5899 (18)	142.4 (18)

Symmetry codes: (i) $-x + 2$, $-y + 1$, $-z + 1$; (ii) $-x + 1$, $-y + 1$, $-z + 1$; (iii) x, $y + 1$, z; (iv) $-x + 1$, $-y$, $-z + 2$.

In summary, we have demonstrated a concise and efficient synthesis of highly substituted benzimidazolylpyrimidines, in

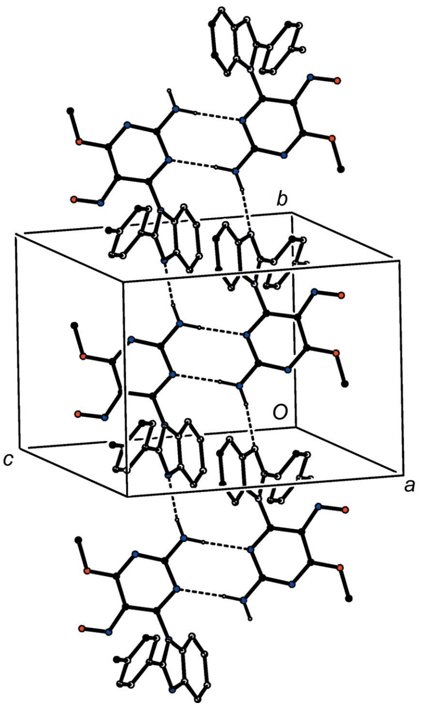


Figure 5
Part of the crystal structure of compound (II), showing the formation of a ribbon along [010] containing alternating $R_2^2(8)$ and $R_4^4(16)$ rings. Hydrogen bonds are drawn as dashed lines and, for the sake of clarity, H atoms bonded to C atoms have been omitted.

which the benzimidazole and nitrosopyrimidine pharmacophores are combined, and we have characterized one product of this type, as well as two immediate precursors on the synthetic pathway.

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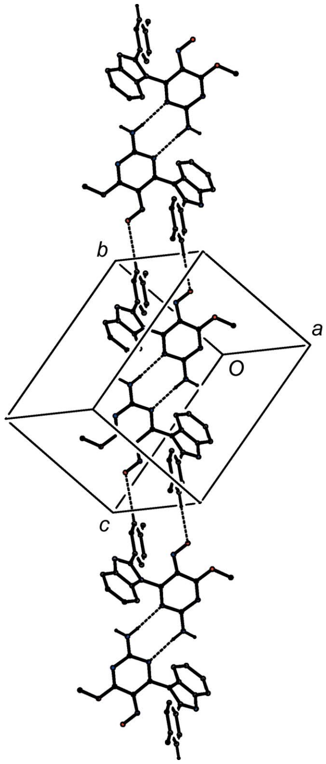

Figure 6
Part of the crystal structure of compound (II), showing the formation of a ribbon along $[01\bar{1}]$ containing alternating $R^2_2(8)$ and $R^2_2(20)$ rings. Hydrogen bonds are drawn as dashed lines and, for the sake of clarity, H atoms bonded to C atoms but not involved in the motif shown have been omitted.

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A concise synthesis of a highly substituted 6-(1*H*-benzimidazol-1-yl)-5-nitrosopyrimidin-2-amine: synthetic sequence and the molecular and supramolecular structures of one product and two intermediates

Justo Cobo, Daniel E. Vicentes, Ricaurte Rodríguez, Antonio Marchal and Christopher Glidewell

Computing details

For both structures, data collection: *APEX3* (Bruker, 2016); cell refinement: *SAINT* (Bruker, 2016); data reduction: *SAINT* (Bruker, 2016); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL2014* (Sheldrick, 2015) and *PLATON* (Spek, 2009).

6-Methoxy-N^4-{2-[(4-methylbenzylidene)amino]phenyl}-5-nitrosopyrimidine-2,4-diamine dimethyl sulfoxide monosolvate (I)

Crystal data

$C_{19}H_{18}N_6O_2·C_2H_6OS$	$F(000) = 928$
$M_r = 440.52$	$D_x = 1.372$ Mg m^{-3}
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
$a = 10.801$ (5) Å	Cell parameters from 4914 reflections
$b = 17.301$ (8) Å	$\theta = 2.1–27.6°$
$c = 11.777$ (7) Å	$\mu = 0.19$ mm^{-1}
$\beta = 104.28$ (2)°	$T = 100$ K
$V = 2132.7$ (19) Å^3	Block, green
$Z = 4$	0.22 × 0.22 × 0.17 mm

Data collection

Bruker D8 Venture diffractometer	20005 measured reflections
Radiation source: INCOATEC high brilliance microfocus sealed tube	4914 independent reflections
Multilayer mirror monochromator	3658 reflections with $I > 2\sigma(I)$
φ and ω scans	$R_{\rm int} = 0.066$
Absorption correction: multi-scan (SADABS; Bruker, 2016)	$\theta_{\max} = 27.6°$, $\theta_{\min} = 2.1°$
$T_{\min} = 0.818$, $T_{\max} = 0.969$	$h = -13\rightarrow14$
	$k = -22\rightarrow22$
	$l = -15\rightarrow15$

Refinement

Refinement on F^2	4914 reflections
Least-squares matrix: full	293 parameters
$R[F^2 > 2\sigma(F^2)] = 0.043$	0 restraints
$wR(F^2) = 0.099$	Hydrogen site location: mixed
$S = 1.04$	

H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0366P)^2 + 0.9653P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.44$ e Å^{-3}
$\Delta\rho_{min} = -0.41$ e Å^{-3}

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	y	z	U_{iso}*/U_{eq}
N1	0.63176 (14)	0.44867 (8)	0.44069 (13)	0.0120 (3)
C2	0.70798 (17)	0.49327 (9)	0.39280 (16)	0.0119 (4)
N3	0.67939 (14)	0.52579 (8)	0.28358 (13)	0.0126 (3)
C4	0.56203 (17)	0.51537 (9)	0.22182 (15)	0.0124 (4)
C5	0.46824 (17)	0.47089 (10)	0.26155 (15)	0.0124 (4)
C6	0.51361 (17)	0.43704 (9)	0.37651 (15)	0.0113 (4)
N21	0.82477 (15)	0.50708 (9)	0.45704 (15)	0.0140 (3)
H21A	0.879 (2)	0.5321 (11)	0.4269 (18)	0.017*
H21B	0.8523 (19)	0.4849 (11)	0.5261 (19)	0.017*
O41	0.52485 (12)	0.54582 (7)	0.11541 (11)	0.0164 (3)
C41	0.62018 (18)	0.58875 (11)	0.07361 (17)	0.0204 (4)
H41C	0.6879	0.5535	0.0639	0.031*
H41A	0.6570	0.6290	0.1306	0.031*
H41B	0.5801	0.6128	−0.0019	0.031*
N51	0.34929 (15)	0.46832 (9)	0.18987 (14)	0.0172 (3)
O51	0.26510 (12)	0.42777 (7)	0.22353 (12)	0.0199 (3)
N61	0.43163 (15)	0.39245 (8)	0.41667 (13)	0.0115 (3)
H61	0.359 (2)	0.3896 (11)	0.3682 (18)	0.014*
C61	0.44691 (17)	0.35231 (9)	0.52304 (15)	0.0113 (4)
C62	0.34263 (17)	0.30489 (10)	0.53073 (16)	0.0129 (4)
C63	0.34837 (18)	0.26217 (10)	0.63204 (17)	0.0164 (4)
H63	0.2799	0.2287	0.6361	0.020*
C64	0.45325 (18)	0.26823 (10)	0.72687 (17)	0.0172 (4)
H64	0.4566	0.2394	0.7962	0.021*
C65	0.55336 (18)	0.31665 (10)	0.71999 (16)	0.0153 (4)
H65	0.6243	0.3217	0.7858	0.018*
C66	0.55184 (17)	0.35804 (10)	0.61841 (16)	0.0136 (4)
H66	0.6221	0.3900	0.6143	0.016*
N62	0.23880 (14)	0.30157 (8)	0.43151 (13)	0.0142 (3)
C77	0.12606 (17)	0.31075 (9)	0.44571 (16)	0.0132 (4)
H77	0.1149	0.3187	0.5224	0.016*
C71	0.01410 (17)	0.30927 (9)	0.34622 (16)	0.0122 (4)
C72	0.02521 (18)	0.28960 (10)	0.23395 (16)	0.0148 (4)
H72	0.1061	0.2753	0.2223	0.018*
C73	−0.08009 (18)	0.29075 (10)	0.14038 (17)	0.0165 (4)

H73	−0.0709	0.2772	0.0647	0.020*
C74	−0.20049 (18)	0.31150 (10)	0.15462 (17)	0.0155 (4)
C75	−0.21199 (17)	0.32966 (10)	0.26681 (16)	0.0149 (4)
H75	−0.2934	0.3428	0.2784	0.018*
C76	−0.10657 (17)	0.32890 (9)	0.36166 (16)	0.0132 (4)
H76	−0.1161	0.3417	0.4375	0.016*
C78	−0.31356 (19)	0.31587 (11)	0.05064 (18)	0.0230 (4)
H78A	−0.3157	0.3667	0.0136	0.034*
H78C	−0.3923	0.3081	0.0764	0.034*
H78B	−0.3064	0.2756	−0.0059	0.034*
S21	0.97174 (4)	0.59113 (2)	0.22222 (4)	0.01328 (11)
O21	1.01515 (12)	0.57943 (7)	0.35309 (11)	0.0185 (3)
C21	0.94880 (19)	0.49656 (10)	0.15963 (19)	0.0211 (4)
H21C	1.0290	0.4675	0.1826	0.032*
H21D	0.9225	0.5007	0.0740	0.032*
H21E	0.8824	0.4697	0.1879	0.032*
C22	1.11243 (18)	0.61524 (10)	0.17569 (18)	0.0189 (4)
H22C	1.1459	0.6649	0.2100	0.028*
H22D	1.0915	0.6191	0.0900	0.028*
H22E	1.1770	0.5749	0.2015	0.028*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0118 (8)	0.0123 (7)	0.0124 (8)	−0.0001 (6)	0.0038 (6)	0.0005 (6)
C2	0.0131 (9)	0.0100 (8)	0.0134 (9)	0.0006 (7)	0.0045 (8)	−0.0013 (7)
N3	0.0130 (8)	0.0134 (7)	0.0121 (8)	0.0014 (6)	0.0046 (6)	0.0005 (6)
C4	0.0149 (9)	0.0123 (8)	0.0110 (9)	0.0041 (7)	0.0052 (8)	0.0004 (6)
C5	0.0132 (9)	0.0131 (8)	0.0112 (9)	0.0018 (7)	0.0034 (7)	−0.0007 (7)
C6	0.0140 (9)	0.0088 (7)	0.0123 (9)	0.0005 (7)	0.0052 (7)	−0.0026 (6)
N21	0.0124 (8)	0.0175 (8)	0.0126 (8)	−0.0027 (6)	0.0043 (7)	0.0023 (6)
O41	0.0154 (7)	0.0218 (7)	0.0122 (7)	−0.0003 (5)	0.0038 (6)	0.0047 (5)
C41	0.0174 (10)	0.0288 (10)	0.0163 (10)	0.0004 (8)	0.0063 (8)	0.0088 (8)
N51	0.0145 (8)	0.0209 (8)	0.0164 (9)	0.0003 (6)	0.0041 (7)	0.0001 (6)
O51	0.0117 (7)	0.0268 (7)	0.0205 (8)	−0.0032 (5)	0.0026 (6)	0.0020 (6)
N61	0.0093 (7)	0.0140 (7)	0.0106 (8)	−0.0007 (6)	0.0014 (6)	−0.0001 (6)
C61	0.0122 (9)	0.0103 (8)	0.0126 (9)	0.0027 (6)	0.0053 (7)	−0.0002 (6)
C62	0.0113 (9)	0.0138 (8)	0.0145 (10)	0.0003 (7)	0.0045 (8)	−0.0020 (7)
C63	0.0143 (9)	0.0154 (8)	0.0211 (11)	−0.0015 (7)	0.0075 (8)	0.0016 (7)
C64	0.0166 (10)	0.0194 (9)	0.0169 (10)	0.0022 (8)	0.0066 (8)	0.0057 (7)
C65	0.0139 (9)	0.0192 (9)	0.0121 (10)	0.0024 (7)	0.0020 (8)	0.0000 (7)
C66	0.0118 (9)	0.0135 (8)	0.0164 (10)	−0.0008 (7)	0.0053 (8)	−0.0014 (7)
N62	0.0111 (8)	0.0152 (7)	0.0159 (9)	−0.0031 (6)	0.0025 (7)	−0.0007 (6)
C77	0.0157 (9)	0.0105 (8)	0.0149 (10)	−0.0019 (7)	0.0064 (8)	0.0007 (7)
C71	0.0113 (9)	0.0088 (8)	0.0160 (10)	−0.0015 (6)	0.0028 (8)	0.0013 (6)
C72	0.0140 (9)	0.0142 (8)	0.0179 (10)	−0.0015 (7)	0.0072 (8)	−0.0004 (7)
C73	0.0213 (10)	0.0158 (9)	0.0134 (10)	−0.0024 (7)	0.0066 (8)	−0.0016 (7)
C74	0.0161 (10)	0.0116 (8)	0.0176 (10)	−0.0006 (7)	0.0019 (8)	0.0033 (7)

C75	0.0111 (9)	0.0118 (8)	0.0221 (11)	0.0009 (7)	0.0048 (8)	0.0017 (7)
C76	0.0153 (9)	0.0099 (8)	0.0155 (10)	−0.0004 (7)	0.0059 (8)	0.0007 (7)
C78	0.0203 (11)	0.0265 (10)	0.0194 (11)	−0.0011 (8)	−0.0002 (9)	0.0049 (8)
S21	0.0120 (2)	0.0138 (2)	0.0145 (2)	−0.00037 (17)	0.00398 (18)	0.00120 (17)
O21	0.0175 (7)	0.0238 (7)	0.0143 (7)	−0.0023 (5)	0.0039 (6)	0.0032 (5)
C21	0.0210 (11)	0.0156 (9)	0.0283 (12)	−0.0048 (8)	0.0091 (9)	−0.0044 (8)
C22	0.0184 (10)	0.0154 (9)	0.0259 (11)	−0.0016 (7)	0.0111 (9)	0.0022 (7)

Geometric parameters (Å, º)

N1—C6	1.328 (2)	C65—H65	0.9500
N1—C2	1.349 (2)	C66—H66	0.9500
C2—N21	1.323 (2)	N62—C77	1.279 (2)
C2—N3	1.368 (2)	C77—C71	1.462 (3)
N3—C4	1.309 (2)	C77—H77	0.9500
C4—O41	1.327 (2)	C71—C72	1.399 (3)
C4—C5	1.439 (2)	C71—C76	1.401 (3)
C5—N51	1.353 (2)	C72—C73	1.375 (3)
C5—C6	1.445 (3)	C72—H72	0.9500
C6—N61	1.345 (2)	C73—C74	1.399 (3)
N21—H21A	0.87 (2)	C73—H73	0.9500
N21—H21B	0.88 (2)	C74—C75	1.393 (3)
O41—C41	1.451 (2)	C74—C78	1.503 (3)
C41—H41C	0.9800	C75—C76	1.384 (3)
C41—H41A	0.9800	C75—H75	0.9500
C41—H41B	0.9800	C76—H76	0.9500
N51—O51	1.286 (2)	C78—H78A	0.9800
N61—C61	1.406 (2)	C78—H78C	0.9800
N61—H61	0.85 (2)	C78—H78B	0.9800
C61—C66	1.389 (3)	S21—O21	1.5100 (16)
C61—C62	1.414 (2)	S21—C21	1.7865 (19)
C62—C63	1.392 (3)	S21—C22	1.787 (2)
C62—N62	1.407 (2)	C21—H21C	0.9800
C63—C64	1.385 (3)	C21—H21D	0.9800
C63—H63	0.9500	C21—H21E	0.9800
C64—C65	1.386 (3)	C22—H22C	0.9800
C64—H64	0.9500	C22—H22D	0.9800
C65—C66	1.391 (3)	C22—H22E	0.9800
C6—N1—C2	116.64 (15)	C65—C66—H66	120.2
N21—C2—N1	117.28 (17)	C77—N62—C62	118.41 (16)
N21—C2—N3	115.21 (16)	N62—C77—C71	121.26 (17)
N1—C2—N3	127.51 (17)	N62—C77—H77	119.4
C4—N3—C2	115.41 (15)	C71—C77—H77	119.4
N3—C4—O41	119.74 (16)	C72—C71—C76	118.75 (17)
N3—C4—C5	123.76 (16)	C72—C71—C77	121.00 (17)
O41—C4—C5	116.49 (16)	C76—C71—C77	120.25 (17)
N51—C5—C4	116.80 (16)	C73—C72—C71	120.48 (17)

N51—C5—C6	128.44 (16)	C73—C72—H72	119.8
C4—C5—C6	114.71 (16)	C71—C72—H72	119.8
N1—C6—N61	120.67 (16)	C72—C73—C74	121.16 (18)
N1—C6—C5	121.86 (16)	C72—C73—H73	119.4
N61—C6—C5	117.47 (16)	C74—C73—H73	119.4
C2—N21—H21A	119.9 (14)	C75—C74—C73	118.34 (17)
C2—N21—H21B	120.4 (13)	C75—C74—C78	121.12 (17)
H21A—N21—H21B	119.0 (19)	C73—C74—C78	120.52 (18)
C4—O41—C41	116.68 (14)	C76—C75—C74	121.00 (17)
O41—C41—H41C	109.5	C76—C75—H75	119.5
O41—C41—H41A	109.5	C74—C75—H75	119.5
H41C—C41—H41A	109.5	C75—C76—C71	120.25 (17)
O41—C41—H41B	109.5	C75—C76—H76	119.9
H41C—C41—H41B	109.5	C71—C76—H76	119.9
H41A—C41—H41B	109.5	C74—C78—H78A	109.5
O51—N51—C5	117.41 (15)	C74—C78—H78C	109.5
C6—N61—C61	130.83 (16)	H78A—C78—H78C	109.5
C6—N61—H61	111.9 (13)	C74—C78—H78B	109.5
C61—N61—H61	117.2 (13)	H78A—C78—H78B	109.5
C66—C61—N61	125.34 (16)	H78C—C78—H78B	109.5
C66—C61—C62	119.58 (16)	O21—S21—C21	105.95 (9)
N61—C61—C62	115.04 (16)	O21—S21—C22	105.72 (9)
C63—C62—N62	123.24 (16)	C21—S21—C22	97.42 (9)
C63—C62—C61	119.68 (17)	S21—C21—H21C	109.5
N62—C62—C61	117.04 (16)	S21—C21—H21D	109.5
C64—C63—C62	120.38 (17)	H21C—C21—H21D	109.5
C64—C63—H63	119.8	S21—C21—H21E	109.5
C62—C63—H63	119.8	H21C—C21—H21E	109.5
C63—C64—C65	119.57 (17)	H21D—C21—H21E	109.5
C63—C64—H64	120.2	S21—C22—H22C	109.5
C65—C64—H64	120.2	S21—C22—H22D	109.5
C64—C65—C66	121.17 (18)	H22C—C22—H22D	109.5
C64—C65—H65	119.4	S21—C22—H22E	109.5
C66—C65—H65	119.4	H22C—C22—H22E	109.5
C61—C66—C65	119.54 (17)	H22D—C22—H22E	109.5
C61—C66—H66	120.2		

C6—N1—C2—N21	178.19 (15)	N61—C61—C62—C63	179.51 (16)
C6—N1—C2—N3	−2.7 (2)	C66—C61—C62—N62	179.76 (15)
N21—C2—N3—C4	−176.88 (15)	N61—C61—C62—N62	1.8 (2)
N1—C2—N3—C4	4.0 (2)	N62—C62—C63—C64	−179.81 (16)
C2—N3—C4—O41	178.97 (14)	C61—C62—C63—C64	2.6 (3)
C2—N3—C4—C5	−2.1 (2)	C62—C63—C64—C65	−0.6 (3)
N3—C4—C5—N51	177.09 (16)	C63—C64—C65—C66	−1.5 (3)
O41—C4—C5—N51	−3.9 (2)	N61—C61—C66—C65	178.21 (16)
N3—C4—C5—C6	−0.6 (2)	C62—C61—C66—C65	0.4 (3)
O41—C4—C5—C6	178.40 (14)	C64—C65—C66—C61	1.6 (3)
C2—N1—C6—N61	179.07 (15)	C63—C62—N62—C77	50.9 (2)

C2—N1—C6—C5	−0.5 (2)	C61—C62—N62—C77	−131.48 (17)
N51—C5—C6—N1	−175.36 (16)	C62—N62—C77—C71	178.98 (14)
C4—C5—C6—N1	2.0 (2)	N62—C77—C71—C72	6.9 (2)
N51—C5—C6—N61	5.0 (3)	N62—C77—C71—C76	−172.06 (16)
C4—C5—C6—N61	−177.63 (14)	C76—C71—C72—C73	1.0 (2)
N3—C4—O41—C41	0.8 (2)	C77—C71—C72—C73	−177.95 (15)
C5—C4—O41—C41	−178.20 (15)	C71—C72—C73—C74	0.0 (3)
C4—C5—N51—O51	178.94 (15)	C72—C73—C74—C75	−1.2 (3)
C6—C5—N51—O51	−3.8 (3)	C72—C73—C74—C78	177.29 (16)
N1—C6—N61—C61	0.5 (3)	C73—C74—C75—C76	1.4 (2)
C5—C6—N61—C61	−179.90 (16)	C78—C74—C75—C76	−177.11 (16)
C6—N61—C61—C66	7.8 (3)	C74—C75—C76—C71	−0.4 (2)
C6—N61—C61—C62	−174.29 (16)	C72—C71—C76—C75	−0.8 (2)
C66—C61—C62—C63	−2.5 (2)	C77—C71—C76—C75	178.13 (15)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N21—H21*A*···O21	0.87 (2)	2.05 (2)	2.922 (3)	173.7 (19)
N21—H21*B*···O21^{i}	0.88 (2)	2.08 (2)	2.885 (3)	152.1 (19)
N61—H61···O51	0.85 (2)	1.88 (2)	2.601 (3)	142.4 (19)

Symmetry code: (i) −*x*+2, −*y*+1, −*z*+1.

N^4-{2-[(Ethoxymethylidene)amino]phenyl}-6-methoxy-5-nitrosopyrimidine-2,4-diamine dimethyl sulfoxide monosolvate (III)

Crystal data

$C_{14}H_{16}N_6O_3 \cdot C_2H_6OS$	$F(000) = 832$
$M_r = 394.46$	$D_x = 1.363$ Mg m^{-3}
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
$a = 10.8498$ (11) Å	Cell parameters from 4608 reflections
$b = 17.2238$ (15) Å	$\theta = 2.3$–27.9°
$c = 11.3806$ (11) Å	$\mu = 0.20$ mm^{-1}
$\beta = 115.351$ (3)°	$T = 100$ K
$V = 1921.9$ (3) Å^3	Block, brown
$Z = 4$	0.20 × 0.17 × 0.13 mm

Data collection

Bruker D8 Venture diffractometer	51879 measured reflections
Radiation source: INCOATEC high brilliance microfocus sealed tube	4606 independent reflections
Multilayer mirror monochromator	3808 reflections with $I > 2\sigma(I)$
φ and ω scans	$R_{int} = 0.066$
Absorption correction: multi-scan (SADABS; Bruker, 2016)	$\theta_{max} = 27.9°$, $\theta_{min} = 2.3°$
$T_{min} = 0.935$, $T_{max} = 0.974$	$h = -14 \rightarrow 14$
	$k = -22 \rightarrow 22$
	$l = -14 \rightarrow 14$

Refinement

Refinement on F^2	Hydrogen site location: mixed
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.037$	$w = 1/[\sigma^2(F_o^2) + (0.0343P)^2 + 1.3229P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.088$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.05$	$\Delta\rho_{max} = 0.35$ e Å^{-3}
4606 reflections	$\Delta\rho_{min} = -0.38$ e Å^{-3}
257 parameters	
0 restraints	

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	y	z	U_{iso}*/U_{eq}
N1	0.62364 (12)	0.45133 (7)	0.43599 (11)	0.0132 (2)
C2	0.68864 (15)	0.49854 (8)	0.38650 (13)	0.0134 (3)
N3	0.63374 (12)	0.53671 (7)	0.26896 (12)	0.0134 (2)
C4	0.50414 (15)	0.52505 (8)	0.19766 (13)	0.0124 (3)
C5	0.42094 (14)	0.47440 (8)	0.23492 (14)	0.0124 (3)
C6	0.49167 (14)	0.43866 (8)	0.36181 (13)	0.0116 (3)
N21	0.82050 (13)	0.51041 (8)	0.45783 (13)	0.0181 (3)
H21A	0.8645 (19)	0.5371 (11)	0.4248 (18)	0.022*
H21B	0.8638 (19)	0.4833 (11)	0.5284 (19)	0.022*
O41	0.44084 (10)	0.56004 (6)	0.08289 (10)	0.0156 (2)
C41	0.52208 (16)	0.61220 (9)	0.04430 (15)	0.0181 (3)
H41A	0.5663	0.6508	0.1128	0.027*
H41B	0.4630	0.6386	−0.0366	0.027*
H41C	0.5918	0.5824	0.0307	0.027*
N51	0.29003 (13)	0.46569 (7)	0.14913 (12)	0.0163 (3)
O51	0.21437 (11)	0.42050 (6)	0.18101 (11)	0.0194 (2)
N61	0.41891 (13)	0.39107 (7)	0.40144 (12)	0.0124 (2)
H61	0.3344 (19)	0.3865 (10)	0.3433 (17)	0.015*
C61	0.45849 (15)	0.34729 (8)	0.51643 (13)	0.0124 (3)
C62	0.35674 (15)	0.29664 (8)	0.51885 (14)	0.0146 (3)
C63	0.38502 (17)	0.25081 (9)	0.62812 (15)	0.0189 (3)
H63	0.3172	0.2166	0.6302	0.023*
C64	0.51191 (17)	0.25470 (9)	0.73433 (15)	0.0204 (3)
H64	0.5308	0.2231	0.8085	0.024*
C65	0.61052 (17)	0.30466 (9)	0.73158 (15)	0.0198 (3)
H65	0.6969	0.3072	0.8044	0.024*
C66	0.58482 (15)	0.35135 (8)	0.62337 (14)	0.0154 (3)
H66	0.6531	0.3857	0.6227	0.018*
N62	0.23363 (13)	0.29167 (7)	0.40440 (12)	0.0164 (3)
C67	0.12132 (17)	0.29543 (9)	0.41230 (16)	0.0206 (3)

H67	0.1223	0.3044	0.4951	0.025*
O67	0.00062 (11)	0.28728 (7)	0.30906 (11)	0.0233 (3)
C68	0.00766 (16)	0.27278 (9)	0.18557 (15)	0.0195 (3)
H68A	0.0664	0.2272	0.1935	0.023*
H68B	0.0468	0.3184	0.1607	0.023*
C69	−0.13509 (17)	0.25776 (10)	0.08446 (17)	0.0275 (4)
H69A	−0.1728	0.2126	0.1101	0.041*
H69B	−0.1334	0.2476	0.0005	0.041*
H69C	−0.1921	0.3033	0.0770	0.041*
S21	0.89988 (4)	0.57171 (2)	0.18998 (3)	0.01387 (9)
O21	0.97955 (11)	0.57988 (6)	0.33640 (10)	0.0180 (2)
C21	0.88050 (17)	0.46953 (9)	0.15983 (15)	0.0195 (3)
H21C	0.9705	0.4448	0.1956	0.029*
H21D	0.8345	0.4602	0.0659	0.029*
H21E	0.8258	0.4475	0.2015	0.029*
C22	1.01965 (16)	0.59012 (9)	0.12422 (15)	0.0192 (3)
H22A	1.0980	0.5553	0.1650	0.029*
H22B	1.0505	0.6441	0.1414	0.029*
H22C	0.9762	0.5810	0.0302	0.029*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0145 (6)	0.0141 (6)	0.0125 (6)	−0.0005 (5)	0.0071 (5)	0.0011 (5)
C2	0.0148 (7)	0.0140 (6)	0.0127 (7)	−0.0001 (5)	0.0072 (6)	−0.0008 (5)
N3	0.0141 (6)	0.0145 (6)	0.0134 (6)	−0.0002 (5)	0.0076 (5)	0.0016 (5)
C4	0.0158 (7)	0.0107 (6)	0.0129 (6)	0.0025 (5)	0.0084 (6)	0.0010 (5)
C5	0.0133 (7)	0.0116 (6)	0.0135 (7)	0.0020 (5)	0.0068 (6)	−0.0002 (5)
C6	0.0142 (7)	0.0091 (6)	0.0135 (6)	0.0017 (5)	0.0079 (5)	−0.0012 (5)
N21	0.0135 (6)	0.0261 (7)	0.0137 (6)	−0.0038 (5)	0.0049 (5)	0.0056 (5)
O41	0.0151 (5)	0.0167 (5)	0.0152 (5)	−0.0004 (4)	0.0068 (4)	0.0065 (4)
C41	0.0191 (8)	0.0197 (7)	0.0177 (7)	−0.0007 (6)	0.0099 (6)	0.0073 (6)
N51	0.0147 (6)	0.0161 (6)	0.0189 (6)	0.0003 (5)	0.0079 (5)	0.0034 (5)
O51	0.0137 (5)	0.0217 (6)	0.0229 (6)	−0.0020 (4)	0.0078 (4)	0.0066 (4)
N61	0.0125 (6)	0.0128 (6)	0.0132 (6)	0.0008 (5)	0.0066 (5)	0.0016 (5)
C61	0.0180 (7)	0.0103 (6)	0.0123 (7)	0.0021 (5)	0.0098 (6)	0.0003 (5)
C62	0.0196 (7)	0.0113 (6)	0.0159 (7)	−0.0004 (5)	0.0107 (6)	−0.0018 (5)
C63	0.0275 (8)	0.0136 (7)	0.0205 (8)	−0.0033 (6)	0.0151 (7)	0.0003 (6)
C64	0.0307 (9)	0.0168 (7)	0.0164 (7)	0.0017 (6)	0.0128 (7)	0.0044 (6)
C65	0.0218 (8)	0.0228 (8)	0.0148 (7)	0.0030 (6)	0.0079 (6)	0.0036 (6)
C66	0.0179 (7)	0.0155 (7)	0.0157 (7)	0.0012 (5)	0.0100 (6)	0.0019 (5)
N62	0.0201 (7)	0.0123 (6)	0.0180 (6)	−0.0040 (5)	0.0094 (5)	−0.0001 (5)
C67	0.0234 (8)	0.0205 (8)	0.0209 (8)	−0.0058 (6)	0.0124 (7)	−0.0011 (6)
O67	0.0189 (6)	0.0295 (6)	0.0234 (6)	−0.0061 (5)	0.0110 (5)	−0.0007 (5)
C68	0.0214 (8)	0.0174 (7)	0.0198 (8)	−0.0038 (6)	0.0091 (6)	0.0015 (6)
C69	0.0233 (9)	0.0284 (9)	0.0258 (9)	−0.0049 (7)	0.0057 (7)	0.0030 (7)
S21	0.01340 (17)	0.01437 (17)	0.01379 (17)	0.00099 (13)	0.00578 (14)	0.00251 (13)
O21	0.0193 (5)	0.0197 (5)	0.0136 (5)	−0.0035 (4)	0.0058 (4)	0.0016 (4)

C21	0.0228 (8)	0.0141 (7)	0.0204 (8)	−0.0020 (6)	0.0081 (7)	−0.0003 (6)
C22	0.0196 (8)	0.0210 (7)	0.0208 (8)	−0.0004 (6)	0.0122 (6)	0.0022 (6)

Geometric parameters (Å, º)

N1—C6	1.3324 (18)	C64—C65	1.384 (2)
N1—C2	1.3476 (18)	C64—H64	0.9500
C2—N21	1.3240 (19)	C65—C66	1.395 (2)
C2—N3	1.3762 (18)	C65—H65	0.9500
N3—C4	1.3034 (19)	C66—H66	0.9500
C4—O41	1.3315 (17)	N62—C67	1.261 (2)
C4—C5	1.4434 (19)	C67—O67	1.341 (2)
C5—N51	1.3437 (19)	C67—H67	0.9500
C5—C6	1.4506 (19)	O67—C68	1.4613 (19)
C6—N61	1.3429 (18)	C68—C69	1.505 (2)
N21—H21A	0.86 (2)	C68—H68A	0.9900
N21—H21B	0.87 (2)	C68—H68B	0.9900
O41—C41	1.4520 (17)	C69—H69A	0.9800
C41—H41A	0.9800	C69—H69B	0.9800
C41—H41B	0.9800	C69—H69C	0.9800
C41—H41C	0.9800	S21—O21	1.5200 (11)
N51—O51	1.2909 (16)	S21—C22	1.7839 (15)
N61—C61	1.4087 (18)	S21—C21	1.7883 (15)
N61—H61	0.874 (18)	C21—H21C	0.9800
C61—C66	1.392 (2)	C21—H21D	0.9800
C61—C62	1.417 (2)	C21—H21E	0.9800
C62—C63	1.392 (2)	C22—H22A	0.9800
C62—N62	1.414 (2)	C22—H22B	0.9800
C63—C64	1.391 (2)	C22—H22C	0.9800
C63—H63	0.9500		

C6—N1—C2	116.53 (12)	C63—C64—H64	120.1
N21—C2—N1	117.28 (13)	C64—C65—C66	120.94 (15)
N21—C2—N3	115.25 (13)	C64—C65—H65	119.5
N1—C2—N3	127.47 (13)	C66—C65—H65	119.5
C4—N3—C2	115.73 (12)	C61—C66—C65	119.52 (14)
N3—C4—O41	120.45 (13)	C61—C66—H66	120.2
N3—C4—C5	123.64 (13)	C65—C66—H66	120.2
O41—C4—C5	115.91 (13)	C67—N62—C62	119.46 (13)
N51—C5—C4	116.96 (13)	N62—C67—O67	122.90 (14)
N51—C5—C6	128.32 (13)	N62—C67—H67	118.6
C4—C5—C6	114.71 (12)	O67—C67—H67	118.6
N1—C6—N61	120.93 (13)	C67—O67—C68	115.28 (12)
N1—C6—C5	121.89 (12)	O67—C68—C69	107.72 (13)
N61—C6—C5	117.18 (13)	O67—C68—H68A	110.2
C2—N21—H21A	118.2 (13)	C69—C68—H68A	110.2
C2—N21—H21B	119.8 (12)	O67—C68—H68B	110.2
H21A—N21—H21B	120.6 (18)	C69—C68—H68B	110.2

C4—O41—C41	116.86 (11)	H68A—C68—H68B	108.5
O41—C41—H41A	109.5	C68—C69—H69A	109.5
O41—C41—H41B	109.5	C68—C69—H69B	109.5
H41A—C41—H41B	109.5	H69A—C69—H69B	109.5
O41—C41—H41C	109.5	C68—C69—H69C	109.5
H41A—C41—H41C	109.5	H69A—C69—H69C	109.5
H41B—C41—H41C	109.5	H69B—C69—H69C	109.5
O51—N51—C5	117.68 (12)	O21—S21—C22	105.61 (7)
C6—N61—C61	130.50 (13)	O21—S21—C21	105.44 (7)
C6—N61—H61	112.2 (11)	C22—S21—C21	98.13 (7)
C61—N61—H61	117.3 (11)	S21—C21—H21C	109.5
C66—C61—N61	125.45 (13)	S21—C21—H21D	109.5
C66—C61—C62	119.86 (13)	H21C—C21—H21D	109.5
N61—C61—C62	114.68 (13)	S21—C21—H21E	109.5
C63—C62—N62	123.29 (13)	H21C—C21—H21E	109.5
C63—C62—C61	119.42 (14)	H21D—C21—H21E	109.5
N62—C62—C61	117.14 (13)	S21—C22—H22A	109.5
C64—C63—C62	120.43 (14)	S21—C22—H22B	109.5
C64—C63—H63	119.8	H22A—C22—H22B	109.5
C62—C63—H63	119.8	S21—C22—H22C	109.5
C65—C64—C63	119.82 (14)	H22A—C22—H22C	109.5
C65—C64—H64	120.1	H22B—C22—H22C	109.5

C6—N1—C2—N21	−178.60 (13)	N1—C6—N61—C61	−0.6 (2)
C6—N1—C2—N3	1.5 (2)	C5—C6—N61—C61	178.58 (13)
N21—C2—N3—C4	179.62 (13)	C6—N61—C61—C66	7.5 (2)
N1—C2—N3—C4	−0.5 (2)	C6—N61—C61—C62	−173.40 (13)
C2—N3—C4—O41	179.17 (12)	C66—C61—C62—C63	−0.7 (2)
C2—N3—C4—C5	−1.4 (2)	N61—C61—C62—C63	−179.83 (13)
N3—C4—C5—N51	−177.41 (13)	C66—C61—C62—N62	−176.28 (12)
O41—C4—C5—N51	2.03 (19)	N61—C61—C62—N62	4.55 (18)
N3—C4—C5—C6	2.1 (2)	N62—C62—C63—C64	175.50 (14)
O41—C4—C5—C6	−178.47 (12)	C61—C62—C63—C64	0.2 (2)
C2—N1—C6—N61	178.48 (12)	C62—C63—C64—C65	0.2 (2)
C2—N1—C6—C5	−0.65 (19)	C63—C64—C65—C66	−0.1 (2)
N51—C5—C6—N1	178.46 (14)	N61—C61—C66—C65	179.82 (13)
C4—C5—C6—N1	−0.97 (19)	C62—C61—C66—C65	0.8 (2)
N51—C5—C6—N61	−0.7 (2)	C64—C65—C66—C61	−0.4 (2)
C4—C5—C6—N61	179.87 (12)	C63—C62—N62—C67	51.4 (2)
N3—C4—O41—C41	−1.46 (19)	C61—C62—N62—C67	−133.18 (15)
C5—C4—O41—C41	179.08 (12)	C62—N62—C67—O67	−176.57 (13)
C4—C5—N51—O51	179.92 (12)	N62—C67—O67—C68	0.6 (2)
C6—C5—N51—O51	0.5 (2)	C67—O67—C68—C69	174.70 (13)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N21—H21*A*···O21	0.86 (2)	2.05 (2)	2.8916 (19)	168.7 (18)

N21—H21*B*···O21$^{\mathrm{i}}$	0.87 (2)	2.05 (2)	2.8737 (18)	157 (2)
N61—H61···O51	0.88 (2)	1.841 (18)	2.5899 (18)	142.4 (18)

Symmetry code: (i) −*x*+2, −*y*+1, −*z*+1.