2-Amino-5-(3,4-dimethoxybenzyl-idene)-1-methylimidazol-4(5H)-one N,N-dimethylformamide monosolvate

Laura M. Tvedte, Kenneth L. Smith, Eric V. Patterson and Russell G. Baughman*

Department of Chemistry, Truman State University, Kirksville, MO 63501-4221, USA
Correspondence e-mail: baughman@truman.edu

The crystal structure of the title compound, $C_{13}H_{15}N_3O_3\cdot C_3H_7NO$, was determined as part of a larger project focusing on creatinine derivatives as potential pharmaceuticals. The molecule is essentially planar, in part because of intramolecular hydrogen bonding. Inversion-related pairs of molecules result from intermolecular hydrogen bonding. The π systems of 2-amino-5-(3,4-dimethoxybenzylidene)-1-methyl-imidazol-4(5H)-one and an inversion-related molecule overlap slightly, indicating a small amount of π–π stacking. Bond lengths, angles and torsion angles are consistent with similar structures, except in the imidazolone ring near the doubly bonded C atom, where significant differences occur.

Comment

As part of a larger project focusing on creatinine derivatives as potential pharmaceuticals, the crystal structure of the title compound, (I) or ADBMI·DMF [where ADBMI is 2-amino-5-(3,4-dimethoxybenzylidene)-1-methylimidazol-4(5H)-one and DMF is N,N-dimethylformamide], was determined (Fig. 1). Hydrogen bonding was observed between atoms O4 and H15A, O3 and H3, and O4 and H3B (Table 2 and Fig. 1). A search of the Cambridge Structural Database (CSD, Version 5.30; Allen, 2002) for structures similar to the seven-membered ring containing atoms O3 and H3, using the PLATON (Spek, 2009) criteria for hydrogen bonding, gave 154 results, showing that aryl H atoms undergoing hydrogen bonding with carbonyl O atoms have been observed many times.

A computational evaluation was performed on ADBMI to investigate aryl hydrogen bonding further. Two rotamers (about the C4—C9 bond) of ADBMI were computed, viz. rotamer A with atom H3 connected to atom O3, and rotamer B with atom H5 connected to atom O3, with the A conformation (as determined crystallographically) preferred. Two transition states were computed between the two rotamers with an energy barrier of 6.0 kcal mol⁻¹ (1 kcal mol⁻¹ =

4.184 kJ mol⁻¹) above the A rotamer. Two interactions exist between lone pairs and the C—H antibonding orbital in each rotamer between atoms O3 and H3, one with the sp-hybridized lone pair on O3 and one with the unhybridized lone pair. These interactions give total energies of 11.2 (rotamer A) and 8.4 kcal mol⁻¹ (rotamer B). The total energy of the A rotamer is approximately 92% of that of a water dimer (12.2 kcal mol⁻¹). Natural atomic charges were computed for atoms O3 and H3/H5 of each rotamer. These charges are −0.61 and 0.30 e, respectively, in rotamer A, and −0.61 and 0.29 e, respectively, in rotamer B. Utilizing these computational quantum molecular calculations in addition to the PLATON criteria for hydrogen bonding, it is concluded that the O3···H3 interaction is at least a weak hydrogen bond.

(I)
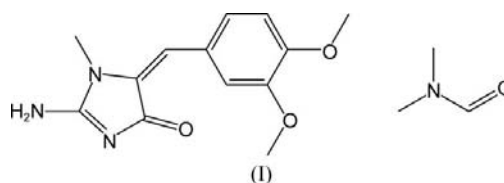
This hydrogen bond has an effect on the conformation of the compound within the crystalline and gas-phase structures and may influence any possible in vivo properties of ADBMI, since rotation about the C4—C9 bond is restricted [C3—C4—C9—C10 = −3.3 (7)°]. Intermolecular hydrogen bonding is also observed with an inversion-related molecule at (2 − x, 1 − y, −z). The combination of these two inversion-related structures leads to interpenetrating noncoplanar planes throughout the crystal structure. The C14=O4···H3A angle (113°) is consistent with sp^2 hybridization on atom O4.

Excluding the H atoms, the molecular planarities for the entire structure of (I), the nonsolvated molecule (ADBMI) and the DMF portion of the structure were determined. The r.m.s. values for these portions are 0.171, 0.067 and 0.003 Å, respectively, which shows the high degree of planarity in (I). The distance between the least-squares plane of ADBMI and that of a different inversion-related molecule at (1 − x, 1 − y, −z) was calculated to be 3.48 (7) Å. The distance between the centroids of the five-membered ring of ADBMI (Cg1B) and the six-membered ring of the inversion-related molecule (Cg1A) was calculated to be 3.763 (2) Å, and the N2A—Cg1B—Cg1A angle was calculated to be 69.7°. A perpendicular view of ADBMI and its inversion-related molecule showed an approximately 20% ring overlap (Pauling, 1960). The small difference between the least-squares plane distance and the centroid–centroid distance (0.283 Å) indicates only a small amount of shifting of the inversion-related molecule.

The two methoxy groups not only point in opposite directions, as would be expected (Ternay, 1976), but are essentially coplanar with the benzene ring. Torsion angles for the dimethoxy portion of the molecule [C7—O2—C2—C1 = −171.2 (4)° and C8—O1—C1—C2 = 175.9 (3)°] are similar to the corresponding angles in the structure of 3,4-dimethoxyphenylacetic acid [175.6 (1) and 170.4 (1)°; Chopra et al., 2003].
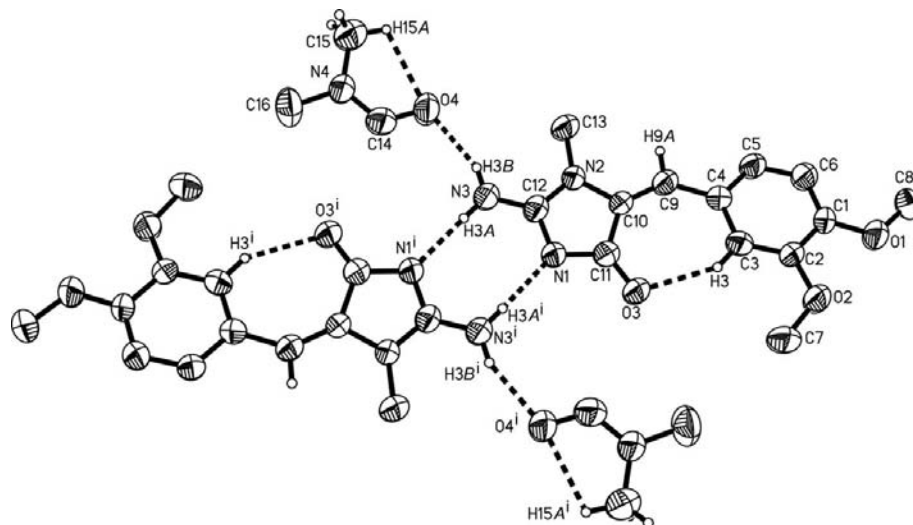
organic compounds

Figure 1
The asymmetric unit of (I), showing the atom-numbering scheme and the inversion-related molecule [symmetry code: (i) $2 - x, 1 - y, -z$]. Displacement ellipsoids are drawn at the 50% probability level. Only H atoms involved in hydrogen bonding and other H atoms attached to donor atoms are shown. Dashed lines indicate hydrogen bonds.

The O3—C11, C10—C11, N2—C12 and C12—N1 bond lengths are within 3σ of those of creatinine (Bell *et al.*, 1995; Allen, 2002). However, the N2—C10 and N1—C11 bond lengths are very different compared to creatinine, with differences of -10.8σ and 4.3σ, respectively. These bond-length differences can be attributed to the fact that creatinine has two H atoms attached to atom C10, while in (I) atom C10, being doubly bonded to atom C9, has none. The N2—C10—C11 bond angle in (I) is also 4.0σ greater than in creatinine (101.5°).

The same portion of the structure was also compared with 3-(2-amino-1-methyl-4-oxo-4,5-dihydro-1*H*-imidazol-5-yl)-3-hydroxyindolin-2-one monohydrate (AMIH; Penthala *et al.*, 2009), a compound that has a portion very similar to the creatinine portion of ADBMI. The N2—C10 bond length in (I) is 12.0σ shorter than the corresponding length in AMIH; C10—C11 is 6.6σ shorter. The N2—C10—C11 bond angle in (I) is 9.0σ wider than that in AMIH. The other angles around C10 are in different bonding environments, as AIMH has no double bond at C10. Another pattern noted is the change in the N1—C12 and N1—C11 bond lengths (-3.3σ and 2.5σ, respectively, compared to AMIH). This can be attributed to some contribution of the tautomeric forms of AMIH, which would cause differences in the bond lengths, leading to larger differences between (I) and AMIH. When accounting for this, it can be noted that (I) follows (within 3σ) the pattern of bond lengths exhibited in creatinine and AMIH.

Experimental

ADBMI was synthesized by coupling creatinine with 3,4-dimethoxybenzaldehyde to afford the desired arylidene in moderate yield (Wållberg *et al.*, 2006; Johnson *et al.*, 2006). Crystals of (I) were grown by slow vapor diffusion of diethyl ether into a solution of ADBMI in DMF. The crystal used was coated with Paratone-N.

Crystal data

$C_{13}H_{15}N_3O_3 \cdot C_3H_7NO$	$V = 1689.0\ (5)\ \text{Å}^3$
$M_r = 334.38$	$Z = 4$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 11.617\ (3)\ \text{Å}$	$\mu = 0.10\ \text{mm}^{-1}$
$b = 17.2235\ (16)\ \text{Å}$	$T = 293\ \text{K}$
$c = 9.062\ (1)\ \text{Å}$	$0.41 \times 0.40 \times 0.23\ \text{mm}$
$\beta = 111.327\ (10)°$	

Data collection

Bruker $P4$ diffractometer	$R_{\text{int}} = 0.055$
3866 measured reflections	3 standard reflections
3009 independent reflections	every 100 reflections
1192 reflections with $I > 2\sigma(I)$	intensity decay: 2.3%

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.057$	217 parameters
$wR(F^2) = 0.144$	H-atom parameters constrained
$S = 0.97$	$\Delta\rho_{\text{max}} = 0.15\ \text{e}\ \text{Å}^{-3}$
3009 reflections	$\Delta\rho_{\text{min}} = -0.15\ \text{e}\ \text{Å}^{-3}$

Geometries were computationally optimized in the gas phase using the M05-2X level of density functional theory (Zhao & Truhlar, 2006) with the 6-31+G(d,p) basis set (Hehre *et al.*, 1972) using *GAUSSIAN03* (Frisch *et al.*, 2003). Natural bond orbital analysis (Glendening *et al.*, 2001; Weinhold & Landis, 2005) was used to generate localized orbitals, to quantify interactions between orbitals and to determine atomic charges.

The approximate positions of all H atoms were first obtained from a difference map. H atoms were then placed in ideal positions and refined as riding atoms, with rigid rotating groups for methyl H atoms. No disordered H atoms were observed. Bond lengths were constrained at C—H = 0.93 Å for aromatic and allyl, and 0.96 Å for methyl H atoms, and at N—H = 0.86 Å for N-bound H atoms. $U_{\text{iso}}(\text{H})$ values were set at $1.5U_{\text{eq}}(\text{C})$ for methyl and at $1.2U_{\text{eq}}(\text{C,N})$ for all other H atoms.

In the final stages of refinement, a few very small or negative F_o values were deemed to be in strong disagreement with their F_c values and 15 reflections were eliminated from the final refinement. The percentage decay of the three standards was calculated as the average of their $\sigma(I)$ values.

Table 1
Selected geometric parameters (Å, °).

N1—C12	1.348 (4)	C4—C9	1.456 (5)
N1—C11	1.364 (4)	C9—C10	1.336 (4)
N2—C12	1.349 (4)	C10—C11	1.500 (5)
N2—C10	1.404 (4)		
C12—N1—C11	105.9 (3)	C9—C10—C11	134.4 (3)
C12—N2—C10	108.3 (3)	N2—C10—C11	102.7 (3)
C10—N2—C13	126.6 (3)	O3—C11—N1	123.9 (3)
C10—C9—C4	135.6 (3)	N1—C11—C10	109.3 (3)
C9—C10—N2	122.9 (3)	N1—C12—N2	113.8 (3)

Table 2
Hydrogen-bond geometry (Å, °).

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
C3—H3⋯O3	0.93	2.18	3.009 (4)	148
N3—H3A⋯N1^i	0.86	2.05	2.906 (4)	176
N3—H3B⋯O4	0.86	2.05	2.853 (4)	156
C15—H15A⋯O4	0.96	2.36	2.768 (5)	105

Symmetry code: (i) $-x + 2, -y + 1, -z$.

Data collection: *XSCANS* (Bruker, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXS86* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL/PC* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL/PC* and *SHELXL97*.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Bell, T. W., Hou, Z., Luo, Y., Drew, M. G. B., Chapoteau, E., Czech, B. P. & Kumar, A. (1995). *Science*, **269**, 671–674.
Bruker (1996). *XSCANS*. Version 2.2. Bruker AXS Inc., Madison, Wisconsin, USA.
Chopra, D., Choudhury, A. R. & Guru Row, T. N. (2003). *Acta Cryst.* E**59**, o433–o434.
Frisch, M. J., *et al.* (2003). *GAUSSIAN03*. Revision E.01. Gaussian Inc., Wallingford, Connecticut, USA.
Glendening, E. D., Reed, A. E., Carpenter, J. E. & Weinhold, F. (2001). *NBO*. Version 3.1. Theoretical Chemistry Institute, University of Wisconsin, Madison, Wisconsin, USA.
Hehre, W. J., Ditchfield, R. & Pople, J. A. (1972). *J. Chem. Phys.* **56**, 2257–2261.
Johnson, S. L., Jung, D., Foring, M., Chen, Y., Satterthwait, A., Rozanov, D. V., Strongin, A. Y. & Pellecchia, M. (2006). *J. Med. Chem.* **49**, 27–30.
Pauling, L. (1960). *The Nature of the Chemical Bond*, 3rd ed., p. 206. Ithaca: Cornell University Press.
Penthala, N. R., Reddy, T. R. Y., Parkin, S. & Crooks, P. A. (2009). *Acta Cryst.* E**65**, o552.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.
Ternay, A. L. Jr (1976). *Contemporary Organic Chemistry*, p. 822. Philadelphia: W. B. Saunders.
Wållberg, A., Nilsson, K., Österlund, K., Peterson, A., Elg, S., Raboisson, P., Bauer, U., Hammerland, L. G. & Mattsson, J. P. (2006). *Bioorg. Med. Chem. Lett.* **16**, 1142–1145.
Weinhold, F. & Landis, C. R. (2005). *Valency and Bonding: A Natural Bond Orbital Donor–Acceptor Perspective*, pp. 16–20. Cambridge University Press.
Zhao, Y. & Truhlar, D. G. (2006). *J. Chem. Theory Comput.* **2**, 1009–1018.