Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Two dibenzodiazepinone molecules with dissimilar dimeric associations and apparent different tautomeric forms

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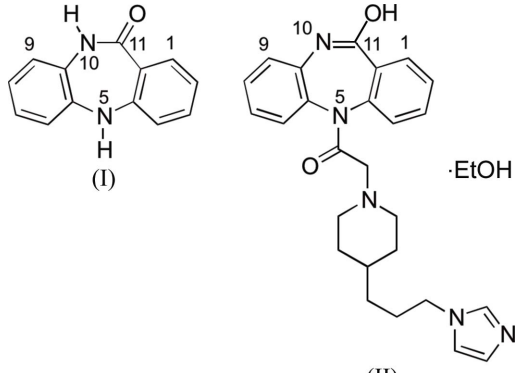
Received 21 March 2012
Accepted 2 May 2012
Online 19 May 2012

In two dibenzodiazepinones, *viz.* the tricyclic core structure, 5*H*-dibenzo[*b*,*e*]diazepin-11(10*H*)-one, $C_{13}H_{10}N_2O$, and an acylated derivative, 1-(11-hydroxy-5*H*-dibenzo[*b*,*e*]diazepin-5-yl)-2-{4-[3-(1*H*-imidazol-1-yl)propyl]piperidin-1-yl}ethanone ethanol monosolvate, $C_{26}H_{29}N_5O_2\cdot C_2H_5OH$, dimeric association *via* hydrogen-bond bridging between the cyclic amide entities is evident, but there are considerable differences between the parent compound and the amidated derivative. Highly consistent with reported structures of related tricyclic lactams, two molecules of the nonsubstituted compound are bridged through two N—H···O hydrogen bonds across a crystallographic centre of symmetry and the bond lengths of the cyclic amide entity correspond to the amino–oxo (lactam) tautomeric form. In contrast, the structure of the derivative shows two similar, but crystallographically unique, molecules hydrogen bonded into a dimeric unit exhibiting an approximate (noncrystallographic) *C*2 axis. The bond lengths of the two derivative cyclic amide groups support their potential presence in the hydroxyimine (lactim) tautomeric forms, with the resulting possibility of intermolecular tautomerism. Likely driving forces for the two extreme configurations are discussed.

Comment

Crystal structures of molecules that contain the dibenzodiazepinone nucleus have not been reported to date, even though the synthesis and crystallization of the parent dibenzodiazepinone, 5*H*-dibenzo[*b*,*e*]diazepin-11(10*H*)-one, (I) (Fig. 1), has been known for decades (Clemo *et al.*, 1924; Giani *et al.*, 1985). Substitution at the 5-position (positional numbering based on systematic IUPAC nomenclature and used throughout, but different from crystallographic positional numbering) of (I) with acyl residues containing one or two aminergic basic entities was reported to be a promising strategy for the development of highly potent ligands for muscarinic receptors (Cohen *et al.*, 1993; Kassiou *et al.*, 1997). With the aim of preparing muscarinic receptor ligands with improved selectivity and potential radioligands for muscarinic receptors, we synthesized dibenzodiazepinone derivatives with basic heterocycles at the terminal 5-position of the side chain of (I). This approach prompted us to synthesize the dibenzodiazepinone derivative 1-(11-hydroxy-5*H*-dibenzo[*b*,*e*]diazepin-5-yl)-2-{4-[3-(1*H*-imidazol-1-yl)propyl]piperidin-1-yl}ethanone ethanol monosolvate, (II) (Fig. 2), which crystallizes from ethanol–diethyl ether as translucent needles. The previously described parent compound (I), a crucial intermediate for the preparation of (II), was crystallized from ethanol–ethyl acetate as a mixture of hexagonal and rhombic plates with a yellow–green appearance.



X-ray crystallographic analyses of the parent compound, (I) (hexagonal plates), and of its amide derivative, (II), reveal consistencies and differences in the molecular and intermolecular structures of the two dibenzodiazepinones. A major and obvious common feature is the hydrogen bonding of two monomers through the dibenzodiazepinone lactam group (Figs. 3*a* and 3*b*). In a second point of similarity, the seven-membered diazepinone rings adopt a puckered conformation (Figs. 1, 2, 3*c* and 3*d*), such that the two aromatic rings are parallel, adopting a butterfly conformation; the puckering is more pronounced in lactam (II) [angles between the benzene rings: (I) 139.28 (11)°, and (II) 120.0 (3)° (molecule *A*) and 126.6 (3)° (molecule *B*).

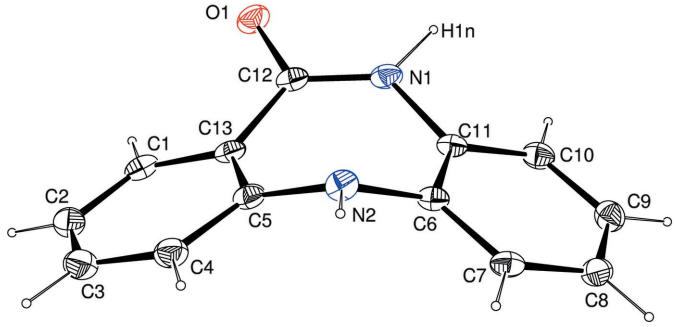


Figure 1
The molecular structure of dibenzodiazepinone (I), showing the crystallographic atom-labelling scheme. Displacement ellipsoids are drawn at the 40% probability level.

  doi:10.1107/S0108270112019622

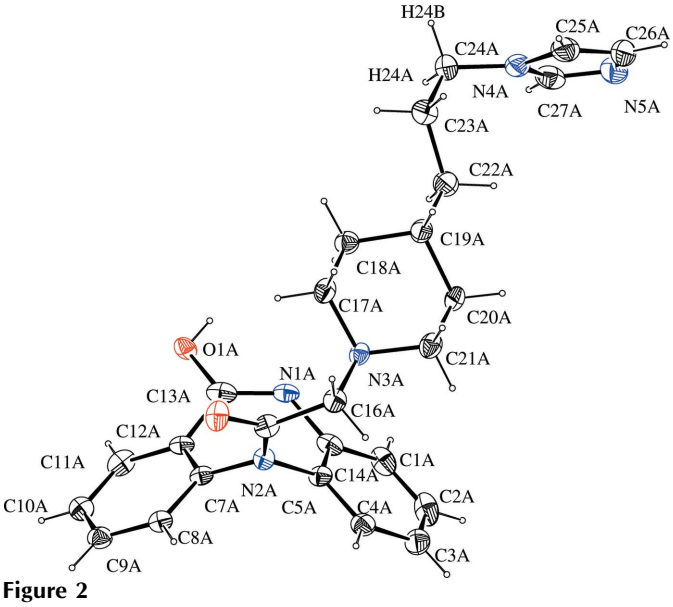


Figure 2
The molecular structure of one of the two symmetry-independent molecules of dibenzodiazepinone (II), showing the crystallographic atom-labelling scheme. Displacement ellipsoids are drawn at the 40% probability level and the ethanol molecules have been omitted for clarity.

Closer examination reveals the first point of difference. In the case of (I), the hydrogen-bonded pair exhibits a centre of inversion, which implies a relative association between the curved dibenzodiazepinone ring systems as two cups held side-by-side, with one cup upright and the other inverted (Fig. 3*c*). A completely different situation is found in the crystal structure of (II). Here, the association between the two butterfly-shaped tricyclic systems is such that the aromatic rings of both molecules are oriented in the same direction. It is noted that in this structure the N5-bound side chains are folded back over the convex surface of the two molecules (Fig. 3*d*). This latter type of dimeric structure normally assumes a *C*2 symmetry, with the axis extended perpendicular to the mean planes of the two tricyclic entities of the pair. In practice there is only an approximate twofold symmetry, as there are minor conformational differences between the two molecules in the dimeric unit of (II).

It should be noted at the outset that the crystallographic data for (II) were relatively weak and there is a level of disorder brought about in part by the presence of disordered solvent in the crystal. However, with this in mind, and within the limits of the data, an overlay of the individual molecules *A*

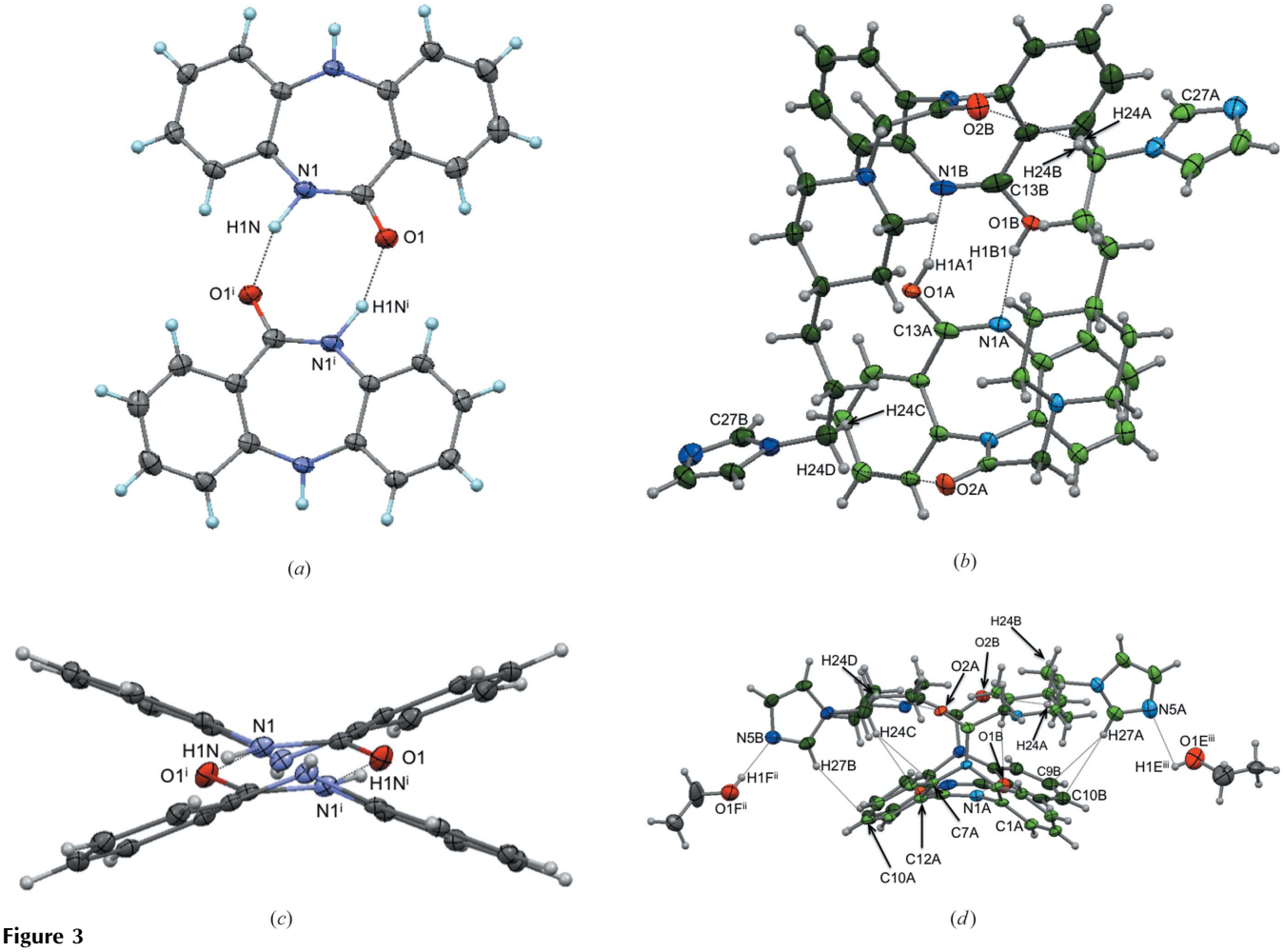


Figure 3
(*a*) Perpendicular and (*c*) parallel views of the dimeric unit in (I) [symmetry code: (i) $-x+1, -y, -z+1$], and (*b*) perpendicular, and (*d*) parallel views of the dimeric unit in (II) [symmetry codes: (ii) $x+1, y, z$; (iii) $x-1, y-1, z$]. Only the major contributing diastereomeric pair is shown for (II). Displacement ellipsoids are drawn at the 40% probability level and dotted lines indicate hydrogen bonds.

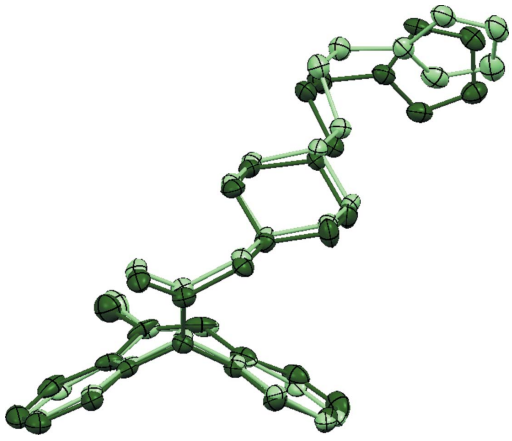
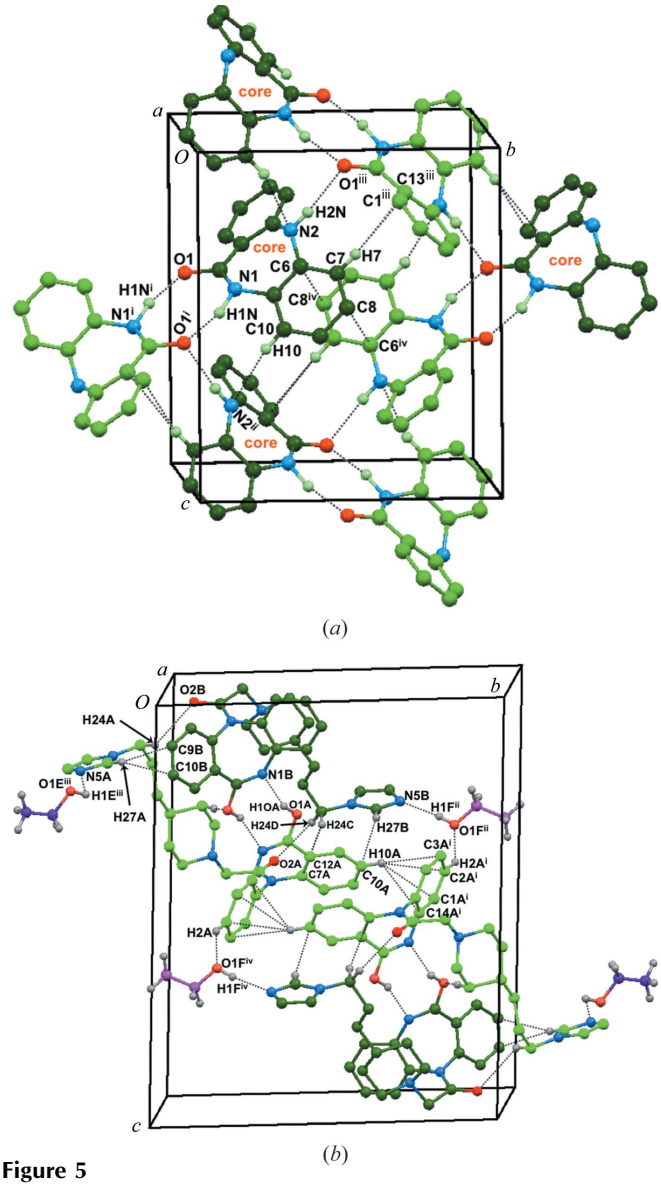


Figure 4
Overlay of the near identical components of the diastereomeric pair *A* (light; pale green in the electronic version of the paper) and *B* (dark; dark green) for (II), in accordance with Figs. 3(*b*), 3(*d*) and 5(*b*). Ellipsoids are drawn at the 40% probability level.

and *B* (Fig. 4) reveals that most differences occur in the orientation of the remote sections of the N5 amide side chain. Compounding these differences is the observation of a degree of apparent disorder in the position of the N—C—O atoms within each of the H-bound partner lactam/lactim moieties. Modelling of this disorder leads to the conclusion that there is the equivalent of an approximately 0.75:0.25 ratio of contributors in which the H/N and C/O atom pairs are interchanged. This amounts to there being present an identical 0.75:0.25 ratio of diastereoisomeric pairs of H-bound molecules in the unit cell. These diastereoisomeric molecules would equate to the *E* and *Z* rotameric molecules that are evident by ^{1}H and ^{13}C NMR spectroscopy in a 1:1 ratio in solution (see below), but fixed in an unequal ratio within the crystallographic constraints in which the side chains remain fixed.

In order to determine the propensity of the symmetry involved in the overall dimeric association of similar tricyclic structures, a search of the Cambridge Structural Database (CSD, Version 5.32; Allen, 2002) for seven-membered lactams fused with two six-membered aromatic rings was carried out. The search gave eight hits, namely dimeric units of dibenzazepinone, (III), dibenzoxazepinone, (IV), dibenzothiazepinone, (V), and four dipyridodiazepinones, (VI*a*)–(VI*e*), all of which show the crystallographic behaviour of (I), *i.e.* a centrosymmetric association of hydrogen-bonded molecules. The type of association found for (II) has not been reported so far. Geometric parameters for the dimeric units of the related lactams (I)–(IV) and (VI*a*)–(VI*e*) are given in Table 1.

In the wider crystal structure of the parent compound, (I), the N5 H atom serves as a hydrogen-bond donor and forms an additional intermolecular hydrogen-bond contact with the lactam carbonyl O atom, over and above the contact of the O atom with the N10 H atom of its partner lactam (Fig. 5*a*). This can not take place in derivative (II), but leads, in (I), to both lone pairs of the carbonyl O atom being involved in hydrogen bonding. As a consequence, there is a hydrogen-bond cross-coupling between hydrogen-bonded dimeric pairs of molecules in (I) that creates a second dimension parallel to (100).



(*a*)

(*b*)

Figure 5
The crystal packing of molecules in the unit cells of (*a*) (I) [symmetry codes: (i) $-x+1, -y, -z+1$; (ii) $x, -y+\frac{1}{2}, z+\frac{1}{2}$; (iii) $-x+1, y+\frac{1}{2}, -z+\frac{1}{2}$; (iv) $-x+1, -y+1, -z+1$] and (*b*) (II) [symmetry codes: (i) $-x+1, -y+1, -z+1$; (ii) $x+1, y, z$; (iii) $x-1, y-1, z$; (iv) $-x, -y+1, -z+1$]. Significant intermolecular interactions are indicated (dotted lines).

This second dimension is reinforced through an additional interaction (2.61 Å) between crystallographic H10*A* and N2^{ii} [symmetry code: (ii) $x, -y+\frac{1}{2}, z+\frac{1}{2}$] (Fig. 5*a*). Furthermore, π–π interactions [3.372 (3) Å] between crystallographic aromatic atom C6 of one molecule and atom C8 of its symmetry-related partner at $(-x+1, -y+1, -z+1)$ and atom C8 of the original molecule and atom C6 of the same $(-x+1, -y+1, -z+1)$ partner, and H$\cdots\pi$ interactions (2.86 and 2.80 Å) between aromatic atom H7 of one molecule and C1/C13 of its symmetry-related partner at $(-x+1, y+\frac{1}{2}, -z+\frac{1}{2})$ are identified in the crystal structure of (I) (*cf* Fig. 5*a*).

In contrast with the situation in (I), the asymmetric unit of (II) comprises two chemically equivalent but crystallographically non-identical hydrogen-bonded partner mol-

ecules. These partner pairs are in turn held together in part by H···π interactions through crystallographic atom H10*A* from one molecule and C14*A*/C1*A*/C2*A*/C3*A* from a benzenoid aromatic ring of its equivalent molecule in an adjacent partner pair (Fig. 5*b*). Cocrystallized ethanol solvent is evident in both the ^{1}H NMR spectrum and the X-ray crystal structure. Present in a 1:1 ratio, the two symmetry-independent molecules are in hydrogen-bond donor contact with the unsubstituted N atoms (N5*A* and N5*B*, respectively) in each of the imidazole heterocycles in the pendant side chains [contacts H1E^{iii}···N5*A* and H1F^{ii}···N5*B* in Figs. 3*d* and 5*b*; symmetry codes: (ii) $x+1, y, z$; (iii) $x-1, y-1, z$]. The ethanol molecule bonded to atom N5*B* is also in a hydrogen-bond acceptor contact with one of the aromatic H atoms (H2*A*) from the partner molecule of an adjacent molecular pair [H2*A*···O1F^{iv}; symmetry code: (iv) $-x, -y+1, -z+1$]. These contacts reinforce the H···π contact in holding the partner pairs together (Fig. 5*b*). In contrast, the second ethanol solvent molecule is slightly disordered, possibly due to a partial escape of the solvent. It is also associated as a hydrogen-bond donor with an imidazole N atom [H1E···N5A^{vi}; symmetry code: (vi) $x+1, y+1, z$], but not as an acceptor.

In addition to the main hydrogen-bond interactions already mentioned between the cyclic amide moieties, there are within the asymmetric dimeric unit of (II) a hydrogen-bond contact between the exocyclic amide carbonyl atom O2*A* of one molecule and atom H24*D* of the methylene group adjacent to the imidazole ring of its partner molecule, and H···π interactions between atoms C7*A* and C12*A* of the original molecule and the same partner methylene H atom (H24*C*), and between atom C10*A* of the original molecule and imidazole atom H27*B* of its partner molecule (Figs. 3*d* and 5*b*). As a further example of the non-equivalence of the two sub-units, only atom H24*A* of the methylene group next to the imidazole ring of the original molecule interacts with exocyclic amide atom O2*B* of the second molecule, while imidazole atom H27*A* from the original molecule participates in an H···π interaction with two atoms, C9*B* and C10*B*, of the adjacent molecule. Both sets of interactions occur across the non-identical molecules of the asymmetric pair and most likely stabilize the complementary back-folding of the N5-bound side chains (Fig. 3*d*).

In the two crystal structures, within the limits imposed by the quality of the data for (II), the cyclic amide (lactam) entities, which form the interface of the dibenzodiazepinone dimeric structure, show significant features in their C—N and C═O bond lengths. The parent compound, (I), contains a relatively short C—N bond [1.331 (3) Å; shorter than for the comparable compounds (III)–(V) and (VI*a*)–(VI*e*), but equal to (VI*b*)] and a relatively long carbonyl bond [1.263 (3) Å; longer than for (III)–(V) and (VI*a*)–(VI*e*)]. These observations indicate the presence of some hydroxyimine character in the molecule but a preference for the amide (keto) tautomer (*cf.* Fig. 6). However, the two monomeric species in the structure of (II) have considerably shorter C—N bonds [1.299 (7) and 1.310 (8) Å] and longer lactam carbonyl bonds [1.310 (6) and 1.309 (6) Å], even than for (I). This provides strong support for primarily hydroxyimine character. Interestingly, the two C—N and C═O bond lengths for the two partner molecules in (II) are the same, within experimental error. This is despite the fact that the two component molecules were refined freely, and similarity restraints (SADI in *SHELXL97*; Sheldrick, 2008) were applied only for the amide moieties of the major (0.75) and minor (0.25) diastereomers, where they occupy the same crystallographic coordinates.

A search of the CSD for bond lengths of doubly hydrogen-bonded amides revealed that of those amides (2091 hits), 89%

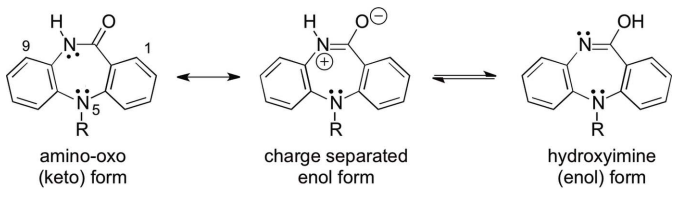


Figure 6
Possible mesomeric and tautomeric structures of the dibenzodiazepinone amide group.

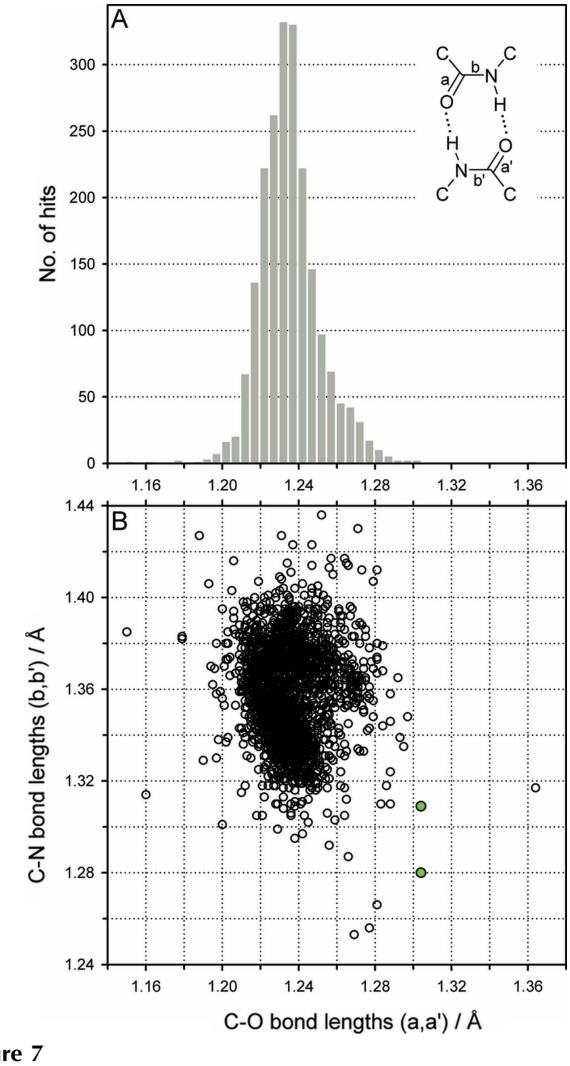


Figure 7
Cambridge Structural Database search for doubly bridged N—H···O-bonded amide dimers (1924 hits). Medial carbonyl bond length (a, a') = 1.235 Å.

had C═O bonds in the range 1.22–1.26 Å (Fig. 7*a*), and 95% had C—N bonds in the range 1.32–1.40 Å. Amongst the outliers, only two cases (highlighted with shading in Fig. 7*b*) had C—N and C═O bond lengths (<1.31 Å and >1.30 Å, respectively) that come close to those observed for lactam (II) (Antoniadis *et al.*, 2005; Romero & Woerpel, 2006).

A referee has rightly questioned the wisdom of placing too much emphasis on these differences, given the poor data quality for (II). However, the untypical values indicated for the bond lengths of the cyclic amide entity in (II) suggest its occurrence as the hydroxyimine (enol) tautomer (*cf.* Fig. 6), and consequently infer an example of intermolecular tautomerism in the crystal structure. This possibility should be investigated further. Such an intermolecular exchange of H atoms in the crystal structure was recently described in a study of 1*H*,2*H*-indazolin-3-one dimers, where oxygen was hydrogen-bonded to oxygen and nitrogen to nitrogen (enol form to keto form) (Perez-Torralba *et al.*, 2010). The source of such a preference for the hydroxyimine structure of this heterocyclic portion of the N5-acyl derivative, (II), remains unknown but it might be brought about by the unique additional intermolecular interactions observed between the acyl side-chain elements in the crystal structure. Resolution of this matter requires further structural studies on similar molecules but fell outside the bounds of the current investigation.

Experimental

Compound (I) was prepared as described previously (Clemo *et al.*, 1924; Giani *et al.*, 1985). It was recrystallized from EtOH–EtOAc (10:90 *v*/*v*) to yield yellow–green rhombic and hexagonal plates [m.p. 532–534 K; literature m.p. 529–530 K (Giani *et al.*, 1985)].

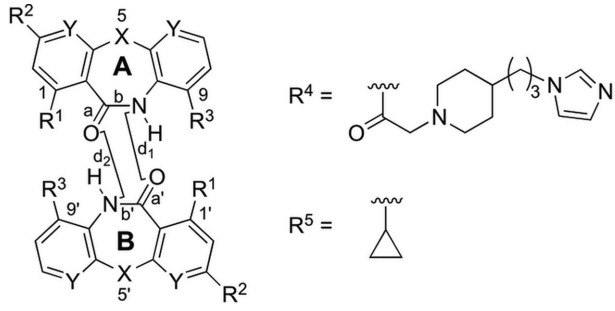
For the preparation of (II), 5-(2-chloroacetyl)-5*H*-dibenzo[*b*,*e*]-[1,4]diazepin-11(10*H*)-one (254 mg, 0.886 mmol) and 4-[3-(1*H*-imidazol-1-yl)propyl]piperidine (180 mg, 0.93 mmol) were dissolved in anhydrous MeCN (2 ml). 5-(2-Chloroacetyl)-5*H*-dibenzo[*b*,*e*]-[1,4]diazepin-11(10*H*)-one was synthesized from (I) and 2-chloroacetyl chloride was prepared as described by Cohen *et al.* (1993). The preparation of 4-[3-(1*H*-imidazol-1-yl)propyl]piperidine was reported by Wei & Weigele (1984), but a different synthetic route was used. A description of the synthetic route for (II), general experimental conditions, and experimental protocols and analytical data for all intermediates for the preparation of (II), as well as ^{1}H and ^{13}C NMR spectra for (II) and all intermediates, are provided as *Supplementary materials*.

Finely ground potassium carbonate (122 mg, 0.886 mmol) was added to the above mixture and the whole kept under stirring in a microwave reactor (Biotage Initiator 8) at 373 K (microwave power 200 W, pressure 200 kPa) for 100 min. Solid material was removed by filtration, the filtrate evaporated to dryness and the residue subjected to column chromatography using mixtures of CH_2Cl_2, Et_2O and MeOH as solvent. The major fraction (CH_2Cl_2–Et_2O–MeOH 20:4:1 to 10:2:1) was evaporated to dryness under reduced pressure, then taken up in CH_2Cl_2 (0.5 ml) and pentane (0.8 ml). Removal of the solvents *in vacuo* afforded (II) as a pale-tan glass (yield 187 mg, 48%; m.p. 368–370 K). R_F = 0.4 (CH_2Cl_2–MeOH 5:1 *v*/*v*). IR (Nujol): 1660, 1600 cm^{-1}.

A portion (150 mg) of this material was dissolved in EtOH (0.8 ml), Et_2O (1 ml) was added and the solution was kept at 253 K to afford white rosettes (*ca* 100 mg), which were kept *in vacuo* at 353 K for 7 h. Separation of the mother liquor and storage at 253 K afforded the ethanol solvate, (II), of the same substance as translucent needles (yield 10 mg; m.p. 371–373 K) that were suitable for X-ray crystal-

Table 1
Selected bond lengths and intermolecular N···O distances (Å) in the hydrogen-bonded dimeric single-crystal X-ray structures of dibenzodiazepinones (I) and (II), and structurally related lactams (III)–(V) and (VI*a*)–(VI*e*).

Where bond lengths *a*, *a*′, *b* and *b*′, and distances d_1 and d_2, are equal due to a centre of symmetry in the dimeric unit (*A* = *B*), the value is given only once. The numbering of atoms is derived from dibenzodiazepinone (I), where *X* = NH, *Y* = CH and R^1 = R^2 = R^3 = H.



Compound	*X*	*Y*	R^1	R^2	R^3	C═O bond length *a*/*a*′	C═N bond length *b*/*b*′	N···O′/N′···O distance d_1/d_2	Reference
(I)	NH	CH	H	H	H	1.263 (3)	1.331 (3)	2.881 (3)	This work
(II)	NR^4	CH	H	H	H	1.310 (6)/1.309 (6)	1.299 (7)/1.310 (8)	2.835 (7)/2.824 (6)	This work
(III)	CH_2	CH	H	H	H	1.239 (2)	1.345 (2)	2.868 (2)	(*a*)
(IV)	O	CH	NO_2	N_3	H	1.237 (2)	1.346 (2)	2.829 (2)	(*b*)
(V)	S	CH	H	H	H	1.238 (3)	1.348 (3)	2.845 (3)	(*c*)
(VI*a*)	NR^5	N	H	H	Me	1.231 (2)	1.356 (2)	2.934 (2)	(*d*)
(VI*b*)	NR^5	N	H	H	Me	1.247 (3)	1.330 (4)	2.938 (4)	(*e*)
(VI*c*)	NR^5	N	H	H	Me	1.240 (2)	1.345 (2)	2.914 (1)	(*f*)
(VI*d*)	NR^5	N	H	H	Me	1.241 (2)	1.350 (2)	2.838 (1)	(*f*)
(VI*e*)	NR^5	N	H	H	Me	1.239 (2)	1.350 (2)	2.898 (1)	(*f*)

References: (*a*) Li *et al.* (2006); (*b*) Samet *et al.* (2007); (*c*) De Souza *et al.* (2006); (*d*) Harrison *et al.* (2007); (*e*) Mui *et al.* (1992); (*f*) Caira *et al.* (2008).

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1N···O1^{i}	1.15 (3)	1.77 (3)	2.881 (3)	161 (2)
C10—H10···N2^{ii}	0.95	2.61	3.463 (3)	149
N2—H2N···O1^{iii}	0.89 (3)	2.21 (3)	3.093 (3)	170 (2)
C7—H7···C1^{iii}	0.95	2.86	3.673 (3)	145

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

lographic analysis (containing one equivalent of cocrystallized EtOH, as evident from NMR spectroscopic and X-ray crystallographic analyses). Analysis calculated for $C_{26}H_{29}N_5O_2\cdot C_2H_6O$: C 68.83, H 7.01, N 14.33%; found: C 68.78, H 7.13, N 14.18%.

Due to a slow rotation about the exocyclic amide group on the NMR time scale, two isomers (ratio 1:1) were evident in the NMR spectra of (II). ^{1}H NMR (700 MHz, [D$_4$]MeOH): δ 1.00–1.11 (*m*, 1H), 1.12–1.30 (*m*, 6.5H), 1.49 (*d*, 0.5H, *J* = 11.8 Hz), 1.56 (*m*, 1H), 1.64 (*d*, 0.5H, *J* = 12.2 Hz), 1.79 (*m*, 2H), 1.90–2.04 (*m*, 2H), 2.50 (*d*, 0.5H, *J* = 9.5 Hz), 2.65 (*d*, 0.5H, *J* = 10.1 Hz), 2.82 (*d*, 1H, *J* = 10.2 Hz), 2.85 (*d*, 1H, *J* = 10.2 Hz), 3.06 (*m*, 0.5H), 3.16 (*m*, 0.5H), 3.20–3.25 (*m*, 1H), 3.64 (*q*, 1.3H, *J* = 7.1 Hz), 4.01 (*t*, 2H, *J* = 7.0 Hz), 6.97 (*t*, 1H, *J* = *ca* 0.9 Hz), 7.13 (*t*, 1H, *J* = *ca* 1.1 Hz), 7.23–7.31 (*m*, 2H), 7.36 (*t*, 0.5H, *J* = 7.2 Hz), 7.42 (*t*, 0.5H, *J* = 7.4 Hz), 7.46–7.52 (*m*, 1.5H), 7.54 (*t*, 0.5H, *J* = 7.4 Hz), 7.58 (*t*, 1H, *J* = 7.7 Hz), 7.65 (*s*, 1H), 7.68 (*m*, 1H), 7.89 (*d*, 0.5H, *J* = 7.5 Hz), 7.92 (*d*, 0.5H, *J* = 7.4 Hz). ^{1}H NMR [600 MHz, [D$_6$]DMSO–D$_2$O 15:1 (*v*/*v*), rosettes]: δ 0.64–0.79 (*m*, 1H), 0.92–1.10 (*m*, 4H), 1.24–1.48 (*m*, 2H), 1.62 (*m*, 2H), 1.73–1.86 (*m*, 2H), 2.11 (*d*, 0.5H, *J* = 10.0 Hz), 2.66 (*d*, 0.5H, *J* = 10.1 Hz), 2.57 (*m*, 1H), 2.86 (*d*, 0.5H, *J* = 14.3 Hz), 2.93 (*d*, 0.5H, *J* = 14.5 Hz), 3.11 (*d*, 0.5H, *J* = 14.5 Hz), 3.29 (*d*, 0.5H, *J* = 14.3 Hz), 3.88 (*br s*, 2H), 6.86 (*s*, 1H), 7.13 (*s*, 1H), 7.14–7.23 (*m*, 2H), 7.25–7.32 (*m*, 1H), 7.37–7.46 (*m*, 2H), 7.54–7.63 (*m*, 3H), 7.73–7.79 (*m*, 1H). ^{13}C NMR [150 MHz, [D$_6$]DMSO–D$_2$O 15:1 (*v*/*v*), rosettes; provided that adjacent signals in the ^{13}C NMR spectra could be unambiguously clarified (using ^{1}H COSY and HSQC spectra) to arise from one carbon nucleus, these signals are depicted as a set of signals (*e.g.* 123.7/123.9 p.p.m.)]: δ 28.1, 31.3/31.67/31.74/31.9, 32.9, 34.4/34.5, 46.5, 52.8/53.0/53.36/53.41, 60.3/60.8, 119.6, 121.7/121.8, 124.9/125.2, 126.4, 127.5, 128.17, 128.24, 128.30, 128.37, 128.5/128.9, 129.2, 130.2, 130.7, 130.8, 132.9/133.2, 134.6, 134.9, 135.0, 135.8, 137.4, 142.6/142.9, 166.8, 169.0/169.4. MS (ESI, MeOH) *m*/*z* (%): 887 (8) [2*M* + H]$^+$, 444 (100) [*M* + H]$^+$. HRMS (ESI, MeOH) *m*/*z*: calculated for $[C_{26}H_{30}N_5O_2]^+$: 444.2394; found: 444.2390.

Compound (I)

Crystal data

$C_{13}H_{10}N_2O$
M_r = 210.23
Monoclinic, $P2_1/c$
a = 7.4767 (16) Å
b = 10.861 (2) Å
c = 12.475 (2) Å
β = 98.277 (6)°
V = 1002.5 (3) Å^3
Z = 4
Mo *K*α radiation
μ = 0.09 mm^{-1}
T = 147 K
0.28 × 0.25 × 0.07 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2007)
T_{min} = 0.975, T_{max} = 0.994
6162 measured reflections
1698 independent reflections
1161 reflections with $I > 2\sigma(I)$
R_{int} = 0.055

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.048
$wR(F^2)$ = 0.120
S = 1.04
1698 reflections
153 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}

Table 3
Hydrogen-bond geometry (Å, °) for (II).

Values for primed *A*′ and *B*′ atoms refer to minor sites of diastereomeric disorder (not shown in Fig. 2 for reasons of clarity).

D—H···A	D—H	H···A	D···A	D—H···A
O1*A*—H1*A*1···N1*B*	0.82	2.05	2.835 (7)	160
O1*B*—H1*B*1···N1*A*	0.82	2.05	2.824 (6)	158
O1*A*′—H1*A*′···N1*B*′	0.82	2.00	2.755 (13)	154
O1*B*′—H1*B*′···N1*A*′	0.82	2.08	2.857 (14)	159
C10*A*—H10*A*···C1*A*^{i}	0.93	2.94	3.655 (8)	135
O1*F*—H1*F*···N5*B*^{v}	0.82	1.97	2.779 (7)	167
O1*E*—H1*E*···N5*A*^{vi}	0.82	2.36	2.70 (3)	106
C2*A*—H2*A*···O1*F*^{iv}	0.93	2.60	3.433 (8)	149

Symmetry codes: (i) $-x+1, -y+1, -z+1$; (iv) $-x, -y+1, -z+1$; (v) $x-1, y, z$; (vi) $x+1, y+1, z$.

Compound (II)

Crystal data

$C_{26}H_{29}N_5O_2\cdot C_2H_6O$
M_r = 489.61
Triclinic, $P\overline{1}$
a = 8.7319 (8) Å
b = 16.0343 (16) Å
c = 19.2802 (18) Å
α = 93.029 (5)°
β = 95.427 (5)°
γ = 93.662 (5)°
V = 2677.1 (4) Å^3
Z = 4
Mo *K*α radiation
μ = 0.08 mm^{-1}
T = 293 K
0.22 × 0.13 × 0.08 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2007)
T_{min} = 0.983, T_{max} = 0.994
35426 measured reflections
9341 independent reflections
3471 reflections with $I > 2\sigma(I)$
R_{int} = 0.143

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.086
$wR(F^2)$ = 0.270
S = 0.99
9341 reflections
690 parameters
88 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.50 e Å^{-3}
$\Delta\rho_{min}$ = −0.67 e Å^{-3}

For (I), the H atoms on N1 and N2 were allowed to refine freely, including their U_{iso} values, without using the stereochemical constraints available in the riding-model option in *SHELX97* (Sheldrick, 2008). For (II), the O-bound H atoms were located in a difference map, but were then geometrically idealized and treated as riding, with O—H = 0.82 Å and U_{iso}(H) = 1.5U_{eq}(O). For both compounds, C-bound H atoms were positioned geometrically and treated as riding, with C—H = 0.93–0.97 Å and U_{iso}(H) = 1.5U_{eq}(C) for solvent methyl groups in (II) and 1.2U_{eq}(C) otherwise.

Crystals of (II), in the form of thin plates, diffracted weakly (37% of the reflections were observed), as reflected in the higher values of R_{int} (0.143), final weighted *R* factor (0.270) and *R* factor (0.086). After the initial model for the molecules had been established and refined, a difference Fourier map contained two strong peaks (1.4 e Å^{-3})

between hydrogen-bonded N/O pairs N1*A*···O1*B* and N1*B*···O1*A*, which as H atoms were not stable in the least-squares refinement. Therefore, H atoms with half-occupancy each were fixed on atoms O1*A* and O1*B* (as the C13—O lengths were >1.30 A). The resulting difference Fourier map still contained two strong peaks (1.4 Å^{-3}) near the centres of the N···O pairs. These were interpreted as traces of O atoms arising from the diastereomeric disorder. This disorder implied that a pair of hydrogen-bonded diasteromers occupied the same location, keeping the positions of all atoms unchanged, and only affecting the positions of atoms N1*A*/C13*A*/O1*A* and N1*B*/C13*B*/O1*B*. The structure was refined with this disorder model, in which alternative positions of N1*A*/C13*A* and N1*B*/C13*B* overlap and were constrained to be identical with C13*A*′/N1*A*′ and C13*B*′/N1*B*′, respectively. At the same time, new positions were generated for atoms O1*A*′ and O1*B*′, accounting for the electron density observed in the difference Fourier map. The full-matrix least-squares refinement thus modelled did not contain any significant residual electron density and the ratio of the two diastereomers converged to 0.751 (4):0.249 (4).

In (II), the crystal lattice contained two ethanol solvent molecules, of which one was found to be orientationally disordered over two positions, *viz*. C1*E*/C2*E*/O1*E* and C1*E*′/C2*E*′/O1*E*′. In this model, atoms C2*E* and C2*E*′ and the H atoms of O1*E* and O1*E*′(H1*E*) shared common positions, respectively. Similarity restraints (the SADI instruction of *SHELXL97*; Sheldrick, 2008) were applied to keep the bond lengths in the two positions similar (s.u. = 0.01 Å). Restraints DELU (0.008) and SIMU (0.008) were applied to keep the atomic displacement parameters of atoms in both the positions similar and within reasonable limits.

For both compounds, data collection: *APEX2* (Bruker, 2007); cell refinement: *APEX2*; data reduction: *APEX2*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL-Plus* (Sheldrick, 2008); software used to prepare material for publication: *SHELXL97*.

This work was substantially supported by the Alexander von Humboldt Foundation through the award to Dr Max Keller of a Feodor Lynen Research Fellowship. The single-crystal X-ray crystallographic analyses, NMR spectroscopic analyses and mass spectrometric analyses were carried out within the UNSW Solid-State and Elemental Analysis Unit, the Nuclear Magnetic Resonance Facility and the Bio-analytical Mass Spectrometry Facility, respectively, which are housed within the Mark Wainwright Analytical Centre, UNSW. These facilities are supported in part by infrastructure funding from the New South Wales Government as part of its co-investment in the National Collaborative Research Infrastructure Strategy. In particular, the authors are grateful to Dr Donald Thomas for expert assistance in acquiring the NMR spectra. Thanks are also extended to Ms Mette Nymand for preliminary synthetic studies towards a higher homologue of compound (II), which gave insight into the reaction conditions required for the preparation of 4-[3-(1*H*-imidazol-1-yl)propyl]-piperidine.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: WQ3014). Services for accessing these data are described at the back of the journal.

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