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2-Bromomethyl-3-(2-ethylphenyl)-4(3*H*)-quinazolinone

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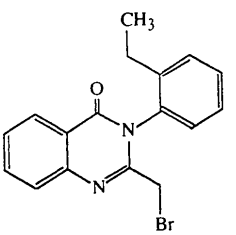
Abstract

The title compound, $C_{17}H_{15}BrN_2O$, crystallizes with two independent molecules having similar configurations in the asymmetric unit. The phenyl substituents are twisted with respect to the almost planar quinazoline moiety, with C3—N2—C13—C14 torsion angles of 76.0 (4) and 79.2 (4)°. The conformation of the molecule corresponds well with that obtained from the ^{1}H NMR spectrum.

Comment

Quinazolinones are versatile compounds showing different biological activities (Amin, Mehta & Samarth, 1970; Johne, 1982). Our continued interest in the synthesis of quinazolinones which act on the central nervous system (CNS) (Ossman & Barakat, 1986) led us to prepare the title compound, (I), as a suitable intermediate for further nucleophilic substitution with amines, alkoxides and thiols. The ^{1}H NMR spectrum of this intermediate showed the methylene protons of both ethyl and bromomethyl groups to be diastereotopic (Barakat, Amin, Aziza & El-Arby, 1994). The protons of the ethyl group constitute an ABX_3 spin system showing two sextets with the proton of each centred at δ 2.45 and 2.33 p.p.m. (J = 7.5 Hz), and a typical triplet of three protons centred at δ 1.13 p.p.m. (J = 7.5 Hz). The protons of the CH_2Br moiety constitute an AB spin system revealing two doublets of one proton each, centred at δ 4.31 and 4.10 p.p.m. (J = 7.5 Hz). This finding prompted us to analyze the structure of this intermediate by X-ray crystallography.



(I)

A view of the two independent molecules of (I) is given in Fig. 1. A comparison of the geometries of the two molecules has shown that all the corresponding bond lengths are equal within two e.s.d.s. The corresponding angles are also similar, except for C17—C18—C19 and C18—C19—C20. This is due to a pseudo-symmetry. The triclinic unit cell can be transformed to a pseudo-monoclinic cell [a = 17.478, b = 7.828, c = 22.396 Å, α = 93.35, β = 102.00, γ = 89.85°, approximate space group *I2/a*] in which the two independent molecules are related by a pseudo-twofold axis, with a small translational component of 0.68 Å along **b** and a pseudo-glide plane of type **a**. This may be due to a packing effect of the ethyl group. Furthermore, bond lengths and angles of the quinazolinone nucleus of the title compound are in fair agreement with those reported for related structures (Fedeli & Mazza, 1974; Huiszoon, 1976; Rogan & Williams, 1980; Törnroos, 1988).

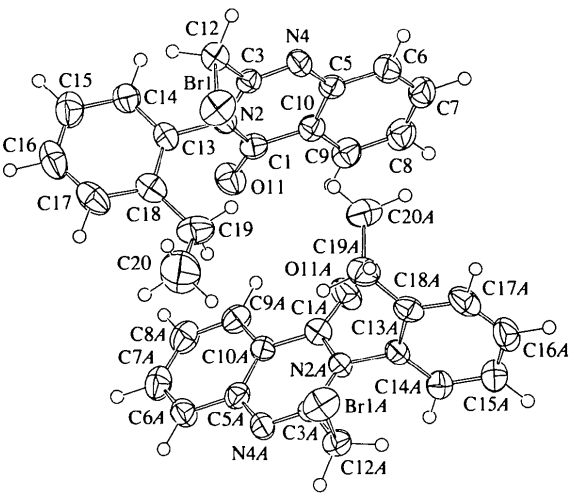


Fig. 1. The molecular structure of the title compound with displacement ellipsoids drawn at the 50% probability level.

The molecules show deviations from planarity which are expected to be a molecular effect rather than an effect caused by packing. The pyrimidone ring adopts a sofa configuration and the displacements of the O atoms from the quinazoline nuclei are 0.143 (4) (for O11) and 0.084 (4) Å (for O11*A*). These values are slightly less than the deviation reported for a related structure (0.175 Å; Fedeli & Mazza, 1974). The Br atoms bonded to the methylene C12 and C12*A* atoms lie on the opposite side of the plane to O11 and O11*A*, with deviations of 1.959 (3) (for Br1) and 1.868 (3) Å (for Br1*A*). The phenyl ring attached to the N2 atom is twisted with a C3—N2—C13—C14 torsion angle of 76.1 (4)° and that attached to N2*A* with a C3*A*—N2*A*—C13*A*—C14*A* torsion angle of 79.3 (4)°. The conformation of the side chains [N2—C3—C12—Br1 83.0 (3) and N2*A*—C3*A*—C12*A*—Br1*A* 84.5 (3), and C13—C18—

C19—C20 158.7 (5) and C13*A*—C18*A*—C19*A*—C20*A* −103.9 (4)°] cause the protons of the ethyl and bromoethyl groups to be magnetically non-equivalent. Accordingly, they exhibited complex patterns of splitting in the ^{1}H NMR spectrum of the title compound (Barakat *et al.*, 1994).

Experimental

The title compound was prepared following the method of Petyunin & Kozhevnikov (1967) and characterized by both elemental and spectral analyses (Barakat *et al.*, 1994). Suitable colourless crystals were obtained from aqueous ethanol.

Crystal data

$C_{17}H_{15}BrN_2O$
M_r = 343.22
Triclinic
$P\bar{1}$
a = 15.890 (5) Å
b = 13.093 (4) Å
c = 7.828 (3) Å
α = 75.480 (10)°
β = 78.250 (10)°
γ = 73.460 (10)°
V = 1495.9 (9) Å^3
Z = 4
D_x = 1.524 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 58 reflections
θ = 16.95–20.3°
μ = 2.748 mm^{-1}
T = 298 K
Needle
0.65 × 0.23 × 0.17 mm
Colourless

Data collection

Stoe Stadi-4 diffractometer
$\omega/2\theta$-scans
Absorption correction: numeric, by integration on crystal shape
T_{min} = 0.550, T_{max} = 0.641
4626 measured reflections
3919 independent reflections

3110 observed reflections [$I > 2\sigma(I)$]
R_{int} = 0.0127
θ_{max} = 22.49°
$h = -17 \rightarrow 16$
$k = -14 \rightarrow 13$
$l = -8 \rightarrow 0$
3 standard reflections
frequency: 90 min
intensity decay: 1.5%

Refinement

Refinement on F^2
$R(F)$ = 0.0348
$wR(F^2)$ = 0.1185
S = 0.957
3919 reflections
379 parameters
H atoms riding
$w = 1/[\sigma^2(F_o^2) + (0.1P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max}$ = 0.014
$\Delta\rho_{max}$ = 0.451 e Å^{-3}
$\Delta\rho_{min}$ = −0.514 e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
Br1	0.38500 (3)	0.95172 (3)	0.00822 (5)	0.0615 (2)
C1	0.3328 (2)	0.8773 (3)	−0.5163 (4)	0.0393 (8)
N2	0.3452 (2)	0.9438 (2)	−0.4120 (4)	0.0361 (6)
C3	0.4255 (2)	0.9265 (3)	−0.3505 (4)	0.0374 (8)
N4	0.4946 (2)	0.8501 (2)	−0.3818 (4)	0.0416 (7)
C5	0.4872 (2)	0.7782 (3)	−0.4796 (4)	0.0390 (8)
C6	0.5616 (2)	0.6924 (3)	−0.5114 (5)	0.0486 (9)
C7	0.5559 (3)	0.6186 (3)	−0.6043 (5)	0.0564 (10)
C8	0.4776 (3)	0.6273 (3)	−0.6647 (5)	0.0569 (10)
C9	0.4045 (2)	0.7105 (3)	−0.6351 (5)	0.0503 (9)
C10	0.4097 (2)	0.7870 (3)	−0.5438 (4)	0.0393 (8)
O11	0.2639 (2)	0.8983 (2)	−0.5769 (4)	0.0553 (7)
C12	0.4330 (2)	1.0006 (3)	−0.2395 (4)	0.0428 (8)
C13	0.2718 (2)	1.0372 (3)	−0.3818 (5)	0.0403 (8)
C14	0.2778 (2)	1.1372 (3)	−0.4863 (5)	0.0491 (9)
C15	0.2107 (3)	1.2289 (3)	−0.4620 (6)	0.0625 (11)
C16	0.1393 (3)	1.2172 (4)	−0.3320 (6)	0.0676 (13)
C17	0.1337 (2)	1.1167 (4)	−0.2303 (6)	0.0584 (11)
C18	0.1998 (2)	1.0222 (3)	−0.2520 (5)	0.0481 (9)
C19	0.1921 (3)	0.9103 (4)	−0.1502 (6)	0.0668 (11)
C20	0.1346 (4)	0.9016 (5)	0.0213 (9)	0.135 (3)
Br1*A*	0.11807 (3)	0.54170 (3)	0.38130 (5)	0.0613 (2)
C1*A*	0.1671 (2)	0.6194 (3)	−0.2486 (4)	0.0404 (8)
N2*A*	0.1565 (2)	0.5513 (2)	−0.0797 (3)	0.0366 (6)
C3*A*	0.0771 (2)	0.5677 (3)	0.0358 (4)	0.0361 (8)
N4*A*	0.0076 (2)	0.6442 (2)	0.0000 (4)	0.0412 (7)
C5*A*	0.0128 (2)	0.7166 (3)	−0.1637 (5)	0.0400 (8)
C6*A*	−0.0624 (2)	0.8009 (3)	−0.2048 (5)	0.0477 (9)
C7*A*	−0.0594 (3)	0.8722 (3)	−0.3657 (5)	0.0536 (10)
C8*A*	0.0170 (3)	0.8631 (3)	−0.4881 (5)	0.0528 (10)
C9*A*	0.0917 (2)	0.7826 (3)	−0.4511 (5)	0.0456 (9)
C10*A*	0.0900 (2)	0.7083 (2)	−0.2884 (4)	0.0376 (8)
O11*A*	0.2363 (2)	0.6000 (2)	−0.3493 (3)	0.0593 (7)
C12*A*	0.0715 (2)	0.4920 (3)	0.2142 (4)	0.0432 (8)
C13*A*	0.2294 (2)	0.4569 (3)	−0.0381 (4)	0.0378 (8)
C14*A*	0.2238 (2)	0.3600 (3)	−0.0682 (5)	0.0483 (9)
C15*A*	0.2906 (3)	0.2666 (3)	−0.0286 (6)	0.0616 (11)
C16*A*	0.3607 (3)	0.2729 (3)	0.0419 (6)	0.0624 (12)
C17*A*	0.3665 (2)	0.3695 (3)	0.0696 (5)	0.0562 (10)
C18*A*	0.3007 (2)	0.4654 (3)	0.0313 (4)	0.0443 (9)
C19*A*	0.3104 (2)	0.5716 (3)	0.0559 (5)	0.0563 (10)
C20*A*	0.3784 (3)	0.6183 (3)	−0.0830 (6)	0.0679 (12)

Table 2. *Selected geometric parameters (Å, °)*

Br1—C12	1.950 (3)	Br1*A*—C12*A*	1.944 (3)
C1—O11	1.214 (4)	C1*A*—O11*A*	1.219 (4)
C1—N2	1.408 (4)	C1*A*—N2*A*	1.405 (4)
N2—C3	1.393 (4)	N2*A*—C3*A*	1.391 (4)
N2—C13	1.460 (4)	N2*A*—C13*A*	1.453 (4)
C3—C12	1.498 (5)	C3*A*—C12*A*	1.499 (5)
N4—C5	1.396 (4)	N4*A*—C5*A*	1.393 (4)
C18—C19	1.508 (6)	C18*A*—C19*A*	1.505 (5)
C19—C20	1.460 (7)	C19*A*—C20*A*	1.512 (5)
C17—C18—C19	122.8 (3)	C17*A*—C18*A*—C19*A*	120.6 (3)
C18—C19—C20	118.0 (4)	C18*A*—C19*A*—C20*A*	113.9 (3)

Data collection: *DIF*4 (Stoe & Cie, 1987*a*). Cell refinement: *DIF*4. Data reduction: *REDU*4 (Stoe & Cie, 1987*b*), *Xtal*3.2 (Hall, Flack & Stewart, 1992). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *Xtal*3.2. Software used to prepare material for publication: *SHELXL*93.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, complete geometry and torsion angles have been deposited with the IUCr (Reference: AB1282). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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A Racemic Bicyclic Acylamidine from a Tripeptide Derivative

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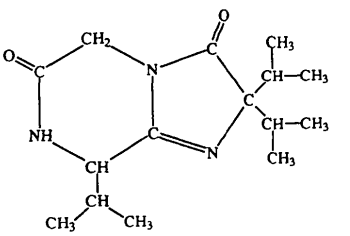
Abstract

The 2,2,8-triisopropyl-4,5,7,8-tetrahydroimidazo[1,2-*a*]-pyrazine-3,6-dione molecule, $C_{15}H_{25}N_3O_2$, has a double bond and two partial double bonds in the bicyclic skeleton, with some π-electron delocalization along C_1'—N_3—C_2'. The conformation parameters of the diisopropyl (Dip) residue reveal that it is in an unusually high-energy conformation. The peptide bond between the glycine and valine residues is *cis* [C_3^{α}—C_3'—N_1—C_1^{α} = −7.0 (3)°]. In the crystal, the molecules are held together in the *ac* plane of the *P2/n* space group by intermolecular hydrogen bonds formed around a twofold axis by molecules related by symmetry centres.

Comment

Peptides containing α,α-disubstituted glycines have received much attention, as amino acids have a high propensity to freeze specific conformations and dramatically slow enzymatic processes (Toniolo & Benedetti, 1988; Di Blasio, Pavone, Lombardi, Pedone & Benedetti, 1993). Recently, the synthesis of a very bulky amino acid, α,α-diisopropylglycine (Dip), and its peptide derivatives by the modified Ugi reaction at high pressure has been reported (Yamada, Yanagi, Omote, Miyazawa, Kuwata, Sugiura & Matsunoto, 1990, 1991). Further studies on the synthesis of various Dip-containing tripeptides have shown the unexpected formation of a bicyclic system (Yamada, Iwamoto, Yanagi, Miyazawa, Kuwata, Saviano & Pavone, 1993). This system was reported as an acylamidine by Rothe, Fahnle, Pudill & Schindler (1979). In this paper, we report the X-ray diffraction analysis of the title compound, (I), performed in order to determine the molecular conformation.



(I)

An *ORTEP* (Johnson, 1965) view of the acylamidine is shown in Fig. 1. The analysis of the geometric parameters reveals the presence of a double bond between N_2 and C_1' [1.276 (2) Å], and partial double bonds between C_1' and N_3 [1.387 (2) Å], and between C_2' and N_3 [1.383 (2) Å] with some π-electron delocalization along C_1'—N_3—C_2'. In addition, the angles N_2—C_1'—N_3 and C_1^{α}—C_1'—N_2 are narrower and wider, respectively, than the sp^2 angles as a result of the steric constraint of the five-membered ring. Two planes can be identified in the bicyclic backbone of the molecule: the first contains the atoms C_1^{α}, C_1', N_2, C_2^{α}, C_2', N_3 and C_3^{α}, while the other contains the atoms C_3^{α}, C_3', N_1 and C_1^{α}. These planes form a dihedral angle of 25.2 (1)°. The peptide bond between the glycine and valine residues is *cis* [C_3^{α}—C_3'—N_1—C_1^{α} = −7.0 (3)°]. This feature allows both O_3 and N_1—H to be involved in intermolecular hydrogen bonds.

The steric hindrance in the bicyclic structure forces the Dip residue to adopt an unusually high-energy conformation [φ = −0.4 (2)° and ψ = 0.5 (2)°]. Additional