169. The Crystal and Molecular Structure of
4-Aza-5-oxo-tricyclo[4.4.0.0³,⁸]decane (Aza-twistanone)

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(22. V. 77)

Die kristalline und molekulare Struktur von
4-Aza-5-oxo-tricyclo[4.4.0.0³,⁸]decan (Aza-twistanon)

Zusammenfassung

Die kristalline Struktur von Aza-twistanon wurde durch eine Röntgenstruktur-analyse untersucht. Die Kristalle gehören zur monoklinen Raumgruppe $P2_1/n$ mit den Zelldimensionen $a = 6,662(6)$, $b = 13,36(2)$, $c = 8,606(9)$ Å, $\beta = 98,97(2)°$, $V = 757$ Å³, $Z = 4$. Die Struktur wurde mit Direktmethoden gelöst und bis zu R = 0,035 verfeinert (mittlere $\sigma(c) = 0,003$ Å³).

Die *cis*-Amidgruppe ist relativ stark deformiert und hat einen Torsionswinkel C_α–C'–N–C_α von 14,5(4)° (Deformation aus der Ebene $\chi_c = 5,0(5)°$ und $\chi_N = 13,5(4,0)°$). Die gegenüberliegende Äthylenbrücke weist einen Torsionswinkel von 25,1(5)° auf. Die entsprechenden Winkel in Twistan betragen je 20°. Das tricyclische Gerüst von Aza-twistanon hat approximative C_2-Symmetrie (Symmetrie von Twistan: D_2).

The *cis*-amide unit occurs in cyclopeptides known for their biological importance as antibiotics, toxin hormones, ion transport regulators *etc.* [1]. It is therefore of interest to study the geometry of this unit under various conditions. In aza-twistanone, the amide group replaces one of the twisted ethylene bridges of the twistane skeleton and is under severe torsional strain. Results of a crystal structure analysis of aza-twistanone are reported in this paper.

Crystal Data. 4-Aza-5-oxo-tricyclo[4.4.0.0³,⁸]decane (aza-twistanone), $C_9H_{13}NO$, Mol.-Wt. = 151,2, monoclinic (unique axis *b*), space group $P2_1/n$, $a = 6.662 \pm 0.006$ Å, $b = 13,36 \pm 0.02$ Å, $c = 8,606 \pm 0.009$ Å, $\beta = 98.97 \pm 0.02°$, $V = 757$ Å³, $D_m = 1.33$ gcm⁻³, $D_c = 1.327$ gcm⁻³, $Z = 4$, $F(0,0,0) = 328$. Approximate dimensions of the crystal used in data collection were $0.2 \times 0.2 \times 0.3$ mm. Linear absorption coefficient $\mu = 0.9$ cm⁻¹ (MoKα-radiation).

The data were collected on a CAD-4 diffractometer in the $\omega/2\theta$ mode with a scan width of $\theta =$ 0.70° + 0.30 tan θ from 1.5° < θ < 25° using graphitemonochromated Mo$K\alpha$ radiation ($\lambda = 0.7107$ Å). The scan speed was varied so as to accumulate 6000 counts per reflection with a time limit of 120 seconds. Corrections were made for *Lorentz* and polarisation factors but not for absorption. A total of 1322 reflexions was collected, of which 1066 were significant [$I > 3\sigma(I)$].

Structure Solution and Refinement. The structure was solved using the MULTAN program [2] adapted to the system IBM 360/44 with 64 K byte memory by *Ramakumar* and *Narasimha Murthy*. All eleven non-hydrogen atoms could be identified in the E-map based on the set of signs with the highest figure of merit. The positional and isotropic thermal parameters were refined block-diagonally using the program written by *Shiono* [3] and modified by Dr *B. S. Reddy*. Hydrogen atoms were then located at stereochemically reasonable positions from a difference map. Further refinement of positional and anisotropic thermal parameters of C, N and O atoms and of positional and isotropic thermal parameters of the hydrogen atoms led to a final R = 0.035 (significant reflexions only). Scattering factors for non-hydrogen atoms were taken from ref. [4], for H-atoms from ref. [5]. The quantity minimised was $\Sigma\omega(|F_o| - K|F_c|)^2$ with $\omega = 1/\sigma^2 (F_o)$.

Final positional and thermal parameters for non-hydrogen atoms are listed in *Table 1*, those for hydrogen atoms in *Table 2*. A table of observed and calculated structure factors can be obtained from the authors on request (*K. V.*).


O CARBON   NITROGEN   OXYGEN
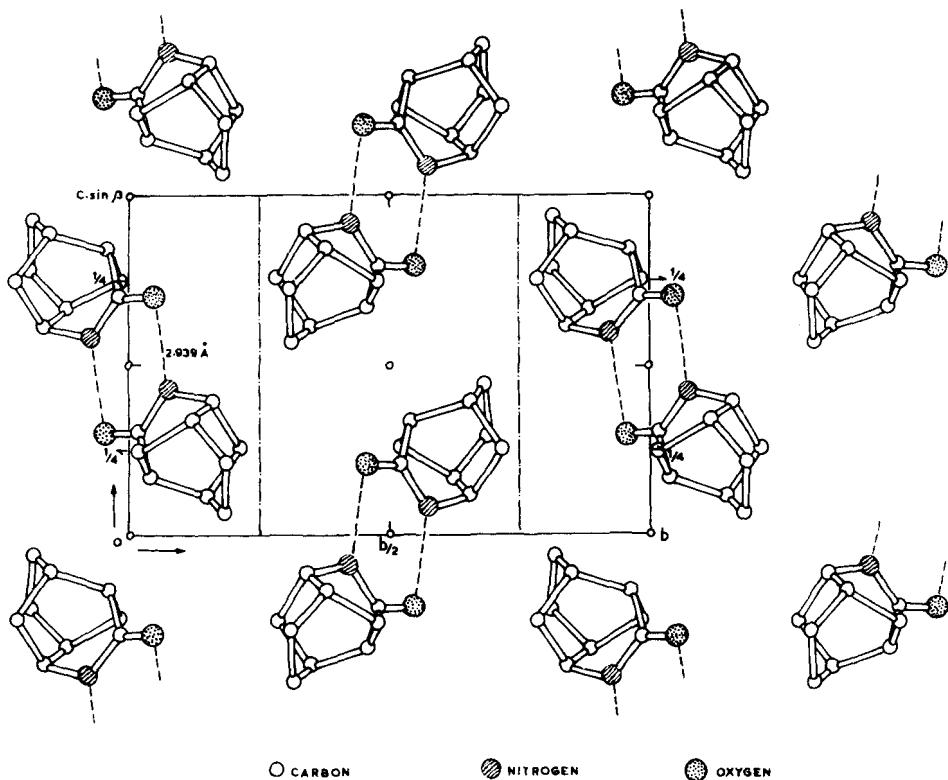
Fig. 1. *Packing of the molecules as viewed down the* a-*axis*

Crystal Packing. The crystal packing is shown in *Fig. 1.* The molecules are organized so as to form centrosymmetrically related hydrogen-bonded dimers. However, the hydrogen bond is weak; N...O = 2.939 (4) Å, N–H...O = 171 (3)° and H–N...O =

Table 1 a. *Fractional coordinates* ($\times 10^5$) *of the heavy atoms with e.s.d.'s in parenthesis*

	x	y	z
C(1)	22628 (44)	15175 (21)	10922 (31)
C(2)	20136 (44)	21626 (21)	25093 (34)
C(3)	32297 (46)	15916 (21)	39024 (31)
N(4)	19074 (39)	7572 (18)	42040 (26)
C(5)	12238 (42)	1869 (21)	29499 (31)
C(6)	24299 (44)	3924 (20)	16308 (33)
C(7)	46320 (47)	2170 (23)	24430 (38)
C(8)	51988 (44)	11880 (22)	33523 (33)
C(9)	58754 (47)	19068 (24)	21358 (37)
C(10)	42901 (51)	18547 (23)	6226 (34)
O(11)	−962 (36)	−4661 (17)	29251 (26)

Table 1 b. *The anisotropic temperature factors* ($\beta_{ij} \times 10^4$) *for the heavy atoms with e.s.d.'s in paranthesis.*
The temperature factor is of the form

$$T = \exp - (\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2hk\beta_{12} + 2hl\beta_{13} + 2kl\beta_{23})$$

|	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	150 (7)	43 (2)	81 (4)	1 (3)	12 (4)	10 (2)
C(2)	163 (8)	35 (2)	120 (4)	8 (3)	43 (5)	2 (2)
C(3)	176 (7)	38 (2)	77 (4)	−19 (3)	36 (4)	−8 (2)
C(4)	194 (7)	47 (2)	81 (3)	−26 (3)	48 (4)	−2 (2)
C(5)	137 (7)	36 (2)	92 (4)	− 6 (3)	25 (4)	3 (2)
C(6)	153 (7)	37 (2)	81 (4)	−11 (3)	29 (4)	−8 (2)
C(7)	165 (7)	37 (2)	123 (4)	10 (3)	39 (5)	2 (2)
C(8)	128 (7)	45 (2)	100 (4)	− 6 (3)	−1 (5)	4 (3)
C(9)	145 (7)	48 (2)	128 (5)	−16 (3)	46 (5)	−1 (3)
C(10)	207 (8)	46 (2)	98 (4)	−13 (4)	52 (5)	7 (3)
O(11)	228 (7)	51 (2)	137 (4)	−46 (3)	62 (4)	−9 (2)
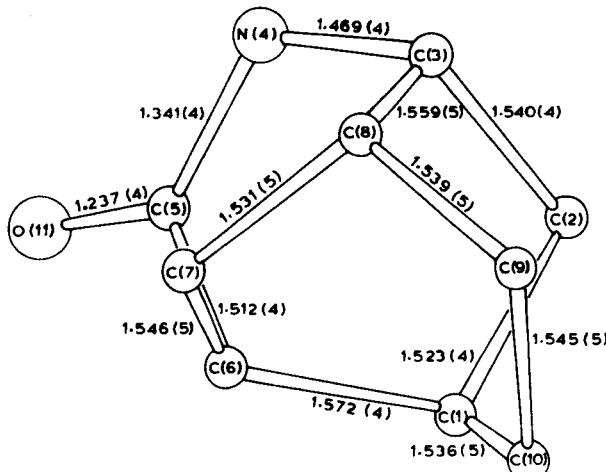
Fig. 2. *Bond lengths* (Å) *involving the heavy atoms* (the standard deviations are indicated in parenthesis)

Table 2. *Fractional coordinates* ($\times 10^4$) *of hydrogen atoms with e.s.d.'s in parenthesis.* The temperature factors are of the form $T = \exp(-B \cdot \sin^2\theta/\lambda^2)$

	x	y	z	$B(\text{Å}^2)$
H(1)	1103 (51)	1592 (25)	189 (37)	3.6 (8)
H(2)	494 (53)	2226 (24)	2645 (36)	3.1 (7)
H(3)	2522 (53)	2844 (23)	2315 (34)	3.2 (7)
H(4)	3532 (45)	2000 (23)	4822 (34)	2.3 (6)
H(5)	1380 (51)	737 (25)	5129 (38)	3.2 (7)
H(6)	2000 (47)	− 68 (25)	778 (34)	2.8 (7)
H(7)	5489 (53)	83 (28)	1619 (39)	3.9 (8)
H(8)	4670 (52)	−390 (25)	3134 (36)	3.3 (8)
H(9)	6228 (50)	1100 (26)	4245 (36)	3.2 (7)
H(10)	7253 (59)	1666 (29)	1916 (41)	4.3 (9)
H(11)	6058 (55)	2620 (27)	2638 (39)	4.0 (8)
H(12)	4125 (49)	2543 (23)	203 (34)	3.1 (7)
H(13)	4821 (55)	1351 (23)	−93 (35)	3.5 (8)

Table 3. *The bond angles* (°) *involving the heavy atoms*

C(2)–C(1)–C(6)	108.4 (3)	C(2)–C(1)–C(10)	104.8 (3)
C(6)–C(1)–C(10)	109.6 (3)	C(1)–C(2)–C(3)	103.5 (3)
C(2)–C(3)–N(4)	104.8 (3)	C(2)–C(3)–C(8)	107.5 (3)
N(4)–C(3)–C(8)	110.3 (3)	C(3)–N(4)–C(5)	115.3 (3)
N(4)–C(5)–C(6)	110.4 (3)	N(4)–C(5)–O(11)	124.5 (3)
C(6)–C(5)–O(11)	125.0 (3)	C(1)–C(6)–C(6)	112.1 (3)
C(1)–C(6)–C(7)	107.1 (3)	C(5)–C(6)–C(7)	102.1 (3)
C(6)–C(7)–C(8)	104.1 (3)	C(3)–C(8)–C(7)	107.2 (3)
C(3)–C(8)–C(9)	109.9 (3)	C(7)–C(8)–C(9)	104.8 (3)
C(8)–C(9)–C(10)	108.1 (3)	C(1)–C(10)–C(9)	107.8 (3)

6 (3)°, in accordance with the observations of *Marsh & Donohue* [6] on other hydrogen-bonded amides. Thus the structure is stabilized by hydrogen bonding between the polar residues and by *van der Waals* contacts between the non-polar groups.

Discussion. Bond distances involving the C, N and O atoms are shown in *Fig. 2*, bond angles in *Table 3*. The C(sp³)–C(sp³) bonds linking methine carbon atoms *i.e.* C(8)–C(3) = 1.559 (5) Å and C(1)–C(6) = 1.572 (4) Å are significantly longer than the standard C–C single bond length of 1.544 Å. Similar lengthening of C–C single bonds has been reported for bridged ring hydrocarbons [7–11].

The standard dimensions of the *cis*-amide group are C'–O = 1.24 Å, C'–N = 1.32 Å, N–C'–O = 123°, N–C'–C$_1^\alpha$ = 118°, O–C'–C$_1^\alpha$ = 119°, C'–N–C$_2^\alpha$ = 126° [12]. In the present structure, the C'–N bond is somewhat longer (1.341 (4) Å), as also observed in tricyclic and tetracyclic spirolactams with highly non-planar amide groups [13]. The angles C(6)–C(5)–N(4) = 110.4 (3)° and C(5)–N(4)–C(3) = 115.3 (3)° are significantly smaller than the corresponding values (118 and 126°) quoted above, which may be attributed to the constraints imposed by the bridging. The four torsion angles around the C'–N bond are $\omega_1(C_1^\alpha-C'-N-C_2^\alpha)$ = 14.5 (4)°, $\omega_2(O-C'-N-H)$ = − 4(3)°, $\omega_3(O-C'-N-C_2^\alpha)$ = − 170.5(3)°, and $\omega_4(C_1^\alpha-C'-N-H)$ = − 179(3)°. The deformation of the *cis*-amide group is then described by the values: $\Delta\omega = \omega_1 = 14.5(4)°$ (torsional strain), $\chi_C = \omega_1 - \omega_3 + \pi = + 5.0(5)°$, and $\chi_N = \omega_2 - \omega_3 + \pi = − 13.5(4.0)°$, charac-

terizing the out-of-plane deformation of C' and N, respectively [14]. Our findings support the observations of *Dunitz & Winkler* [15], also *Ramachandran & Kolaskar* [16], and *Kolaskar et al.* [17], that the pyramidal distortion at the C' atom is smaller than at the nitrogen atom. It has been suggested by *Kolaskar* [18] that the torsional
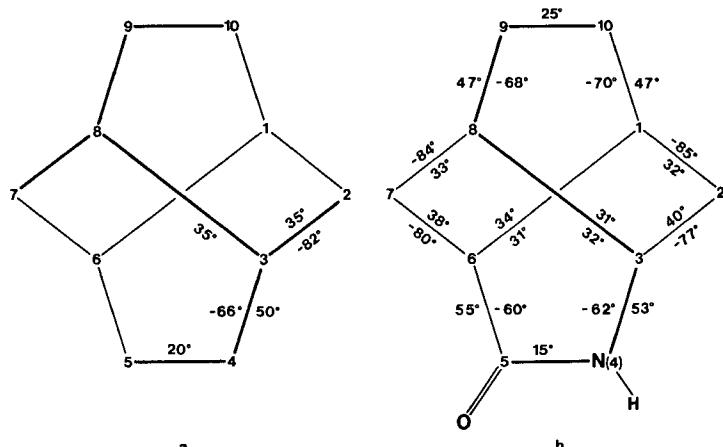

Fig. 3. *Torsion angles in twistane* (a) *and in aza-twistanone* (b). The values for twistane were obtained by empirical force field calculations [19]. The e.s.d. of the values for aza-twistanone are about 1°. Twistane has D_2-symmetry, the skeleton of aza-twistanone has an approximate C_2-symmetry
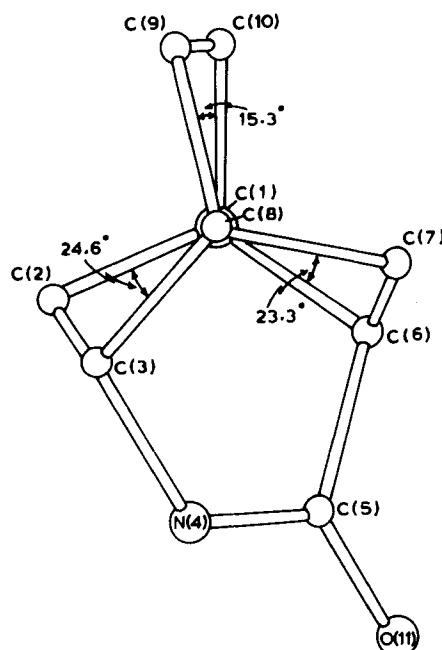
Fig. 4. *A view of the molecule down the C(8)–C(1) direction showing the twisted bicyclo[2.2.2]octane moiety*

angle [$\Delta\omega$] about the C'–N bond in the case of a *cis*-amide unit is correlated with the pyramidal distortion at the nitrogen [χ_N] through a relation $\chi_N \approx \Delta\omega$, as found in the present study.

The torsion angles in the skeleton of aza-twistanone, as observed in the crystal structure, and those of twistane, as obtained from empirical force field calculations [19], are given in *Fig.3*. The molecular symmetry of twistane is D_2 (222). The substitution of an ethylene bridge by an amide group leads to particular deformations in the tricyclic skeleton. The largest effect concerns the torsion angles around the amide and the opposite ethylene bridge. In twistane the torsion angles of the two (equivalent) ethylene bridges are each 20°, in aza-twistanone the corresponding values are 15° (amide) and 25°. The remaining torsion angles in the aza-twistanone skeleton are changed by small amounts (2 to 5°) compared with the twistane values, but in a way as to preserve an approximate twofold axis passing through the mid points of amide and ethylene. A projection of the aza-twistanone molecule along the axis C(8)...C(1) (*Fig.4*) shows the twisted bicyclo[2.2.2]octane (BO) moiety with three unequal twist angles, the smallest opposite the amide group. In twistane the BO unit has twist angles of 12, 23, and 23°, the smallest value belonging to an ethylene bridge.

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