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# Structure of 4-Isovaleryl-2-morpholinocarbonyl-6-trifluoromethylfuro[3,2-*b*]indole

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**Abstract.** $C_{21}H_{21}F_3N_2O_4$, $M_r = 422{\cdot}40$, monoclinic, $P2_1/n$, $a = 22{\cdot}614$ (2), $b = 14{\cdot}287$ (1), $c = 6{\cdot}193$ (1) Å, $\beta = 91{\cdot}05$ (1)°, $V = 2000{\cdot}5$ (3) Å$^3$, $Z = 4$, $D_m = 1{\cdot}401$ (3), $D_x = 1{\cdot}403$ Mg m$^{-3}$, $\lambda$(Cu $K\alpha$) = 1·5405 Å, $\mu = 1{\cdot}14$ mm$^{-1}$, $F(000) = 880$, $T = 277$ K, final $R = 0{\cdot}071$ for 2713 observed reflections. The furo[3,2-*b*]-indole ring system is planar, whereas the morpholino ring is in a chair conformation. An intramolecular weak C—H···O interaction contributes to the conformational stability. The crystal structure is stabilized solely by van der Waals contacts.

**Introduction.** The crystal structure of the title compound has been determined as part of a structure–activity relationship study on furo[3,2-*b*]indoles which possess potent analgesic and anti-inflammatory activities using the acetic acid writhing method in mice and the carrageenin edema method in rats (Kawashima, Amanuma, Sato, Okuyama, Nakashima, Sota & Moriguchi, 1986). The title compound has been obtained from ethyl 6-trifluoromethyl-4*H*-furo[3,2-*b*]-indole-2-carboxylate (Nakashima, Kawashima, Amanuma, Sota & Kameyama, 1984). The furo-[3,2-*b*]indole nucleus was first synthesized by Tanaka, Yakushijin & Yoshina (1977).

**Experimental.** Colorless needle-shaped crystals from hexane and chloroform. Crystal 0·2 × 0·3 × 0·4 mm. $D_m$ by flotation. Rigaku AFC-5 automated four-circle diffractometer, graphite-monochromated Cu $K\alpha$ radiation; cell dimensions by least-squares refinement of 20 reflections with $57 < 2\theta < 60°$; intensity data $2\theta_{max} = 126°$, $\omega$–$2\theta$ scan technique. Three standard reflections (12,3,0, $\bar{4}72$, 914), monitored every 100 reflections, 2% intensity fluctuation. 3724 independent reflections. $-26 < h < 26$, $0 < k < 17$, $0 < l < 7$, 2713 with $|F_o| > 3\sigma(F_o)$. No correction for absorption. Structure solved by direct methods using *MULTAN*84 (Main, Germain & Woolfson, 1984). Positional and thermal parameters for all non-H atoms refined by block-diagonal least squares. H atoms located in a difference Fourier map or added in geometrically reasonable positions; their positional and isotropic thermal parameters included in the subsequent refinement. $R = 0{\cdot}071$, $wR = 0{\cdot}073$ for 2713 reflections, $S = 1{\cdot}46$; $\sum w(|F_o| - |F_c|)^2$ minimized, unit weights. *HBLS*V (Ashida, 1979) used for block-diagonal refinement. $(\Delta/\sigma)_{mean}$ and $(\Delta/\sigma)_{max}$ 0·07 and 0·53 for non-H atoms. Final $\Delta\rho$ excursions ±0·4 e Å$^{-3}$. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974). Calculations carried out on a PANAFACOM U-1200 and ACOS 850 at the Computing Center for Research in Agriculture, Forestry and Fishery.

**Discussion.** Final atomic coordinates for non-H atoms with their estimated standard deviations are given in Table 1.* Bond distances and angles are given in Table 2. An *ORTEP* (Johnson, 1976) drawing of the molecule with the numbering of atoms is shown in Fig. 1.

The furo[3,2-*b*]indole tricyclic ring system is planar with a maximum deviation of 0·03 (1) Å at C(8a); the substituents C(9) and C(21) are displaced on the same side of the plane by 0·11 (1) and 0·16 (1) Å respectively while C(16) is displaced on the opposite side by 0·15 (1) Å. The morpholino ring is in a chair conformation with torsion angles 56·1 (5), −57·0 (5), 59·5 (5), −59·4 (6), 55·7 (5) and −54·5 (5)° about the N(10)–C(11), C(11)–C(12), C(12)–O(13), O(13)–C(14), C(14)–C(15) and C(15)–N(10) bonds respectively. These parameters are in good agreement with those found in morpholino-related structures (Swaminathan, Sundaralingam, Chattopadhyaya & Reese, 1980; Ponnuswamy & Trotter, 1984). The bond distances and angles in the morpholino ring are also in good agreement with those found in the related structures mentioned above. However, the exocyclic bond angles around N(10) are markedly different from the corresponding values and, in this case, the sum of

* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and complete geometric data have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43459 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. *Final positional and equivalent isotropic thermal parameters for the non-*H *atoms with e.s.d.'s in parentheses*

$B_{eq} = \frac{4}{3}\sum_i\sum_j \beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

| | $x$ | $y$ | $z$ | $B_{eq}$ (Å$^2$) |
|---|---|---|---|---|
| F(21*A*) | 0·6857 (1) | 0·4417 (2) | 0·2203 (5) | 6·0 |
| F(21*B*) | 0·7451 (2) | 0·5086 (2) | 0·0048 (6) | 7·3 |
| F(21*C*) | 0·7718 (2) | 0·3847 (3) | 0·1698 (6) | 8·5 |
| O(1) | 0·6331 (1) | 0·1779 (2) | −0·8200 (5) | 3·6 |
| O(9) | 0·5228 (1) | 0·1518 (2) | −1·2340 (5) | 4·7 |
| O(13) | 0·6116 (2) | −0·1337 (2) | −1·2526 (6) | 5·5 |
| O(16) | 0·5218 (1) | 0·4312 (3) | −0·2341 (6) | 5·9 |
| N(4) | 0·5678 (1) | 0·3335 (2) | −0·4648 (6) | 3·5 |
| N(10) | 0·6046 (2) | 0·0619 (3) | −1·1961 (6) | 3·9 |
| C(2) | 0·5781 (2) | 0·1793 (3) | −0·9237 (7) | 3·5 |
| C(3) | 0·5394 (2) | 0·2367 (3) | −0·8215 (7) | 3·5 |
| C(3a) | 0·5709 (2) | 0·2730 (3) | −0·6417 (7) | 3·3 |
| C(4a) | 0·6239 (2) | 0·3320 (3) | −0·3591 (7) | 3·4 |
| C(5) | 0·6432 (2) | 0·3799 (3) | −0·1805 (8) | 3·7 |
| C(6) | 0·7015 (2) | 0·3671 (3) | −0·1157 (8) | 3·9 |
| C(7) | 0·7403 (2) | 0·3076 (4) | −0·2242 (8) | 4·5 |
| C(8) | 0·7203 (2) | 0·2577 (3) | −0·4024 (7) | 4·5 |
| C(8a) | 0·6622 (2) | 0·2701 (3) | −0·4727 (8) | 3·6 |
| C(8b) | 0·6266 (2) | 0·2360 (3) | −0·6468 (7) | 3·6 |
| C(9) | 0·5663 (2) | 0·1284 (3) | −1·1283 (7) | 3·6 |
| C(11) | 0·5937 (2) | 0·0183 (3) | −1·4101 (7) | 4·2 |
| C(12) | 0·5709 (2) | −0·0792 (4) | −1·3809 (9) | 5·0 |
| C(14) | 0·6210 (2) | −0·0933 (4) | −1·0446 (9) | 5·2 |
| C(15) | 0·6456 (2) | 0·0055 (3) | −1·0584 (8) | 4·3 |
| C(16) | 0·5174 (2) | 0·3778 (3) | −0·3840 (8) | 4·2 |
| C(17) | 0·4608 (2) | 0·3565 (3) | −0·5109 (8) | 4·1 |
| C(18) | 0·4051 (2) | 0·3928 (3) | −0·3993 (9) | 4·5 |
| C(19) | 0·3527 (2) | 0·3822 (4) | −0·558 (1) | 6·6 |
| C(20) | 0·3953 (3) | 0·3427 (6) | −0·189 (1) | 9·1 |
| C(21) | 0·7258 (2) | 0·4247 (4) | 0·0707 (9) | 5·0 |

Table 2. *Bond distances* (Å) *and angles* (°) *for the non-*H *atoms*

| | | | |
|---|---|---|---|
| F(21*A*)–C(21) | 1·330 (6) | F(21*B*)–C(21) | 1·341 (7) |
| F(21*C*)–C(21) | 1·328 (7) | O(1)–C(2) | 1·391 (5) |
| O(1)–C(8b) | 1·367 (5) | O(9)–C(9) | 1·219 (6) |
| O(13)–C(12) | 1·435 (7) | O(13)–C(14) | 1·424 (7) |
| O(16)–C(16) | 1·204 (6) | N(4)–C(3a) | 1·398 (6) |
| N(4)–C(4a) | 1·418 (6) | N(4)–C(16) | 1·403 (6) |
| N(10)–C(9) | 1·356 (6) | N(10)–C(11) | 1·480 (6) |
| N(10)–C(15) | 1·487 (6) | C(2)–C(3) | 1·364 (6) |
| C(2)–C(9) | 1·481 (6) | C(3)–C(3a) | 1·411 (6) |
| C(3a)–C(8b) | 1·368 (6) | C(4a)–C(5) | 1·365 (7) |
| C(4a)–C(8a) | 1·432 (7) | C(5)–C(6) | 1·383 (7) |
| C(6)–C(7) | 1·403 (7) | C(6)–C(21) | 1·513 (7) |
| C(7)–C(8) | 1·383 (7) | C(8)–C(8a) | 1·387 (7) |
| C(8a)–C(8b) | 1·419 (7) | C(11)–C(12) | 1·498 (7) |
| C(14)–C(15) | 1·521 (7) | C(16)–C(17) | 1·520 (7) |
| C(17)–C(18) | 1·539 (7) | C(18)–C(19) | 1·532 (9) |
| C(18)–C(20) | 1·50 (1) | | |

| | | | |
|---|---|---|---|
| C(2)–O(1)–C(8b) | 104·2 (3) | C(12)–O(13)–C(14) | 111·4 (4) |
| C(3a)–N(4)–C(4a) | 107·1 (4) | C(9)–N(10)–C(11) | 118·3 (4) |
| C(9)–N(10)–C(15) | 126·7 (4) | C(11)–N(10)–C(15) | 112·2 (4) |
| O(1)–C(2)–C(3) | 111·8 (4) | C(2)–C(3)–C(3a) | 105·5 (4) |
| N(4)–C(3a)–C(8b) | 108·5 (4) | C(3)–C(3a)–C(8b) | 107·0 (4) |
| N(4)–C(4a)–C(8a) | 109·1 (4) | C(5)–C(4a)–C(8a) | 121·4 (4) |
| C(4a)–C(5)–C(6) | 117·2 (4) | C(5)–C(6)–C(7) | 122·9 (5) |
| C(6)–C(7)–C(8) | 119·7 (5) | C(7)–C(8)–C(8a) | 118·6 (5) |
| C(4a)–C(8a)–C(8) | 120·2 (5) | C(4a)–C(8a)–C(8b) | 104·2 (4) |
| O(1)–C(8b)–C(3a) | 111·5 (4) | C(3a)–C(8b)–C(8a) | 111·1 (4) |
| O(9)–C(9)–N(10) | 122·6 (4) | N(10)–C(9)–C(2) | 120·2 (4) |
| N(10)–C(11)–C(12) | 109·6 (4) | O(13)–C(12)–C(11) | 110·7 (4) |
| O(13)–C(14)–C(15) | 112·0 (4) | N(10)–C(15)–C(14) | 108·0 (4) |
| F(21*A*)–C(21)–F(21*B*) | 106·2 (4) | F(21*A*)–C(21)–F(21*C*) | 107·2 (4) |
| F(21*A*)–C(21)–C(6) | 112·9 (4) | F(21*B*)–C(21)–F(21*C*) | 105·6 (4) |
| F(21*B*)–C(21)–C(6) | 111·7 (4) | F(21*C*)–C(21)–C(6) | 112·9 (4) |

the three bond angles around N(10) is 357·2°. This indicates the nitrogen orbital is $sp^2$ hybridized and may contribute largely to the formation of a $\pi$ bond between N(10) and the exocyclic $sp^2$-hybridized C(9) atom. Indeed, this bond distance, 1·356 (6) Å, is considerably shorter than the corresponding values of 1·391 Å for the N($sp^3$)–C($sp^2$) bond (Swaminathan *et al.*, 1980) and 1·457 Å for the N($sp^3$)–C($sp^3$) bond (Ponnuswamy & Trotter, 1984). The conformation about the C(2)–C(9) bond [torsion angle O(1)–C(2)–C(9)–N(10) = 14·9 (7)°] may be attributed to a weak intramolecular C–H···O interaction [C(15)···O(1) = 2·888 (6) Å, O(1)···H(15b) = 2·14 (5) Å, C(15)–

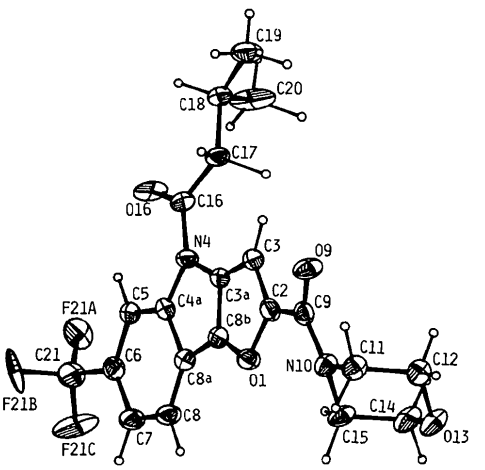


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of the molecule and the numbering for the individual atoms. The thermal ellipsoids are at 30% probability.

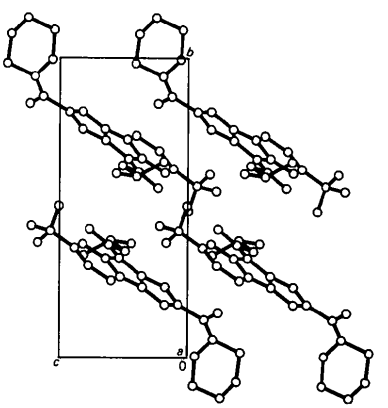


Fig. 2. Molecular packing viewed down the *a* axis. Upper layered molecules are omitted for clarity.

H(15b)···O(1) = 120 (3)°]. The widening of the exocyclic angle C(9)–N(10)–C(15) = 126·7 (4)° can also be attributed to the above interaction.

Bond distances and angles in the trifluoromethyl group are in good agreement with those found in related structures (Murthy & Vijayan, 1979; Lenstra, Gupta, Vanhoeck & Lemière, 1984). Fig. 1 shows that the trifluoromethyl group may possibly rotate around the C(6)–C(21) bond. This is consistent with the observation of relatively high standard deviations of positional and thermal parameters of F(21*A*), F(21*B*) and F(21*C*), and may result in the relatively high *R* value in the present structure analysis. In the isovaleryl substituent, the N(4)–C(16)–C(17)–C(18)–C(19) chain takes approximately a *trans* zigzag conformation with torsion angles of 170·9 (4) and 170·6 (4)°, while C(20) is in a *gauche* position [−65·4 (6)°] against the C(16)–C(17) bond.

Fig. 2 shows the packing of the molecule. The fluoromethyl group is stacked over the furo[2,3-*b*]-indole ring system of the adjacent molecule, where the closest van der Waals contacts of 3·154 (6) and 3·433 (6) Å are between F(21*A*) and C(8a) and between F(21*C*) and C(8).

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# Garuganin-II,* an Antibiotic


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**Abstract.** $C_{22}H_{24}O_5$, $M_r = 368{\cdot}41$, monoclinic, *Pc*, $a = 17{\cdot}180$ (2), $b = 11{\cdot}180$ (2), $c = 10{\cdot}052$ (1) Å, $\beta = 94{\cdot}08$ (1)°, $V = 1925{\cdot}8$ (5) Å$^3$, $Z = 4$, $D_m$(flotation) $= 1{\cdot}25$ (1), $D_x = 1{\cdot}271$ Mg m$^{-3}$, $\lambda$(Cu $K\alpha$) $= 1{\cdot}5418$ Å, $\mu = 0{\cdot}646$ mm$^{-1}$, $F(000) = 784$, $T \simeq 298$ K, $R = 0{\cdot}027$ for 2647 observed reflections. Garuganin-II exists as two independent molecules which are grossly similar. The biphenyl rings are twisted by dihedral angles of 41·4 (1) and 38·6 (1)° in the two molecules. The carbonyl bond at the aliphatic ansa bridge joining the non-adjacent positions of the biphenyl group is nearly equi-inclined (67–77°) to the biphenyl rings.


**Introduction.** Garuganin-II is one of a series of compounds extracted from the plant *Garuga pinnata*. The structures of this molecule and its chemical isomer garuganin-I (Pattabhi, Krishnaswamy & Gabe, 1984) resemble the ansamycin antibiotics (Brufani & Cellai, 1984). The ansamycin antibiotics are macrocyclic antibiotics characterized by an aliphatic ansa bridge joining two non-adjacent positions of an aromatic system. The structure determination of garuganin-II is part of a programme of work on the structure–activity relations of antibiotics.

* IUPAC name: 1-hydroxy-4,6,12-trimethoxytricyclo-[12.3.1.1$^{3,7}$]nonadeca-2(18),3,5,7(19),11,15,17-heptaen-10-one.

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