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6-Amino-2-(fluoromethyl)-3-(2-methylphenyl)quinazolin-4(3*H*)-one

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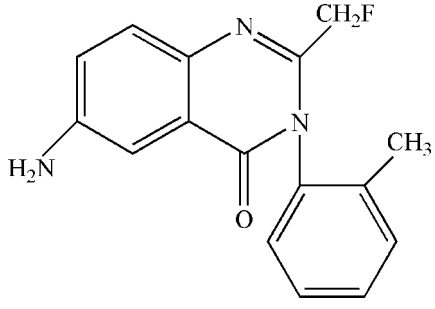
Key indicators: single-crystal X-ray study; T = 291 K; mean σ(C–C) = 0.004 Å; disorder in main residue; R factor = 0.063; wR factor = 0.154; data-to-parameter ratio = 13.5.

In an effort to discover a novel and potent muscle relaxant, the title compound, $C_{16}H_{14}FN_3O$, has been synthesized. In the molecule, the pendant benzene ring is nearly perpendicular to the quinazoline system [dihedral angle = 87.60 (12)°]. Intermolecular N—H···F, N—H···O and C—H···O hydrogen bonding helps to stabilize the crystal structure. The fluoromethyl group shows rotational disorder, equally over two positions.

Related literature

For general background, see: Chou *et al.* (1948); Witt & Bergman (2003); Michael (2005); Tani *et al.* (1979). For related structures, see: Allen *et al.* (1987); Etter (1983); Böcskei *et al.* (1995).



Experimental

Crystal data

$C_{16}H_{14}FN_3O$
M_r = 283.30
Monoclinic, $P2_1/c$
a = 6.3100 (13) Å
b = 12.310 (3) Å
c = 17.658 (4) Å
β = 90.24 (3)°
V = 1371.6 (5) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 291 (2) K
0.30 × 0.26 × 0.24 mm

Data collection

Bruker SMART APEX CCD diffractometer
Absorption correction: none
5223 measured reflections
2691 independent reflections
2172 reflections with $I > 2\sigma(I)$
R_{int} = 0.019

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.063
$wR(F^2)$ = 0.154
S = 1.06
2691 reflections
200 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.39 e Å^{-3}
$\Delta\rho_{min}$ = −0.36 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N3—H3A···O1^{i}	0.86	2.33	3.132 (3)	155
N3—H3C···F2^{ii}	0.90	2.43	3.229 (4)	147
C3—H3···O1^{i}	0.93	2.49	3.294 (3)	145

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

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Bruker, 2000); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

The authors thank the Centre for Testing and Analysis at Nanjing University for the data collection.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: XU2266).

References

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supplementary materials

Acta Cryst. (2007). E**63**, o3109 [**doi:10.1107/S1600536807026670**]

6-Amino-2-(fluoromethyl)-3-(2-methylphenyl)quinazolin-4(3*H*)-one

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Comment

Quninazolin-4(3*H*)-one is an alkaloid (Chou *et al.*, 1948). Due to their biological activity, substituted quinazolin-4(3*H*)-ones represent one of the most interesting groups of heterocycles. In particular, quinazolin-4(3*H*)-one alkaloids such as asperlicin C, possessing cholecystokinin antagonist properties, and benzomalvins, which are neuro-kinin receptor antagonists, have attracted significant attention (Witt & Bergman, 2003; Michael, 2005). A number of derivatives of 6-amino-2-(fluoromethyl)-3-(2-methylphenyl)-3*H*-quinazolin-4-one have aroused considerable interest owing to their potent muscle relaxing activity and low toxicity (Tani *et al.*, 1979).

The title compound (Figure 1) consists of a quinazoline ring with an amino group at C4, a disordered fluoromethyl substitutent at C8 and a 2-methylphenyl group at N1. The quinazoline fragment is nearly planar, with a maximum deviation from the least-squares plane of 0.034 (2) Å. The phenyl ring attached to N1 atom is orthogonal to the quinzaoline plane with a C1—N1—C10—C15 torsion angle of 85.0 (3)°. The bond lengths and bond angles are within the reported values (Allen *et al.*, 1987). The distance of C1—O1 bond (1.203 (3) Å) is significantly shorter than the values for some analogous structures (Etter, 1983; Böcskei *et al.*, 1995).

The fluoromethyl group is disordered over two positions, corresponding to rotation of approximately 120° about the single C8—C9 bond, with a major-minor ratio of about 50:50. Three intermolecular hydrogen bonding (N—H···F, N—H···O and C—H···O) (Table 1), as observed in the packing diagram (Fig. 2), are effective in stabilizing the crystal structure.

Experimental

$SnCl_2{\cdot}2H_2O$ (13.56 g, 60 mmol) was added to a solution of 2-(fluoromethyl)-3-(2-methylphenyl)-6-nitro-3*H*-quinazolin-4-one (3.13 g, 10 mmol) in methanol (150 ml) below 273.15 K. After stirring at room temperature for 12 h, the reaction mixture was poured into ice water (300 ml) and neutralized with $NaHCO_3$ solution. The mixture was extracted with chloroform (600 ml), dried over $MgSO_4$, and then concentrated to dryness *in vacuo*. The crude product was purified by column chromatography on silica gel, eluent is petroleum ether/ethyl acetate (4:1) to give the title compound (yield 1.21 g, 42.6%). The crystals of (I) suitable for X-ray structure determination were obtained from heptane-ethyl acetate mixed solvent at room temperature. Analysis calcd. for $C_{16}H_{14}FN_3O$: C 67.83, H 4.98, N 14.83%; Found: C 67.81, H 4.91, N 14.85%.

Refinement

The fluoromethyl group is disordered over two sites with equal occupancy factors. Amino H atoms were located in a difference Fourier map and other H atoms were placed in calculated positions with C—H = 0.93–0.96 Å, and refined in riding model with U_{iso}(H)=1.2U_{eq}(C,*N*), or 1.5U_{eq}(C) for methyl.

Figures

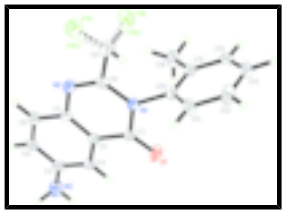

Fig. 1. The molecular structure of (I) (thermal ellipsoids are shown at 30% probability levels).

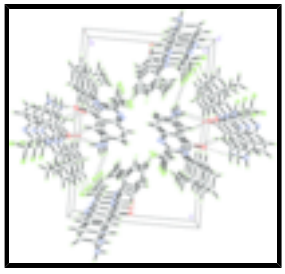

Fig. 2. A packing diagram for (I) (Dashed lines indicate hydrogen bonds).

6-Amino-2-(fluoromethyl)-3-(2-methylphenyl)quinazolin-4(3*H*)-one

Crystal data

$C_{16}H_{14}FN_3O$	F_{000} = 592
M_r = 283.30	D_x = 1.372 Mg m^{-3}
Monoclinic, $P2_1/c$	Melting point: 470 K
Hall symbol: -P 2ybc	Mo $K\alpha$ radiation λ = 0.71073 Å
a = 6.3100 (13) Å	Cell parameters from 732 reflections
b = 12.310 (3) Å	θ = 2.1–25.5º
c = 17.658 (4) Å	μ = 0.10 mm^{-1}
β = 90.24 (3)º	T = 291 (2) K
V = 1371.6 (5) Å^3	Block, yellow
Z = 4	0.30 × 0.26 × 0.24 mm

Data collection

Bruker SMART APEX CCD diffractometer	2172 reflections with $I > 2\sigma(I)$
Radiation source: sealed tube	R_{int} = 0.019
Monochromator: graphite	θ_{max} = 26.0º
T = 291(2) K	θ_{min} = 2.0º
φ and ω scans	h = −7→7
Absorption correction: none	k = −15→15
5223 measured reflections	l = −21→21
2691 independent reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.063$	H-atom parameters constrained
$wR(F^2) = 0.154$	$w = 1/[\sigma^2(F_o^2) + (0.0562P)^2 + 1.1526P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.06$	$(\Delta/\sigma)_{max} < 0.001$
2691 reflections	$\Delta\rho_{max} = 0.39$ e Å^{-3}
200 parameters	$\Delta\rho_{min} = -0.36$ e Å^{-3}
Primary atom site location: structure-invariant direct methods	Extinction correction: none

Special details

Experimental. IR (KBr): 3468, 3369, 3065, 3040, 2956, 2925, 1672, 1628, 1608, 1489, 1357, 1274, 1107, 1030, 838, 761 cm^{-1}; ^{1}HN-MR (*d*-Acetone, 300 MHz): σ 2.13 (s, 3H, CH_3), 4.08 (s, 2H, NH_2), 4.85(s, 1H, CH_2F), 5.01 (s, 1H, CH_2F) 7.15–7.67 (m, 7H, ArH).

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2$sigma(F^2) is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}	Occ. (<1)
C1	0.3272 (4)	0.37992 (19)	0.06660 (14)	0.0351 (5)	
C2	0.2262 (3)	0.29811 (18)	0.01924 (13)	0.0311 (5)	
C3	0.0418 (4)	0.3265 (2)	−0.02108 (14)	0.0378 (6)	
H3	−0.0084	0.3975	−0.0197	0.045*	
C4	−0.0646 (4)	0.2485 (2)	−0.06276 (14)	0.0395 (6)	
C5	0.0130 (4)	0.1430 (2)	−0.06377 (14)	0.0435 (6)	
H5	−0.0587	0.0902	−0.0914	0.052*	
C6	0.1975 (4)	0.1146 (2)	−0.02386 (14)	0.0403 (6)	
H6	0.2497	0.0440	−0.0259	0.048*	
C7	0.3005 (4)	0.19287 (19)	0.01852 (13)	0.0333 (5)	
C8	0.5704 (4)	0.23229 (19)	0.10110 (13)	0.0334 (5)	
C9	0.7671 (5)	0.2024 (2)	0.14313 (18)	0.0559 (8)	
H9A	0.7379	0.1994	0.1964	0.067*	0.50
H9C	0.8160	0.1327	0.1262	0.067*	0.50
H9B	0.8744	0.2560	0.1338	0.067*	

F1	0.8229 (5)	0.1004 (3)	0.1308 (2)	0.0569 (9)	0.50
F2	0.7462 (5)	0.1867 (3)	0.21687 (18)	0.0554 (8)	0.50
C10	0.5861 (3)	0.40942 (19)	0.16752 (14)	0.0346 (6)	
C11	0.7616 (4)	0.4745 (2)	0.15056 (15)	0.0425 (6)	
H11	0.8214	0.4735	0.1025	0.051*	
C12	0.8429 (4)	0.5396 (2)	0.20645 (19)	0.0557 (8)	
H12	0.9575	0.5847	0.1962	0.067*	
C13	0.7555 (5)	0.5383 (2)	0.27761 (17)	0.0523 (8)	
H13	0.8140	0.5810	0.3158	0.063*	
C14	0.5837 (4)	0.4750 (2)	0.29274 (15)	0.0425 (6)	
H14	0.5252	0.4767	0.3410	0.051*	
C15	0.4929 (4)	0.4076 (2)	0.23813 (14)	0.0364 (5)	
C16	0.3045 (5)	0.3415 (3)	0.25512 (18)	0.0569 (8)	
H16A	0.1814	0.3747	0.2329	0.085*	
H16B	0.2867	0.3367	0.3090	0.085*	
H16C	0.3225	0.2699	0.2346	0.085*	
N1	0.5001 (3)	0.33912 (16)	0.10830 (11)	0.0328 (5)	
N2	0.4853 (3)	0.16129 (16)	0.05817 (12)	0.0379 (5)	
N3	−0.2479 (4)	0.2761 (2)	−0.10214 (15)	0.0563 (7)	
H3C	−0.2256	0.2587	−0.1510	0.068*	
H3A	−0.2934	0.3419	−0.1011	0.068*	
O1	0.2752 (3)	0.47363 (14)	0.07204 (12)	0.0544 (6)	

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0318 (12)	0.0284 (12)	0.0451 (14)	0.0018 (9)	−0.0125 (10)	−0.0001 (10)
C2	0.0304 (11)	0.0321 (12)	0.0309 (11)	0.0006 (9)	−0.0084 (9)	0.0007 (9)
C3	0.0352 (12)	0.0393 (13)	0.0389 (13)	0.0000 (10)	−0.0164 (10)	0.0014 (10)
C4	0.0374 (13)	0.0440 (14)	0.0369 (13)	−0.0099 (11)	−0.0137 (10)	0.0058 (11)
C5	0.0550 (16)	0.0387 (14)	0.0365 (13)	−0.0176 (12)	−0.0145 (11)	−0.0029 (11)
C6	0.0457 (14)	0.0305 (12)	0.0447 (14)	−0.0049 (11)	−0.0105 (11)	−0.0040 (10)
C7	0.0303 (11)	0.0342 (12)	0.0352 (12)	−0.0017 (9)	−0.0002 (9)	0.0016 (10)
C8	0.0276 (11)	0.0389 (13)	0.0338 (12)	0.0036 (9)	−0.0015 (9)	−0.0023 (10)
C9	0.0507 (17)	0.0490 (16)	0.068 (2)	0.0209 (13)	−0.0260 (15)	−0.0128 (14)
F1	0.0510 (18)	0.0493 (19)	0.070 (2)	−0.0051 (15)	−0.0137 (16)	−0.0006 (16)
F2	0.0490 (18)	0.069 (2)	0.0482 (19)	−0.0034 (16)	−0.0059 (15)	−0.0051 (16)
C10	0.0257 (11)	0.0329 (12)	0.0450 (14)	0.0122 (9)	−0.0143 (10)	−0.0088 (10)
C11	0.0417 (14)	0.0442 (14)	0.0416 (14)	−0.0082 (11)	−0.0028 (11)	−0.0052 (11)
C12	0.0375 (14)	0.0478 (16)	0.082 (2)	−0.0119 (12)	−0.0077 (14)	−0.0150 (15)
C13	0.0586 (17)	0.0409 (15)	0.0571 (18)	−0.0022 (13)	−0.0304 (15)	−0.0072 (13)
C14	0.0517 (15)	0.0404 (14)	0.0353 (13)	0.0042 (12)	−0.0125 (11)	−0.0020 (11)
C15	0.0309 (11)	0.0343 (12)	0.0440 (14)	0.0076 (9)	−0.0041 (10)	−0.0053 (10)
C16	0.0514 (17)	0.0582 (18)	0.0611 (19)	−0.0227 (14)	0.0034 (14)	−0.0093 (15)
N1	0.0300 (10)	0.0308 (10)	0.0375 (11)	0.0019 (8)	−0.0132 (8)	−0.0031 (8)
N2	0.0386 (11)	0.0300 (10)	0.0450 (12)	0.0034 (8)	−0.0108 (9)	−0.0038 (9)
N3	0.0448 (13)	0.0524 (15)	0.0716 (17)	−0.0076 (11)	−0.0076 (12)	−0.0127 (12)
O1	0.0524 (11)	0.0316 (9)	0.0790 (14)	0.0153 (8)	−0.0330 (10)	−0.0144 (9)

Geometric parameters (Å, °)

C1—O1	1.203 (3)	C9—H9B	0.9600
C1—N1	1.407 (3)	F1—H9C	0.4086
C1—C2	1.454 (3)	F2—H9A	0.3969
C2—C7	1.378 (3)	C10—C15	1.381 (4)
C2—C3	1.406 (3)	C10—C11	1.400 (4)
C3—C4	1.382 (3)	C10—N1	1.460 (3)
C3—H3	0.9300	C11—C12	1.369 (4)
C4—N3	1.389 (3)	C11—H11	0.9300
C4—C5	1.388 (4)	C12—C13	1.375 (4)
C5—C6	1.403 (4)	C12—H12	0.9300
C5—H5	0.9300	C13—C14	1.363 (4)
C6—C7	1.381 (3)	C13—H13	0.9300
C6—H6	0.9300	C14—C15	1.393 (3)
C7—N2	1.412 (3)	C14—H14	0.9300
C8—N2	1.274 (3)	C15—C16	1.473 (4)
C8—N1	1.394 (3)	C16—H16A	0.9600
C8—C9	1.490 (3)	C16—H16B	0.9600
C9—F1	1.322 (4)	C16—H16C	0.9600
C9—F2	1.324 (5)	N3—H3C	0.8999
C9—H9A	0.9601	N3—H3A	0.8599
C9—H9C	0.9599		
O1—C1—N1	120.8 (2)	C8—C9—H9B	109.4
O1—C1—C2	126.2 (2)	H9A—C9—H9B	109.5
N1—C1—C2	113.00 (19)	H9C—C9—H9B	109.5
C7—C2—C3	120.7 (2)	C15—C10—C11	122.9 (2)
C7—C2—C1	120.6 (2)	C15—C10—N1	118.6 (2)
C3—C2—C1	118.6 (2)	C11—C10—N1	118.5 (2)
C4—C3—C2	119.8 (2)	C12—C11—C10	118.4 (3)
C4—C3—H3	120.1	C12—C11—H11	120.8
C2—C3—H3	120.1	C10—C11—H11	120.8
C3—C4—N3	119.9 (2)	C13—C12—C11	120.1 (3)
C3—C4—C5	119.1 (2)	C13—C12—H12	120.0
N3—C4—C5	121.0 (2)	C11—C12—H12	120.0
C4—C5—C6	121.3 (2)	C14—C13—C12	120.6 (3)
C4—C5—H5	119.4	C14—C13—H13	119.7
C6—C5—H5	119.4	C12—C13—H13	119.7
C7—C6—C5	119.1 (2)	C13—C14—C15	122.0 (3)
C7—C6—H6	120.5	C13—C14—H14	119.0
C5—C6—H6	120.5	C15—C14—H14	119.0
C2—C7—C6	120.1 (2)	C10—C15—C14	116.1 (2)
C2—C7—N2	122.3 (2)	C10—C15—C16	122.7 (2)
C6—C7—N2	117.5 (2)	C14—C15—C16	121.2 (2)
N2—C8—N1	124.6 (2)	C15—C16—H16A	109.5
N2—C8—C9	118.4 (2)	C15—C16—H16B	109.5
N1—C8—C9	116.9 (2)	H16A—C16—H16B	109.5
F1—C9—F2	92.9 (3)	C15—C16—H16C	109.5

F1—C9—C8	112.0 (3)	H16A—C16—H16C	109.5
F2—C9—C8	116.1 (3)	H16B—C16—H16C	109.5
F1—C9—H9A	100.1	C8—N1—C1	122.38 (19)
C8—C9—H9A	109.5	C8—N1—C10	120.48 (18)
F2—C9—H9C	102.1	C1—N1—C10	116.64 (18)
C8—C9—H9C	109.5	C8—N2—C7	116.8 (2)
H9A—C9—H9C	109.5	C4—N3—H3C	106.8
F1—C9—H9B	115.9	C4—N3—H3A	119.8
F2—C9—H9B	110.0	H3C—N3—H3A	107.3

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3A···O1^{i}	0.86	2.33	3.132 (3)	155
N3—H3C···F2^{ii}	0.90	2.43	3.229 (4)	147
C3—H3···O1^{i}	0.93	2.49	3.294 (3)	145

Symmetry codes: (i) −*x*, −*y*+1, −*z*; (ii) *x*−1, −*y*+1/2, *z*−1/2.

Fig. 1

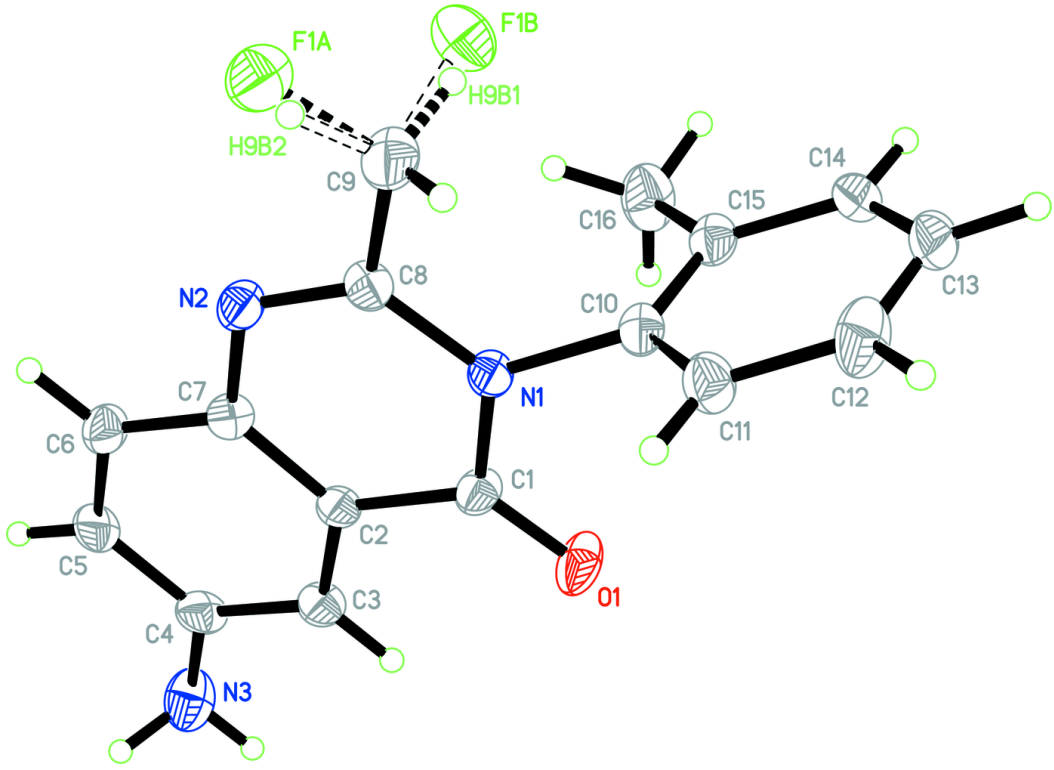
F1A
F1B
H9B1
H9B2
C9
C8
N2
C7
C6
C5
C4
N3
C3
C2
C1
O1
N1
C10
C16
C15
C14
C13
C12
C11

Fig. 2