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4-(3-Chloroanilino)benzoic acid

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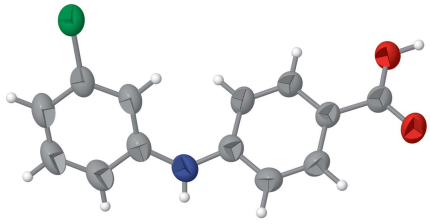
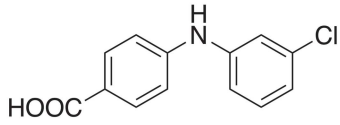
Structural data: full structural data are available from iucrdata.iucr.org

The title compound, $C_{13}H_{10}ClNO_2$, was synthesized by a Buchwald–Hartwig reaction and its crystal structure was investigated for the first time. Crystallization in a variety of solvents led to the discovery of one crystal form. High-quality single crystals were obtained by slow evaporation and the crystal structure was determined by single-crystal X-ray diffraction. The molecules in the crystal structures are highly twisted [the dihedral angle between the aromatic rings is 34.66 (6)°] and pair up to form acid–acid dimers.

3D view



Chemical scheme



Structure description

The title compound (Fig. 1) was first synthesized by Adeniji *et al.* (2011). It is a potent and selective aldo-keto reductase AKR1C2 and AKR1C3 inhibitor, which is efficacious in a prostate cancer model and is a potential therapeutic agent for the treatment of castration-resistant prostate cancer (CRPC) (Adeniji *et al.*, 2012). There is only one molecule in the asymmetric unit of the crystal structure. As a result of the repulsion between the carbon-bonded H atoms *ortho* to NH on both aromatic rings, the molecule is twisted as evidenced by the dihedral angle between the two aromatic rings [34.66 (6)°]. In the crystal, the molecules form acid–acid dimers *via* O—H···O hydrogen bonds (Table 1, Fig. 2).

Synthesis and crystallization

In this work, the title compound was successfully prepared by a Buchwald–Hartwig reaction (Fig. 3) (Hou *et al.*, 2015) using 4-chlorobenzoic acid and 3-chloroaniline as starting materials. Crystallization was conducted by slow evaporation in avariety of solvents in a clean fume hood. Crystals suitable for single-crystal X-ray diffraction (Fig. 4) were obtained by slow evaporation of an acetonitrile solution.

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···O2^{i}	0.90 (4)	1.78 (4)	2.6359 (19)	160 (4)

Symmetry code: (i) $-x+1, -y+1, -z+2$.

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

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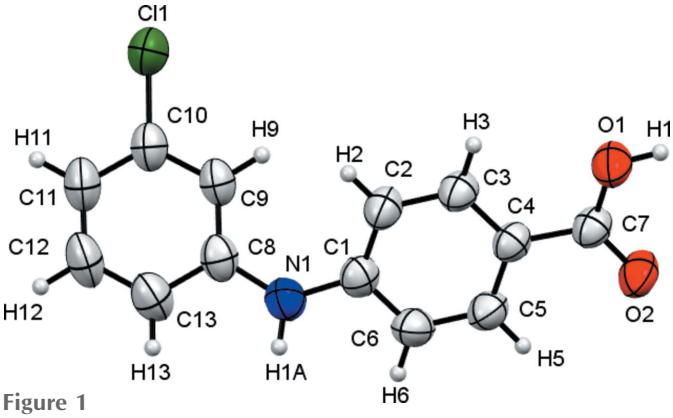

Figure 1
Molecular structure of the title compound generated with *Mercury* (Macrae *et al.*, 2020), with displacement ellipsoids drawn at the 50% probability level.

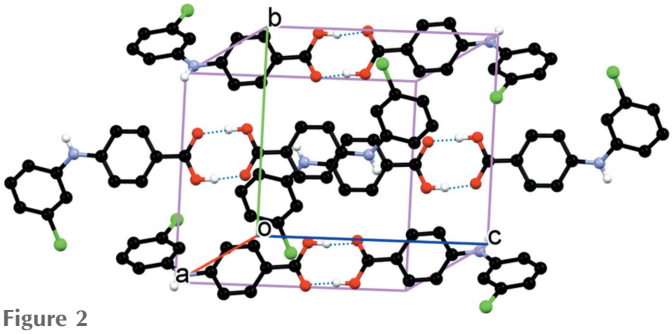

Figure 2
Packing of the molecules of the title compound. For clarity, H atoms bonded to C are omitted.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{13}H_{10}ClNO_2$
M_r	247.67
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	288
a, b, c (Å)	10.8865 (2), 10.31441 (18), 11.0885 (2)
β (°)	113.817 (3)
V (Å^3)	1139.08 (5)
Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	2.88
Crystal size (mm)	0.15 × 0.13 × 0.09
Data collection	
Diffractometer	Rigaku Oxford Diffraction, Synergy Custom system, HyPix
Absorption correction	Multi-scan (*CrysAlis PRO*; Meyer, 2015)
T_{min}, T_{max}	0.375, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	7087, 2278, 2045
R_{int}	0.025
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.633
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.047, 0.143, 1.08
No. of reflections	2278
No. of parameters	162
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.35, −0.37

Computer programs: *CrysAlis PRO* (Rigaku OD, 2022), *SHELXS* (Sheldrick, 2008), *SHELXL2018/3* (Sheldrick, 2015), *Mercury* (Macrae *et al.*, 2020) and *OLEX2* (Dolomanov *et al.*, 2009).

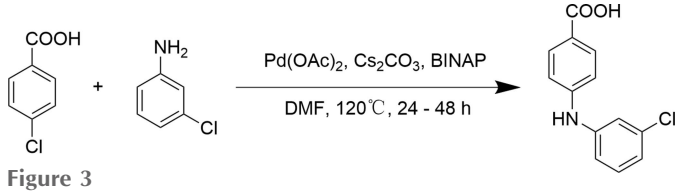

Figure 3
Synthesis of the title compound.

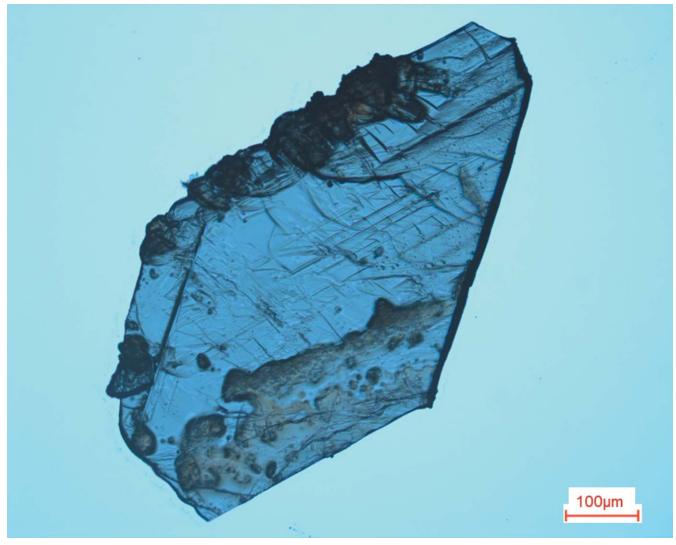

Figure 4
A representative crystal of the title compound.

full crystallographic data

IUCrData (2023). **8**, x230598 [https://doi.org/10.1107/S2414314623005989]

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Crystal data

$C_{13}H_{10}ClNO_2$
M_r = 247.67
Monoclinic, $P2_1/c$
a = 10.8865 (2) Å
b = 10.31441 (18) Å
c = 11.0885 (2) Å
β = 113.817 (3)°
V = 1139.08 (5) Å^3
Z = 4
$F(000)$ = 512
D_x = 1.444 Mg m^{-3}
Cu $K\alpha$ radiation, λ = 1.54184 Å
Cell parameters from 5783 reflections
θ = 4.3–77.1°
μ = 2.88 mm^{-1}
T = 288 K
Block, clear light colourless
0.15 × 0.13 × 0.09 mm

Data collection

Rigaku Oxford Diffraction, Synergy Custom system, HyPix diffractometer
Radiation source: Rotating-anode X-ray tube, Rigaku (Cu) X-ray Source
Mirror monochromator
Detector resolution: 10.0000 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (CrysAlisPro; Rigaku OD, 2022)
T_{min} = 0.375, T_{max} = 1.000
7087 measured reflections
2278 independent reflections
2045 reflections with $I > 2\sigma(I)$
R_{int} = 0.025
θ_{max} = 77.4°, θ_{min} = 4.4°
h = −13→13
k = −12→12
l = −13→14

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.143
S = 1.08
2278 reflections
162 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.085P)^2 + 0.1891P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.35 e Å^{-3}
$\Delta\rho_{min}$ = −0.37 e Å^{-3}

Special details

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

Refinement. The positions of all H atoms were obtained from the difference Fourier map. H atoms bonded to N1 and O1 were freely refined. Other H atoms were positioned geometrically with C—H = 0.93 Å and constraioned to ride on their parent atoms with U_{iso}(H) = 1.2U_{eq}(C).

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
Cl1	1.08885 (6)	0.18033 (6)	0.52451 (6)	0.0806 (3)
O1	0.56772 (18)	0.39086 (13)	0.91797 (17)	0.0746 (4)
H1	0.553 (4)	0.394 (4)	0.992 (4)	0.150 (15)*
O2	0.53662 (16)	0.60395 (13)	0.90499 (15)	0.0729 (4)
N1	0.72634 (17)	0.52920 (19)	0.43865 (17)	0.0663 (4)
C1	0.69502 (16)	0.51613 (18)	0.54768 (17)	0.0547 (4)
C2	0.69426 (18)	0.39841 (17)	0.60907 (19)	0.0583 (4)
H2	0.718984	0.322720	0.579069	0.070*
C3	0.65700 (18)	0.39349 (16)	0.71420 (19)	0.0566 (4)
H3	0.658316	0.314588	0.755293	0.068*
C4	0.61751 (16)	0.50519 (15)	0.75936 (17)	0.0511 (4)
C5	0.61631 (19)	0.62229 (17)	0.69628 (19)	0.0594 (4)
H5	0.588815	0.697547	0.724422	0.071*
C6	0.6552 (2)	0.62786 (19)	0.5931 (2)	0.0634 (5)
H6	0.655065	0.707079	0.552966	0.076*
C7	0.57147 (17)	0.50230 (15)	0.86682 (18)	0.0542 (4)
C8	0.80918 (17)	0.4555 (2)	0.39658 (17)	0.0577 (4)
C9	0.89546 (17)	0.3606 (2)	0.47289 (16)	0.0573 (4)
H9	0.897922	0.340034	0.555486	0.069*
C10	0.97786 (19)	0.2970 (2)	0.42486 (18)	0.0612 (5)
C11	0.9792 (2)	0.3250 (2)	0.3038 (2)	0.0717 (6)
H11	1.035995	0.281079	0.273724	0.086*
C12	0.8938 (2)	0.4199 (3)	0.22921 (19)	0.0781 (6)
H12	0.893432	0.441247	0.147575	0.094*
C13	0.8084 (2)	0.4843 (2)	0.27326 (19)	0.0710 (5)
H13	0.750126	0.547161	0.220491	0.085*
H1A	0.707 (3)	0.599 (2)	0.404 (2)	0.076 (7)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0851 (4)	0.0895 (4)	0.0837 (4)	0.0171 (3)	0.0512 (3)	0.0098 (2)
O1	0.1076 (11)	0.0517 (7)	0.0901 (10)	−0.0001 (7)	0.0662 (9)	−0.0001 (6)
O2	0.0978 (10)	0.0509 (7)	0.0929 (10)	−0.0024 (6)	0.0623 (9)	−0.0109 (6)
N1	0.0644 (9)	0.0749 (11)	0.0663 (10)	0.0075 (8)	0.0333 (8)	0.0120 (8)
C1	0.0453 (8)	0.0623 (10)	0.0569 (9)	−0.0007 (7)	0.0212 (7)	0.0001 (7)
C2	0.0618 (10)	0.0515 (9)	0.0731 (11)	−0.0036 (7)	0.0390 (9)	−0.0076 (7)
C3	0.0606 (9)	0.0455 (8)	0.0723 (10)	−0.0027 (7)	0.0358 (8)	−0.0023 (7)
C4	0.0475 (8)	0.0486 (9)	0.0595 (9)	−0.0019 (6)	0.0240 (7)	−0.0047 (6)
C5	0.0633 (10)	0.0486 (9)	0.0721 (11)	0.0066 (7)	0.0332 (9)	0.0002 (7)
C6	0.0666 (10)	0.0548 (10)	0.0750 (11)	0.0087 (8)	0.0351 (9)	0.0136 (8)

C7	0.0550 (9)	0.0467 (9)	0.0659 (10)	−0.0043 (6)	0.0296 (8)	−0.0070 (7)
C8	0.0507 (8)	0.0720 (11)	0.0533 (9)	−0.0104 (8)	0.0242 (7)	−0.0046 (8)
C9	0.0551 (9)	0.0723 (11)	0.0502 (8)	−0.0082 (8)	0.0273 (7)	−0.0039 (7)
C10	0.0599 (9)	0.0727 (11)	0.0584 (10)	−0.0078 (8)	0.0316 (8)	−0.0064 (8)
C11	0.0725 (12)	0.0946 (15)	0.0601 (10)	−0.0076 (10)	0.0392 (9)	−0.0102 (10)
C12	0.0794 (13)	0.1123 (18)	0.0515 (10)	−0.0099 (12)	0.0357 (9)	−0.0001 (10)
C13	0.0648 (11)	0.0932 (15)	0.0552 (10)	−0.0058 (10)	0.0244 (8)	0.0064 (9)

Geometric parameters (Å, º)

Cl1—C10	1.746 (2)	C4—C7	1.468 (2)
O1—H1	0.90 (4)	C5—H5	0.9300
O1—C7	1.290 (2)	C5—C6	1.372 (3)
O2—C7	1.246 (2)	C6—H6	0.9300
N1—C1	1.389 (2)	C8—C9	1.383 (3)
N1—C8	1.396 (3)	C8—C13	1.396 (3)
N1—H1A	0.80 (3)	C9—H9	0.9300
C1—C2	1.394 (3)	C9—C10	1.380 (3)
C1—C6	1.395 (3)	C10—C11	1.379 (3)
C2—H2	0.9300	C11—H11	0.9300
C2—C3	1.381 (3)	C11—C12	1.374 (3)
C3—H3	0.9300	C12—H12	0.9300
C3—C4	1.392 (2)	C12—C13	1.383 (3)
C4—C5	1.393 (2)	C13—H13	0.9300
C7—O1—H1	115 (3)	O1—C7—C4	117.19 (15)
C1—N1—C8	131.05 (18)	O2—C7—O1	122.19 (16)
C1—N1—H1A	113.1 (18)	O2—C7—C4	120.62 (15)
C8—N1—H1A	114.2 (19)	C9—C8—N1	123.47 (16)
N1—C1—C2	124.18 (17)	C9—C8—C13	118.95 (18)
N1—C1—C6	117.08 (17)	C13—C8—N1	117.50 (19)
C2—C1—C6	118.66 (16)	C8—C9—H9	120.4
C1—C2—H2	119.8	C10—C9—C8	119.14 (16)
C3—C2—C1	120.39 (16)	C10—C9—H9	120.4
C3—C2—H2	119.8	C9—C10—Cl1	118.36 (14)
C2—C3—H3	119.6	C11—C10—Cl1	118.92 (16)
C2—C3—C4	120.79 (16)	C11—C10—C9	122.7 (2)
C4—C3—H3	119.6	C10—C11—H11	121.2
C3—C4—C5	118.60 (16)	C12—C11—C10	117.70 (19)
C3—C4—C7	122.12 (15)	C12—C11—H11	121.2
C5—C4—C7	119.22 (15)	C11—C12—H12	119.4
C4—C5—H5	119.6	C11—C12—C13	121.21 (18)
C6—C5—C4	120.76 (17)	C13—C12—H12	119.4
C6—C5—H5	119.6	C8—C13—H13	119.8
C1—C6—H6	119.6	C12—C13—C8	120.3 (2)
C5—C6—C1	120.78 (17)	C12—C13—H13	119.8
C5—C6—H6	119.6		

Cl1—C10—C11—C12	−178.04 (17)	C4—C5—C6—C1	0.9 (3)
N1—C1—C2—C3	−177.58 (17)	C5—C4—C7—O1	176.54 (17)
N1—C1—C6—C5	176.83 (17)	C5—C4—C7—O2	−2.8 (3)
N1—C8—C9—C10	−177.07 (18)	C6—C1—C2—C3	−1.1 (3)
N1—C8—C13—C12	176.3 (2)	C7—C4—C5—C6	−178.23 (17)
C1—N1—C8—C9	−10.4 (3)	C8—N1—C1—C2	−28.5 (3)
C1—N1—C8—C13	172.68 (19)	C8—N1—C1—C6	155.0 (2)
C1—C2—C3—C4	1.1 (3)	C8—C9—C10—Cl1	178.49 (14)
C2—C1—C6—C5	0.1 (3)	C8—C9—C10—C11	0.8 (3)
C2—C3—C4—C5	0.0 (3)	C9—C8—C13—C12	−0.7 (3)
C2—C3—C4—C7	177.14 (16)	C9—C10—C11—C12	−0.4 (3)
C3—C4—C5—C6	−1.0 (3)	C10—C11—C12—C13	−0.7 (3)
C3—C4—C7—O1	−0.6 (3)	C11—C12—C13—C8	1.2 (3)
C3—C4—C7—O2	−179.92 (17)	C13—C8—C9—C10	−0.2 (3)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O2^{i}	0.90 (4)	1.78 (4)	2.6359 (19)	160 (4)

Symmetry code: (i) −*x*+1, −*y*+1, −*z*+2.