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Isopropyl 2-[2-(2,6-dichloroanilino)-phenyl]acetate

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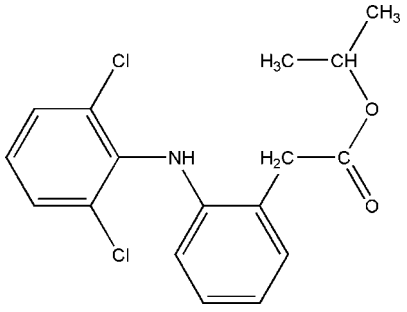
Key indicators: single-crystal X-ray study; T = 123 K; mean σ(C–C) = 0.002 Å; R factor = 0.038; wR factor = 0.093; data-to-parameter ratio = 17.9.

In the title compound, $C_{17}H_{17}Cl_2NO_2$, the NH group exhibits an intramolecular hydrogen bond to the carbonyl O atom and no intermolecular hydrogen bonding, in contrast with previous studies. The dihedral angle between the two benzene rings is 58.57 (5)°. The ester group is planar, the greatest deviation from planarity being 0.0135 (11) Å for the ether O atom.

Related literature

For related literature, see: Abo-Ghalia *et al.* (1999); Alvarez-Larena *et al.* (1992); Corell *et al.* (1979); Evens (1979); Kass (1982); Lipka (1978, 1980); Moser *et al.* (1990); Robinson (1977); Scherrer & Whitehouse (1974).



Experimental

Crystal data

$C_{17}H_{17}Cl_2NO_2$
M_r = 338.22
Monoclinic, $P2_1/c$
a = 17.548 (6) Å
b = 9.443 (3) Å
c = 9.719 (3) Å
β = 93.959 (4)°
V = 1606.7 (9) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.41 mm^{-1}
T = 123 (2) K
0.45 × 0.25 × 0.15 mm

Data collection

Rigaku/MSC Mercury CCD diffractometer
Absorption correction: none
12744 measured reflections
3670 independent reflections
3428 reflections with $I > 2\sigma(I)$
R_{int} = 0.061

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.093
S = 1.10
3670 reflections
205 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.31 e Å^{-3}
$\Delta\rho_{min}$ = −0.32 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1	0.90 (2)	2.05 (2)	2.859 (2)	149 (2)

Data collection: *CrystalClear* (Molecular Structure Corporation & Rigaku, 2001); cell refinement: *CrystalClear*; data reduction: *TEXSAN* (Molecular Structure Corporation & Rigaku, 2004); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97* and *TEXSAN*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: EZ2110).

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supplementary materials

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Isopropyl 2-[2-(2,6-dichloroanilino)phenyl]acetate

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Comment

The anti-phlogistic nonsteroidal anti-inflammatory drug (NSAID) (2-[(2,6-Dichlorophenyl)amino]-phenylacetic acid, common name diclofenac, is a potent *cyclo*-oxygenase inhibitor. It therapeutically interferes with the arachidonic acid cascade prior to the biosynthesis of the inflammatory prostaglandins. Consequently, the drug has a universal anti-phlogistic potency represented by generalized anti-inflammatory, anti-pyretic, anti-rheumatic and analgesic characteristics (Robinson, 1977; Kass, 1982; Evens, 1979; Scherrer & Whitehouse, 1974). However, several undesired side effects of the drug, particularly its ulcerogenicity, frequently restrict its remedial recommendation and it is contra-indicated for patients with a high risk of gastro-intestinal ulcers (Corell *et al.*, 1979). New non-proteinogenic amino acid conjugates of diclofenac have been synthesized and biologically screened for their anti-inflammatory, analgesic and ulcerogenic activity in rats (Abo-Ghalia *et al.*, 1999). We are interested in the synthesis of more potent, less ulcerogenic drugs that hopefully replace diclofenac, and present here the crystal structure of the title compound (I).

The bond lengths and angles in (I) are normal for this kind of molecule (Lipka, 1978, 1980; Moser *et al.*; 1990). The bond angles C(6)—N(1)—H(1) and C(7)—N(1)—H(1) are both 113.0 (1)°. The bond length N(1)—C(7) [1.418 (2) Å] is larger than N(1)—C(6) [1.393 (2) Å] suggesting a greater delocalization of the N lone pair toward the chlorinated ring. The bond lengths C(14)—O(1) [1.209 (2) Å] and C(14)—O(2) [1.333 (2) Å] indicate double and partial double bond character, respectively. The dihedral angle between the two benzene rings is 58.57 (5)°. The N(1)—H(1) is involved in intramolecular H-bonding to the carbonylic O(1) (Alvarez-Larena *et al.*; 1992).

Experimental

Diclofenac sodium (1.0 g, 3.1 mmol) and anhydrous potassium carbonate (1.0 g, 7.2 mmol) were added to dry acetone (30 ml) and the mixture was stirred for 20 min. Neat isopropyl iodide (0.785 ml, 7.83 mmol) in excess was then added and the resulting mixture was heated under reflux for 6 h. The reaction mixture was filtered when hot. The resultant cakes were washed with dry acetone 5 × 2 ml. The combined filtrate and washings were evaporated under reduced pressure to afford compound (I) as an oily material which solidified after 5 d at room temperature (70% yield). Melting point 363–366 K. Block-shaped single crystals were obtained by recrystallization from acetone.

Refinement

The H atom on the N atom was refined isotropically. Other H atoms were placed in idealized positions and treated as riding atoms with the C—H distance in the range 0.95–0.99 Å and U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(C_{methyl}).

Figures

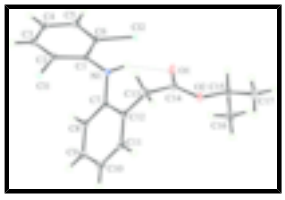


Fig. 1. Molecular structure of (I) showing atom-labelling scheme and displacement ellipsoids at the 30% probability level. The intramolecular hydrogen bond is shown by a dashed line.

Isopropyl 2-[2-(2,6-dichloroanilino)phenyl]acetate

Crystal data

$C_{17}H_{17}Cl_2NO_2$	F_{000} = 704
M_r = 338.22	D_x = 1.398 Mg m^{-3}
Monoclinic, $P2_1/c$	Melting point: 363 K
Hall symbol: -P 2ybc	Mo $K\alpha$ radiation λ = 0.71070 Å
a = 17.548 (6) Å	Cell parameters from 4977 reflections
b = 9.443 (3) Å	θ = 3.0–27.5º
c = 9.719 (3) Å	μ = 0.41 mm^{-1}
β = 93.959 (4)º	T = 123 (2) K
V = 1606.7 (9) Å^3	Block, colorless
Z = 4	0.45 × 0.25 × 0.15 mm

Data collection

Rigaku/MSC Mercury CCD diffractometer	3670 independent reflections
Radiation source: fine-focus sealed tube	3428 reflections with $I > 2\sigma(I)$
Monochromator: graphite	R_{int} = 0.061
Detector resolution: 14.62 pixels mm^{-1}	θ_{max} = 27.5º
T = 123(2) K	θ_{min} = 3.0º
ω scans	h = −16→22
Absorption correction: none	k = −12→12
12744 measured reflections	l = −11→12

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)]$ = 0.038	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2)$ = 0.093	$w = 1/[\sigma^2(F_o^2) + (0.0391P)^2 + 0.7365P]$ where $P = (F_o^2 + 2F_c^2)/3$
S = 1.10	$(\Delta/\sigma)_{max}$ = 0.002

3670 reflections	$\Delta\rho_{max} = 0.31$ e Å^{-3}
205 parameters	$\Delta\rho_{min} = -0.32$ e Å^{-3}
Primary atom site location: structure-invariant direct methods	Extinction correction: none

Special details

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 $F^2 > 2\text{sigma}(F^2)$ 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}
N1	0.20829 (8)	0.00238 (14)	0.81278 (14)	0.0176 (3)
H1	0.2551 (14)	−0.036 (2)	0.822 (2)	0.041 (6)*
C1	0.15347 (8)	−0.07425 (15)	0.87884 (15)	0.0150 (3)
C2	0.07450 (9)	−0.06102 (15)	0.84548 (15)	0.0152 (3)
C3	0.02096 (9)	−0.13894 (16)	0.91175 (16)	0.0178 (3)
H3	−0.0320	−0.1244	0.8893	0.021*
C4	0.04477 (9)	−0.23810 (16)	1.01071 (16)	0.0192 (3)
H4	0.0083	−0.2903	1.0577	0.023*
C5	0.12211 (9)	−0.26066 (17)	1.04063 (16)	0.0188 (3)
H5	0.1390	−0.3313	1.1053	0.023*
C6	0.17464 (8)	−0.17985 (16)	0.97592 (15)	0.0158 (3)
Cl1	0.04071 (2)	0.05250 (4)	0.71474 (4)	0.01864 (11)
Cl2	0.27143 (2)	−0.21169 (4)	1.01691 (4)	0.02223 (11)
C7	0.20896 (8)	0.15202 (16)	0.80276 (15)	0.0163 (3)
C8	0.16317 (9)	0.23666 (17)	0.88131 (16)	0.0185 (3)
H8	0.1321	0.1938	0.9459	0.022*
C9	0.16256 (9)	0.38265 (17)	0.86589 (17)	0.0214 (3)
H9	0.1306	0.4390	0.9189	0.026*
C10	0.20854 (10)	0.44656 (17)	0.77316 (17)	0.0233 (3)
H10	0.2079	0.5465	0.7616	0.028*
C11	0.25537 (9)	0.36304 (17)	0.69773 (16)	0.0214 (3)
H11	0.2874	0.4071	0.6355	0.026*
C12	0.25671 (9)	0.21573 (16)	0.71063 (15)	0.0172 (3)
C13	0.30776 (9)	0.12827 (18)	0.62396 (16)	0.0201 (3)
H13A	0.2779	0.0492	0.5806	0.024*
H13B	0.3262	0.1880	0.5494	0.024*
C14	0.37563 (9)	0.06929 (17)	0.71054 (17)	0.0211 (3)
O1	0.37023 (7)	−0.01740 (15)	0.80056 (15)	0.0362 (3)

O2	0.44207 (6)	0.12335 (12)	0.67675 (11)	0.0209 (2)
C15	0.51089 (9)	0.07400 (18)	0.75893 (17)	0.0225 (3)
H15	0.5055	−0.0287	0.7814	0.027*
C16	0.52004 (11)	0.1592 (2)	0.89044 (19)	0.0337 (4)
H16A	0.5287	0.2588	0.8681	0.051*
H16B	0.5638	0.1231	0.9482	0.051*
H16C	0.4736	0.1509	0.9404	0.051*
C17	0.57594 (10)	0.0941 (3)	0.6674 (2)	0.0390 (5)
H17A	0.5659	0.0396	0.5822	0.059*
H17B	0.6236	0.0611	0.7155	0.059*
H17C	0.5806	0.1948	0.6448	0.059*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0136 (6)	0.0152 (6)	0.0242 (7)	0.0011 (5)	0.0032 (5)	0.0029 (5)
C1	0.0168 (7)	0.0137 (7)	0.0148 (7)	−0.0001 (5)	0.0019 (5)	−0.0018 (5)
C2	0.0168 (7)	0.0130 (7)	0.0156 (7)	0.0017 (5)	−0.0004 (5)	−0.0017 (5)
C3	0.0141 (7)	0.0179 (7)	0.0213 (7)	−0.0011 (6)	0.0013 (6)	−0.0042 (6)
C4	0.0203 (8)	0.0180 (7)	0.0195 (7)	−0.0039 (6)	0.0039 (6)	−0.0009 (6)
C5	0.0234 (8)	0.0165 (7)	0.0163 (7)	0.0000 (6)	0.0005 (6)	0.0007 (6)
C6	0.0134 (7)	0.0171 (7)	0.0165 (7)	0.0015 (6)	−0.0016 (5)	−0.0023 (6)
Cl1	0.01741 (19)	0.01788 (18)	0.02003 (19)	0.00138 (13)	−0.00299 (13)	0.00181 (13)
Cl2	0.01558 (19)	0.0220 (2)	0.0285 (2)	0.00267 (14)	−0.00263 (14)	0.00416 (15)
C7	0.0132 (7)	0.0175 (7)	0.0174 (7)	−0.0012 (6)	−0.0041 (5)	0.0022 (6)
C8	0.0158 (7)	0.0205 (7)	0.0189 (7)	−0.0024 (6)	−0.0016 (6)	−0.0004 (6)
C9	0.0195 (8)	0.0204 (7)	0.0235 (8)	0.0015 (6)	−0.0052 (6)	−0.0043 (6)
C10	0.0270 (9)	0.0158 (7)	0.0258 (8)	−0.0025 (6)	−0.0069 (7)	0.0021 (6)
C11	0.0211 (8)	0.0218 (8)	0.0207 (8)	−0.0054 (6)	−0.0043 (6)	0.0053 (6)
C12	0.0135 (7)	0.0219 (8)	0.0157 (7)	−0.0011 (6)	−0.0034 (5)	0.0022 (6)
C13	0.0151 (7)	0.0260 (8)	0.0191 (7)	−0.0005 (6)	0.0013 (6)	0.0042 (6)
C14	0.0158 (7)	0.0252 (8)	0.0224 (8)	−0.0001 (6)	0.0022 (6)	0.0021 (6)
O1	0.0168 (6)	0.0452 (8)	0.0467 (8)	0.0018 (6)	0.0022 (5)	0.0264 (7)
O2	0.0131 (5)	0.0285 (6)	0.0207 (6)	−0.0007 (4)	−0.0005 (4)	0.0053 (5)
C15	0.0133 (8)	0.0284 (8)	0.0252 (8)	0.0000 (6)	−0.0037 (6)	0.0064 (7)
C16	0.0332 (10)	0.0355 (10)	0.0307 (10)	−0.0012 (8)	−0.0100 (8)	0.0013 (8)
C17	0.0145 (8)	0.0663 (14)	0.0363 (10)	0.0045 (9)	0.0022 (7)	0.0140 (10)

Geometric parameters (Å, °)

N1—C1	1.3952 (19)	C10—C11	1.385 (2)
N1—C7	1.416 (2)	C10—H10	0.9500
N1—H1	0.90 (2)	C11—C12	1.397 (2)
C1—C6	1.405 (2)	C11—H11	0.9500
C1—C2	1.407 (2)	C12—C13	1.516 (2)
C2—C3	1.387 (2)	C13—C14	1.516 (2)
C2—Cl1	1.7354 (15)	C13—H13A	0.9900
C3—C4	1.386 (2)	C13—H13B	0.9900
C3—H3	0.9500	C14—O1	1.207 (2)

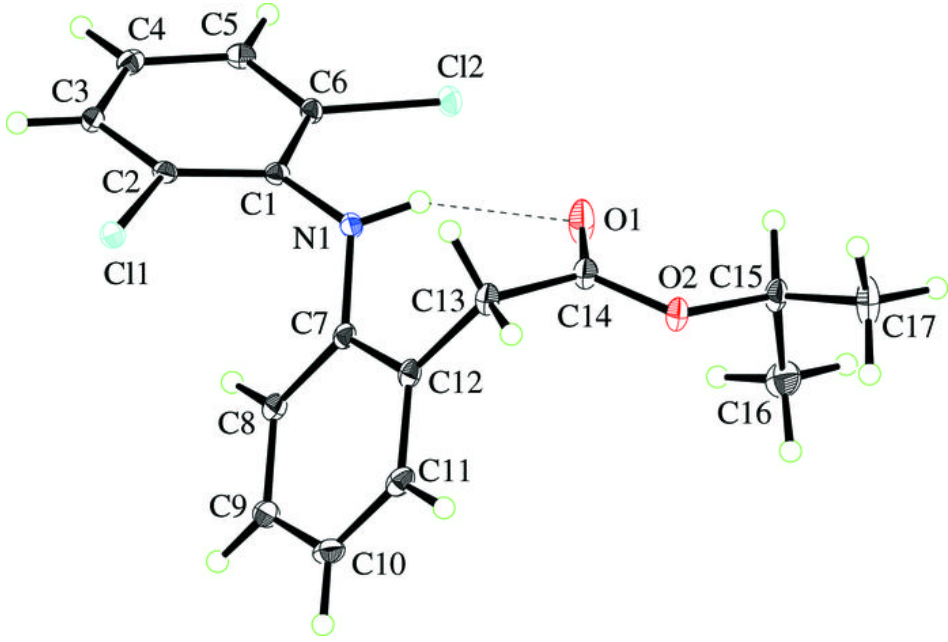
C4—C5	1.385 (2)	C14—O2	1.3344 (19)
C4—H4	0.9500	O2—C15	1.4766 (19)
C5—C6	1.381 (2)	C15—C17	1.507 (2)
C5—H5	0.9500	C15—C16	1.509 (3)
C6—Cl2	1.7438 (16)	C15—H15	1.0000
C7—C8	1.397 (2)	C16—H16A	0.9800
C7—C12	1.403 (2)	C16—H16B	0.9800
C8—C9	1.387 (2)	C16—H16C	0.9800
C8—H8	0.9500	C17—H17A	0.9800
C9—C10	1.388 (2)	C17—H17B	0.9800
C9—H9	0.9500	C17—H17C	0.9800
C1—N1—C7	123.94 (13)	C10—C11—H11	119.1
C1—N1—H1	113.5 (15)	C12—C11—H11	119.1
C7—N1—H1	113.6 (15)	C11—C12—C7	118.50 (14)
N1—C1—C6	121.23 (14)	C11—C12—C13	119.98 (14)
N1—C1—C2	123.19 (14)	C7—C12—C13	121.51 (14)
C6—C1—C2	115.36 (13)	C14—C13—C12	111.31 (13)
C3—C2—C1	122.29 (14)	C14—C13—H13A	109.4
C3—C2—Cl1	117.36 (12)	C12—C13—H13A	109.4
C1—C2—Cl1	120.33 (11)	C14—C13—H13B	109.4
C4—C3—C2	119.96 (14)	C12—C13—H13B	109.4
C4—C3—H3	120.0	H13A—C13—H13B	108.0
C2—C3—H3	120.0	O1—C14—O2	123.47 (15)
C5—C4—C3	119.59 (14)	O1—C14—C13	123.62 (15)
C5—C4—H4	120.2	O2—C14—C13	112.90 (13)
C3—C4—H4	120.2	C14—O2—C15	116.23 (12)
C6—C5—C4	119.65 (14)	O2—C15—C17	105.38 (14)
C6—C5—H5	120.2	O2—C15—C16	108.97 (14)
C4—C5—H5	120.2	C17—C15—C16	113.10 (16)
C5—C6—C1	122.97 (14)	O2—C15—H15	109.8
C5—C6—Cl2	118.09 (12)	C17—C15—H15	109.8
C1—C6—Cl2	118.94 (12)	C16—C15—H15	109.8
C8—C7—C12	119.65 (14)	C15—C16—H16A	109.5
C8—C7—N1	121.69 (14)	C15—C16—H16B	109.5
C12—C7—N1	118.66 (14)	H16A—C16—H16B	109.5
C9—C8—C7	120.67 (15)	C15—C16—H16C	109.5
C9—C8—H8	119.7	H16A—C16—H16C	109.5
C7—C8—H8	119.7	H16B—C16—H16C	109.5
C8—C9—C10	120.12 (15)	C15—C17—H17A	109.5
C8—C9—H9	119.9	C15—C17—H17B	109.5
C10—C9—H9	119.9	H17A—C17—H17B	109.5
C11—C10—C9	119.25 (15)	C15—C17—H17C	109.5
C11—C10—H10	120.4	H17A—C17—H17C	109.5
C9—C10—H10	120.4	H17B—C17—H17C	109.5
C10—C11—C12	121.78 (15)		
C7—N1—C1—C6	−130.59 (16)	N1—C7—C8—C9	−177.48 (14)
C7—N1—C1—C2	55.1 (2)	C7—C8—C9—C10	−0.9 (2)
N1—C1—C2—C3	179.53 (14)	C8—C9—C10—C11	−0.7 (2)

C6—C1—C2—C3	4.9 (2)	C9—C10—C11—C12	1.1 (2)
N1—C1—C2—Cl1	1.1 (2)	C10—C11—C12—C7	0.1 (2)
C6—C1—C2—Cl1	−173.52 (11)	C10—C11—C12—C13	178.82 (14)
C1—C2—C3—C4	−2.7 (2)	C8—C7—C12—C11	−1.7 (2)
Cl1—C2—C3—C4	175.78 (12)	N1—C7—C12—C11	177.93 (13)
C2—C3—C4—C5	−1.3 (2)	C8—C7—C12—C13	179.61 (13)
C3—C4—C5—C6	2.8 (2)	N1—C7—C12—C13	−0.8 (2)
C4—C5—C6—C1	−0.3 (2)	C11—C12—C13—C14	107.44 (16)
C4—C5—C6—Cl2	179.91 (12)	C7—C12—C13—C14	−73.86 (18)
N1—C1—C6—C5	−178.14 (14)	C12—C13—C14—O1	66.2 (2)
C2—C1—C6—C5	−3.4 (2)	C12—C13—C14—O2	−113.82 (15)
N1—C1—C6—Cl2	1.62 (19)	O1—C14—O2—C15	−1.5 (2)
C2—C1—C6—Cl2	176.35 (11)	C13—C14—O2—C15	178.45 (13)
C1—N1—C7—C8	12.6 (2)	C14—O2—C15—C17	155.43 (15)
C1—N1—C7—C12	−166.97 (14)	C14—O2—C15—C16	−82.92 (17)
C12—C7—C8—C9	2.1 (2)		

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O1	0.90 (2)	2.05 (2)	2.859 (2)	149 (2)

Fig. 1


C4
C5
C6
Cl2
C3
C2
C1
N1
O1
Cl1
C13
C14
O2
C15
C17
C7
C12
C8
C16
C11
C9
C10