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The crystal structure of *N*-benzyl-2-chloro-*N*-(*p*-tolyl) acetamide, C₁₆H₁₆ClNO

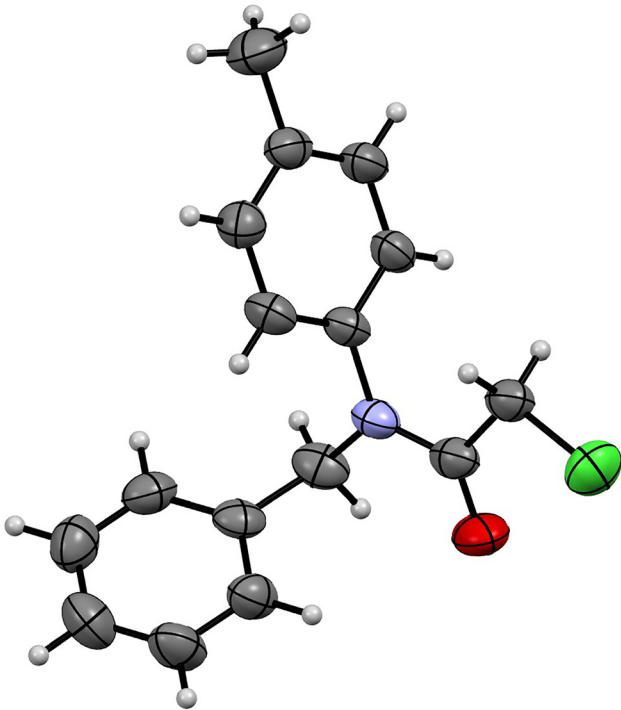


Table 1: Data collection and handling.

Crystal:	Colourless needle
Size:	0.20 × 0.19 × 0.18 mm
Wavelength:	Mo Kα radiation (0.71073 Å)
μ:	0.26 mm ⁻¹
Diffractionmeter, scan mode:	New Gemini, ω
θ _{max} , completeness:	26.1°, >99 %
N(hkl) _{measured} , N(hkl) _{unique} , R _{int} :	5452, 2747, 0.056
Criterion for I _{obs} , N(hkl) _{gt} :	I _{obs} > 2σ(I _{obs}), 2016
N(param) _{refined} :	174
Programs:	SHELX ^{1,2} , OLEX2 ³

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	x	y	z	U _{iso} [*] /U _{eq}
Cl4	1.29708 (10)	0.84145 (12)	0.49615 (6)	0.0744 (4)
O2	0.9871 (3)	0.8763 (3)	0.41374 (13)	0.0681 (7)
N4	0.8798 (3)	0.7564 (2)	0.49972 (13)	0.0464 (5)
C6	1.1470 (3)	0.8030 (3)	0.53936 (16)	0.0506 (6)
H6A	1.1579	0.7058	0.5614	0.061 [*]
H6B	1.1481	0.8703	0.5828	0.061 [*]
C12	0.9055 (3)	0.7800 (3)	0.64340 (16)	0.0481 (6)
H12	0.9127	0.8800	0.6387	0.058 [*]
C15	0.6784 (3)	0.6403 (3)	0.39544 (15)	0.0462 (6)
C17	0.8885 (3)	0.6922 (3)	0.57668 (15)	0.0431 (6)
C19	0.8737 (3)	0.5441 (3)	0.58417 (16)	0.0500 (6)
H19	0.8614	0.4848	0.5394	0.060 [*]
C23	0.9117 (3)	0.7176 (3)	0.71729 (17)	0.0531 (7)
H23	0.9259	0.7766	0.7622	0.064 [*]
C30	0.5576 (3)	0.5591 (4)	0.40520 (16)	0.0545 (7)
H30	0.5099	0.5838	0.4452	0.065 [*]
C32	0.8973 (3)	0.5702 (4)	0.72574 (16)	0.0512 (7)
C34	0.9989 (3)	0.8150 (3)	0.47790 (16)	0.0498 (6)
C35	0.7483 (3)	0.6011 (4)	0.33546 (18)	0.0554 (7)
H35	0.8294	0.6542	0.3281	0.066 [*]
C40	0.8771 (3)	0.4840 (3)	0.65829 (17)	0.0530 (7)
H40	0.8657	0.3845	0.6628	0.064 [*]
C41	0.7304 (3)	0.7707 (3)	0.44685 (18)	0.0545 (7)
H41A	0.7296	0.8540	0.4124	0.065 [*]
H41B	0.6602	0.7896	0.4794	0.065 [*]
C55	0.6977 (4)	0.4840 (4)	0.28679 (19)	0.0672 (9)
H55	0.7454	0.4578	0.2471	0.081 [*]
C59	0.5769 (4)	0.4057 (4)	0.2968 (2)	0.0675 (9)
H59	0.5422	0.3277	0.2633	0.081 [*]
C62	0.9030 (5)	0.5037 (5)	0.8068 (2)	0.0816 (11)
H62A	1.0029	0.5081	0.8390	0.122 [*]
H62B	0.8714	0.4044	0.8001	0.122 [*]
H62C	0.8381	0.5564	0.8326	0.122 [*]
C67	0.5075 (4)	0.4424 (4)	0.3562 (2)	0.0653 (8)
H67	0.4268	0.3885	0.3633	0.078 [*]

<https://doi.org/10.1515/ncrs-2024-0117>
Received March 8, 2024; accepted April 11, 2024;
published online April 24, 2024

Abstract

C₁₆H₁₆ClNO, monoclinic, *P*2₁/*n* (no. 14), *a* = 9.2566 Å, *b* = 9.2270(7) Å, *c* = 17.2231(14) Å, β = 103.745(8)°, *V* = 1428.9(2) Å³, *Z* = 4, *R*_{gt}(*F*) = 0.0655, *wR*_{ref}(*F*²) = 0.2113, *T* = 293 K.

CCDC no.: 2312788

The crystal structure is shown in the figure above. Tables 1 and 2 contain details of the measurement method and a list of atoms including atomic coordinates and displacement parameters (Table 3).

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Table 3: Fractional atomic coordinates and displacement parameters (Å²).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> ₁₁	<i>U</i> ₂₂	<i>U</i> ₃₃	<i>U</i> ₂₃	<i>U</i> ₁₃	<i>U</i> ₁₂
Cl4	12970.8 (10)	8414.5 (12)	4961.5 (6)	0.0697 (6)	0.0874 (7)	0.0750 (6)	−0.0001 (4)	0.0346 (5)	−0.0070 (4)
O2	9871 (3)	8763 (3)	4137.4 (13)	0.0912 (17)	0.0686 (14)	0.0417 (11)	0.0135 (10)	0.0104 (11)	−0.0056 (12)
N4	8798 (3)	7564 (2)	4997.2 (13)	0.0521 (12)	0.0511 (13)	0.0322 (11)	−0.0008 (8)	0.0026 (9)	0.0015 (9)
C6	11470 (3)	8030 (3)	5393.6 (16)	0.0620 (16)	0.0516 (15)	0.0391 (13)	−0.0030 (11)	0.0137 (12)	−0.0019 (11)
C12	9055 (3)	7800 (3)	6434.0 (16)	0.0505 (14)	0.0528 (14)	0.0405 (14)	−0.0118 (11)	0.0099 (11)	−0.0062 (11)
C15	6784 (3)	6403 (3)	3954.4 (15)	0.0404 (12)	0.0621 (15)	0.0319 (12)	0.0046 (10)	0.0005 (9)	0.0099 (10)
C17	8885 (3)	6922 (3)	5766.8 (15)	0.0426 (12)	0.0531 (14)	0.0325 (12)	−0.0062 (10)	0.0067 (9)	0.0024 (10)
C19	8737 (3)	5441 (3)	5841.7 (16)	0.0563 (14)	0.0529 (15)	0.0382 (13)	−0.0081 (11)	0.0060 (11)	0.0036 (11)
C23	9117 (3)	7176 (3)	7172.9 (17)	0.0561 (15)	0.0660 (17)	0.0377 (13)	−0.0100 (12)	0.0123 (11)	−0.0085 (13)
C30	5576 (3)	5591 (4)	4052.0 (16)	0.0525 (15)	0.0726 (18)	0.0405 (14)	0.0116 (12)	0.0151 (11)	0.0060 (13)
C32	8973 (3)	5702 (4)	7257.4 (16)	0.0387 (12)	0.0764 (18)	0.0381 (13)	0.0022 (12)	0.0085 (10)	−0.0063 (11)
C34	9989 (3)	8150 (3)	4779.0 (16)	0.0676 (17)	0.0430 (13)	0.0376 (13)	−0.0016 (10)	0.0100 (12)	0.0018 (11)
C35	7483 (3)	6011 (4)	3354.6 (18)	0.0436 (13)	0.0766 (19)	0.0468 (15)	−0.0052 (14)	0.0124 (11)	−0.0034 (12)
C40	8771 (3)	4840 (3)	6582.9 (17)	0.0532 (14)	0.0553 (15)	0.0494 (15)	0.0026 (12)	0.0100 (12)	−0.0013 (12)
C41	7304 (3)	7707 (3)	4468.5 (18)	0.0545 (16)	0.0577 (15)	0.0460 (15)	0.0004 (12)	0.0013 (12)	0.0151 (12)
C55	6977 (4)	4840 (4)	2867.9 (19)	0.0620 (17)	0.092 (2)	0.0504 (17)	−0.0196 (16)	0.0182 (14)	−0.0033 (16)
C59	5769 (4)	4057 (4)	2968 (2)	0.0608 (18)	0.070 (2)	0.064 (2)	−0.0146 (16)	−0.0001 (15)	−0.0042 (14)
C62	9030 (5)	5037 (5)	8068 (2)	0.089 (3)	0.105 (3)	0.0526 (19)	0.0156 (18)	0.0197 (17)	−0.014 (2)

1 Source of material

Benzaldehyde (1 g, 9.42 mmol) was added to the stirred anhydrous magnesium sulfate (15 g), then dichloromethane (100 ml), finally 4-methylaniline (1.01 g, 9.42 mmol), and the reaction mixture was stirred for 6 h at room temperature. The reaction mixture was filtered and the filtrate was concentrated to obtain the crude product (*E*)-1-phenyl-*N*-(*p*-tolyl)methanimine, light yellow clear oil (1.77 g, yield 96.2 %). To (*E*)-1-phenyl-*N*-(*p*-tolyl)methanimine (1 g, 5.12 mmol) in a solution in anhydrous methanol (150 ml), we slowly added sodium borohydride (0.77 g, 20.48 mmol) for 0.5 h at low temperature, then moved to room temperature for 2 h. The solvent was steamed and dried, and a small amount of dichloromethane and dilute hydrochloric acid were added to regulate pH = 1–2. The product was washed three times with dichloromethane (30 ml), the combined organic phase, dried with anhydrous magnesium sulfate, and steamed to obtain light yellow solid (0.96 g, yield 95.02 %).⁴ We added triethylamine (1.06 ml, 7.60 mmol) to a solution of *N*-benzyl-4-methylaniline (1 g, 5.07 mmol) in dichloromethane (100 ml), and then added chloroacetyl chloride (1.03 g, 9.12 mmol) dropwise after a 0.5 h ice salt bath. After addition, we stabilize at low temperature for 1 h. Transferred to room temperature and stirred for 9 h. Then we extracted the organic layer from a saturated salt aqueous solution and merged the organic layers. We dried with anhydrous magnesium sulfate, filtered, and evaporated the filtrate to

obtain a light yellow solid (1.24 g, yield 89.36 %). The compounds were dissolved in dichloromethane/methanol. The solvent was then slowly volatilized in the air at low temperatures. A few days later, the crystals of the compound were obtained. ¹H-NMR (600 MHz, DMSO-d₆) *d* 7.31–7.27 (m, 2H), 7.26–7.21 (m, 1H), 7.21–7.17 (m, 4H), 7.12–7.08 (m, 2H), 4.86 (s, 2H), 4.06 (s, 2H), 2.29 (s, 3H). ¹³C-NMR (151 MHz, DMSO-d₆) *d* 165.66, 138.14, 136.93, 130.07, 129.22, 128.33, 127.90 (*d*, *J* = 21.8 Hz), 52.66, 42.35, 20.57. MS(ESI):*m/z* = 274.0900 [M+H]⁺; FTIR (KBr, cm^{−1}), 3003.12 (C–H methyl), 2933.69 (C–H methylene), 1668.40 (C=O ketone), 1508.31 (C=C benzene double bonds), 1398.37 (C–N amide bond), 752.23 (C–Cl carbon chlorine single bond).

2 Experimental details

Hydrogen atoms were placed in their geometrically idealized positions and constrained to ride on their parent atoms.

3 Comment

The amide bond is undoubtedly one of the most important structural motifs in nature.^{5,6} Amides are not only restricted to biological systems but also undeniably present in an enormous array of molecules, along with major marketed drugs. In addition, the US FDA approved drugs like imatinib (Bcr-Abl tyrosine-kinase inhibitor), nilotinib (tyrosine-kinase inhibitor), ponatinib (multi-targeted

tyrosine-kinase inhibitor), dasatinib (tyrosine-kinase inhibitor), afatinib (tyrosine kinase inhibitor), methotrexate (dihydrofolate reductase inhibitor) and carfilzomib (selective proteasome inhibitor) which are used for the treatment of different types of cancers also carry amide bond as an indispensable structural motif.⁷ And the acylation of amine is one of the most widely practiced reactions in the pharmaceutical industry.⁸ The crystal molecular packing of the title compound was formed by hydrogen bonds and van der Waals interactions. The hydrogen bond in the molecular structure of the target compound includes one intramolecular C41–H41A...O2 (2.750 Å) hydrogen bond. The above mentioned interactions play an important role in the stability of the crystal structure. Geometric parameters are all in the expected ranges.⁹

Author contribution: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: This work was supported by the Excellent youth project of Heilongjiang Natural Science Foundation (YQ2021H027), and the project of Cultivating Young Innovative Talents in Heilongjiang Province (UNPYST-2020056), and National Fund Cultivation Program of Jiamusi University (JMSUGPZR2022-007).

Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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