J Chem Crystallogr (2010) 40:919–923
DOI 10.1007/s10870-010-9763-1

ORIGINAL PAPER

Synthesis, Characterization and Crystal Structure of 2-Nitro-*N*-[2,4-dichlorophenyl]-*N*-(2-methylbenzoyl)benzamide

Aamer Saeed · Shahid Hussain · Naeem Abbas · Michael Bolte

Received: 28 July 2008 / Accepted: 7 May 2010 / Published online: 19 May 2010

Abstract The title benzamide was synthesized in two steps by refluxing N-(2,4-dichlorophenyl)-2-nitrobenzamide with thionyl chloride in dry toluene to afford 2,4-dichloro-N-[chloro(2-nitrophenyl]methylene)benzenamine intermediate followed by treatment with 2-methyl benzoic acid in presence of triethyl amine. The structure was confirmed by spectroscopic and elemental analysis. The crystal structure was determined from single crystal X-ray diffraction data. It crystallizes in the monoclinic space group P 21/c with unit cell dimensions $a = 10.4122(7)$, $b = 12.9613(7)$ and $c = 15.5518(10)$ Å. The dihedral angle between the two aromatic rings is 82.32(4)°. The N2 and N3 nitro groups are oriented with respect to their attached phenyl rings at dihedral angles of 1.97(3)° and 15.73(3)°, respectively.

Keywords X-ray crystallography · 2-Nitro-*N*-aroylbenzamide · Synthesis

Introduction

The benzanilide core is present in compounds with such a wide range of biological activities that it has been called a privileged structure. N-substituted benzamides are well known anticancer compounds and the mechanism of action for N-substituted benzamide-induced apoptosis has been studied, using declopramide as a lead compound [1]. N-substituted benzamides inhibit nuclear factor-B and nuclear factor of activated T cells activity while inducing activator protein 1 activity in T lymphocytes [2]. Various N-substituted benzamides exhibit potent antiemetic activity [3]. *O*-Aryloxylation of N-substituted benzamides induced by the copper(II)/trimethylamine N-oxide system has been studied [4]. N,N-Disubstituted amides constitute an extremely important and rare subclass of amides which are versatile building blocks for the synthesis of a variety of heterocycles as well as exhibit a wide spectrum of bioactivities. N-Alkylated 2-nitrobenzamides are intermediates toward dibenzo[*b*,*e*][1,4]diazepines [5]. N-Acyl-2-nitrobenzamides are precursors towards 2,3-disubstitued 3H-quinazoline-4-ones. Thus, reaction of 2-nitrobenzamides with thionyl chloride affords the imidoyl chloride as an unstable intermediate which is treated directly with Boc-protected amino acids to afford the corresponding chiral N-acyl-2-nitrobenzamide. Reductive cyclization of the latter lead to quinazoline-4-ones without any racemization [6].

The title compound was synthesized in continuation of our interest in the synthesis of novel heterocycles and for the systematic study of its complexation behavior.

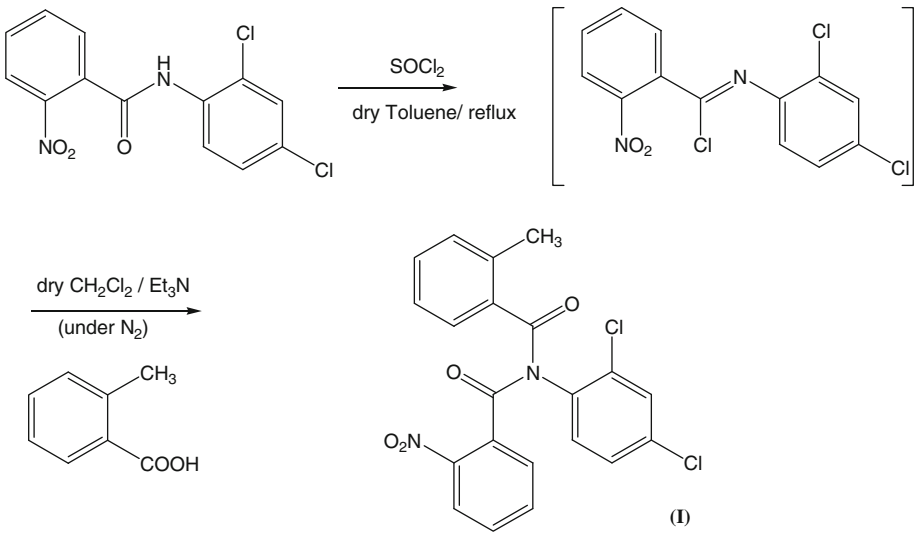
Results and Discussion

The synthesis started with N-(2,4-dichlorophenyl)-2-nitrobenzamide prepared according to procedure reported earlier. It was refluxed with thionyl chloride in dry toluene to afford 2,4-dichloro-N-[chloro(2-nitrophenyl)methylene] benzenamine as air sensitive intermediate which was used as such in the nest step involving treatment with 2-methylbenzoic acid in presence of base to afford in high yield (Scheme 1).

A. Saeed (✉) · S. Hussain · N. Abbas
Department of Chemistry, Quaid-I-Azam University, Islamabad 45320, Pakistan
e-mail: aamersaeed@yahoo.com

M. Bolte
Institut für Anorganische Chemie, J.-W.-Goethe-Universität, Max-von-Laue-Str.7, 60438 Frankfurt, Germany

Scheme 1 Synthesis of 2-nitro-*N*-[2,4-dichlorophenyl]-*N*-(2-methylbenzoyl)benzamide



Absence of IR absorptions for free NH, and absorptions for two carbonyls at 1678 and 1644 was noticed. ^{1}H and ^{13}C-NMR spectra supported the structure.

X-Ray Data Collection and Structure Refinement

Experimental data are listed in Table 1. The atomic coordinates and equivalent isotropic displacement parameters for non-hydrogen atoms are reported in Table 2. The selected bond lengths and angles and hydrogen-bond geometry are given in Tables 3 and 4, respectively. Crystallographic data were recorded on a STOE IPDS-II diffractometer [7] using Mo K_α radiation ($\lambda = 0.71073$ Å) at $T = 173$ K. An absorption correction was applied using the MULABS [8] option in PLATON [9]. The structure was solved by direct methods and refined by full-matrix least-squares using SHELXL-97 against F^2 using all data [10]. All non-H atoms were refined anisotropically. H atoms were positioned geometrically at distances of 0.95 Å (aromatic CH) and 0.98 Å (methyl groups) from the parent C atoms; a riding model was used during the refinement process and the U_{iso}(H) values were constrained to be 1.2 U_{eq}(aromatic C) or 1.5 U_{eq}(methyl C).

The X-ray structural determination of the title compound **1** confirms the assignment of its structure from spectroscopic data. The molecular structure of the title compound **1** along with the atom-numbering scheme is depicted in Fig. 1.

Geometric parameters are in the usual ranges. The central N atom is in a trigonal planar environment. The sum of its bond angles is 359.5°. The nitrophenyl ring makes dihedral angles of 48.9° and 12.8° with the methylphenyl and dichlorophenyl ring. The dihedral angles between the methylphenyl ring and the dichlorophenyl ring is 61.4°. A packing diagram is shown in Fig. 2.

Table 1 Crystal data and structure refinement

Empirical formula	$C_{21}H_{14}Cl_2N_2O_4$
Formula weight	429.24
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P21/c
Unit cell dimensions	
	$a = 10.4122(7)$ Å, $\alpha = 90°$
	$b = 12.9613(7)$ Å, $\beta = 106.986(5)°$
	$c = 15.5518(10)$ Å, $\gamma = 90°$
Volume	2007.2(2) Å^3
Z	4
Density (calculated)	1.420 Mg/m^3
Absorption coefficient	0.354 mm^{-1}
$F(000)$	880
Crystal size	0.49 × 0.47 × 0.47 mm^3
Theta range for data collection	3.75–25.61°
Index ranges	$-9 \le h \le 12$, $-15 \le k \le 15$, $-18 \le l \le 18$
Reflections collected	22,101
Independent reflections	3,749 [$R_{(int)} = 0.0492$]
Completeness to $\theta = 25.00°$	99.6%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8513 and 0.8457
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3749/0/263
Goodness-of-fit on F^2	1.060
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0416$, $wR_2 = 0.1053$
R indices (all data)	$R_1 = 0.0465$, $wR_2 = 0.1089$
Largest diff. peak and hole	0.435 and −0.482 e Å^{-3}

Table 2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$)

	x	*y*	*z*	U(eq)
Cl(1)	2605(1)	4465(1)	818(1)	39(1)
Cl(2)	−451(1)	7849(1)	571(1)	71(1)
N(1)	4856(1)	5778(1)	1971(1)	25(1)
C(1)	5623(2)	5790(1)	1354(1)	27(1)
C(2)	5354(2)	5442(1)	2872(1)	28(1)
N(2)	8147(2)	6795(2)	2427(2)	57(1)
O(1)	5148(1)	6154(1)	612(1)	38(1)
O(2)	6485(2)	5101(1)	3165(1)	50(1)
O(3)	7083(2)	7264(1)	2239(1)	55(1)
O(4)	9182(3)	7130(2)	2948(3)	129(1)
C(11)	6982(2)	5278(1)	1591(1)	27(1)
C(12)	8181(2)	5767(2)	2036(2)	38(1)
C(13)	9423(2)	5302(2)	2158(2)	52(1)
C(14)	9476(2)	4325(2)	1833(2)	51(1)
C(15)	8304(2)	3811(2)	1395(1)	44(1)
C(16)	7056(2)	4289(2)	1265(1)	35(1)
C(21)	4427(2)	5551(1)	3445(1)	26(1)
C(22)	4740(2)	6272(1)	4150(1)	29(1)
C(23)	3898(2)	6326(2)	4701(1)	40(1)
C(24)	2801(2)	5680(2)	4573(2)	47(1)
C(25)	2517(2)	4963(2)	3886(2)	45(1)
C(26)	3328(2)	4895(2)	3315(1)	36(1)
C(27)	5959(2)	6964(2)	4315(2)	44(1)
C(31)	3560(2)	6274(1)	1650(1)	24(1)
C(32)	2458(2)	5746(1)	1102(1)	27(1)
C(33)	1222(2)	6230(2)	769(1)	34(1)
C(34)	1105(2)	7252(2)	995(1)	36(1)
C(35)	2183(2)	7803(2)	1533(1)	33(1)
C(36)	3413(2)	7306(1)	1855(1)	28(1)

U(eq) is defined as one-third of the trace of the orthogonalized Uij tensor

Experimental

Melting points were recorded using a digital Gallenkamp (SANYO) model MPD.BM 3.5 apparatus and are uncorrected. ^{1}H-NMR (300 MHz) spectra were determined in $CDCl_3$ at 300 MHz using a Bruker machine. FTIR spectra were recorded on an FTS 3000 MX spectrophotometer. Mass Spectra (EI, 70 eV) on a MAT 312 instrument, and elemental analyses were conducted using a LECO-183 CHNS analyzer.

Synthesis of 2-Nitro-*N*-(2,4-dichlorophenyl)-*N*-(2-methylbenzoyl)benzamide

Thionyl chloride (0.12 mol) was added dropwise to a stirred solution of 2-nitro-*N*-(2, 4-dichlorophenyl)benzamide

Table 3 Bond lengths (Å) and angles (°)

Cl(1)–C(32)	1.7362(18)
Cl(2)–C(34)	1.7425(19)
N(1)–C(2)	1.412(2)
N(1)–C(1)	1.417(2)
N(1)–C(31)	1.446(2)
C(1)–O(1)	1.211(2)
C(1)–C(11)	1.508(2)
C(2)–O(2)	1.215(2)
C(2)–C(21)	1.499(3)
N(2)–O(3)	1.222(3)
N(2)–O(4)	1.224(3)
N(2)–C(12)	1.469(3)
C(11)–C(16)	1.389(3)
C(11)–C(12)	1.391(3)
C(12)–C(13)	1.388(3)
C(13)–C(14)	1.371(4)
C(13)–H(13)	0.9500
C(14)–C(15)	1.383(4)
C(14)–H(14)	0.9500
C(15)–C(16)	1.400(3)
C(15)–H(15)	0.9500
C(16)–H(16)	0.9500
C(21)–C(26)	1.392(3)
C(21)–C(22)	1.405(3)
C(22)–C(23)	1.395(3)
C(22)–C(27)	1.514(3)
C(23)–C(24)	1.383(3)
C(23)–H(23)	0.9500
C(24)–C(25)	1.381(4)
C(24)–H(24)	0.9500
C(25)–C(26)	1.395(3)
C(25)–H(25)	0.9500
C(26)–H(26)	0.9500
C(27)–H(27A)	0.9800
C(27)–H(27B)	0.9800
C(27)–H(27C)	0.9800
C(31)–C(32)	1.392(2)
C(31)–C(36)	1.393(2)
C(32)–C(33)	1.388(3)
C(33)–C(34)	1.385(3)
C(33)–H(33)	0.9500
C(34)–C(35)	1.387(3)
C(35)–C(36)	1.390(3)
C(35)–H(35)	0.9500
C(36)–H(36)	0.9500
C(2)–N(1)–C(1)	123.97(15)
C(2)–N(1)–C(31)	121.00(14)
C(1)–N(1)–C(31)	114.51(14)
O(1)–C(1)–N(1)	119.73(16)
O(1)–C(1)–C(11)	119.82(16)

Table 3 Bond lengths (Å) and angles (°)

N(1)–C(1)–C(11)	120.27(15)
O(2)–C(2)–N(1)	121.28(16)
O(2)–C(2)–C(21)	122.19(16)
N(1)–C(2)–C(21)	116.52(15)
O(3)–N(2)–O(4)	122.9(2)
O(3)–N(2)–C(12)	118.85(19)
O(4)–N(2)–C(12)	118.2(2)
C(16)–C(11)–C(12)	117.68(18)
C(16)–C(11)–C(1)	117.75(17)
C(12)–C(11)–C(1)	124.24(17)
C(13)–C(12)–C(11)	122.3(2)
C(13)–C(12)–N(2)	118.1(2)
C(11)–C(12)–N(2)	119.48(18)
C(14)–C(13)–C(12)	119.2(2)
C(14)–C(13)–H(13)	120.4
C(12)–C(13)–H(13)	120.4
C(13)–C(14)–C(15)	120.1(2)
C(13)–C(14)–H(14)	119.9
C(15)–C(14)–H(14)	119.9
C(14)–C(15)–C(16)	120.4(2)
C(14)–C(15)–H(15)	119.8
C(16)–C(15)–H(15)	119.8
C(11)–C(16)–C(15)	120.3(2)
C(11)–C(16)–H(16)	119.9
C(15)–C(16)–H(16)	119.9
C(26)–C(21)–C(22)	120.81(17)
C(26)–C(21)–C(2)	120.09(17)
C(22)–C(21)–C(2)	118.94(16)
C(23)–C(22)–C(21)	117.98(18)
C(23)–C(22)–C(27)	120.84(18)
C(21)–C(22)–C(27)	121.19(17)
C(24)–C(23)–C(22)	121.4(2)
C(24)–C(23)–H(23)	119.3
C(22)–C(23)–H(23)	119.3
C(25)–C(24)–C(23)	120.0(2)
C(25)–C(24)–H(24)	120.0
C(23)–C(24)–H(24)	120.0
C(24)–C(25)–C(26)	120.1(2)
C(24)–C(25)–H(25)	120.0
C(26)–C(25)–H(25)	120.0
C(21)–C(26)–C(25)	119.65(19)
C(21)–C(26)–H(26)	120.2
C(25)–C(26)–H(26)	120.2
C(22)–C(27)–H(27A)	109.5
C(22)–C(27)–H(27B)	109.5
H(27A)–C(27)–H(27B)	109.5
C(22)–C(27)–H(27C)	109.5
H(27A)–C(27)–H(27C)	109.5
H(27B)–C(27)–H(27C)	109.5

Table 3 continued

C(32)–C(31)–C(36)	119.09(16)
C(32)–C(31)–N(1)	120.78(15)
C(36)–C(31)–N(1)	120.07(16)
C(33)–C(32)–C(31)	120.95(17)
C(33)–C(32)–Cl(1)	118.56(14)
C(31)–C(32)–Cl(1)	120.50(13)
C(34)–C(33)–C(32)	118.55(18)
C(34)–C(33)–H(33)	120.7
C(32)–C(33)–H(33)	120.7
C(33)–C(34)–C(35)	122.03(18)
C(33)–C(34)–Cl(2)	118.06(15)
C(35)–C(34)–Cl(2)	119.91(15)
C(34)–C(35)–C(36)	118.46(17)
C(34)–C(35)–H(35)	120.8
C(36)–C(35)–H(35)	120.8
C(35)–C(36)–C(31)	120.91(17)
C(35)–C(36)–H(36)	119.5
C(31)–C(36)–H(36)	11

Table 4 Hydrogen coordinates (×104) and isotropic displacement parameters (Å2 × 103) for (**1**)

	x	*y*	*z*	U(eq)
H(13)	10,225	5,657	2,464	62
H(14)	10,321	4,001	1,909	61
H(15)	8,346	3,130	1,180	53
H(16)	6,257	3,935	954	42
H(23)	4,081	6,819	5,174	48
H(24)	2,243	5,729	4,957	56
H(25)	1,768	4,515	3,801	54
H(26)	3,132	4,405	2,841	43
H(27A)	5,961	7,460	4,791	65
H(27B)	5,928	7,337	3,761	65
H(27C)	6,776	6,544	4,499	65
H(33)	473	5,867	396	41
H(35)	2,083	8,504	1,679	39
H(36)	4,165	7,674	2,220	34

(0.1 mol) in toluene (10 mL) and the reaction mixture refluxed for 4 h. After completion of reaction the contents were concentrated in vacuo and the residue was taken up in dichloromethane (5 mL). The latter was added drop-wise with continuous stirring to a solution of 2-methyl benzoic acid in dichloromethane at 0–5 °C. The reaction mixture was stirred overnight at room temperature. The reaction mixture was quenched and diluted with distilled water, washed with 10% aqueous citric acid followed by $NaHCO_3$, dried over anhydrous sodium sulfate and concentrated in vacuo. The residue was recrystallized from ethanol. Yield

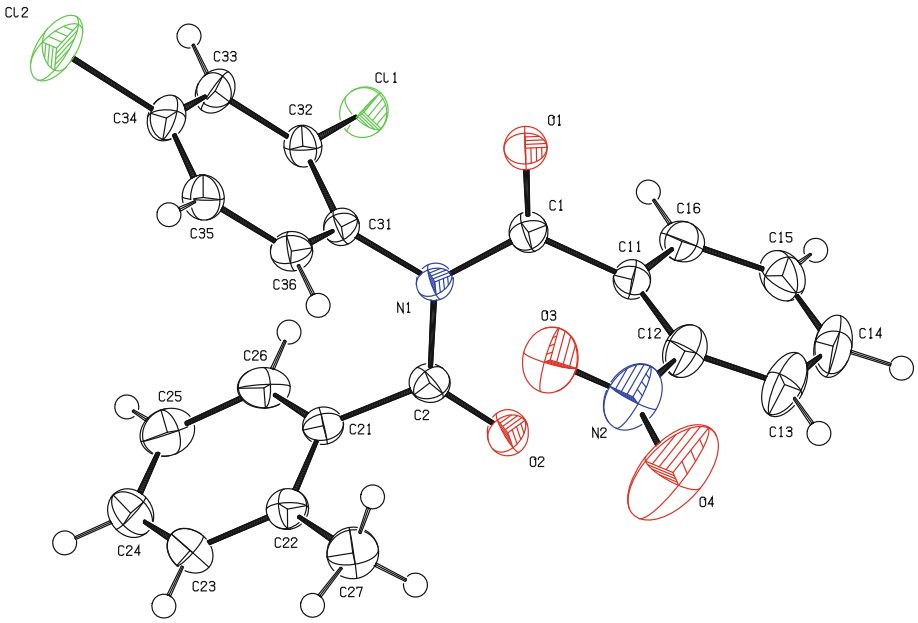


Fig. 1 The molecular structure of the title molecule, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level

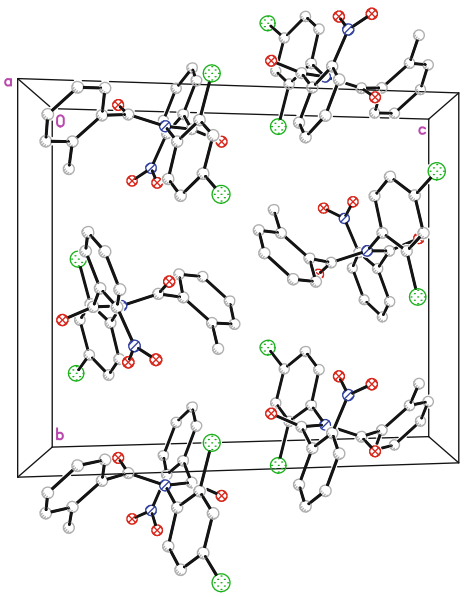


Fig. 2 A packing diagram of (I)

66%; m. p. 122–123 °C; R_f 0.23 *; IR (KBr): ν/cm^{-1} 3021, 1678 (C=O), 1644 (C=O), 1583 (Ar C=C), 1308 (C–N); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.19–8.25 (m, 4H′, Ar–H), 7.25–7.45 (m, 3H, C–Ar–H), 7.12–7.33 (m, 4H″, N–Ar–H), 2.35 (s, 3H, CH_3); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 175.0, 168.2, 163.4, 155.3, 144.5, 144.0, 138.5, 137.0, 136.4, 136.1, 134.5, 129.1, 128.8, 122.0, 49.4, 28.2, 18.9, 17.0. Anal. Calcd. for C 55.9; H 2.7; N 6.52%. Found: C 55.98, H 2.84; N 6.41%.

Supplementary Material

Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre (deposition number: CCDC 691753). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [e-mail: deposit@ccdc.cam.ac.uk].

Acknowledgments Naeem Abbas gratefully acknowledges a research scholarship from HEC Islamabad under HEC Indigenous Ph.D Scholarship 5000 Scheme.

References

1. Olsson AR, Lindgren H, Pero RW, Leanderson T (2002) Br J Cancer 86:971–978
2. Lindgren H, Pero RW, Ivars F, Leanderson T (2001) Mol Immunol 38:267–277
3. Vega-noverola AP, Soto JM, Noguera FP, Mauri JM, Spickett, GWR (1989) USP 4877780
4. Reinaud O, Capdevielle P, Maumy M (1991) J Chem Soc, Perkin Trans 1:2129–2134
5. Zhichkin P, Kesicki E, Treiberg J, Bourdon L, Ronsheim M, Ooi HC, White S, Judkins A, Fairfax D (2007) Org Lett 5:1415–1418
6. Beccalli EM, Broggini G, Paladinoa G, Zonia C (2005) Tetrahedron 61:61–68
7. Stoe & Cie (2001) X-Area. Area-Detector Control and Integration Software. Stoe & Cie, Darmstadt, Germany
8. Blessing RH (1995) Acta Cryst A51:33–38
9. Spek AL (2003) J Appl Cryst A36:7–13
10. Sheldrick GM (2008) Acta Cryst A64:112–122