Journal of Chemical Crystallography, Vol. 33, No. 12, December 2003 (© 2003)

Synthesis, characterization, and crystal structure of 1-(4-chloro-benzoyl)-3-naphthalen-1-yl-thiourea

Hakan Arslan,[(1,2)*] Ulrich Flörke,[(3)] and Nevzat Külcü[(1)]

Received August 19, 2002

1-(4-Chloro-benzoyl)-3-naphthalen-1-yl-thiourea has been synthesized and characterized by elemental analysis, IR spectroscopy, and mass spectrometry. The crystal and molecular structure of the title compound has been determined from single crystal X-ray diffraction data. It crystallizes in the triclinic space group P-1, with $a = 6.962(1)$ Å, $b = 10.770(3)$ Å, $c = 11.738(2)$ Å, $\alpha = 65.76(2)^\circ$, $\beta = 80.03(1)^\circ$, $\gamma = 84.86(2)^\circ$, and $D_{calc} = 1.432\,g\,cm^{-1}$ for $Z = 2$. The thermal behavior of the compound has been studied by DTA and TG. The antibacterial activities of the title compound were investigated for three Gram (+) and two Gram (−) bacteria by employing broth microdilution method and subsequently, inhibitory activity against yeast-like fungi was also determined.

KEY WORDS: Thioureas; synthesis; X-ray structures; DTA/TG; antibacterial activities.

Introduction

The biological activities of the complexes with thiourea derivatives have been well documented and thiourea derivatives have been successfully screened for various biological actions.[1–4] Thiourea derivatives have been found to be useful ligands for the potential determination of traces of the transition metals by means of normal phase chromatography.[5] The complexation capacity of these compounds has been reported in several papers.[5,6] These derivative compounds can induce a large alternation of electronic effects of the ligands and therefore a change of the properties, particularly the redox behavior of the metallic complexes.[7–10]

In previous studies, metal complexes of N, N-dialkyl-N'-benzoylthiourea derivatives having such properties were synthesized and their thermal behaviour was examined.[11–13] On the basis of the literature search, we could not find synthesis and characterization of 1-(4-chloro-benzoyl)-3-naphthalen-1-yl-thiourea (BNT) compound. In this paper we report the preparation, characterization, chemical structural properties, thermal behaviors, decomposition kinetics, and microbiological activities of BNT.

Experimental

Instrumentation

Infrared spectra were recorded in the range 4000–400 cm^{-1} on a Shimadzu 435 spectrophotometer, using KBr pellets. Mass spectra were

[(1)] Department of Chemistry, Faculty of Arts and Sciences, Mersin University, 33343 Mersin, Turkey.
[(2)] School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, Georgia.
[(3)] Department of Inorganic and Analytical Chemistry, University of Paderborn, Paderborn, Germany.
* To whom correspondence should be addressed; e-mail: arslanh@mersin.edu.tr.

1074-1542/03/1200-0919/0

recorded on a VG Autospec, with the FAB technique. Elemental analyses were carried out on a Carlo Erba MOD 1106 instrument. Melting point determinations were performed with a digital melting point instrument from Electrothermal model 9200.

The DTA and TG curves are obtained with Shimadzu DT-40 model simultaneously with DTA and TG apparatus. Experimental data: heating rate, 10 K min^{-1}; atmosphere, nitrogen; flow rate of furnace atmosphere, 60 mL min^{-1}; crucible, Platinum; sample size, 6 mg; reference substance, α-Al_2O_3.

Single crystal X-ray data were collected on a Bruker AXS P4 diffractometer using monochromated Mo K_α radiation. Standard reflections monitored after every 300 reflections showed only random deviations. LP corrections were applied. The structure was solved by direct and conventional Fourier methods. Full-matrix least-squares refinement were based on F^2. Programs used for calculations was SHELXTL[14]. Further details concerning data collection and refinement are given in Table 1.

Table 1. Summary of Crystallographic Data and Parameters of 1-(4-Chloro-Benzoyl)-3-Naphthalen-1-yl-Thiourea

Empirical formula	$C_{18}H_{13}N_2OSCl$
Formula weight	340.81
CCDC deposit no.	CCDC-189945
Temperature	203(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	$a = 6.962(1)$ Å
	$b = 10.770(3)$ Å
	$c = 11.738(2)$ Å
	$\alpha = 65.76(2)^\circ$
	$\beta = 80.03(1)^\circ$
	$\gamma = 84.86(2)^\circ$
Volume	790.2(3) $Å^3$
Z	2
Density (calculated)	1.432 Mg/m^3
Absorption coefficient	0.379 mm^{-1}
$F(000)$	352
Crystal size	$0.50 \times 0.42 \times 0.40$ mm^3
Theta range for data collection	2.07–24.99°
Index ranges	$-1 \le h \le 8, -11 \le k \le 11,$ $-13 \le l \le 13$
Reflections collected	3419
Independent reflections	2695 [$R_{int} = 0.0229$]
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2695/0/209
Goodness-of-fit on F^2	1.065
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0317$, $wR_2 = 0.0782$
R indices (all data)	$R_1 = 0.0348$, $wR_2 = 0.0803$
Largest diff. peak and hole	0.233 and −0.256 e.$Å^{-3}$

Synthesis of the compound

All chemicals used for the preparation of the compound were of reagent grade quality. The compound was obtained in acetone using the method given in the previous study of Arslan *et al.*[15,16] The 4-chloro-benzoylisothiocyanate was obtained from 4-chloro-benzoyl chloride (5×10^{-2} mol) and KSCN (5×10^{-2} mol) at 40°C (30 min). A solution of the naphthalen-1-ylamine was added to the mixture for 15 min at room temperature and stirred for 2 h. The solid organic phase was filtered and recrystallized from ethanol/dichloromethane (1:1).

1-(4-Chloro-benzoyl)-3-naphthalen-1-yl-thiourea (BNT). Color: white. Yield: 87%, m.p. 183–185°C. *Anal.* required for $C_{18}H_{13}N_2OSCl$: C, 63.4; H, 3.8; N, 8.2. Found: C, 63.5; H, 3.9; N, 8.3%. IR (KBr pellet, cm^{-1}): ν(N—H) 3186 (s, br), ν(C═O) 1670 (s). MS(FAB), m/z (%) = 341 (M^{+1}, 100), 185 (37), 139 (40), 201 (25), and 111 (35).

Antimicrobiological activity studies

Antibacterial activities of the compound were tested against Gram (+) and Gram (−) bacteria such as *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853), *Enterococcus faecalis* (ATCC 29212), *Staphylococcus aureus* (ATCC 25923), and *Staphylocccus epidermidis* (ATCC 12228), and the antifungal activities of compounds against some yeast like fungi such as *Candida albicans* (ATCC 90028), *Candida krusei* (ATCC 6258), *Candida glabrata* (ATCC 32554), and *Candida parapsilosis* (ATCC 22019). Minimal inhibitory concentrations

(MICs) were determined by broth microdilution method following the procedures recommended by the National Committee for Clinical Laboratory Standards.[17,18] Amikacin and Flucanozole were used as reference compounds for bacteria and fungi, respectively.

Mueller-Hinton broth (Difco Laboratories, Detroit, MI) was used when testing bacterial strains. For Candida species, Saboraud Dextroz broth (Difco) was used. The inoculum density was 1×10^6 cfu/mL for bacteria and fungi. The compounds under investigation were dissolved in 100% dimethysulfoxide. The solutions in the test medium were furnished the required concentration ranging from 1024 to 0.5 μg/mL. The microtiter plates were incubated at 35°C and read visually after 24 h. For Candida species, incubation period was 48 h. The MIC values were recorded as the lowest concentrations of the substances that had no visible turbidity.

Results and discussion

We herein report the synthesis and full characterization (by elemental analysis, IR spectroscopy, mass spectrometry, and single crystal X-ray diffraction methods) of 1-(4-chloro-benzoyl)-3-naphthalen-1-yl-thiourea. All of the characterization data are in agreement with the molecular structure of 1-(4-chloro-benzoyl)-3-naphthalen-1-yl-thiourea. The IR region between 2900 and 3300 cm^{-1} shows a group of peaks corresponding to the aromatic C—H absorption bands and the N—H stretching vibration is observed in the region around 3186 cm^{-1} as a broad band.

1-(4-Chloro-benzoyl)-3-naphthalen-1-yl-thiourea melts at 458 K with simultaneous decomposition. The first mass loss is observed at 458 K in the TG profile. The DTA/TG/DTG profiles of BNT are shown in Fig. 1. From the TG curve, it appeared that the sample decomposes in two stages over the temperature range 298–675 K. The first decomposition occurs between 298 and 513 K with a mass loss of 69.1% and the second decomposition starts at 513 K and ends at 675 K with a 30.9% mass loss. From the corresponding DTA profile, three endothermic peaks are noted, the first between 458 and 467 K with a maximum at 458 K, second between 467 and 515 K with a maximum at 493 K, and the third between

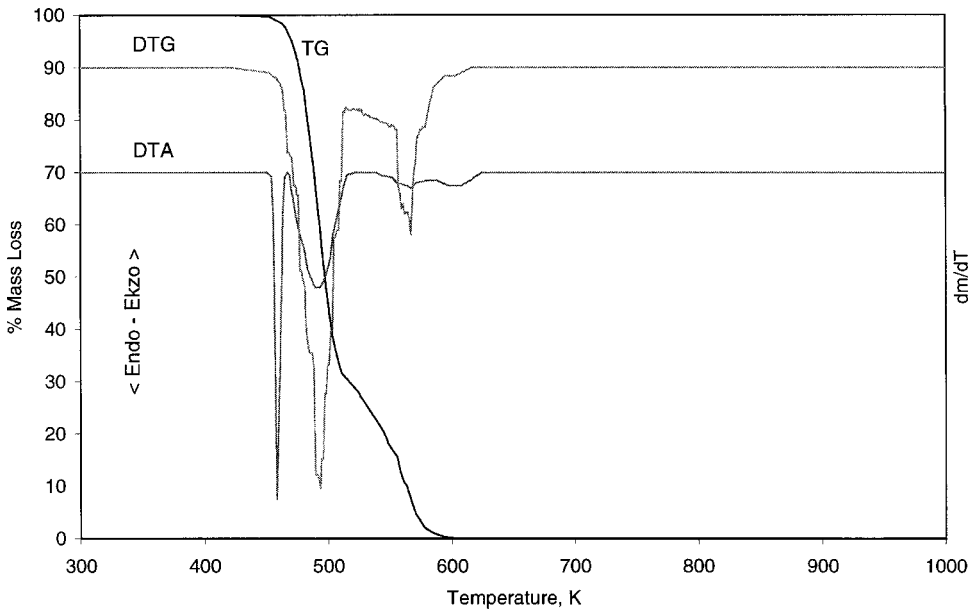

Fig. 1. DTA/TG/DTG diagram of 1-(4-chloro-benzoyl)-3-naphthalen-1-yl-thiourea.

Table 2. Kinetic Data of 1-(4-Chloro-Benzoyl)-3-Naphthalen-1-yl-Thiourea

Stage	Parameters[a]	Coats–Redfern method	Horowitz–Metzger method
I	E^*	155.4	158.8
	A	3.3×10^{14}	5.7×10^{14}
	ΔS^*	28.8	33.2
	r	0.9991	0.9993
II	E^*	101.5	100.9
	A	1.5×10^{7}	1.5×10^{7}
	ΔS^*	−86.1	−112.6
	r	0.9525	0.9416

[a] Unit of parameters: E^* in kJ mole^{-1}, A in s^{-1}, ΔS^* in J mole^{-1} K^{-1}, r: correlation coefficient of the linear plot.

515 and 676 K with a maximum at 567 K. The end product of the first stage is chloro-benzene radical (·C$_6$H$_4$Cl) and this is confirmed by results of TG and mass spectrum data (111 m/z). In the second stage, chloro-benzene radical undergoes pyrolysis.

Coats–Redfern[19] and Horowitz–Metzger[20] methods were used to evaluate the decomposition kinetics. From the TG curves, activation energy E^*, entropies ΔS^*, and preexponential factor A, of the thermal decomposition have been elucidated. The decomposition kinetic parameters are presented in Table 2.

The molecular structure of 1-(4-chloro-benzoyl)-3-naphthalen-1-yl-thiourea, showing the atom numbering scheme and selected bond lengths and angles are given in Fig. 2 and Table 3, respectively. Table 4 lists the nonhydrogen atomic coordinates. In the molecule the overall

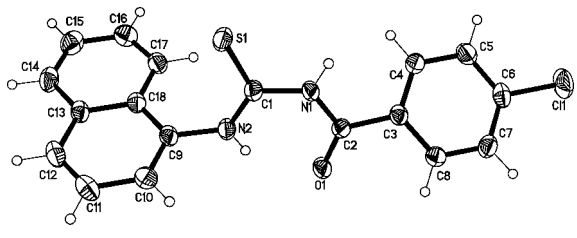

Fig. 2. Molecular structure of BNT in the crystal showing the atom numbering scheme. Thermal ellipsoids are shown at the 50% probability level.

Table 3. Selected Bond Lengths (Å) and Angles (°) of BNT

Bond lengths			
C(1)−N(1)	1.3974(19)	C(2)−O(1)	1.224(2)
C(1)−S(1)	1.6696(17)	C(2)−C(3)	1.488(2)
C(1)−N(2)	1.327(2)	N(2)−C(9)	1.4408(19)
N(1)−C(2)	1.377(2)	C(6)−Cl	1.7372(16)
Bond Angles			
N(2)−C(1)−N(1)	116.72(14)	C(1)−N(1)−C(2)	128.11(13)
N(2)−C(1)−S(1)	124.47(12)	N(1)−C(2)−O(1)	122.77(14)
C(9)−N(2)−C(1)	123.59(13)	N(1)−C(2)−C(3)	115.88(13)
C(2)−C(3)−C(4)	121.68(14)	N(2)−C(9)−C(10)	118.36(14)

bond lengths and angles in the naphthalene, substituted benzene, and the thiourea moiety are as expected, i.e. C(1)−S(1) bond length of 1.6696(17) Å and C(2)−O(1) of 1.224(2) Å, both typical double bonds for thiourea derivatives. The C−N bond lengths are all shorter than normal C−N single bond lengths of 1.479 Å[16],

Table 4. Atomic Coordinates (10^4) and Equivalent Isotropic Displacement Parameters (10^3 Å^2) for BNT

	x/a	y/b	z/c	U_{eq}^a
Cl(1)	14556(1)	3295(1)	−3678(1)	51(1)
S(1)	3018(1)	226(1)	1435(1)	35(1)
O(1)	5872(2)	4337(1)	−844(1)	34(1)
N(1)	5626(2)	2030(1)	−127(1)	27(1)
N(2)	3132(2)	2848(1)	986(1)	28(1)
C(1)	3918(2)	1793(2)	750(1)	27(1)
C(2)	6550(2)	3247(2)	−841(1)	26(1)
C(3)	8473(2)	3160(2)	−1591(1)	25(1)
C(4)	9792(2)	2094(2)	−1120(2)	29(1)
C(5)	11662(2)	2126(2)	−1769(2)	32(1)
C(6)	12183(2)	3226(2)	−2895(2)	32(1)
C(7)	10882(2)	4281(2)	−3399(2)	33(1)
C(8)	9028(2)	4256(2)	−2736(2)	30(1)
C(9)	1324(2)	2790(2)	1815(2)	27(1)
C(10)	−311(2)	3357(2)	1288(2)	32(1)
C(11)	−2099(2)	3371(2)	2057(2)	37(1)
C(12)	−2201(2)	2802(2)	3341(2)	36(1)
C(13)	−528(2)	2213(2)	3917(2)	28(1)
C(14)	−616(3)	1614(2)	5244(2)	36(1)
C(15)	1008(3)	1074(2)	5785(2)	39(1)
C(16)	2813(3)	1113(2)	5016(2)	37(1)
C(17)	2967(2)	1653(2)	3732(2)	30(1)
C(18)	1287(2)	2215(2)	3142(2)	26(1)

[a] U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

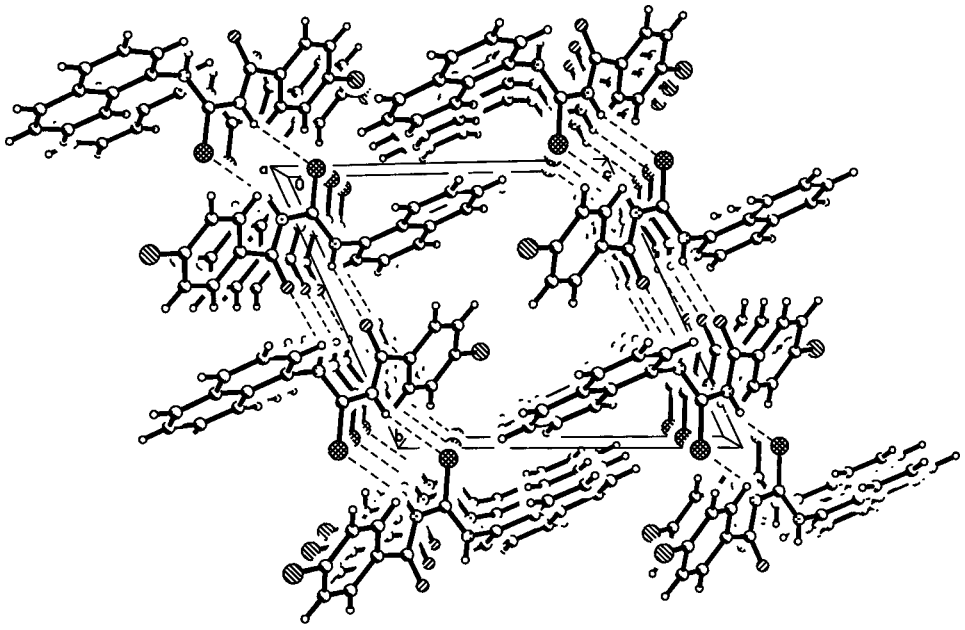

Fig. 3. Crystal packing diagram viewed along [100].

being C(2)−N(1)=1.377(2) Å, C(1)−N(1) = 1.3974(19) Å and C(1)−N(2) = 1.327(2) Å. All the other bond lengths fall within the expected range. The unit H−N(2)−C(1)−N(1)−C(2)−O(1) forms an intramolecular hydrogen bond N(2)−H···O(1) of 1.996 Å (N−H 0.87 Å) to give a six-membered ring; the N(2)−H−O(1) angle is 133.4°. The conformation of the molecule with respect to the thiocarbonyl and carbonyl moieties is definitely twisted as reflected by the torsional angles O(1)−C(2)−N(1)−C(1) and C(2)−N(1)−C(1)−N(2) of −4.8(3)° and −4.2(2)°, respectively.

The crystal packing shows intermolecular hydrogen bonding patterns N(1)−H(1A)···S(1) $(-x+1, -y, -z)$ with H···S 2.420 Å, N−H···S 151.8°; N(2)−H(2A)···O(1) $(-x+1, -y+1, -z)$ with H···O 2.244 Å, N−H···O 139.7°; and C(11)−H(11A)···O(1) $(-x, -y+1, -z)$ with H···O 2.489 Å, C−H···O 155.9°. These values are normalized for N−H 1.030 Å and C−H 1.080 Å. Figure 3 depicts the crystal packing along [100].

Antibacterial activities of the compound were tested against Gram (+) and Gram (−) bacteria. The results obtained from the antibacterial and antifungal efficacy studies were found as: bacteria/fungi (MIC value (μg/mL)/reference MIC value (μg/mL)): *Escherichia coli* (256/1), *Pseudomonas aeruginosa* (128/2), *Enterococcus faecalis* (128/32), *Staphylocccus aureus* (128/4), *Staphylocccus epidermidis* (128/4), *Candida albicans* (256/0.5), *Candida krusei* (256/32), *Candida glabrata* (512/4), and *Candida parapsilosis* (256/2). It was determined that the benzoylthiourea derivative under investigation inhibit the growth of some Gram (+) and Gram (−) bacteria and fungi at different levels but the antibacterial efficacy is better than antifungal activity. The highest MIC value (512 μg/mL) was found against the growth of *Candida glabrata*.

Acknowledgments

This work was supported by Mersin University Research Fund (Project No. FEF.K.HA.99.1).

We thank Dr. N. Duran for the interpretation of antimicrobiological activity.

Supplementary material CCDC-189945 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033; email: deposit@ccdc.cam.ac.uk].

References

1. Frech, F.A.; Blanz, E.J. *Cancer Res.* **1965**, *25*, 1454.
2. Blanz, E.J.; French, F.A. *Cancer Res.* **1965**, *28*, 2419.
3. Frech, F.A.; Blanz, E.J. *J. Med. Chem.* **1966**, *9*, 585.
4. Frech, F.A.; Blanz, E.J.; Amaral, J.R.D.; French, D.A. *J. Med. Chem.* **1970**, *13*, 1117.
5. König, K.H.; Schuster, M.; Schneeweis, G.; Steinbrech, B. *Zeit. Anal. Chem.* **1984**, *319*, 66.
6. Schuster, M.; Kugler, B.; König, K.H. *J. Anal. Chem.* **1990**, *338*, 717.
7. Guttmann, M.; Lubert, K.H.; Beyer, L. *Fresenius J. Anal. Chem.* **1996**, *356*, 263.
8. Shen, X.; Shi, X.; Kang, B.; Tong, Y.; Liu, Y.; Gu, L.; Liu, Q.; Huang, Y. *Polyhedron* **1998**, *18*, 33.
9. Mohamadou, A.; Dechamps-Olivier, I.; Barbier, J.P. *Polyhedron* **1994**, *13*, 3277.
10. Dechamps-Olivier, I.; Guillion, E.; Mohamadou, A.; Barbier, J.P. *Polyhedron* **1996**, *15*, 3617.
11. Özpozan, N.; Özpozan, T.; Arslan, H.; Karipcin, F.; Külcü, N. *Thermochim. Acta* **1999**, *336*, 97.
12. Özpozan, N.; Arslan, H.; Özpozan, T.; Özdeş, N.; Külcü, N. *Thermochim. Acta* **2000**, *343*, 127.
13. Özpozan, N.; Arslan, H.; Özpozan, T.; Merdivan, M.; Külcü, N. *J. Ther. Anal.* **2000**, *61*, 955.
14. Sheldrick, G.M. *SHELXTL, Structure Determination Software Program*, Version 5.10; Bruker Analytical X-ray Systems, Inc.: Madison, WI, 1998.
15. Arslan, H.; Flörke, U.; Külcü, N. *Transit. Metal Chem.* **2003**, *28*, 816.
16. Arslan, H.; Flörke, U.; Külcü, N. *Acta Crystallogr. Sect. E*, **2003**, *E59*, o641.
17. National Committee for Clinical Laboratory Standards. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. Approved Standard, M7-A4; Viallanova, PA, 1997.
18. National Committee for Clinical Laboratory Standards. *Reference Methods for Broth Dilution Antifungal Susceptibility Testing Yeasts*. Approved Standard, M27-A; Viallanova, PA, 1997.
19. Coats, A.W.; Redfern, J. P. *Nature* **1964**, 201, 68.
20. Horowitz, H.H.; Metzger, G. *Anal. Chem.* **1963**, 35, 1464.