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ORIGINAL PAPER

Dual Roles of *N,N*-Dimethylformamide in Benzothiazoles Synthesis from *N*-Benzoyl-*N*′-(2,4,6-trichlorophenyl)thiourea

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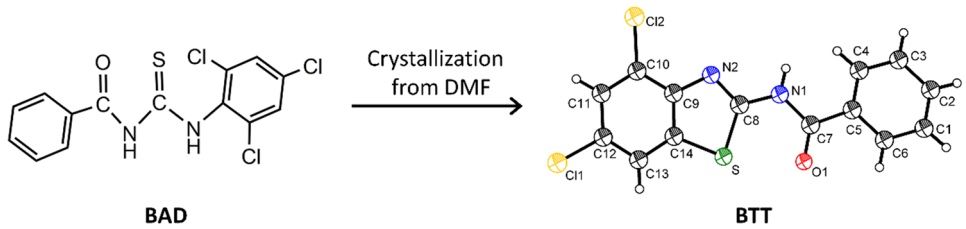
Abstract

N,N-Dimethylformamide (DMF) is not only a common polar solvent in chemistry, but also a reaction reagent, a catalyst and a stabilizer. In this paper, a new reaction was found accidently where DMF acted as both solvent and catalyst. By dissolving *N*-benzoyl-*N*′-(2,4,6-trichlorophenyl)-thiourea (BAD) in DMF and evaporating the solvent slowly, single crystals were obtained but their composition was determined to be 2-benzoylamino-4,6-dichloro-benzothiazole (BTT) with DMF molecule (BTT–DMF), not BAD. The single crystals of BAD could be obtained by crystallization from the solvents of acetonitrile or ethanol. The crystal structures of BAD and BTT–DMF were measured and analysed. Based on the hydrogen bonding interactions in their crystal structures, a possible reaction mechanism was proposed. All in all, DMF is a really multifunctional chemical, it may still have other potential functions which are interesting and valuable to be developed.

Graphic Abstract

A new reaction was found by dissolving *N*-benzoyl-*N*′-(2,4,6-trichlorophenyl)-thiourea (BAD) in DMF and evaporation of the solvent slowly to grow single crystals.



Keywords *N,N*-dimethylformamide · Catalyst · Solvent · Crystal structure · Arylthiourea · Benzothiazole

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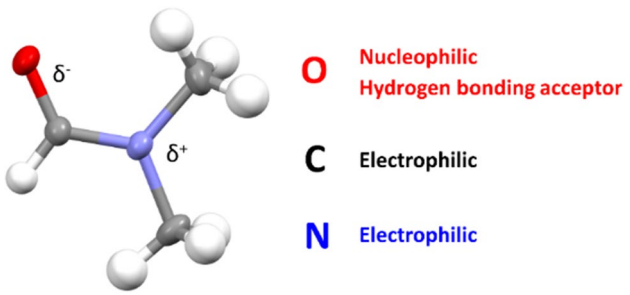
Introduction

N,N-dimethylformamide (DMF) is a common polar solvent with formula of $(CH_3)_2NCHO$. It can dissolve various classes of compounds, and has a high boiling point of 153 °C. Not only as a solvent, DMF also plays other roles in the chemical world, particularly in organic chemistry e.g. as a reaction reagent to supply building block units such as CHO, O, CO, $(CH_3)_2$ and CH_3 [1–3]; as a ligand to form metallic complexes [4]; as a catalyst in organic reactions [5]. In addition, DMF can be used as a stabilizer for preparation of some metal nanoparticles [5, 6]. Why DMF exhibits so many functions? The reason can be found from its unique molecular structure, in which there is a nucleophilic O atom, an electrophilic N atom, an active H atom, and two hydrophobic CH_3 groups (Scheme 1). So, it can act as an electrophilic reagent to attack a nucleus, as well as a nucleophilic reagent to attack an electro-rich atom [1, 5, 7]. Although the steric obstacles of the two methyl groups can block the electrophilic activity of the N atom, the electronegative activity of the O atom is improved due to the pushing electron behavior from the two methyl groups, resulting in the O atom being a good hydrogen bond acceptor [8]. The active H atom in the HC=O group is a good hydrogen bond donor, it can form a relatively stable ring complex with another molecule who has both hydrogen bond donor and acceptor, particularly together with its neighbor O atom [9]. All in all, DMF attracts increasing attention from chemists to study its new functions and applications.

In this paper, a new reaction was found accidently by using DMF as the solvent to grow single crystals of *N*-benzoyl-*N′*-(2,4,6-trichlorophenyl)thiourea (BAD). The BAD was synthesized in acetonitrile with a higher yield than that synthesized in ethanol or DMF. To obtain the BAD single crystals suitable for X-ray diffraction analysis, three solvents were employed to grow its single crystals. We were surprised to find that the chemical composition of the single crystals obtained from DMF was not BAD at all, although the composition of the single crystals from acetonitrile and ethanol were still BAD. A reaction mechanism was proposed mainly based on the analysis of their crystal structures.



Scheme 1 Molecular structure of *N,N*-dimethylformamide

Experimental

Chemicals and Instruments

Analytical grade reagents of *N,N*-Dimethylformamide (DMF, 99.5%) and ethanol (99.7%) were purchased from Tianjin Damao Chemical Reagent Factory (Tianjin, China). Acetonitrile (99.0%) was from Xilong Science Co., Ltd. (Guangdong, China). Benzoic acid (99.5%), sodium thiocyanate (NaSCN, 98%) and benzoyl isothiocyanate (96%) were from J&K Scientific (Shanghai, China). Thionyl chloride ($SOCl_2$, 99%) and 2,4,6-trichlorophenylamine (98%) were bought from Macklin (Shanghai, China). All the reagents were used without further purification.

UV spectra were recorded on Varian Cary 50 UV–Vis spectrophotometer (Agilent Technologies, USA). IR spectra were recorded on a FTIR-Tensor27 spectrophotometer (Bruker, Germany) using KBr discs in the range of 4000–600 cm^{-1}. Mass spectroscopy determination was performed on GCMS-2010 (Shimadzu, Japan). ^1H NMR spectra were recorded on DD2-400MR (Agilent Technologies, USA) using $CDCl_3$ as the solvent. The melting point was determined using a WRS-1B digital melting-point apparatus (Shanghai YiCe Apparatus & Equipment co., LTD, China). The crystal data of the compounds were collected on a CAD4/PC X-ray single crystal diffractometer (Enraf Noius, Netherlands).

Synthesis of BAD and BTT and Their Single Crystals

N-benzoyl-*N′*-(2,4,6-trichlorophenyl)-thiourea (BAD) was synthesized as following procedure: benzoic acid (1.22 g, 0.01 mol) and $SOCl_2$ (7.3 mL, 0.1 mol) were mixed together and refluxed in oil bath (100 °C) for 4 h, then the residual $SOCl_2$ was removed by evaporation under vaccum to get benzoylchloride. The benzolychloride was dissolved in acetonitrile (20 mL), then NaSCN (1.22 g, 0.015 mol) was added at room temperature (25 °C). After removal of unreacted NaSCN by filtration, 2,4,6-trichlorophenylamine (1.96 g, 0.01 mol) dissolved in acetonitrile (5 mL) was added, then the mixture was stirred and refluxed in oil bath (100 °C) for 2 h. After the solvent evaporation under vacuum, crude product (light yellow) was obtained and re-crystallized from acetonitrile. The final product was colorless, yield of 83%.

BAD was also synthesized in ethanol and DMF separately as following procedure. At first, benzoyl isothiocyanate (1.63 g, 0.01 mol) was dissolved into ethanol (or DMF, 20 mL); then, add 2,4,6-trichlorophenylamine (1.96 g, 0.01 mol) dissolved in ethanol (or DMF, 5 mL) with stirring

Table 1 Crystal structure and refinement details

Compound name	*N*-benzoyl-*N*′-(2,4,6-trichlorophenyl)-thiourea	2-benzoylamino-4,6-dichloro-benzothiazole, *N,N*-dimethylformamide
Chemical formula	$C_{28}H_{18}Cl_6N_4O_2S_2$	$C_{14}H_8Cl_2N_2OS,(CH_3)_2NCHO$
CCDC Deposit No.	643496	643497
Color	Colorless	Colorless
Crystal dimensions (mm)	0.40×0.30×0.30	0.30×0.30×0.20
Formula weight	719.28	396.28
Crystal system	Monoclinic	Monoclinic
Space group	P21/n	C2/c
Unit cell dimensions		
a (Å)	7.8170(16)	17.402(4)
b (Å)	36.372(7)	8.1280(16)
c (Å)	10.745(2)	26.551(5)
β (°)	90.96(3)	106.60(3)
Cell volume	3054.6(11)	3599.1(12)
Z	4	8
Density (calculated, g.cm^{-3})	1.564	1.463
Absorption coefficient (mm^{-1})	0.734	0.493
Diffractometer	Nonius CAD4	Nonius CAD4
Radiation	MoKα (*λ* = 0.71073)	MoKα (*λ* = 0.71073)
θ range (°)	1.12–25.99	1.60–25.98
Reflections collected/unique	6437/5994	3526/2176
Range of *h*, *k*, *l*	−9:9, 0:44, 0:13	−21:20, 0:10, 0:32
Absorption correction	Psi-scan	Psi-scan
Data/restraints/parameters	5994/0/379	3526/0/226
Goodness-of-fit on F^2	1.080	1.097
Final R indices [$I > 2\sigma(I)$]	$R = 0.0659$, $wR = 0.1574$	$R = 0.0629$, $wR = 0.1273$
R indices (all data)	$R = 0.1229$, $wR = 0.1928$	$R = 0.1132$, $wR = 0.2024$
Largest feature (e/Å^3)	0.324 and −0.364	0.474 and −0.446
Temperature (K)	293(2)	293(2)

at room temperature; finally, the mixture was heated in oil bath (100 °C) for 2 h. After cooling down, the solvent was removed under vacuum to obtain crude product, which was re-crystallized in acetonitrile. The final yield of BAD was 17% in ethanol and 35% in DMF.

Crystals of 2-benzoylamino-4,6-dichloro-benzothiazole (BTT) with DMF molecules were obtained by the following prodedure. At first, BAD (0.20 g, 0.56 mmol) was dissolved in DMF (10 mL) in a beaker (50 mL); then, the beaker was sealed by cling wrap with several holes and put in the fume-hood at room temperature (25 °C). Colorless crystals presented in the beaker after a week. The crystals were collected by filtration using filter paper until the DMF was evaporated completely. The solid crystals were washed with DMF (2 mL) once and ethanol twice (each time 5 mL) to remove the residues, then dried at room temperature to obtain the crystals of BTT with DMF molecule (BTT–DMF). The pure BTT compound can be obtained by drying at 50 °C for 12 h to remove the DMF in the crystal. Finally, the yield of BTT was ~46%.

Compounds Characterization

Compound BAD: m.p. = 192–193 °C; ^{1}H NMR ($CDCl_3$, *δ*): 12.01 (1H, s, NHCO), 9.38 (1H, s, NHCS), 7.91 (2H, d, ArH), 7.65 (1H, t, ArH), 7.53 (2H, t, ArH), 7.44 (2H, s, ArH); IR (KBr, cm^{-1}, *ν*): 3383 (m), 3355 (m), 3176 (m), 3130 (m), 3086 (m), 1659 (s), 1600 (s), 1580 (s), 1555 (s), 1497 (s), 1382 (m), 1319 (m), 1266 (m), 1188 (m), 1158 (s), 1086 (m). The ^{1}H NMR and IR characterizations agreed with the reference reported [12].

Compound BTT: m.p. = 207–209 °C; ^{1}H NMR ($CDCl_3$, *δ*): 8.02-7.44 (7H, m, ArH); MS (M^+, m/z) = 322; IR (KBr, cm^{-1}, *ν*): 3378 (m), 3077 (m), 1678 (s), 1589 (s), 1538 (s), 1432 (m), 1387 (m), 1283 (m), 1144 (m), 1077 (m). The melting point agreed with the reference reported [18].

Table 2 Hydrogen bond lengths (Å) and bond angles (°)

D–H···A	D–H	H···A	D···A	∠DHA
In the single crystal of BAD				
N1–H1A···O2	0.86	2.38	3.221 (5)	166
N2–H2A···S2^{i}	0.86	2.74	3.369 (5)	131
N2–H2A···O1	0.86	2.03	2.664 (5)	130
N3–H3A···O1^{ii}	0.86	2.52	3.324 (5)	157
N4–H4B···S1	0.86	2.70	3.302 (5)	128
N4–H4B···O2	0.86	2.01	2.681 (5)	134
C1–H1B···Cl5^{iii}	0.93	2.74	3.633 (7)	161
C11–H11A···Cl6^{iv}	0.93	2.81	3.717 (6)	166
In the single crystal of BTT-DMF				
N1–H1A···O2^{v}	0.86	1.96	2.802 (7)	167
C4–H4A···O2^{v}	0.93	2.34	3.181 (9)	150
C6–H6A···O1	0.93	2.46	2.771 (9)	100
C13–H13A···O1^{vi}	0.93	2.51	3.387 (7)	157
C16–H16A···O2	0.96	2.36	2.776 (9)	105
C17–H17A···N2^{v}	0.93	2.50	3.236 (9)	136

Symmetry transformations used to generate the equivalent atoms: i: x, y, 1 + z; ii: x, y, −1 + z; iii: 1/2 + x, 1/2 − y, 1/2 + z; iv: 2 − x, −y, 2 − z; v: −1/2 − x, 1/2 − y, −z; vi: 1/2 − x, 1/2 − y, −z

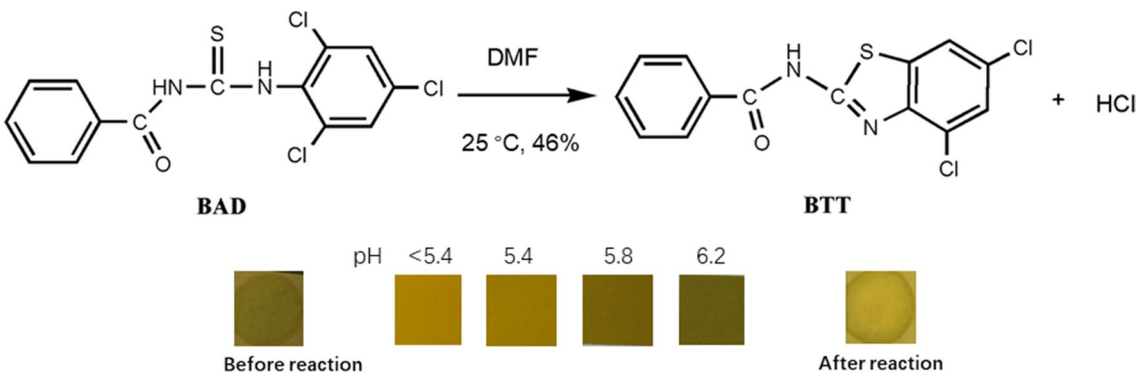
X-Ray Crystallography

The single crystals of BAD or BTT–DMF was mounted on an Enraf–Nonius CAD-4 diffractometer with MoKα radiation ($\lambda = 0.71073$ Å). The angle of the $\omega/2\theta$ scan mode was in the range 1.60°–25.98°. Psi-scan corrections were employed. The crystal structure was resolved by direct methods using SHELX97 software. The non-hydrogen atoms were refined anisotropically and hydrogen atoms isotropically. H atoms were positioned geometrically and treated as riding model, with C–H = 0.93 Å, N–H = 0.86 Å and U_{iso} (H) = 1.2 U_{eq} (C, N). Crystal and structure refinement data is shown in Table 1 and selected hydrogen bond lengths and bond angles are in Table 2.

Results and Discussion

N-benzoyl-*N*′-(2,4,6-trichlorophenyl)thiourea (BAD), which showed potential biological activities [10–12], was synthesized in acetonitrile in a yield of 83%, a little lower than that synthesized in tetrahydrofuran [12]. We also used ethanol and DMF separately as the reaction solvent to synthesize BAD by the same experimental procedure. The yield of BAD was much lower in ethanol (17%) and DMF (35%) comparing with the yield in acetonitrile, demonstrating the reaction solvent can significantly affect the product yield.

In order to obtain the BAD single crystals suitable for X-ray diffraction analysis, different solvents were employed to grow single crystals by solvent evaporation method. We were surprised to find that the chemical composition of the single crystals obtained from DMF was not BAD, although the chemical composition of the single crystals from acetonitrile and ethanol were both still BAD. The BAD single crystals can also be obtained from the mixture of ethanol/dichloromethane (1/1, v/v) [12]. As shown in Scheme 2, BAD was firstly dissolved into DMF, after 7 days of solvent evaporation at room temperature (25 °C), single crystals presented in the solution. The single crystals were collected by filtration using filter paper and determined by X-ray diffraction method. The analytical result demonstrated that the chemical composition in the single crystal was 2-benzoylamino-4,6-dichlorobenzothiazole (BTT) with DMF molecule (BTT–DMF), not BAD at all. To confirm this result, we repeated the recrystallization experiment and measured the pH changes of the solution before and after reaction. Clearly, the pH decreased after the crystallization (Scheme 2), suggesting



Scheme 2 Synthesis of 2-benzoylamino-4,6-dichloro-benzothiazole (**BTT**) from *N*-benzoyl-*N*′-(2,4,6-trichlorophenyl)thiourea (**BAD**) in DMF at room temperature by slow solvent evaporation method. pH value was measured by the pH test strip before and after the reaction

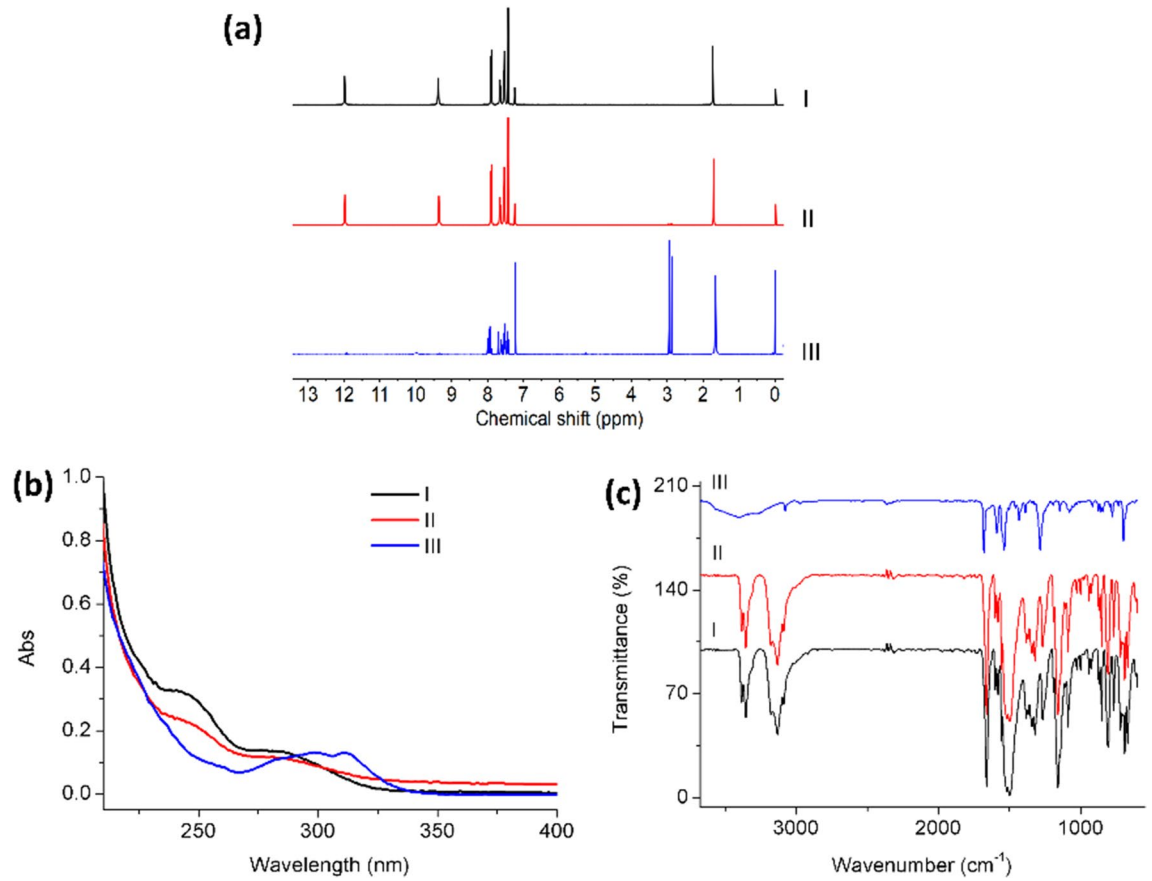


Fig. 1 ^{1}H NMR (**a**), UV (**b**) and IR (**c**) spectra of the compounds of I, II and III recrystallized from acetonitrile, ethanol and DMF, respectively

that hydrochloric acid molecules might generate during the reaction process.

The compounds recrystallized from acetonitrile(I), ethanol(II) and DMF(III), were all characterized by ^{1}H NMR, UV and IR (Fig. 1). From their ^{1}H NMR spectra (Fig. 1a), it is clear to see that the peaks at chemical shifts of 12.0 and 9.4 ppm (two protons of NH groups in BAD) were only found in the spectra of compounds I and II, demonstrating that compound III was different from compounds I and II. The peaks at chemical shifts of 2.8 and 2.9 ppm in the spectrum of compound III were due to the DMF molecules in the crystal. As shown in Fig. 1b, comparing with the UV spectra of compounds I and II, the UV absorption band of compound III showed a red shift, indicating there was a bigger aromatic ring in III than the benzyl ring in I and II. From their IR spectra in Fig. 1c, it is also easy to see that compound III was different from compounds I and II, which were the same. So, we were now completely sure of that the crystals recrystallized from acetonitrile and ethanol were BAD, while the crystals from DMF were BTT–DMF. As the active H in the CONH group of BTT formed a hydrogen bond with the DMF molecule, it was difficult to observe its ^{1}H NMR signal here (Fig. 2).

To study if co-solvents could affect the reaction, we performed the recrystallization of BAD in the co-solvents of DMF/acetonitrile (1/1, v/v) and DMF/ethanol (1/1, v/v) instead of pure DMF at room temperature. The composition of the crystals precipitated from the co-solvents were determined to be BAD, demonstrating that the addition of acetonitrile or ethanol in DMF would inhibit the reaction, which might due to the BAD crystal was prior to precipitate in ethanol or acetonitrile comparing with DMF by solvent evaporation method. In addition, different BAD solutions (100 mg in 5 mL DMF, or DMF/acetonitrile (1/1, v/v), or DMF/ethanol (1/1, v/v), respectively) were prepared and sealed in separate tubes and kept at temperature of 50 °C for 7 days. The compound in these solutions was determined by UV, and the result showed that the BAD didn't change, indicating that BAD could not convert to BTT at a high temperature (50 °C) even in DMF. Based on these investigations, we speculated that the reaction might happen at the interface of the liquid and the crystal when the crystal was growing.

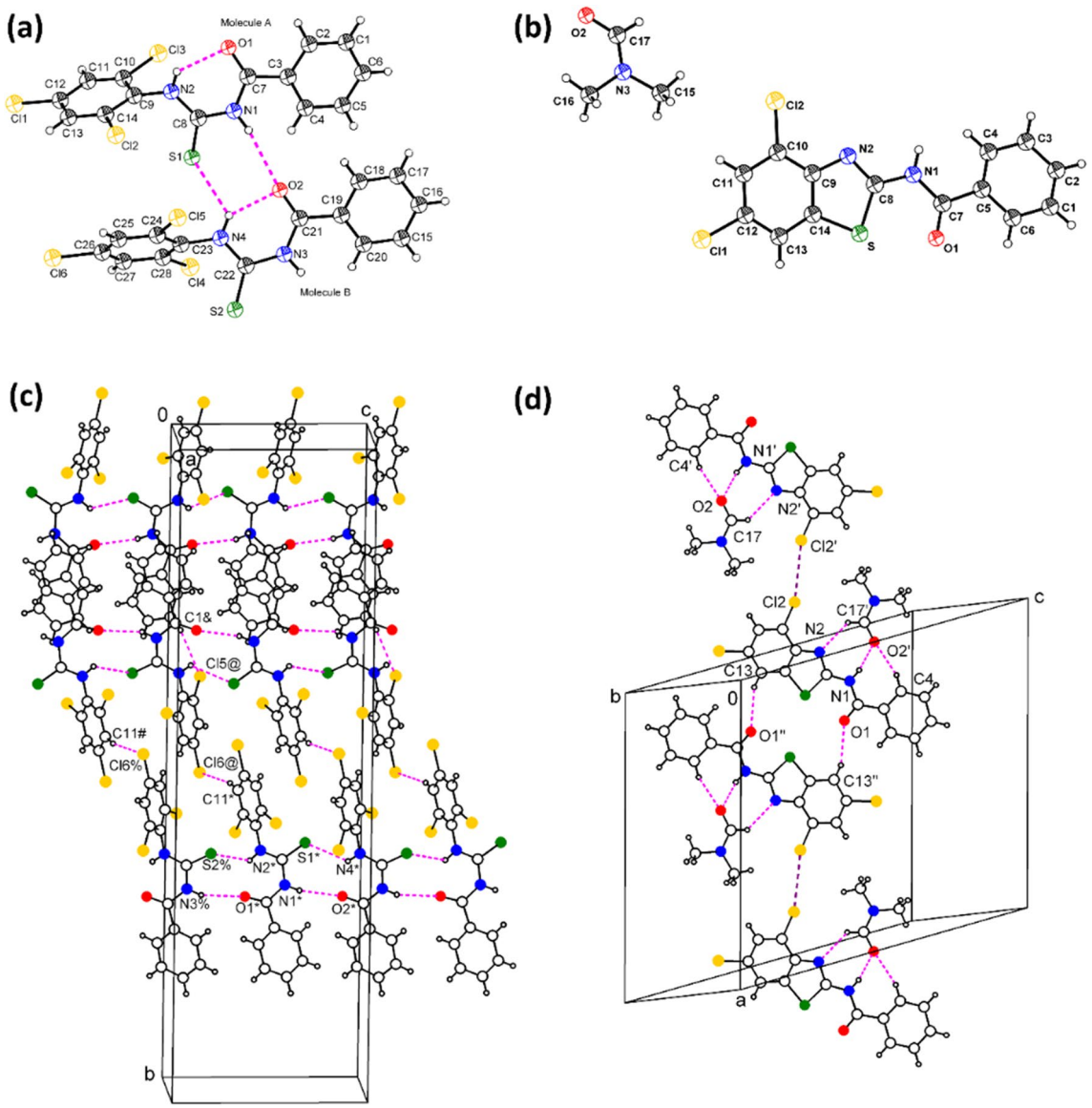
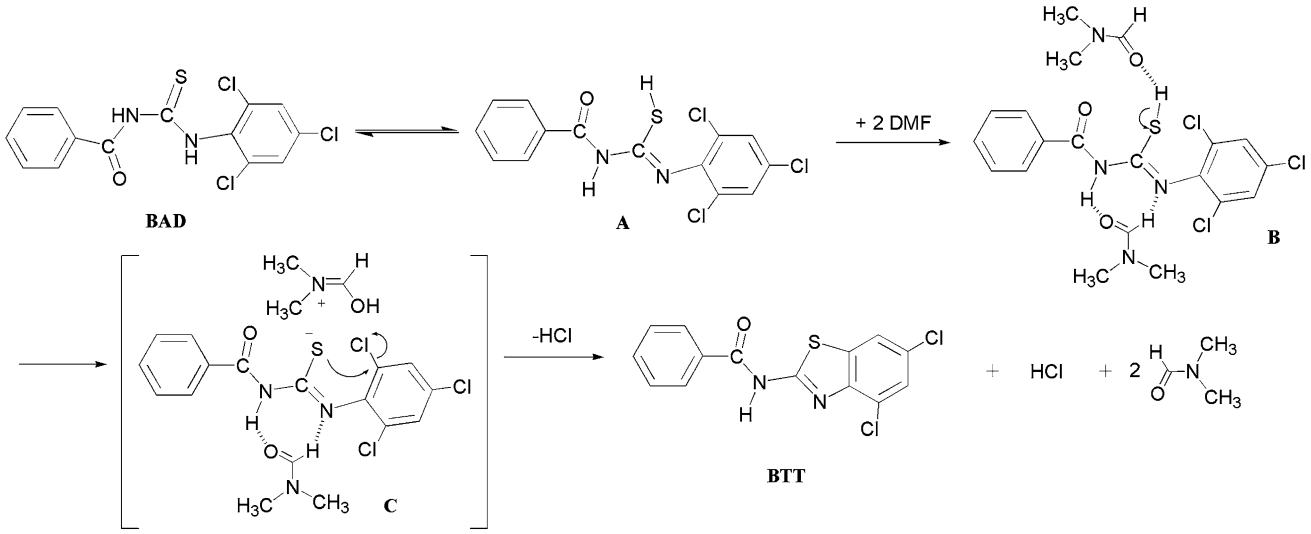


Fig. 2 Molecular structure of BAD (**a**, CCDC643496) and BTT–DMF (**b**, CCDC643497) with displacement ellipsoids at the 50% probability level. The packing structure of BAD (**c**) and BTT–DMF (**d**) to show the intermolecular hydrogen bond interactions. Dashed lines mean hydrogen bonds

BTT is one of the benzothiazole derivatives, which have wide applications and can be synthesized from many starting materials such as phenylthiourea derivatives [13–18]. BTT was firstly reported by Papke et al. using 2-amino-4,6-dichloro-benthiazole as the starting material to react with benzoyl chloride without catalyst, and recrystallized from pyridine/ethanol in a yield of 95% [18]. However, in order to obtain benzothiazoles from phenylthiourea derivatives, all the reported reactions required metal catalysts such as Pd or Cu catalysts together with some bases [19, 20], Fe catalysts together with some oxidants [21, 22], or Cs_2CO_3 [23, 24]. Moreover, these reactions were usually performed at a high temperature (80–130 °C). In our knowledge, there is no report to synthesize benzothiazoles from phenylthiourea derivatives without catalyst at room temperature. In this paper, BTT was obtained by recrystallization of BAD in DMF at room temperature. As DMF can act as catalyst in some organic reactions [5], we speculated that it might also play a role of catalyst during the recrystallization process and help BAD convert to BTT. So, next question is how about the catalytic mechanism?

To investigate the reaction mechanism, we analyzed the hydrogen bonds in the single crystals of BAD and BTT–DMF (Tables 1, 2). As shown in Fig. 2, in the BAD crystal there was no solvent molecule, while DMF molecules were observed in the BTT-DMF crystals, indicating DMF



Scheme 3 A possible reaction mechanism catalysed by DMF for conversation of BAD to BTT

might take part in the conversion process of BAD to BTT. Two isomers of BAD were stabilized by the intramolecular N–H···O hydrogen bonds, as well as the intermolecular N–H···O and N–H···S hydrogen bonds (Fig. 2a), which further linked the isomers into a ribbon (Fig. 2c) [12]. Different ribbons were linked together into three dimensional (3D) structure of BAD by the intermolecular C–H···Cl hydrogen bonds [25]. However, in the BTT–DMF crystal, there were no intramolecular and intermolecular N–H···O and N–H···S hydrogen bonds (Fig. 2b, d). Instead, the solvent molecule of DMF formed intermolecular C–H···O, N–H···O and C–H···N hydrogen bonds to stabilize the BTT molecular structure into a plane. The planes were further linked into 3D structure by the intermolecular C–H···O hydrogen bonds and the Cl···Cl weak interactions. As shown in Fig. 2d, the short distance of Cl2···Cl2^{i} [symmetry code: (i) −1/2−x, 1/2−y, −z] was determined to be 3.478(2) Å (C10–Cl2···Cl2 ^{i} = 159.1(2)°), which is a little longer than 3.364(3) Å (C–Cl···Cl = 158.1(3)°) reported in the crystal of *N*-(2,4-dichlorophenoxyacetyl)-*N'*-(4-nitrophenyl)thiourea [26], suggesting the halogen bonding interaction is also important for the crystal structure packing. By comparing the hydrogen bonds in these two crystal structures, we speculated that DMF might help BAD convert to BTT through hydrogen bond interactions.

Based on the catalytic mechanisms using metal or base catalysts to synthesize benzothiazoles from phenylthiourea derivatives [19–24], a possible reaction mechanism was proposed in Scheme 3. The nucleophilic O atom of DMF might attack the proton in the thiol group of conformation A, at the same time another DMF molecule could form a complex with BTT through hydrogen bond interactions and try to stabilize the complex into a planar structure (complex B in Scheme 3), which could give the negative S atom more chance to attack the C nucleus of C–Cl group in the benzene ring to form a transition state C (Scheme 3). Then, the negative Cl would leave and react with the positive proton-conjugated DMF to generate a HCl molecule. Finally, BTT-DMF crystals were formed. Computational study was employed to investigate the proposed reaction mechanism by using the density functional method (DFT) in Gaussian 09 program [27]. Unfortunately, the calculation results suggested the complex B and the transition state C had high potential energy barriers, more efforts are still needed and in process to reveal the real reaction mechanism.

In summary, a new DMF-catalyzed reaction was reported here. In the solvent of DMF, the phenylthiourea derivative BAD could convert to the benzothiazole derivative BTT during the single crystal growing process by slow solvent evaporation method. Such synthetic method took a long time, but the product was easy to purify and the reaction at room temperature could save thermal energy as well. The reaction mechanism is still unclear and requires more efforts to be figured out.

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Compliance with Ethical Standards

Conflict of interest All authors states that there is no conflict of interest.

References

1. Ding ST, Jiao N (2012) *N*,*N*-Dimethylformamide: a multipurpose building block. Angew Chem Int Ed 51(37):9226–9237. https://doi.org/10.1002/anie.201200859
2. Liu WB, Chen C, Zhou P (2017) *N*,*N*-Dimethylformamide (DMF) as a source of oxygen to access alpha-hydroxy arones via the alpha-hydroxylation of arones. J Org Chem 82(4):2219–2222. https://doi.org/10.1021/acs.joc.6b02751
3. Xia HM, Zhang FL, Ye T, Wang YF (2018) Selective alpha-monomethylation by an amine-borane/*N*,*N*-dimethylformamide system as the methyl source. Angew Chem Int Ed 57(36):11770–11775. https://doi.org/10.1002/anie.201804794
4. Kovala-Demertzi D, Kourkoumelis N, West DX, Valdes-Martinez J, Hernandez-Ortega S (1998) A trinuclear palladium(II) complex with bridging 2-hydroxyacetophenone *N*-4-ethylthiosemicarbazone ligands—an unusual dimethylformamide promoted deprotonation and aggregation. Eur J Inorg Chem 6:861–863. https://doi.org/10.1002/(SICI)1099-0682(199806)1998:6%3c861:AID-EJIC861%3e3.0.CO;2-Y
5. Heravi MM, Ghavidel M, Mohammadkhani L (2018) Beyond a solvent: triple roles of dimethylformamide in organic chemistry. Rsc Adv 8(49):27832–27862. https://doi.org/10.1039/c8ra04985h
6. Pastoriza-Santos I, Liz-Marzan LM (2009) *N*,*N*-Dimethylformamide as a reaction medium for metal nanoparticle synthesis. Adv Funct Mater 19(5):679–688. https://doi.org/10.1002/adfm.200801566
7. Muzart J (2009) *N*,*N*-Dimethylformamide: much more than a solvent. Tetrahedron 65(40):8313–8323. https://doi.org/10.1016/j.tet.2009.06.091
8. Venkatesu P (2010) Thermophysical contribution of *N*,*N*-dimethylformamide in the molecular interactions with other solvents. Fluid Phase Equilib 298(2):173–191. https://doi.org/10.1016/j.fluid.2010.07.010
9. Lei Y, Li HR, Pan HH, Han SJ (2003) Structures and hydrogen bonding analysis of *N*,*N*-dimethylformamide and *N*,*N*-dimethylformamide-water mixtures by molecular dynamics simulations. J Phys Chem A 107(10):1574–1583. https://doi.org/10.1021/jp026638+
10. Li QJ, Yang CL (2008) Synthesis and crystal structure of a compound with two conformational isomers: *N*-(2-methylbenzoyl)-*N*′-(4-nitrophenyl)thiourea. J Chem Crystallogr 38(12):927–930. https://doi.org/10.1007/s10870-008-9413-z
11. Li QJ, Wang XF, Xie XQ, Yang CL (2009) Synthesis and crystal structure of centrosymmetric 4,4′-bis(*N*′-substituted acylthioureido)biphenyls. Chin J Org Chem 29(3):409–413
12. Rauf MK, Talib A, Badshah A, Zaib S, Shoaib K, Shahid M, Florke U, Imtiaz ud D, Iqbal J (2013) Solution-phase microwave assisted parallel synthesis of *N*,*N*′-disubstituted thioureas derived from benzoic acid: biological evaluation and molecular docking studies. Eur J Med Chem 70:487–496. https://doi.org/10.1016/j.ejmech.2013.10.012
13. Li Y, Wang YL (2006) Progress in the synthesis of 2-substituent-benzothiazoles. Chin J Org Chem 26(6):878–884. https://doi.org/10.3321/j.issn:0253-2786.2006.06.023
14. Zhu N, Zhang ZW, Gao M, Han LM, Suo QL, Hong HL (2013) New progress in the synthesis of 2-substituent-benzothiazole derivatives. Chin J Org Chem 33(7):1423–1436. https://doi.org/10.6023/cjoc201212014
15. Banerjee S, Payra S, Saha A (2017) A review on synthesis of benzothiazole derivatives. Curr Organocatal 4(3):164–181. https://doi.org/10.2174/2213337205666180119143539
16. Keri RS, Patil MR, Patil SA, Budagumpi S (2015) A comprehensive review in current developments of benzothiazole-based molecules in medicinal chemistry. Eur J Med Chem 89:207–251. https://doi.org/10.1016/j.ejmech.2014.10.059
17. Rauf MK, Zaib S, Talib A, Ebihara M, Badshah A, Bolte M, Iqbal J (2016) Solution-phase microwave assisted parallel synthesis, biological evaluation and in silico docking studies of *N*,*N*′-disubstituted thioureas derived from 3-chlorobenzoic acid. Bioorgan Med Chem 24(18):4452–4463. https://doi.org/10.1016/j.bmc.2016.07.042
18. Papke K, Pohloude R (1967) Uber Die Rhodanierung Halogen-substituierter Aniline.24. Uber Organische Rhodanverbindungen. Pharmazie 22(5):229–233
19. Joyce LL, Batey RA (2009) Heterocycle formation via palladium-catalyzed intramolecular oxidative C–H bond functionalization: an efficient strategy for the synthesis of 2-aminobenzothiazoles. Org Lett 11(13):2792–2795. https://doi.org/10.1021/ol900958z
20. Guo YJ, Tang RY, Zhong P, Li JH (2010) Copper-catalyzed tandem reactions of 2-halobenzenamines with isothiocyanates under ligand- and base-free conditions. Tetrahedron Lett 51(4):649–652. https://doi.org/10.1016/j.tetlet.2009.11.086
21. Qiu JW, Zhang XG, Tang RY, Zhong P, Li JH (2009) Iron-catalyzed tandem reactions of 2-halobenzenamines with isothiocyanates leading to 2-aminobenzothiazoles. Adv Synth Catal 351(14–15):2319–2323. https://doi.org/10.1002/adsc.200900450
22. Wang JK, Zong YX, Zhang XX, Gao Y, Li ZL, Yue GR, Quan ZJ, Wang XC (2014) Synthesis of *N*-benzothiazol-2-yl-amides by an iron-catalyzed oxidative C(sp(2))–H functionalization. Synlett 25(15):2143–2148. https://doi.org/10.1055/s-0034-1378547
23. Feng EG, Huang H, Zhou Y, Ye DJ, Jiang HL, Liu H (2010) Metal-free synthesis of 2-substituted (N, O, C) benzothiazoles via an intramolecular C–S bond formation. J Comb Chem 12(4):422–429. https://doi.org/10.1021/cc9001839
24. Mostafavi H, Islami MR, Ghonchepour E, Tikdari AM (2018) Synthesis of 1H-1,3-benzimidazoles, benzothiazoles and 3H-imidazo[4,5-c]pyridine using DMF in the presence of HMDS as a reagent under the transition-metal-free condition. Chem Pap 72(12):2973–2978. https://doi.org/10.1007/s11696-018-0540-5
25. Rauf MK, Bolte M, Badshah A (2009) 1-(4-Chlorobenzoyl)-3-(2,4,6-trichlorophenyl)thiourea hemihydrate. Acta Crystallogr Sect E Crystallogr Commun 65:O143–U2501. https://doi.org/10.1107/s1600536808041251
26. Li QJ, Yang CL, Xie XQ (2007) *N*-(2,4-Dichlorophenoxyacetyl)-*N*′-(2,4,6-trichlorophenyl)thiourea. Acta Crystallogr Sect E Crystallogr Commun 63:o773–o774. https://doi.org/10.1107/S1600536806054201
27. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Petersson GA, Nakatsuji H, Li X, Caricato M, Marenich A, Bloino J, Janesko BG, Gomperts R, Mennucci B, Hratchian HP, Ortiz JV, Izmaylov AF, Sonnenberg JL, Williams-Young D, Ding F, Lipparini F, Egidi F, Goings J, Peng B, Petrone A, Henderson T, Ranasinghe D, Zakrzewski VG, Gao J, Rega N, Zheng G, Liang W, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Vreven T, Throssell K, Montgomery JA Jr, Peralta JE, Ogliaro F, Bearpark M, Heyd JJ, Brothers E, Kudin KN, Staroverov VN, Keith T, Kobayashi R, Normand J, Raghavachari K, Rendell A, Burant JC, Iyengar SS, Tomasi J, Cossi M, Millam JM, Klene M, Adamo C, Cammi R, Ochterski JW, Martin RL, Morokuma K, Farkas O, Foresman JB, Fox DJ (2009) Gaussian 09. Gaussian Inc, Wallingford