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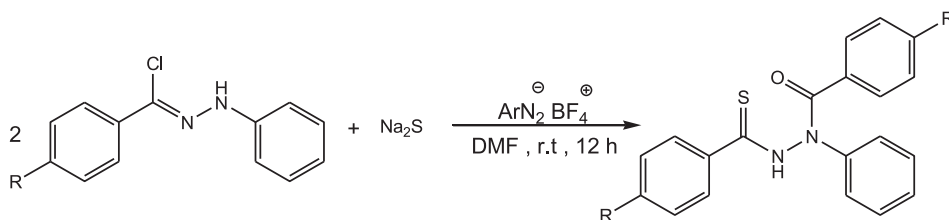
# One-pot synthesis of *N*-phenyl-*N'*-(arylcarbonothioyl)-*N*-arylhydrazide derivatives from hydrazoneyl chlorides with sodium sulfide and aryldiazonium salts

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The one-pot synthesis of *N*-phenyl-*N'*-(arylcarbonothioyl)-*N*-arylhydrazides is described by the reaction between two equiv. of hydrazoneyl chloride and sodium sulfide in the presence of aryldiazonium fluoroborates in DMF at room temperature.



**Keywords:** hydrazide; hydrazoneyl chloride; sodium sulfide; aryldiazonium fluoroborates

## 1. Introduction

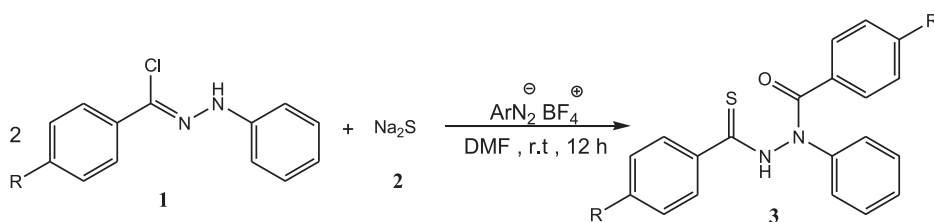
The development of rapid, practical, and environmentally benign synthetic routes for the construction of libraries of organic molecules from relatively simple starting materials is one of the most important targets in organic synthesis.[1] Toward this goal, the cascade, domino, and tandem reactions are an extremely powerful tool for delivering the molecular diversity needed in the combinatorial strategies for the synthesis of biologically active compounds.[2,3] Preparative protocols in which at least two consecutive transformations are carried out in the same reaction vessel offer a number of advantages such as automated, high-throughput, and fast generation of organic compounds to the organic chemists.[4,5] Furthermore, the discovery of novel multicomponent reactions can be considered as a field of undoubted current importance for academic research that also satisfies a practical interest in applied science.[6–9] Hydrazide derivatives can be targeted for synthesis via multicomponent reactions because they are a very interesting class of compounds with various applications in organic synthesis

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and in industry.[10,11] In recent years, broad study of hydrazides and their derivatives have demonstrated diverse biological activities such as analgesic, chemotherapeutic, anti-fungicidal, antibacterial, and anti-inflammatory properties.[12,13] On the other hand, hydrazides have been described as useful starting materials for the synthesis of azo heterocycles, such as indoles, carbazoles, pyrazoles, triazines, indazolones, and indazoles.[14–16] Different reagents and procedures have been employed over the decades to prepare hydrazides that often suffer from low yield, harsh conditions, and multistep synthetic procedures. Until recently, only one synthetic approach has been reported for the synthesis of *N'*-*N'*-arylbenzothiohydrazides.[17] The thiohydrazide scaffold with variety of functional groups is a chemosensor for recognition of  $\text{Hg}^{+2}$  in aqueous solution and consequently, because monitoring of mercury in the environment and industrial waste streams is important, this area of research is in high demand.[18] Following our interest in the development of new multicomponent reactions,[19] we considered the possibility of the synthesis of functionalized *N*-phenyl-*N'*-(arylcarbonothioyl)-*N*-arylhydrazides in a single synthetic operation from hydrazonoyl chlorides and sodium sulfide in the presence of diazonium salts.

## 2. Results and discussion

Our investigation started with the synthesis of hydrazonoyl chlorides from *N'*-arylbenzohydrazides in the presence of  $\text{CCl}_4$  and  $\text{Ph}_3\text{P}$  at room temperature. Subsequently we chose to study the behavior of these nitrogen-containing compounds **1** in a multicomponent reaction with sodium sulfide in the presence of aryldiazonium fluoroborate in DMF solvent (Scheme 1). Control



3	R	Ar	Yield %
3a	Cl	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	80
3a	Cl	4-MeOC <sub>6</sub> H <sub>4</sub>	75
3a	Cl	4-ClC <sub>6</sub> H <sub>4</sub>	76
3a	Cl	C <sub>6</sub> H <sub>5</sub>	70
3b	Me	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	85
3b	Me	4-MeOC <sub>6</sub> H <sub>4</sub>	80
3b	Me	4-ClC <sub>6</sub> H <sub>4</sub>	81
3b	Me	C <sub>6</sub> H <sub>5</sub>	76
3c	H	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	83
3c	H	4-MeOC <sub>6</sub> H <sub>4</sub>	80
3c	H	4-ClC <sub>6</sub> H <sub>4</sub>	77
3c	H	C <sub>6</sub> H <sub>5</sub>	76

Scheme 1. Synthesis of *N*-phenyl-*N'*-(arylcarbonothioyl)-*N*-arylhydrazides from hydrazonoyl chlorides and sodium sulfide in the presence of aryldiazonium fluoroborate.

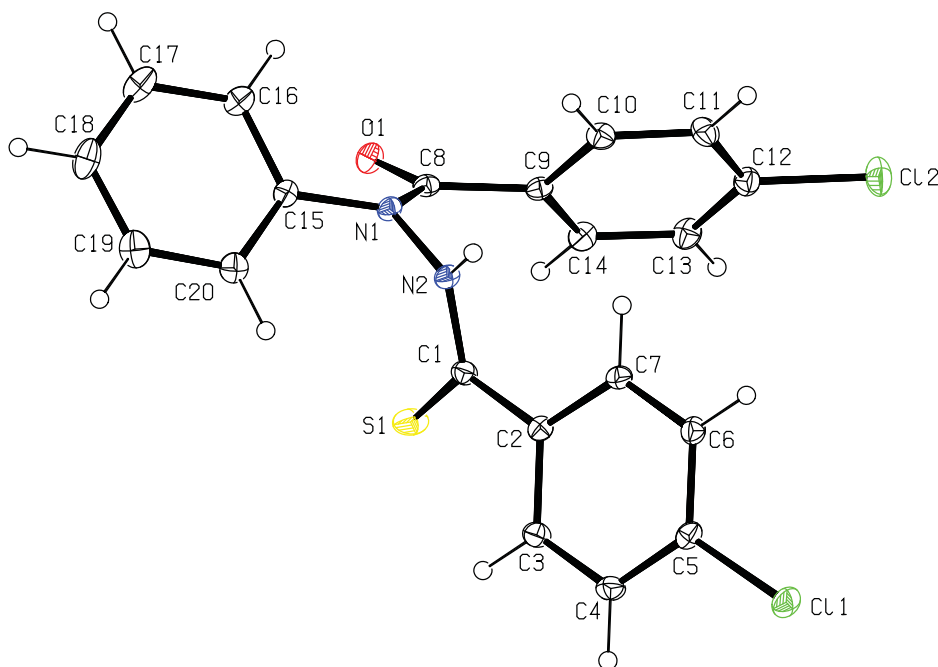


Figure 1. Single-crystal X-ray structure of 4-chloro-*N'*-(4-chlorophenylcarbonothioyl)-*N*-phenylbenzohydrazide structure **3a**.

studies demonstrated that the thiohydrazides **3** were not obtained from the hydrazonoyl chlorides **1** and sodium sulfide **2** in the absence of the aryldiazonium salts. In a pilot experiment, the stable crystalline *N*-phenyl-*N'*-(arylcarbonothioyl)-*N*-arylhydrazides were isolated by repeated chromatography and their structures supported by IR, NMR, elemental analyses, and mass spectrometry data. The IR spectrum of **3a** showed absorptions at  $3471\text{ cm}^{-1}$  due to the NH group and at  $1666\text{ cm}^{-1}$  for the carbonyl. In the  $^1\text{H}$  NMR (400 MHz) spectrum, the NH hydrogen appeared as a singlet at 10.36 ppm. The aromatic protons showed three doublets with  $^3J_{\text{HH}} = 8.4$  Hz and multiplets between  $\delta$  7.28 and 7.31 ppm. The  $^1\text{H}$ -decoupled  $^{13}\text{C}$  NMR spectra of **3a** showed 14 signals in agreement with the 4-chloro-*N'*-(4-chlorophenylcarbonothioyl)-*N*-phenylbenzohydrazide structure. The structure of **3a** was unambiguously confirmed by an X-ray crystallographic analysis (Figure 1). The unit cell packing of molecules in the crystal structure of compound **3a** is shown in Figure 2.

In conclusion, we have devised an easy approach for the new synthesis of *N*-phenyl-*N'*-(arylcarbonothioyl)-*N*-arylhydrazides from hydrazonoyl chlorides and sodium sulfide in the presence of diazonium salts. The simple purification and good yield of products are advantages of this new synthesis. Although the mechanism of formation of these new compounds and the role of aryldiazonium fluoroborates are ambiguous,<sup>[20,21]</sup> we anticipate that further investigations of the present method can clarify its mechanism and further expand its scope and limitations.

### 3. Experimental design

All reagents were obtained commercially and used without further purification. Hydrazonoyl chloride compounds **1** were prepared according to [22]. An electrothermal-9100 apparatus was used for melting points. The data of IR, NMR, Elemental analyzer, and mass were recorded by

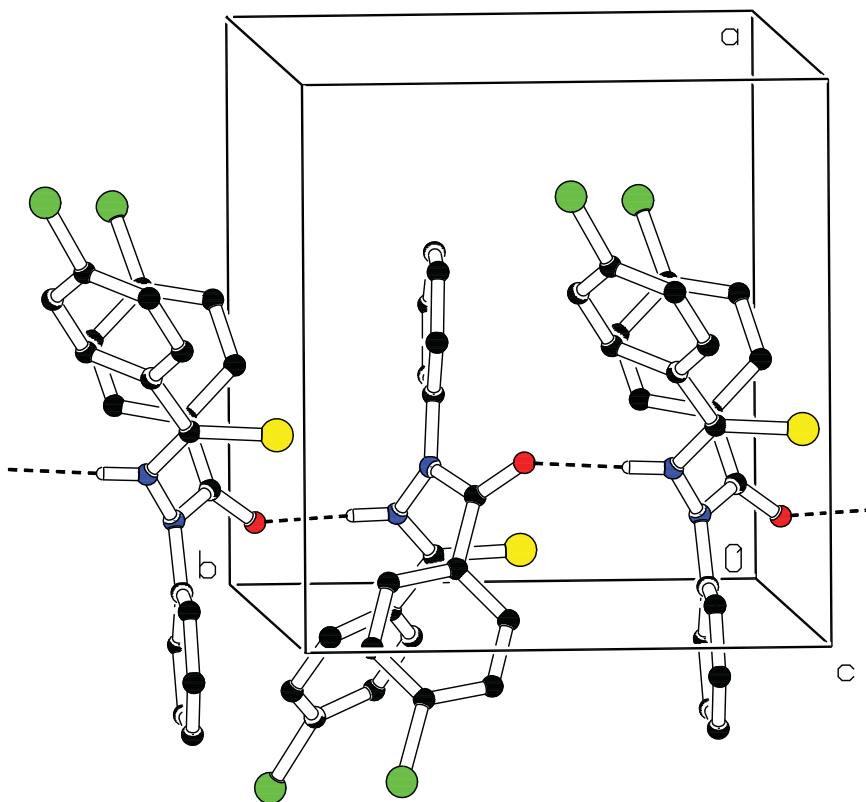


Figure 2. Unit cell packing of **3a**, showing hydrogen bond interactions.

Shimadzu-IR-460 spectrometer, Bruker DRX-400, Vario EL III CHNOS, and Finnigan-MAT-8430EI-MS, respectively.

### 3.1. General procedure for the preparation of **3**

Sodium sulfide hydrate **2** (1 mmol) was added to a magnetically stirred solution of hydrazonoyl chloride **1** (2 mmol) in 5 mL DMF at room temperature. The reaction mixture was stirred for 45 min, and then aryldiazonium tetrafluoroborate (2 mmol) was added and the reaction mixture was stirred for 10 h at this temperature. Then, H<sub>2</sub>O (8 ml) was added to this solution and stirred for 20 min. The mixture was extracted with AcOEt (15 ml), dried (MgSO<sub>4</sub>), and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography using hexan/AcOEt (4:1) as eluent to give products **3a–c**.

#### 3.1.1. 4-Chloro-*N'*-(4-chlorophenylcarbonothioyl)-*N*-phenylbenzohydrazide (**3a**)

Yellow crystal, m.p: 168C. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3471, 3292, 3248, 1666, 1525, 1484, 1260, 1091, 831, 751. <sup>1</sup>H NMR (400.1 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.23 (2 H, d, <sup>3</sup>*J*<sub>HH</sub> = 8.4 Hz, 2 CH), 7.28–7.31 (7 H, m, 7 CH), 7.49 (2 H, d, <sup>3</sup>*J*<sub>HH</sub> = 8.4 Hz, 2 CH), 7.74 (2 H, d, <sup>3</sup>*J*<sub>HH</sub> = 8.4 Hz, 2 CH), 10.36 (1 H, s, NH). <sup>13</sup>C NMR (100.6 MHz, CDCl<sub>3</sub>):  $\delta$  = 125.2 (2 CH), 127.7 (2 CH), 128.4 (2 CH), 128.6 (2 CH), 128.7 (2 CH), 129.2 (2 CH), 130.5 (CH), 132.1 (C), 136.6 (C), 137.6 (C), 138.3 (C), 141.1 (C), 168.6 (C=O), 198.0 (C=S). MS *m/z* 401 (M<sup>+</sup>, 15). Anal. Calcd for

$C_{20}H_{14}Cl_2N_2OS$  (401.31): C 59.86%, H 3.52%, N 6.98%, S 7.99%. Found: C 59.64%, H 3.48%, N 6.92%, S 7.83%.

### 3.1.2. 4-Methyl-*N'*-(4-methylphenylcarbonothioyl)-*N*-phenylbenzohydrazide (**3b**)

Yellow crystal, m.p: 153 C. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3470, 3293, 3245, 1668, 1593, 1489, 1265, 1073, 748.  $^1\text{H}$  NMR (400.1 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.32 (3 H, s, Me), 2.36 (3 H, s, Me), 7.04 (2 H, d,  $^3J_{\text{HH}}$  = 8.0 Hz, 2 CH), 7.11 (2 H, d,  $^3J_{\text{HH}}$  = 8.0 Hz, 2 CH), 7.20–7.28 (3 H, m, 3 CH), 7.33 (2 H, d,  $^3J_{\text{HH}}$  = 8.0 Hz, 2 CH), 7.48 (2 H, d,  $^3J_{\text{HH}}$  = 8.0 Hz, 2 CH), 7.68 (2 H, d,  $^3J_{\text{HH}}$  = 8.0 Hz, 2 CH), 10.29 (1 H, s, NH).  $^{13}\text{C}$  NMR (100.6 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 21.4 (Me), 21.5 (Me), 125.1 (2 CH), 127.0 (CH), 127.3 (2 CH), 128.7 (2 CH), 128.9 (2 CH), 129.1 (2 CH), 129.2 (CH), 131.0 (C), 135.9 (C), 141.7 (C), 142.3 (C), 169.7 (C=O), 199.3 (C=S). MS  $m/z$  360 ( $\text{M}^+$ , 10). Anal. Calcd for  $\text{C}_{22}\text{H}_{20}\text{N}_2\text{OS}$  (360.47): C 73.30%, H 5.59%, N 7.77%, S 8.90%. Found: C 73.42%, H 5.64%, N 7.80%, S 8.94%.

### 3.1.3. *N*-phenyl-*N'*-(phenylcarbonothioyl)-benzohydrazide (**3c**)

Yellow crystal, m.p: 157C. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3468, 3290, 3253, 1659, 1514, 1413, 1253, 870.  $^1\text{H}$  NMR (400.1 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.21–7.29 (5 H, m, 5 CH), 7.32–7.40 (5 H, m, 5 CH), 7.47 (1 H, t,  $^3J_{\text{HH}}$  = 7.2 Hz, CH), 7.62 (2 H, d,  $^3J_{\text{HH}}$  = 6.8 Hz, 2 CH), 7.75 (2 H, d,  $^3J_{\text{HH}}$  = 7.2 Hz, 2 CH), 10.19 (1 H, s, NH).  $^{13}\text{C}$  NMR (100.6 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 125.1 (CH), 127.2 (CH), 127.2 (2 CH), 128.0 (2 CH), 128.5 (2 CH), 128.9 (CH), 129.0 (2 CH), 131.1 (2 CH), 131.7 (2 CH), 134.0 (C), 134.1 (C), 138.9 (C), 169.6 (C=O), 199.7 (C=S). MS  $m/z$  332 ( $\text{M}^+$ , 20). Anal. Calcd for  $\text{C}_{20}\text{H}_{16}\text{N}_2\text{OS}$  (332.40): C 72.26%, H 4.85%, N 8.43%, S 9.65%. Found: C 72.33%, H 4.79%, N 8.38%, S 9.70%.

## Disclosure statement

No potential conflict of interest was reported by the authors.

## Supplemental material

CCDC 1047625 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at [http://www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

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