



## An Efficient, Facial and Green Synthesis of Substituted Thiourea

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A series of novel substituted N,N'-di(arylaminothiocarbonyl)terephthalamide and 1,4-di(aryloylthioureido)benzene were synthesized by the reaction of terephthaloyl dichloride, ammonium thiocyanate and primary amines, 1,4-phenylenediamine and acyl halide derivatives. The reaction has been completed within 0.5 h in solvent-free condition by grinding the mixture of reactants and afforded the substituted thiourea in good yields.

**Key Words:** High substituted thiourea, Arylamines, Terephthaloyl dichloride, Grinding chemistry.

### INTRODUCTION

Thiourea are important compounds as building blocks in the synthesis of heterocycles<sup>1,2</sup>. For example, thioureas condense with  $\alpha$ -halo carbonyl compounds to afford 2-amino-1,3-thiazoles<sup>3,4</sup>. Benzothiazoles can be prepared from aryl thioureas in the presence of bromine<sup>5</sup>. The use of thioureas to make iminothiazolines<sup>6</sup>, thiohydantoin<sup>7,8</sup>, 1,3,5-triazines<sup>9</sup> and 2-amino-oxazolidines<sup>10</sup> was also described recently. Many methods for the synthesis of thiourea have been reported *e.g.*, N-substituted thioureas are commonly prepared from the reaction of amines with alkali metal thiocyanates in the presence of a strong acid, aroyl isothiocyanates with amines followed by basic hydrolysis, isothiocyanates with ammonia or amines.

Several new methods for the preparation of substituted thioureas have been recently reported<sup>11</sup>. However, these methods have several drawbacks, namely, the need for the high reaction temperature, long reaction time, the use of noxious reagents and special starting materials. Therefore, development of mild, efficient and environmentally friendly methods is still desired.

We present here a mild, efficient and green approach method under solvent free conditions by grinding the reactants to give N-aryl-N'-aroyl(acyl)thioureas in good yields. Thus, a mixture of ammonium thiocyanate (12 mmol) and a bis-functional acid chloride (6 mmol) was grinded without solvent for 10 min. Then, an arylamine (12 mmol) was added and mixed for 20 min. The product was recrystallized from EtOH. The results obtained are shown in **Scheme-I**.

In the same manner, a mixture of 1,4-phenylenediamine, ammonium thiocyanate and acyl halide derivative under

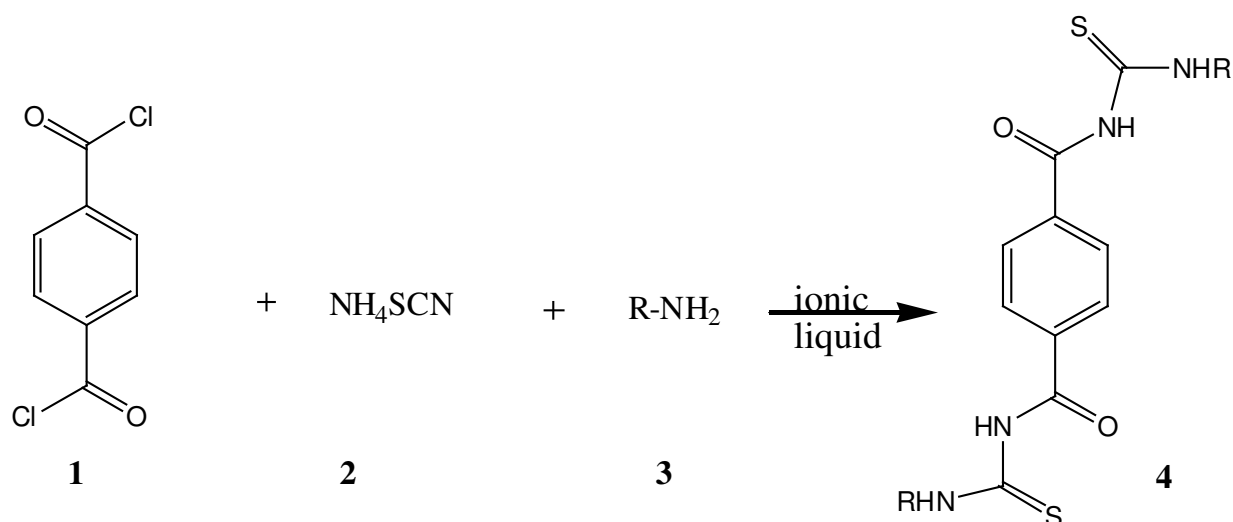
solvent free conditions produced substituted thiourea **5** in good yields and short times (**Scheme-II**).

The structures of compounds **4a-d** and **5a-d** were deduced from their elemental analyses and their IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra. The mass spectra of these compounds displayed molecular ion peak at appropriate m/z values. The <sup>1</sup>H NMR spectrum of **4a** in CDCl<sub>3</sub> showed two singlets for NH ( $\delta$  = 9.33 and 11.12) protons, along with multiplets for the aromatic ( $\delta$  = 7.33-8.44) protons. The <sup>13</sup>C NMR spectrum of **4a** showed eight signals in agreement with the proposed structure. Partial assignments of these resonances are given in experimental section. The <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of **4b-d** are similar to those for **4a** except for the aromatic moieties, which exhibited characteristic signals with appropriate chemical shifts.

### EXPERIMENTAL

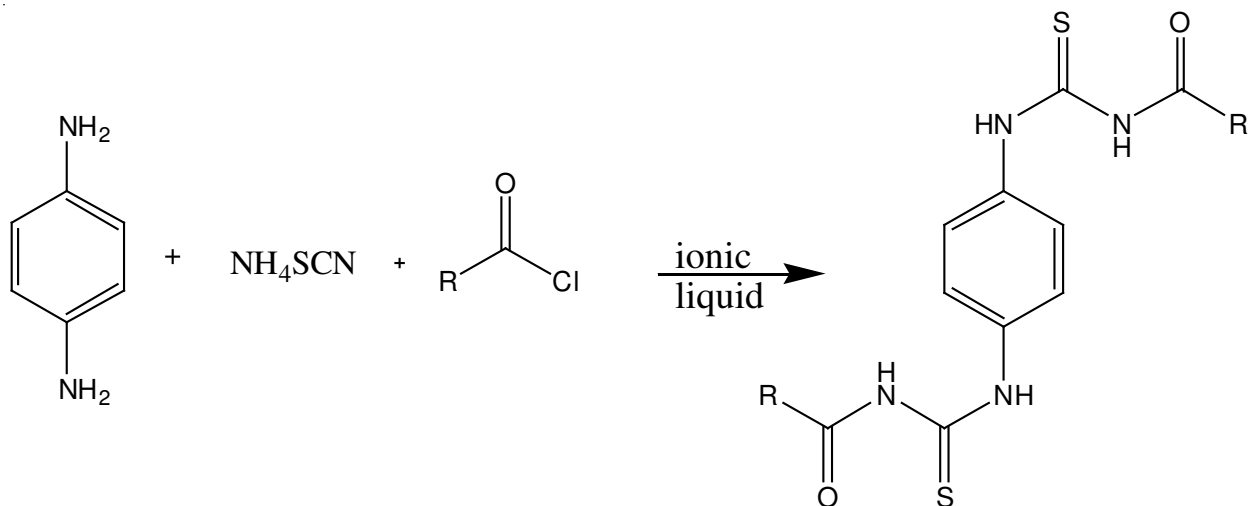
Compounds were obtained from Merck and were used without further purification. The following instruments were used: melting points, Electrothermal-9100 apparatus, uncorrected, IR spectra, Shimadzu IR-460 spectrometer; <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra, Bruker DRX-300 Avance instrument; in CDCl<sub>3</sub> at 400 MHz and 75 MHz, respectively,  $\delta$  in ppm; EI-MS (70 eV): finnigan-MAT-8430 mass spectrometer, in m/z. Elemental analyses data were in agreement with the proposed structures.

**General procedure for the preparation of substituted N,N'-di(arylaminothiocarbonyl)terephthalamides 4(a-d):** To a solid ammonium thiocyanate (12 mmol), was added solid terephthaloyl dichloride (6 mmol) and grinded for 10 min.



4	R	Yield %
a	Ph	84
b	4-Me-Ph	72
c	4-Et-Ph	79
d	Benzyl	81

Scheme-I



5	R	Yield %
a	Ph	91
b	4-Cl-Ph	86
c	3-Cl-Ph	93
d	4-Et-Ph	88

Scheme-II

Then to the solid crude, was added an appropriate N-arylamine (12 mmol) and then grinded for 20 min (monitored by TLC using hexane:ethyl acetate 1:1 v/v as eluent). The precipitated solids triturated and were washed with ethanol and filtered. The products were crystallized from absolute ethanol.

**N,N'-Di(phenylaminothiocarbonyl)terephthalamide (4a):** Colourless solid, yield: 84 %, m.p. 212-214 °C, IR (KBr,

$\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3323 (NH), 3180 (NH), 1520 (C=O), 1230 (C=S);  $^1\text{H}$  NMR 400 MHz ( $\text{CDCl}_3$ ): 7.33-8.44 (14H, m, arom), 9.33 (1H, s, NH), 11.12 (1H, s, NH),  $^{13}\text{C}$  NMR: 122-136 (6C, arom), 163 (C=O), 181.4 (C=S). EI-MS: 434 (12,  $\text{M}^+$ ), 250 (38), 162 (46), 132 (58), 76 (100), 28 (16).

**N,N'-Di((4-methylphenyl)aminothiocarbonyl)terephthalamide (4b):** Pale yellow powder, yield: 72 %, m.p. 218-

220 °C, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3330 (NH), 3210 (NH), 1538 (C=O), 1222 (C=S);  $^1\text{H NMR}$  400 MHz ( $\text{CDCl}_3$ ): 1.63 (6H, s,  $\text{CH}_3$ ), 7.22-8.38 (12H, m, arom), 9.48 (1H, s, NH), 11.66 (1H, s, NH),  $^{13}\text{C NMR}$ : 27.3 ( $\text{CH}_3$ ), 121-133 (6C, arom), 168 (C=O), 183.3 (C=S). EI-MS: 462 (18,  $\text{M}^+$ ), 310 (23), 192 (37), 162 (72), 91 (100), 28 (22).

**N,N'-Di((4-ethylphenyl)aminothiocarbonyl)terephthalamide (4c):** Pale yellow powder, yield: 79 %, m.p. 215-217 °C, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3327 (NH), 3194 (NH), 1533 (C=O), 1218 (C=S);  $^1\text{H NMR}$  400 MHz ( $\text{CDCl}_3$ ): 1.02 (6H, t,  $\text{CH}_3$ ), 1.71 (4H, q,  $\text{CH}_2$ ), 7.14-8.27 (12H, m, arom), 9.39 (1H, s, NH), 11.21 (1H, s, NH),  $^{13}\text{C NMR}$ : 22.1 ( $\text{CH}_3$ ), 38.4 ( $\text{CH}_2$ ), 118-130 (6C, arom), 166 (C=O), 179.8 (C=S). EI-MS: 490 (14,  $\text{M}^+$ ), 338 (23), 220 (29), 162 (68), 105 (100), 28 (17).

**N,N'-Di(benzylaminothiocarbonyl)terephthalamide (4d):** Pale yellow powder, yield: 81 %, m.p. 216-218 °C, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3397 (NH), 3217 (NH), 1570 (C=O), 1228 (C=S);  $^1\text{H NMR}$  400 MHz ( $\text{CDCl}_3$ ): 4.12 (4H, d,  $\text{CH}_2$ ), 7.30-8.36 (12H, m, arom), 9.41 (1H, s, NH), 11.26 (1H, s, NH),  $^{13}\text{C NMR}$ : 51.3 ( $\text{CH}_2$ ), 115-134 (6C, arom), 163.2 (C=O), 180.6 (C=S). EI-MS: 462 (23,  $\text{M}^+$ ), 310 (33), 192 (46), 162 (59), 91 (100), 28 (21).

**1,4-Di(benzoylthioureido) benzene (5a):** Yellow crystal, yield: 91 %, m.p. 240-242 °C, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3354 (NH), 3308 (NH), 1555 (C=O), 1217 (C=S);  $^1\text{H NMR}$  400 MHz ( $\text{CDCl}_3$ ): 6.80-8.36 (14H, m, arom), 10.23 (1H, s, NH), 11.96 (1H, s, NH),  $^{13}\text{C NMR}$ : 115-134 (6C, arom), 168.5 (C=O), 184.7 (C=S). EI-MS: 434 (28,  $\text{M}^+$ ), 224 (46), 106 (28), 105 (100), 28 (17).

**1,4-Di((4-chlorobenzoyl)thioureido)benzene (5b):** Yellow crystal, yield: 86 %, m.p. 236-238 °C, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3360 (NH), 3312 (NH), 1549 (C=O), 1214 (C=S);  $^1\text{H NMR}$  400 MHz ( $\text{CDCl}_3$ ): 6.84-8.44 (12H, m, arom), 10.20 (1H, s, NH), 11.88 (1H, s, NH),  $^{13}\text{C NMR}$ : 121-133 (6C, arom), 169 (C=O), 185.9 (C=S). EI-MS: 503 (8,  $\text{M}^+$ ), 224 (100), 140 (38), 28 (22).

**1,4-Di((3-chlorobenzoyl)thioureido)benzene (5c):** White yellow crystal, yield: 93 %, m.p. 234-235 °C, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3357 (NH), 3321 (NH), 1553 (C=O), 1215 (C=S);  $^1\text{H NMR}$  400 MHz ( $\text{CDCl}_3$ ): 6.87-8.39 (12H, m, arom), 10.12 (1H, s, NH), 11.92 (1H, s, NH),  $^{13}\text{C NMR}$ : 121-133 (8C, arom), 174.3 (C=O), 182 (C=S).

**1,4-Di((4-ethylbenzoyl)thioureido)benzene (5d):** White yellow crystal, yield: 88 %, m.p. 243-245 °C, IR (KBr,  $\nu_{\max}$ ,

$\text{cm}^{-1}$ ): 3357 (NH), 3321 (NH), 1553 (C=O), 1215 (C=S);  $^1\text{H NMR}$  400 MHz ( $\text{CDCl}_3$ ): 1.16 (6H, t,  $\text{CH}_3$ ), 1.83 (4H, q,  $\text{CH}_2$ ), 6.92-8.54 (12H, m, arom), 10.08 (1H, s, NH), 11.74 (1H, s, NH),  $^{13}\text{C NMR}$ : 127-137 (6C, arom), 178 (C=O), 189 (C=S).

## RESULTS AND DISCUSSION

The work described presents the synthesis of new *bisthiourea* derivatives. The *hitherto* unreported thioureas **4a-d** and **5a-d** were successfully synthesized *via* a biphasic reacting between terephthaloyl chloride, ammonium thiocyanate and a primary amine under a phase transfer catalysis condition. The products **4a-d** were recrystallized from ethanol and fully characterized by IR,  $^1\text{H NMR}$ ,  $^{13}\text{C NMR}$  and mass spectrometry.

In conclusion, we have reported a mild, simple, efficient and environmental friendly method for the synthesis of N,N'-di(arylaminothiocarbonyl)terephthalamide and 1,4-di(aryloylthioureido)benzene derivatives under biphasic condition with the aid of tetrabutylammonium bromide as a phase transfer catalyst.

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