

# A Convenient Method for the Synthesis of Bis-Ureas Using Bis(*O*-Nitrophenyl) Carbonate as Starting Material

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**Abstract:** A general method for the preparation of bis-ureas from bis(*o*-nitrophenyl)carbonate have been developed. Directional urea synthesis is achieved by sequential amine addition to bis(*o*-nitrophenyl)carbonate in two steps: as a first step bis(*o*-nitrophenyl) carbonate is reacted with benzyl amine to form benzyl-*o*-nitrophenyl carbamate; in the second step the carbamate is reacted with a variety of diamines in toluene to yield bis-ureas.

**Keywords:** bis(*o*-nitrophenyl) carbonate, carbamate, bis-urea.

## 1. Introduction

Bis-urea compounds are well-suited for material science. Bis-urea grafted molecules or polymers give rise to strong hydrogen bonding interactions that have been used to obtain gelling agents[1,2], to structure inorganic materials[3] and also in polymeric assemblies[4]. Recently, it has been demonstrated that bis-ureas are guest-host molecules that exhibits molecular recognition[4].

The reaction of amines or diamines with isocyanates[1, 3-5] or diisocyanate[6-8] is the key step in the preparation of bis-ureas. This method is very inconvenient because isocyanates and diisocyanates are prepared from phosgene, a very dangerous reagent.

Our attention was directed toward bis(*o*-nitrophenyl) carbonate **1**, a mild reagent, that can be used in organic synthesis instead of phosgene or its derivative. We already reported its reactivity in reaction with primary and secondary amines and have successfully obtained di- and trisubstituted ureas [9-11].

In this paper we wish to report the use of bis(*o*-nitrophenyl) carbonate in the synthesis of bis-ureas **3**.

## 2. Experimental

Melting points were determined on a Boetius apparatus (Carl Zeiss Jena). The IR spectra were recorded in KBr pellet for solid compounds and reaction monitoring was carried out in thermostated silicon cells of 0.137 mm thickness on a Jasco FT/IR-430 instrument. TLC analyses were carried out on pre-coated plates silica gel 60 F<sub>254</sub>(Merk). Spots visualization was achieved by exposing the plates under a UV 254 lamp. Bis(*o*-nitrophenyl)carbonate **1** was obtained by our published method [12]. All reagents were purchased from chemical suppliers and used without further purification

**General Procedure for the Preparation of trisubstituted ureas.** Compound **1** (0.2 g, 0.657mmoli)

was dissolved in toluene (10 mL) and the first amine (1.2 equiv.) was added. The reaction mixture was stirred at room temperature until no carbonate could be further detected by TLC (eluent: dichloromethane). The reaction mixture was washed with 1M HCl solution (5 mL), dried on anhydrous MgSO<sub>4</sub> and filtered. The diamine (2.5 equiv.) was then added to the filtrate and the resulting reaction mixture was heated under reflux conditions until no residual carbamate was detectable by TLC (eluent: dichloromethane). The insoluble bis-urea obtained was filtered off and washed with cold toluene.

**Bis(benzylcarbamoyl)ethyldiamine 3a.** Obtained in 86% yield as a white solid; m.p.= 240-242°C  
IR (KBr, cm<sup>-1</sup>): 3330i, 3031s, 1621i, 1575i, 1264m, 697.

**Bis(benzylcarbamoyl)1,2-propyldiamine 3b.** Obtained in 95% yield as a white solid; m.p.= 228-230°C  
IR (pastilă KBr): 3330i, 3031s, 1623i, 1568i, 1260m, 694.

**Bis(benzylcarbamoyl)1,3-propyldiamine 3c.** Obtained in 86% yield as a white solid; m.p.= 217-219°C  
IR (KBr, cm<sup>-1</sup>): 3355i, 3031, 2919, 2870,1621i, 1578i, 1287, 695.

**Bis(benzylcarbamoyl)1,4-butyldiamine 3d.** Obtained in 92% yield as a white solid; m.p.= 245-247°C  
IR (KBr, cm<sup>-1</sup>): 3338i, 3031,2939, 2863, 1618i, 1573i, 1268, 695.

**Bis(benzylcarbamoyl)1,6-hexamethyldiamine 3e.** Obtained in 90% yield as a white solid; m.p.= 224-226°C  
IR (KBr, cm<sup>-1</sup>): 3346i, 3031, 2932. 2856, 1618i, 1576i, 1254, 695.

**Bis(benzylcarbamoyl)1,2-cyclohexyldiamine 3f.** Obtained in 91% yield as a white solid; m.p.= 255-257°C  
IR (KBr, cm<sup>-1</sup>): 3346i, 3031, 2932m, 2856, 1618i, 1576i, 1254, 695.

**Bis(benzylcarbamoyl)1,2-phenyldiamine 3g.** Obtained in 76% yield as a white solid; m.p.= 197-199°C  
IR (KBr, cm<sup>-1</sup>): 3294i, 3030, 1686i, 1629i, 1247, 696

### 3. Results and discussion

An efficient and straightforward two-step synthetic route for bis-ureas **3** using bis(*o*-nitrophenyl) carbonate **1** has been developed. As a first step, bis(*o*-nitrophenyl) carbonate **1** is reacted with benzyl amine to produce the intermediate, *N*-benzyl-*o*-nitrophenyl carbamate **2** (Scheme 1). The second step is formation of bis-ureas **3** by treatment of this intermediate with various diamines (Scheme 3).

The synthesis of *N*-benzyl-*o*-nitrophenyl carbamate **2** was based on the published procedure for the preparation of *o*-nitrophenyl carbamates[13], but without the isolation of this intermediate. This to obtain bis-ureas **3** a carbamate

solution which also contains *o*-nitrophenol was treated with a diamine in the molar ratio carbamate: diamine =2.5:1. The reactions we carried out in toluen because in the second step the transformation of carbamate occur more slowly and it was necessary to increase the reaction temperature to reflux.

Following our protocol with aliphatic diamine isolation of bis-ureas **3a-f** was achieved from the reaction mixture by precipitation after one hour, in yields between 86-95% (Table I).

When *o*-phenylenediamine, an aromatic diamine, was used 0.1 equiv. 4-dimethylaminopyridine was added as a catalyst, producing bis(benzylcarbamoyl)-*o*-phenylenediamine **3g** with a yield only 76%, after two hours.

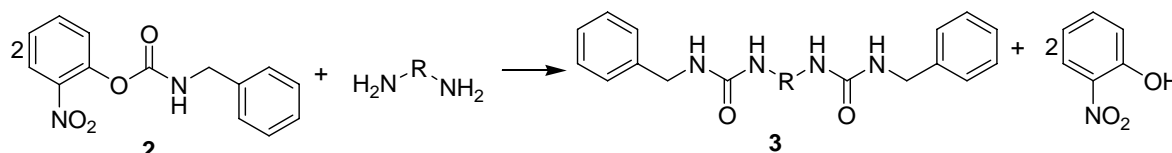
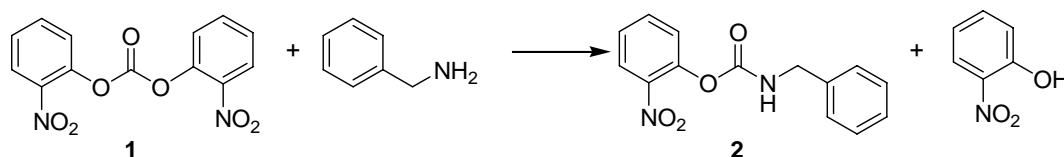


TABLE I. Preparation of bis-urea from primary diamines

Diamine	$\eta$ (%)	m. p. (°C)	$\nu_{\text{C=O}}$ (cm <sup>-1</sup> )	Bis-urea <b>3</b>
	86	240-242	1621	3a
	95	228-230	1623	3b
	86	217-219	1621	3c
	92	245-247	1618	3d
	90	224-226	1618	3e
	91	255-257	1618	3f
	76	197-199	1629	3g

### 4. Conclusions

We have developed a convenient two-step synthesis procedure for the preparation of bis-ureas using bis(*o*-nitrophenyl) carbonate as a starting material.

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