

Short Note

## ***N,N'*-(1,2-Phenylene)-bis[4-(azidomethyl)benzamide]**

Jürgen Bachl<sup>1</sup> and David D. Díaz<sup>1,2,\*</sup>

<sup>1</sup> Institut für Organische Chemie, Universität Regensburg, Universitätsstr. 31, 93040 Regensburg, Germany

<sup>2</sup> ICMA, CSIC-Universidad de Zaragoza, Pedro Cerbuna 12, 50009 Zaragoza, Spain

\* Author to whom correspondence should be addressed;

E-Mail: David.Diaz@chemie.uni-regensburg.de

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**Abstract:** The synthesis of *N,N'*-(1,2-phenylene)-bis[4-(azidomethyl)benzamide] (**2**) by direct nucleophilic disubstitution of the suitable dihalogen precursor **1** with NaN<sub>3</sub> is reported. The structure of the title compound was fully characterized by FT-IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, EI-MS, elemental analysis and melting point determination.

**Keywords:** *o*-phenylenediamine; azide; benzamide; nucleophilic substitution

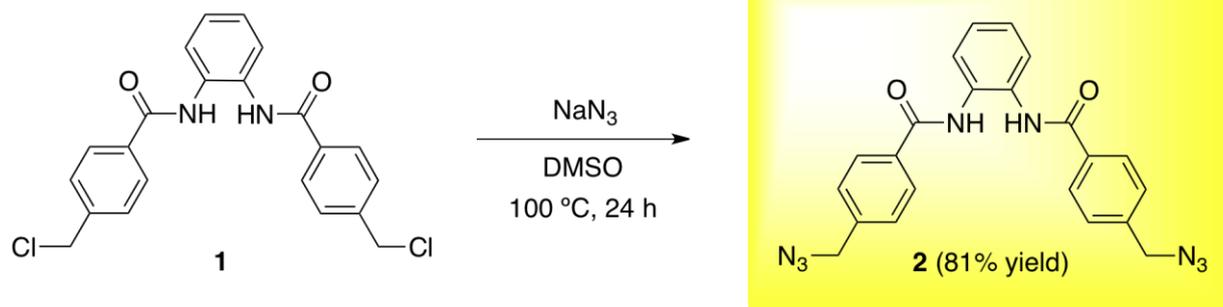
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Organic azides (R-N<sub>3</sub>) are an important class of energy-rich and versatile intermediates for organic synthesis [1] that have drawn great interest since the late 19<sup>th</sup> century [2]. They currently engage a key interdisciplinary position at the interfaces between chemistry, biomedicine and materials science [3]. The industrial interest in these compounds derives from their use as precursors for the synthesis of amines [3,4], nitrenes [5], heterocycles such as triazoles and tetrazoles [3,6], as latent amino groups in the synthesis of natural products [3], as detonators [7], blowing agents for polymeric foams [3], and functional groups in pharmaceuticals as illustrated by azidonucleosides in the AIDS treatment [8] and their bioconjugation *via* Staudinger ligation [9]. Moreover, in the last decade organic azides have emerged as a key component of the powerful ‘click’ chemistry [10]. In particular, polyvalent azides are valued cross-linking agents and monomers in materials science [11,12].

Herein, we report the synthesis of *N,N'*-(1,2-phenylene)-bis[4-(azidomethyl)benzamide] (**2**). This compound represents a versatile building block for the synthesis of a library of 3,1,5-benzoxadiazepines with potential bioactivities that could lead to potential new drug candidates [13]. The preparation of **2** was carried out by double nucleophilic substitution of the suitable dihalogen

precursor **1** with  $\text{NaN}_3$  in DMSO at 100 °C for 24 h (Scheme 1). Dihalogen precursor **1** was prepared by double nucleophilic addition of *o*-phenylenediamine on 4-(chloromethyl)benzoyl chloride as reported previously [14].

Scheme 1.



## Experimental Section

### General

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded at 25 °C on a Bruker Avance 300 spectrometer in  $\text{CDCl}_3$  as solvent, and chemical shifts are reported relative to  $\text{Me}_4\text{Si}$  ( $\delta = 0$ ) [15]. The low-resolution mass spectrum was obtained by using a Varian MAT 311A spectrometer. Elemental analysis was performed on a Heraeus Mikro-Rapid analyzer. The infrared spectrum was recorded using a Diamond ATR (attenuated total reflection) accessory (Golden Gate) on a Bio-Rad Excalibur FTS 3000 MX spectrophotometer. The melting point (mp) was measured in a Büchi 510 and is uncorrected. Thin-layer chromatography was carried out on Merck aluminium sheets coated with silica gel 60 F<sub>254</sub>. Compounds were visualized by use of 254 nm UV light and/or iodine as staining reagent. All solvents were of p.a. grade or purified by standard techniques [16]. Anhydrous sodium sulfate was used for drying solutions.

### Safety Note

Although the title compound was found to be a stable solid ( $\text{C/N} = 2.75$ ) at room temperature, highly energy-rich organic azides ( $\text{C/N} < 1$ ) should never be isolated and they should be stored away from sources of heat, light, pressure, and shock. Azide-containing reaction mixtures should not be concentrated through rotary evaporation or distillation.

### Synthesis of *N,N'*-(1,2-phenylene)-bis[4-(azidomethyl)benzamide] (**2**)

To a 50 mL round-bottomed flask equipped with a stirring bar and condenser were added *N,N'*-(1,2-phenylene)-bis[4-(chloromethyl)benzamide] (**1**) (500 mg, 1.21 mmol), sodium azide (236 mg, 3.63 mmol), and DMSO (10 mL). The mixture was heated at 100 °C for 24 h, cooled, and water (30 mL) and brine (10 mL) were added. The mixture was extracted five times with EtOAc, and the combined organic phases were washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ), filtered, and concentrated. The final

traces of solvent were removed under vacuum to yield **2** (417 mg, 81%) as a white solid: TLC  $R_f$  (AcOEt/hexane 1:1) 0.44; m.p. = 116–118 °C;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ /ppm = 4.46 (s, 2H), 6.84–6.47 (m, 1H), 7.34–7.26 (m, 1H), 7.48 (d,  $J$  = 8.4 Hz, 2H), 8.04 (d,  $J$  = 8.3 Hz, 2H), 9.61 (s, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ /ppm = 54.28, 125.88, 126.17, 128.29, 128.32, 130.58, 133.30, 139.68, 166.06; FT-IR (ATR)  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 3225 (N-H stretching), 2086 ( $\text{N}_3$  asymmetric stretching), 1646 (C=O stretching, amide I band), 1505 (N-H bending, amide II band), 1252 ( $\text{N}_3$  symmetric stretching); MS (ESI)  $m/z$  427 [ $\text{MH}^+$ ]. Elemental analysis calculated for  $\text{C}_{22}\text{H}_{18}\text{N}_8\text{O}_2$ : C, 61.96; H, 4.25; N, 26.28; found: C, 62.09; H, 4.69; N, 26.89.

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