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Short Note

N,N'-1,2-Phenylenebis[4-(chloromethyl)benzamide]

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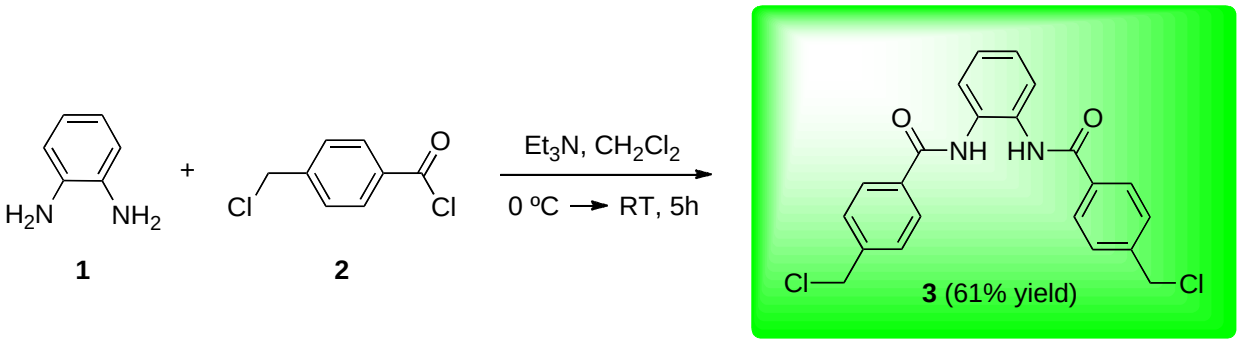
Abstract: *N,N'*-1,2-Phenylenebis[4-(chloromethyl)benzamide] (**3**) was obtained in 61% yield by nucleophilic acyl substitution of 4-(chloromethyl)benzoyl chloride (**2**) with 1,2-phenylenediamine (**1**) under basic conditions. The title compound was characterized by FT-IR, ^{1}H NMR, ^{13}C NMR, low- and high-resolution EI-MS, and melting point.

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

Substituted benzamides have been in clinical use for many years as anti-emetics, anti-arrhythmics, neuroleptics, and/or anti-psychotics in the treatment of various disorders [1]. They also constitute versatile intermediates for the synthesis of anti-tumor and anti-inflammatory agents [2], protease inhibitors [3], dyes [4], and have been extensively used as sensitizers for radio- or chemotherapies [5]. On the other hand, benzyl chloride derivatives are widely used as synthetic building blocks. They constitute, for instance, the precursors to benzyl esters, which are commonly employed in industry as plasticizers, flavorants, and perfumes [6]. Hence, organic molecules bearing both functionalities may be of practical interest.

We report here the synthesis of *N,N'*-1,2-phenylenebis[4-(chloromethyl)benzamide] (**3**) by nucleophilic acyl substitution of 4-(chloromethyl)benzoyl chloride (**2**) with 1,2-phenylenediamine (**1**) in the presence of Et_3N (Scheme 1) [7].

Scheme 1.



Experimental Section

General

^{1}H and ^{13}C NMR spectra were recorded at 25 ℃ on a Bruker 400 spectrometer in DMSO-d_6 as solvent, and chemical shifts are reported relative to residual solvent peaks [8]. The low-resolution mass spectrum was obtained using a Varian MAT 311A spectrometer. 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 an Opti Melt MPA 100 instrument and is uncorrected. Thin-layer chromatography was carried out on Merck aluminium sheets coated with silica gel 60 F_{254}. Compounds were visualized by use of 254 nm UV light and/or phosphomolybdic acid 20% (wt.) solution in ethanol with heating. All solvents were of p.a. grade or were purified by standard techniques [9]. Anhydrous sodium sulfate was used for drying solutions. 1,2-Phenylenediamine (**1**) and 4-(chloromethyl)benzoyl chloride (**2**) were purchased from commercial suppliers and used as received without further purification.

*Synthesis of N,N'-1,2-phenylenebis[4-(chloromethyl)benzamide] (**3**)*

To a stirred solution of 1,2-phenylenediamine (**1**) (500 mg, 4.55 mmol) and Et_3N (1.59 mL, 11.4 mmol) in CH_2Cl_2 (20 mL) kept at 0 ℃ was added dropwise (using a pressure-compensated addition funnel) a solution of 4-(chloromethyl)benzoyl chloride (**2**) (1.75 g, 9.09 mmol) in CH_2Cl_2 (20 mL). The reaction mixture was allowed to stir for 5 h at room temperature, after which time TLC analysis showed full conversion of the starting materials. The organic phase was washed with H_2O (15 mL × 2) and brine (15 mL × 2), dried (Na_2SO_4), filtered, and concentrated. The solid residue was recrystallized from CH_2Cl_2/pentane, affording product **3** (1.1 g, 61% yield [10]) as a white crystalline solid: TLC R_f (AcOEt/hexane 1:1) 0.40; mp = 191–193 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm = 4.83 (s, 4H), 7.31 (dd, J = 6.0, 3.6 Hz, 2H), 7.59 (d, J = 8.4 Hz, 4H), 7.67 (dd, J = 6.0, 3.6 Hz, 2H), 7.96 (d, J = 8.4 Hz, 4H), 10.08 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ/ppm = 45.23 (2C), 125.51 (2C), 125.80 (2C), 127.81 (4C), 128.83 (4C), 131.19 (2C), 133.97 (2C), 141.22 (2C), 164.92 (2C); FT-IR (ATR) ν_{max} (cm^{-1}) 3287 (N-H stretching), 1644 (C=O stretching, amide I band), 1514 (N-H bending, amide II band), 1305, 1267 (C-H stretching, CH_2Cl), 672, 476; MS (ESI) *m/z* 412 [M^{+}]. HRMS calculated for $C_{22}H_{18}Cl_2N_2O_2$ 412.07453; found 412.07426.

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