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Short Note

N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine

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Abstract

This work reports the synthesis of a previously uncharacterized N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine derivative, a member of the aromatic diamine Schiff base family that has not been documented in the existing literature. The full set of ^{1}H NMR, ^{13}C NMR and mass spectrometry data provides definitive confirmation of the successful construction and full structural consistency of the target product.

Keywords: N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine; synthesis; structural characterization

1. Introduction

N-(1-Arylethyl)benzene-1,2-diamine features a unique structural arrangement where the amino group is adjacent to the active imino moiety, which significantly enhances the reactivity of this class of compounds and serves as a critical intermediate for the synthesis of potent HIV-1 non-nucleoside reverse transcriptase aryl benzimidazolone derivatives. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) are capable of achieving maximal and sustained suppression of in vivo viral replication, enabling patients to attain and maintain immune function reconstitution, while reducing the morbidity and mortality associated with both HIV infection and non-AIDS-related diseases [1]. A series of highly potent NNRTIs developed by modifying the benzimidazolone scaffold using indole methyl ether and methyl sulfide as template molecules have demonstrated promising outcomes in clinical anti-HIV studies, exhibiting exceptional antiviral potency, favorable pharmacokinetic properties, high selectivity, and remarkable structural diversity [2]. Accordingly, the synthetic methodology for benzimidazolone derivatives has attracted growing research attention from the medicinal chemistry community.

Typical synthetic methods for derivatives structurally similar to *N*-(1-arylethyl)benzene-1,2-diamine are listed as follows: (I) palladium-catalyzed reaction of o-dibromobenzene with 1,2-propanediamine derivatives [3]; (II) reaction of aromatic ketones with vinyl Grignard reagents [4]; (III) reaction of 2-fluoronitrobenzene with aliphatic amines to synthesize 2-iminonitrobenzene, followed by further reduction of the nitro group [5]; (IV) dehydrohalogenation reaction of o-haloaniline with benzylamine [6]; (V) palladium-catalyzed dehydrohalogenation reaction of 2-haloaniline with benzylamine [2]; and (VI) monoaminoalkylation reaction of o-phenylenediamine under potassium carbonate catalysis [7].

Herein, we describe the synthesis of the hitherto-unreported N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine (Figure 1). A battery of complementary analytical methods was adopted to verify both the structure and phase purity of this newly obtained molecule. ^{1}H and ^{13}C NMR spectra allowed unambiguous assignment of all proton and carbon

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signals consistent with the expected molecular skeleton. Furthermore, high-resolution mass spectrometry (HRMS) provides definitive core evidence for the identity of N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine, by accurately determining the exact mass-to-charge ratio of the molecule and delivering molecular weight data that is in excellent agreement with the theoretically calculated value of the target molecular formula.

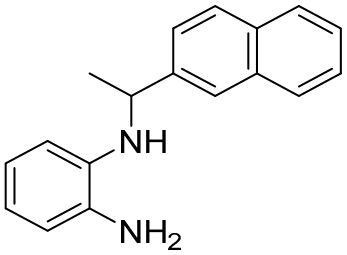
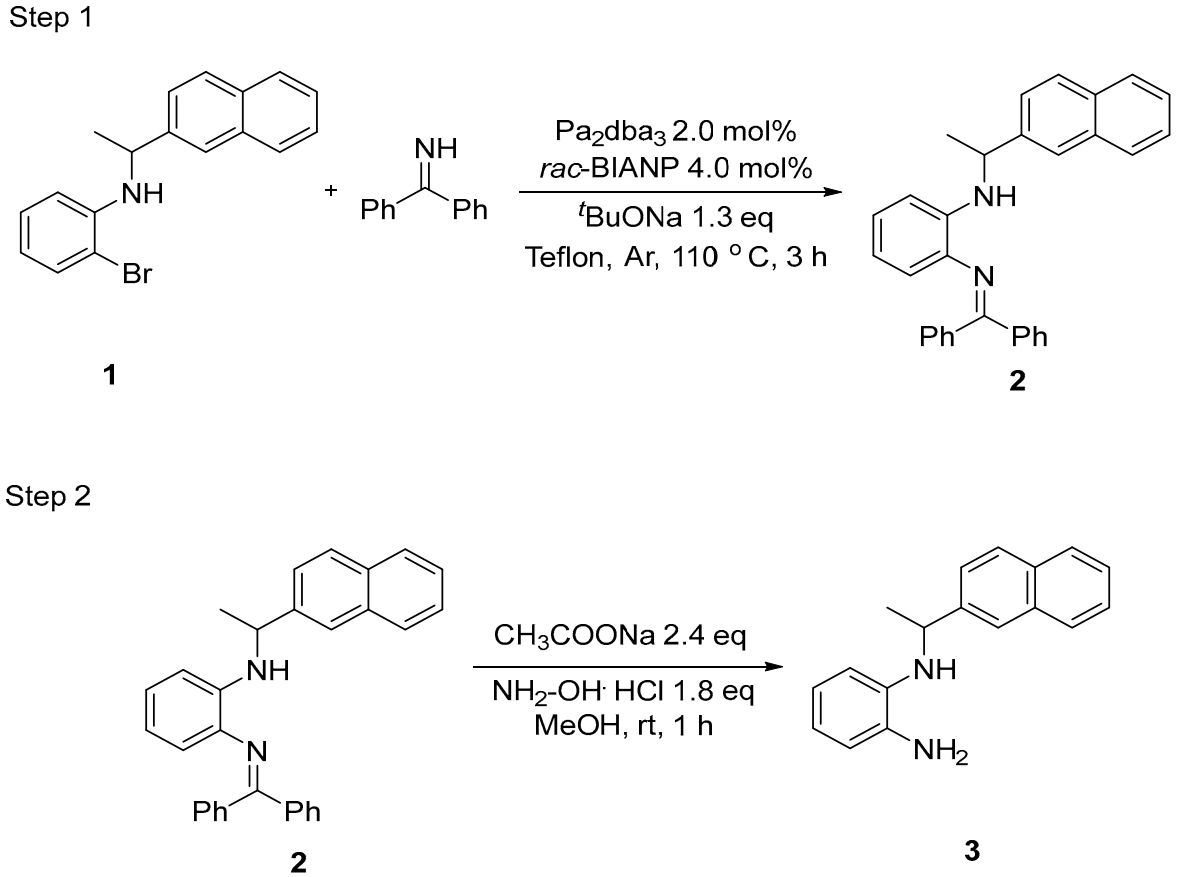


Figure 1. Structural formula of N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine **3**.

2. Results

The successful synthesis of N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine is described. 2-Bromo-*N*-(1-(naphthalen-2-yl)ethyl)aniline is first converted into 2-((diphenylmethylene)amino)-*N*-(1-(naphthalen-2-yl)ethyl)aniline, and subsequent deprotection with sodium acetate and hydroxylamine hydrochloride affords the target N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine (Scheme 1).



Scheme 1. Synthesis of N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine (**3**).

The structure of the synthesized compound was unambiguously confirmed by comprehensive spectral characterization, including ^{1}H NMR, ^{13}C NMR, and high-resolution mass spectrometry (HRMS).

^{1}H NMR spectroscopic analysis verifies that all 18 anticipated protons of the target compound can be clearly detected. A broad smooth resonance at δ 3.53 ppm, integrating for three protons, is unambiguously assigned to the exchangeable protons of the amino and imino functionalities. The well-resolved doublet at δ 1.61 ppm (3H) corresponds to the aliphatic methyl group, and the distinct quartet at δ 4.64 ppm (1H) is attributed to the adjacent methine moiety. All the above ^{1}H NMR signals are fully consistent with the proposed molecular structure of the target compound (see Supplementary Figure S1). The ^{13}C NMR spectrum unambiguously presents all 18 expected carbon signals of the target molecule, at δ 25.20 ppm and δ 53.75 ppm, which are unambiguously assigned to the methyl carbon atom and the adjacent methine carbon atom in the molecular skeleton, respectively (see Supplementary Figure S2). HRMS: m/z [M + Na]$^+$ call for $C_{18}H_{18}N_3Na^+$: 285.1362; Found: 285.1358 (see Supplementary Figure S3).

3. Materials and Methods

^{1}H and ^{13}C NMR spectra were recorded on a Bruker NEO 400 MB spectrometer (Bruker, Billerica, MA, USA) in $CDCl_3$ with Me_4Si as an internal reference. High-resolution mass spectrometry (HRMS) data were obtained on a Q Exactive Plus mass spectrometer (Thermo Fisher Scientific, Bremen, Germany) with a heated electrospray ionization (HESI-II) source, and only molecular and parent ion peaks (m/z) are listed. Thin-layer chromatography (TLC) was performed on 0.2 mm silica gel 60 plates (Qingdao Marine Chemical, Qingdao, China).

All starting materials were commercially available from Energy Chemical. All solvents and reagents were of analytical grade and used directly without additional purification, unless otherwise specified in the experimental section. Flash column chromatography was carried out on an automated system with silica gel as the stationary phase, employing a binary eluent system composed of hexane and ethyl acetate. Pre-coated silica gel GF-254 plates were used for all thin-layer chromatography (TLC) monitoring throughout the reactions.

The target compound is obtained via a two-step sequential synthetic protocol:

Step 1: Tris(dibenzylideneacetone)dipalladium(0) (0.183 g, 2.0 mol%) and 2,2′-bis(diphenylphosphino)-1,1′-binaphthalene (0.248 g, 4.0 mol%) were dissolved in toluene, with all manipulations carried out under a dry argon atmosphere. The resulting mixture was heated in a preheated oil bath for 0.5 h to complete the pre-activation of the catalytic system. After the system was cooled to room temperature, 2-bromo-*N*-(1-(naphthalen-2-yl)ethyl)aniline (1.0 mmol, 0.326 g), benzophenone imine (1.3 mmol, 0.235 g) and sodium tert-butoxide (1.3 mmol, 0.125 g) were introduced. The reaction mixture was stirred at 110 °C for 2.5 h under an inert atmosphere. After cooling to room temperature, the mixture was diluted with diethyl ether and filtered through a Celite pad to remove insoluble residues, and the solvent was removed in vacuo to yield a dark brown–black crude residue. Subsequent purification via flash chromatography (10:1 hexane/CH_2Cl_2) afforded the desired Compound **2** as a yellow oil. The TLC analysis (2:1 hexane/CH_2Cl_2) indicated an R_f of 0.14.

Step 2: Compound **2** (1.0 mmol, 0.426 g), sodium acetate (2.4 mmol, 0.197 g), and hydroxylamine hydrochloride (2.4 mmol, 0.079 g) were charged into a reaction vessel containing 8 mL of methanol. The mixture was stirred at 25 °C for 1 h. Upon reaction completion, the biphasic system was formed by adding NaOH and CH_2Cl_2 for liquid–liquid extraction. The organic layer was collected, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to remove volatile solvents. The resulting crude oil was purified by flash chromatography on silica gel with a step-gradient elution (6:1 hexane/EtOAc, then 4:1 hexane/EtOAc) to give Compound **3** as a reddish-brown oil (136 mg, 52% yield). The TLC analysis (4:1 hexane/CH_2Cl_2) indicated an R_f of 0.19. The isolated product slowly turns

light red on standing, whether dissolved in organic solvent or stored as a neat substance. Analytical TLC was carried out on silica gel plates with 30% hexane/ethyl acetate as the mobile phase.

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Reddish-brown oily liquid (136 mg, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82–7.76 (m, 4H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.43 (td, *J* = 7.5, 6.3, 4.2 Hz, 2H), 6.71 (d, *J* = 9.0 Hz, 1H), 6.61 (t, *J* = 4.6 Hz, 2H), 6.45 (d, *J* = 9.2 Hz, 1H), 4.64 (q, *J* = 6.6 Hz, 1H), 3.53 (s, 3H), 1.61 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.73, 136.97, 133.84, 133.56, 132.74, 128.40, 127.81, 127.63, 125.94, 125.45, 124.46, 124.28, 120.79, 118.44, 116.73, 113.21, 53.75, 25.21. HRMS: *m*/*z* $(M + H)^+$ calcd for $C_{18}H_{19}N_2^+$: 263.1543; Found: 263.1540.

Supplementary Materials: The following supporting information can be downloaded online. Figure S1: ^{1}H NMR of N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine (**3**); Figure S2: ^{13}C NMR of N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine (**3**); Figure S3: HRMS [$(M + H)^+$] N^1-(1-(naphthalen-2-yl)ethyl)benzene-1,2-diamine (**3**).

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Data Availability Statement: The raw data supporting the conclusions of this article will be made available by the authors on request.

Conflicts of Interest: The authors declare no conflicts of interest.

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