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SYNTHESIS AND STRUCTURES OF SOME BINAPHTHYL DERIVATIVES VIA SUZUKI CROSS COUPLING REACTION

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Abstract. Four new binaphthyl derivatives **2a**, **2b**, **2c** and **2d** have been synthesized successfully *via* Suzuki reaction of 2,2'-dibromo-1,1'-binaphthalene (**1)** and phenylboronic acid derivatives in high yield. Structures of all samples were determined by ^{1}H NMR, ^{13}C NMR, HMBC, HSQC, and MS spectra that referred to a strong agreement between spectral data and structures.

Keywords: binaphthyl derivative, Suzuki cross coupling reaction, asymmetric catalyst.

1. Introduction

Binaphthalene and its derivatives have been isolated from various plant sources or synthesized from microorganisms [1]. Recently, the synthesis of binaphthyl derivatives has garnered increasing attention from researchers due to the widespread occurrence of the binaphthalene framework in various natural products and analogous compounds such as gossypol, exhibiting intriguing biological activities [2], [3]. Moreover, owing to the distinctive optical properties of the binaphthalene framework, its derivatives have found utility as asymmetric catalysts in synthesizing an α-amino acid [4], highly optically selective reduction of ketones to alcohols [5], [6], asymmetric alkylations or arylations of aldehydes [7], and the asymmetric hydrogenation of imines into amines [8]. Particularly, binaphthalene derivatives exhibit the capability to form complexes with triarylamine, yielding fluorescent quenching probes for Fe^{3+} ions. For example: Four compounds 6,6-TB-1, 6,6-TB-2, 7,7-OMeTB-1, 7,7-TB-2 (Figure 1) [9].

Due to these remarkable applications of binaphthyl derivatives, numerous research groups have developed several synthetic methodologies. The most prevalent methods involve coupling two naphthalene rings through the Ullmann reaction [10], the decomposition of diazonium salts (Pschorr reaction [11], [12] and Gomberg-Bachmann-Hey reaction [13]-[15], or utilizing relatively weak Lewis acids such as $TiCl_4$ as oxidizing agents [16]. Recently, several modern synthesis methods have been published, for instance: employing the Palladium-catalyzed cross-coupling reaction of triorganoindium

reagents [17]; direct synthesis through coupling of 2-naphthol derivatives using transition metal catalysts [18]; electrochemical synthesis via transition-metal-free oxidative homocoupling [19]. In this paper, we report a simple procedure for synthesizing binaphthyl derivatives via the Suzuki reaction of 2,2'-dibromo-1,1'-binaphthalene (**1)** and various phenylboronic acid derivatives, aiming to discover new materials and novel asymmetric catalysts for future applications.

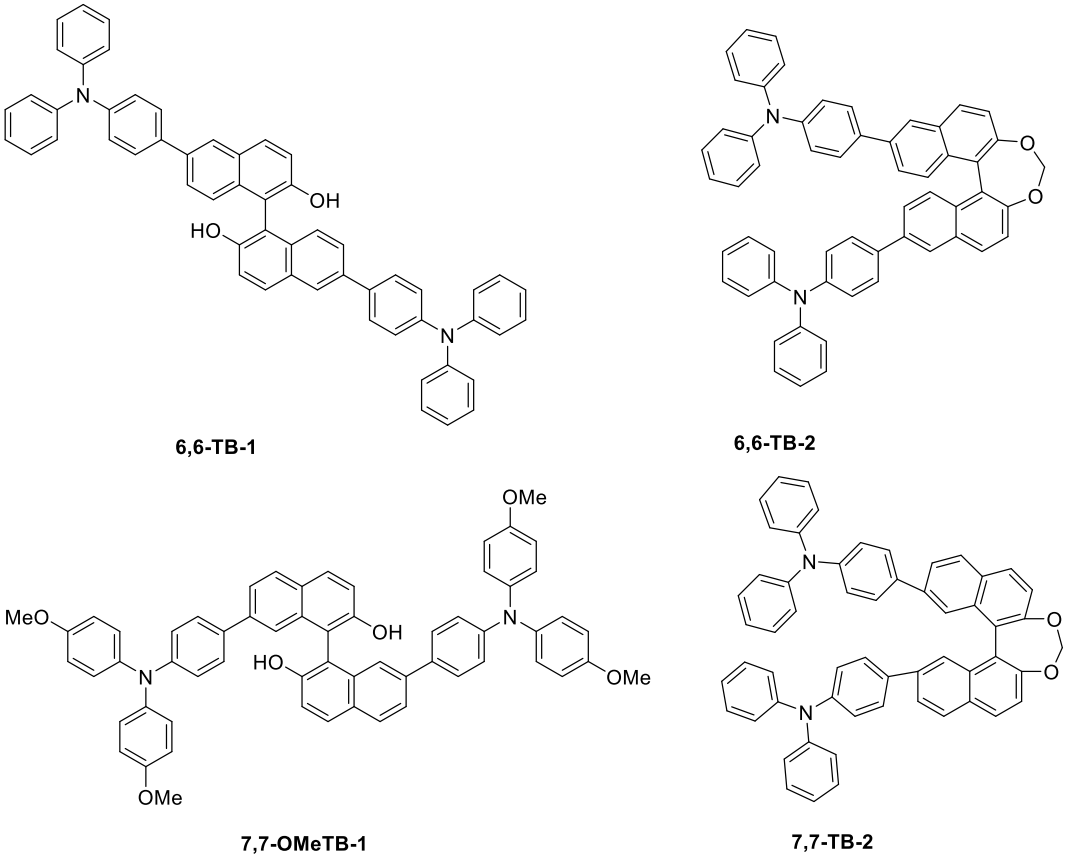


Figure 1. Structure of some binaphthalene derivatives [9]

2. Content

2.1. Experiments

2.1.1. Chemicals and equipment

Solvents and other chemicals were purchased from Sigma-Aldrich, Merck Corp, Aladdin, Vietnam or other Chinese companies and were used as received unless indicated. The 1D and 2D NMRs spectra were recorded on the Bruker Avance 600 NMR spectrometer in chloroform-d ($CDCl_3$). Mattson 4020 GALAXY Series FT-IR, LC-MSD-Trap-SL spectrometers were used to take IR and MS spectra. Progress of the reaction was monitored by thin-layer chromatography (TLC). The melting point determination was screened on a Gallenkamp melting-point apparatus in the opening of a capillary tube.

2.1.2. Synthetic procedure

General experimental procedure for the synthesis of Binaphthyl derivatives, ***2a – 2d****.*

To a solution of K_2CO_3 (380 mg, 2.75 mmol), $PdCl_2$ (1.24 mg, 0.007 mmol), 2-phenylimidazole (2 mg, 0.014 mmol), 2,2'-dibromo-1,1'-binaphthalene (**1**, 409.93 mg, 1 mmol) and aryl boronic acid (3 mmol) in anhydrous DMF (16 mL) was degassed with argon. Then the resulting mixture was stirred at 120°C for 17h - 48 hours under an argon atmosphere. The mixture was cooled and then poured into ice-water (250 mL) containing 1M HCl (2 mL) aqueous solution and extracted with $CHCl_3$ (5 × 20 mL). The combined organic layers were washed with brine (2 × 30 mL) and dried with Na_2SO_4. Removal of solvent followed by column chromatography purification (silica gel, hexane–$CHCl_3$) afforded the coupling products **2a-d**

*Synthesis of 2,2'-bis(4-methoxyphenyl)-1,1'-binaphthalene (**2a**)*

Following the general procedure from K_2CO_3 (380 mg, 2.75 mmol), $PdCl_2$ (1.24 mg, 0.007 mmol), 2-phenylimidazole (2 mg, 0.014 mmol), 2,2'-dibromo-1,1'-binaphthalene (**1**, 409.93 mg, 1 mmol) and (4-methoxyphenyl)boronic acid (456.18 mg, 3 mmol) and anhydrous DMF (16 mL) gave 2,2'-bis(4-methoxyphenyl)-1,1'-binaphthalene (**2a**) (0.428g, 92%, mp = 276 ^oC); ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.93 (d, J = 7.8 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.47 (td, J = 1.2, 6.6 Hz, 1H), 7.39 (d, J = 8.4 Hz, 1H), 7.35 (d, J = 9.0 Hz, 1H), 7.31 (m, 1H), 6.44 (m, 2H), 6.39 (m, 2H), 3.68 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 158.0, 139.2, 134.6, 134.1, 134.0, 132.2, 130.2, 128.7, 128.1, 127.9, 127.4, 126.5, 125.3, 112.5, 55.1. ESI-MS m/z: $[M-H]^-$ 465.

*Synthesis of 2,2'-di-p-tolyl-1,1'-binaphthalene (**2b**)*

Following the general procedure from K_2CO_3 (380 mg, 2.75 mmol), $PdCl_2$ (1.24 mg, 0.007 mmol), 2-phenylimidazole (2 mg, 0.014 mmol), 2,2'-dibromo-1,1'-binaphthalene (**1**, 409.93 mg, 1 mmol) and *p*-tolylboronic acid (408.21 mg, 3 mmol) and anhydrous DMF (16 mL) gave 2,2'-di-p-tolyl-1,1'-binaphthalene (**2b**) (0.386g, 89%, mp = 217 ^oC); ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.92 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.46 (td, J = 1.2, 6.6 Hz, 1H), 7.39 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.30 (td, J = 1.2, 6.6 Hz, 1H), 6.69 (d, J = 7.8 Hz, 2H), 6.36 (d, J = 7.8 Hz, 2H), 2.19 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 139.6, 138.5, 135.5, 134.5, 134.2, 132.2, 128.9, 128.6, 128.1, 127.8, 127.7, 127.4, 126.3, 125.4, 20.1; ESI-MS m/z: $[M+H]^+$ 436.

*Synthesis of 2,2'-bis(4-butylphenyl)-1,1'-binaphthalene (**2c**)*

Following the general procedure from K_2CO_3 (380 mg, 2.75 mmol), $PdCl_2$ (1.24 mg, 0.007 mmol), 2-phenylimidazole (2 mg, 0.014 mmol), 2,2'-dibromo-1,1'-binaphthalene (**1**, 409.93 mg, 1 mmol) and (4-butylphenyl)boronic acid (534.36 mg, 3 mmol) and anhydrous DMF (16 mL) gave 2,2'-bis(4-butylphenyl)-1,1'-binaphthalene (**2c**) (0.441g, 85%, mp = 239^0C); ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.90 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.43 (td, J = 1.2, 6.6 Hz, 1H), 7.37 (d, J = 8.4 Hz, 1H), 7.30 (d, J = 3.6 Hz, 1H), 7.27 (td, J = 1.2, 6.6 Hz, 1H), 6.66 (d, J = 7.8 Hz, 2H), 6.33 (dd, J = 1.6, 6.6 Hz, 2H), 2.44 (t, J = 7.8 Hz, 2H), 1.49 (m, 2H), 1.28 (m, 2H), 0.89 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, MHz, $CDCl_3$) δ (ppm): 140.6, 138.7, 134.7, 134.2, 133.9, 132.3, 129.0, 128.7, 128.1, 128.0, 127.5, 127.2, 126.5, 125.4, 35.2, 33.6, 22.3, 14.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{40}H_{39}$ 519.3072, found 519.3046.

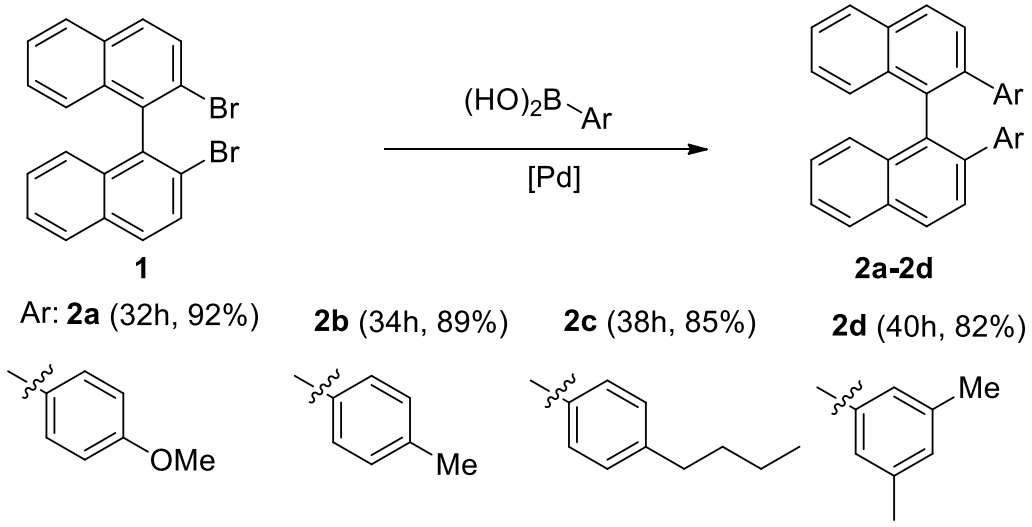
*Synthesis of 2,2'-bis(3,5-dimethylphenyl)-1,1'-binaphthalene (**2d**)*

Following the general procedure from K_2CO_3 (380 mg, 2.75 mmol), $PdCl_2$ (1.24 mg, 0.007 mmol), 2-phenylimidazole (2 mg, 0.014 mmol), 2,2'-dibromo-1,1'-binaphthalene (**1**, 409.93 mg, 1 mmol) and (3,5-dimethylphenyl)boronic acid (450.27 mg, 3 mmol) and anhydrous DMF (16 mL) gave 2,2'-bis(3,5-dimethylphenyl)-1,1'-binaphthalene (**2d**) (0.379g, 82%, mp = 226 ^oC); ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.91 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.46 (t, J = 8.4 Hz, 2H), 7.34 (m, 2H), 6.64 (s, 1H), 6.11 (s, 2H), 1.93 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 141.3, 139.79, 136.1, 134.7, 134.5, 132.1, 128.4, 127.9, 127.7, 127.6, 127.5, 127.0, 126.3, 125.3, 29.71, 21.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{36}H_{31}$ 463.2428, found 463.2442.

2.2. Results and discussion

2.2.1. Synthesis

Synthesis of binaphthyl derivatives **2a** - **2d** was completed following Scheme 1. The Suzuki reaction between 2,2'-dibromo-1,1'-binaphthalene (**1)** and various phenylboronic acid derivatives was carried to form 4 novel derivatives with excellent yield, up to 92% over a duration ranging from 32 to 40 hours. This reaction exhibited a prolonged reaction time (> 24 hours), likely influenced by spatial constraints, attributed to the necessity of coupling two aromatic rings onto the 1,1'-binaphthalene frameworks. Additionally, the size of the substituent groups in the phenylboronic acid derivatives also impacted the reaction duration, with compound **2d** exhibiting an extended reaction time (up to 40 hours) due to the bulkiness of its substituent group.



Scheme 1. Synthesis of binaphthyl derivatives 2a – 2d

2.2.2. Structural determination

The structure of the **2a** - **2d** was determined by modern spectroscopic methods. Compound **2a** was chosen for precise structural analysis through ^1H NMR, ^{13}C NMR, HSQC, HMBC, and MS spectra. First of all, the negative mass spectrum showed a base peak at *m/z* 465 au. This indicated that the molecular weight of compound **2a** must be 466 g/mol, matching the designed product, expectedly.

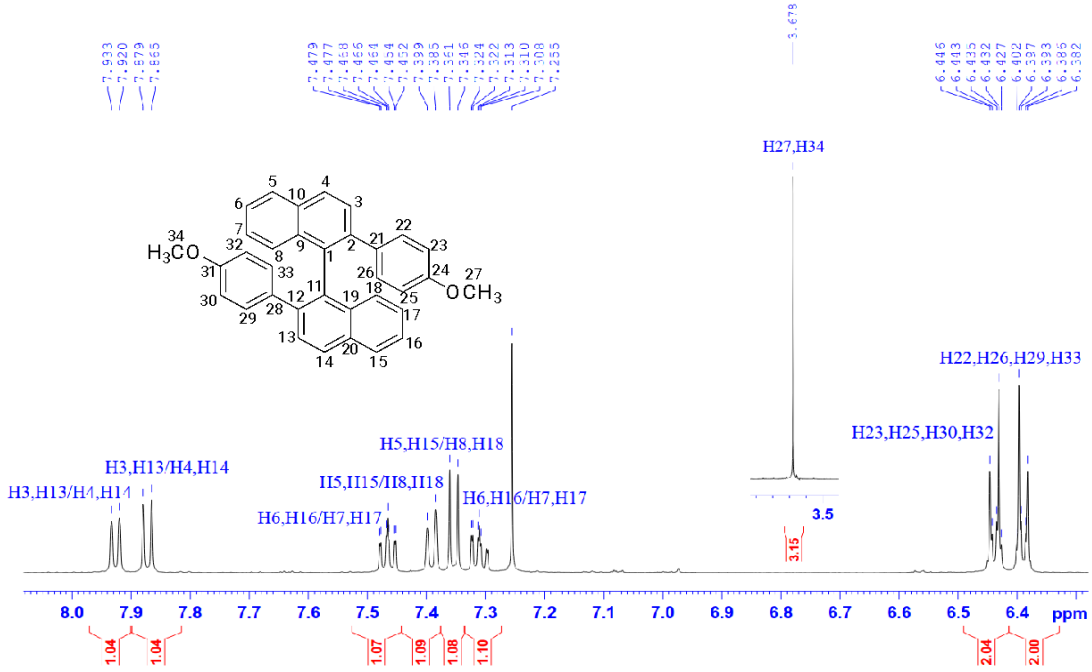


Figure 2. ^{1}H NMR spectrum of compound 2a

The ^{1}H NMR spectrum fully shows the resonance signal of the protons of compound **2a**. Based on the chemical shift, spectral pattern, and constant spin-spin interaction, the signal of the protons of compound **2a** can be accurately attributed. ^{1}H NMR spectrum of compound **2a** indicated 26 protons, a singlet peak at δ = 3.68 ppm was for H27, H34. In addition, there were two multiplet peaks at δ = 6.39 and 6.43 ppm, which were ether for either H22, H26, H29, H33 or H23, H25, H30, H32. There were two doublet peaks at δ = 7.93 and 7.87 ppm with a splitting constant of about 7.8 and 8.4 Hz, which were assigned for either H3, H13, or H4, H14. Similarly, there were two doublet peaks at δ = 7.35 and 7.39 ppm with a splitting constant of about 8.4 and 9.0 Hz, which were for ether H5, H15, or H8, H18. Finally, two signals including a doublet-triplet signal at δ = 7.49 ppm with a splitting constant of 1.2, 6.6 Hz, and a multiplet signal at δ = 7.31 ppm are predicted to possibly correspond to H6, H16, or H7, H17 (Figure 2).

The ^{13}C NMR spectrum of compound **2a** indicated 15 peaks associated with 34 carbon atoms (because several C signals overlap in chemical shifts). Certainly, a peak at 55.1 ppm was assigned for C27 and C34, and a peak at 158.0 ppm was assigned for C24, and C31 (Because it directly bonds to an electron-withdrawing oxygen atom). The remaining 13 signals are for aromatic carbons. To determine the resonance signal of the remaining aromatic carbons, relying on the HSQC and HMBC spectrum of **2a** is necessary.

From the results of the HSQC spectrum analysis, the signal of C3, C4, C5, C6, C7, C8, C13, C14, C15, C16, C17, C18, C22, C26, C29, C33 can be shown. From the results of the HMBC spectrum analysis, the signal of the remaining C atoms is determined (Figure 3).

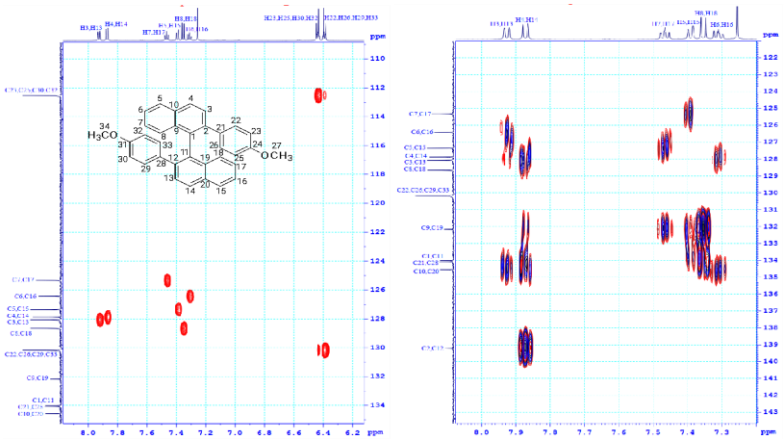


Figure 3. Parts of HSQC and HMBC spectra of compound 2a

3. Conclusions

Assembling of 2,2'-dibromo-1,1'-binaphthalene (**1**) and phenylboronic acid derivatives derived to form 04 binaphthyl derivatives **2a-d** in up to 92% yield for 32 to 40 hours. The size of substituents of phenylboronic acids might affect the yield. The structures of the synthesized compounds were accurately determined using modern spectroscopic methods including ^{1}H NMR, ^{13}C NMR, HMBC, HSQC, and MS spectra.

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