

Coupling reaction of 1,2,3,4-tetrahydro-1,10-phenanthroline: synthesis and crystal structure of 6,6'-bis(1,2,3,4-tetrahydro-1,10-phenanthroline)

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Abstract: The coupling reaction of 1,2,3,4-tetrahydro-1,10-phenanthroline (*tphen*) with silver salt as oxidative coupling agent is investigated, which can afford a new heterocyclic compound, namely 6,6'-bis(1,2,3,4-tetrahydro-1,10-phenanthroline) (**1**). The accurate structures of compound **1** are confirmed and investigated by X-ray single crystal diffraction. The result proves that the coupling reaction of *tphen* mainly affords its C6-coupling product. Crystal data of **1**: Monoclinic, space group C2/c, $a = 25.745(8) \text{ \AA}$, $b = 6.706(2) \text{ \AA}$, $c = 10.834(4) \text{ \AA}$, $\beta = 90^\circ$, $Z = 4$, $V = 1870.3(11) \text{ \AA}^3$.

Keywords: 6,6'-bis(1,2,3,4-tetrahydro-1,10-phenanthroline), 1,2,3,4-tetrahydro-1,10-phenanthroline, silver salt, coupling reaction

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I. Introduction

1,2,3,4-tetrahydro-1,10-phenanthroline (*tphen*) is an organic heterocyclic base, whose zirconium or hafnium complexes can be homogeneous metallocene catalysts for olefin polymerization [1]. It also have potential application for fluorescent dyes and acid-base indicators because *tphen* and its dimethyl substitutes can display bright yellow color (with green fluorescence, neutral form) or red color (ionic form) [2-4]. However, at room temperature, *tphen* itself is a yellow oil with weak thermal stability and leach resistant, which is not suitable for high performance organic dyes. Thus, it is necessary to explore new substitutes of *tphen* with relatively high molecule weights and melting points. By now, reduction of 1,10-phenanthrolines is still the main synthesis strategy to obtain *tphens* [4-10]. Though various reduction reagents can be used for this synthesis strategy, it is still stunted by the limit of substrates and relatively weak selectivity, which can only afford *tphen* itself and its dialkyl derivatives.

The structure of *tphen* can be recognized as the condensation product of quinoline and piperidine. It is notable that, the amino group in its piperidine ring can display electron-donating effect and result in an increasing of electron cloud density of its C6 position carbon atom, i.e. the contraposition of the N1 amino group, which is favor for the attack of electrophilic reagent. So organic modification of the C6 position can be the key for designing new derivatives of *tphen*. As described in our previous reports, the bromination reaction of *tphen* can afford its C6-substituted product, namely 6-bromo-1,2,3,4-tetrahydro-1,10-phenanthroline with high regioselectivity and an isolated yield of 90 % [11], while a more complex C6-substituted *tphen* molecule, i.e. bis(1,2,3,4-tetrahydro-1,10-phenanthroline-6-yl) methane, can be obtained by a condensation reaction of *tphen* and formaldehyde (HCHO) with an isolated yield of 83.8 % [12].

It is known that silver ion can be oxidative coupling agent for some coupling reaction [13-18]. In order to explore new synthesis strategy for the derivatives of *tphen*, we chose silver sulfate and *tphen* as substrate, and investigated the coupling reaction between them. From this reaction, we successfully obtained a new heterocyclic compound, namely 6,6'-bis(1,2,3,4-tetrahydro-1,10-phenanthroline) (**1**) (See Fig. 1). This compound can be prepared as single crystals and structural characterized by X-ray single crystal diffraction.

II. Experimental Section

2.1 Materials and methods

The *tphen* was prepared according to the solvent-free hydrogenation reaction of 1,10-phenanthrolines and phosphorous acid (H_3PO_3) as yellow oil [3]. The silver sulfate (Ag_2SO_4), silver nitrate (AgNO_3), dichloromethane, ethyl acetate, hexane and hydrochloric acid (HCl, 37% water solution) and were all purchased as analytical reagent from Sinopharm Chemical Reagent Co., Ltd. The elemental analysis data (C, H and N) were obtained from a Perkin-Elmer 240B elemental analyzer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX-400 spectrometer. The powder X-ray diffraction (PXRD) patterns were obtained with a

Bruker D8 advanced diffractometer with Cu K α radiation ($\lambda = 1.54056 \text{ \AA}$) at 40 kV and 40 mA and a scan speed of 4° min^{-1} (20).

2.2 The coupling reaction of *tphen* and synthesis of 6,6'-bis(1,2,3,4-tetrahydro-1,10-phenanthroline) (**1**) 0.0432 g (0.23 mmol) *tphen*, 0.0366 g Ag₂SO₄ (0.12 mmol) and 10 mL distilled water were mixed in a 25 mL round-bottom flask with magnetic stirring bar and condenser. The reaction mixture was re-fluxed at 100 °C for 5 hours by magnetically stirring. A kind of mixed precipitates contained yellow and gray powders was gradually formed from the solution.

After that, 30 mL distilled water was added to the reaction mixture. Then, 1:1 aqueous hydrochloric acid was slowly dropped onto the mixture by strong stirring, the yellow precipitates were dissolved and the color of the mixture would generally turned into red. The rest of gray precipitate was filtrated, washed with distilled water and dried in air. Gray powders are obtained and proved to be pure silver (match the PDF card number 4-783 [19]) (See Fig. 2).

Then, 30 % aqueous NaOH was slowly dropped onto the red solution by strong stirring, and the color of the mixture would generally turned into yellow. The resulting products were then extracted with dichloromethane (3 \times 30 mL). The combined organic extract was washed with brine, dried over MgSO₄, filtered and concentrated *in vacuo*. Column chromatography (1 : 4 ethylacetate-hexane, R_f = 0.50) gave 6,6'-bis(1,2,3,4-tetrahydro-1,10-phenanthroline) (**1**, 0.0193g, 45.8 % yield based on *tphen*) as a yellow crystalline powder. Melting point: 213~216 °C. ¹H NMR (300 MHz, CDCl₃): $\delta = 8.67$ (d, 2H, $J = 3.9$ Hz), 7.68 (d, 2H, $J = 8.4$ Hz), 7.13 (dd, 2H, $J = 5.4, 4.5$ Hz), 6.05 (bs, 2H, NH), 3.59 (t, 4H, $J = 5.1$ Hz), 2.95 (t, 2H, $J = 6.3$ Hz), 2.12 (quintet, 2H, $J = 5.4$) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 146.6, 140.0, 137.1, 134.8, 131.2, 127.2, 123.3, 120.3, 116.1, 41.3, 26.9, 21.8$ ppm (See Fig S-1). EI-MS: m/z calcd for C₂₄H₂₂N₄⁺: 366.2; found: 366.2.

2.3 Single crystal growth of **1**

Single crystals of **1** were obtained with a mixed solvent evaporation method: 0.0164 g yellow powder of **1** was dissolved in 8 mL dichloromethane at room temperature to form clean solution, then 1 mL hexane was added to the solution and uniformly mixed. The resulted solution was placed in a test tube at room temperature for 3 days. Bright yellow, lamellar single crystals for X-ray single crystal diffraction were obtained and dried in air. Yield: 0.0156g, 95% (based on the powder of **1**). Elemental analysis, %: Found: C 78.13, H 6.22, N 15.01; Calculated for C₂₄H₂₂N₄: C 78.66, H 6.05, N 15.29.

2.4 X-ray crystallographic analysis

Crystallographic measurements of compounds **1** was manipulated on a Bruker SMART CCD area-detector diffractometer. Its structure was analyzed by using graphite monochromated Mo K α radiation ($\lambda = 0.71073 \text{ \AA}$) and solved with direct methods by using SHELXS-97 program [20]. Non-hydrogen atoms were anisotropically refined and the hydrogen atoms were placed on calculated positions in riding mode with temperature factors fixed at 1.2 times U_{eq} of the parent atoms. Crystallographic data and structural refinement parameters are listed in Table 1.

III. Result and discussion

3.1 Structure of **1**

Compound **1** was a stable, bright yellow crystalline solid at room temperature, which was crystallized in *Monoclinic* crystal system and *Pc* space group. As shown in Fig. 3, the molecule of **1** could be recognized as the directly connection of two *tphen* units, while the connection positions of the two *tphen* units were both located at the C6 carbon atom (the contraposition of the amino group). The piperidine rings in *tphen* units showed twisted chair conformations (corresponding angles $\angle \text{C1C2C3} = 113.16^\circ$, $\angle \text{C4C12N1} = 120.88^\circ$, dihedral angles $\angle \text{C2C3C4C12} = -8.99^\circ$, $\angle \text{C2C1N1C12} = 34.90^\circ$), which was similar to the molecular conformation of other C-6 substitutes of *tphen* [11-12]. Connected C–C bond length of the two *tphen* units (C6–C6A = 1.497 Å) was in the normal **range**. In addition, the two *tphen* units of **1** are not coplanar, and the angle between the quinoline rings of the two *tphen* units is 62.36° , which was smaller than that of bis(1,2,3,4-tetrahydro-1,10-phenanthroline-6-yl) methane [12].

Adjacent molecules of **1** were connected by weak C–H \cdots N hydrogen bonds (C1–H1A \cdots N2#1 = 3.665(2) Å) between piperidine ring and neighboring quinoline ring, forming a two-dimensional (2D) supramolecular layer (See Fig. 4a). On the other hand, molecules of **1** in neighboring 2D supramolecular layers were overlapped, and generated $\pi\cdots\pi$ stacking interactions among their aromatic rings, with a face to face distance of 3.55 Å, and a center to center distance of 4.88 Å, which expanded the 2D supramolecular layers of **1** to a three dimensional (3D) block supramolecular structure (See Fig. 4b).

3.2 Coupling reaction of *tphen* with silver salt

In order to further investigate the coupling reaction of *tphen* with silver salt, a series of control experiments were carried out and the results were listed in Table 2. It could be observed that, the coupling reaction needed relatively high temperature, which better reacted at 100 °C for 5 hours. However, compared with the C-6 bromination and condensation reaction of *tphen*, the coupling reaction with Ag₂SO₄ showed a relatively low yield (45.8 %) and excessive Ag₂SO₄ or longer react time could not enhance the yields of **1** evidently. It was probably because that *tphen* was insoluble in water and could not contact with silver ion adequately. However, if added ethanol to increase the solubility of *tphen*, the yield would be greatly reduced, and only trace amount of products could be obtained. The reason might be that hot ethanol could react with silver ion and compete with *tphen*.

On the other hand, instead of Ag₂SO₄, using AgNO₃ could also afford compound **1** but with lower yield. It might be that AgNO₃ could form strong oxidizing nitric acid and lead to other side reactions. Using sulfuric acid or nitric acid alone could not lead to any reaction of *tphen*, indicating that silver ion was the key factor of the reaction. In addition, except for compound **1**, no other reaction product was observed from this coupling reaction by now, which proved that the coupling reaction of *tphen* could afford its C6 condensation product with high regioselectivity.

IV. Conclusion

In this paper, we have investigated the coupling reaction of *tphen* with silver salt for the first time, and synthesized a new heterocyclic compound, namely 6,6'-bis(1,2,3,4-tetrahydro-1,10-phenanthroline)(**1**). The accurate structure of **1** are confirmed and investigated by X-ray single crystal diffraction. The result proves that the coupling reaction of *tphen* with the help of silver salt can afford its C6-condensation product with high regioselectivity, and the organic modification of the C6 position can be an effective strategy for designing and synthesizing new derivatives of *tphen*. Compared with *tphen* itself, **1** displays much higher melting point, and is very stable at room temperature, thus can be better organic dyes.

Acknowledgements

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, including ¹H NMR, ¹³C NMR and crystallographic CIF file of compound **1**.

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Figures And Tables

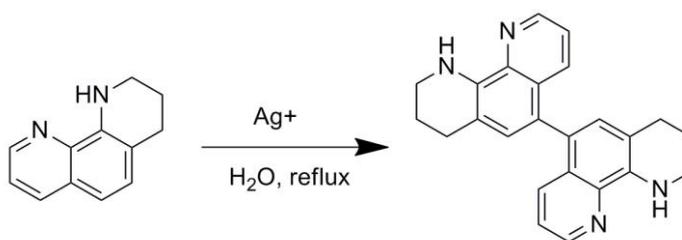


Figure 1 The coupling reaction of tphen with silver salt

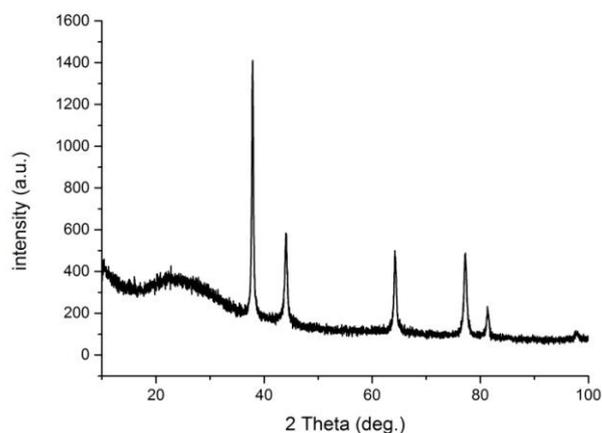


Figure 2 The PXRD diffraction pattern of the reduction product of silver salt in the coupling reaction

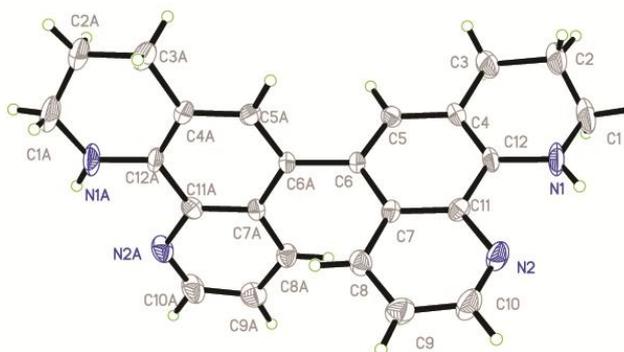


Figure 3. The ORTEP drawing of compound 1 with the thermal ellipsoids at 30% probability.

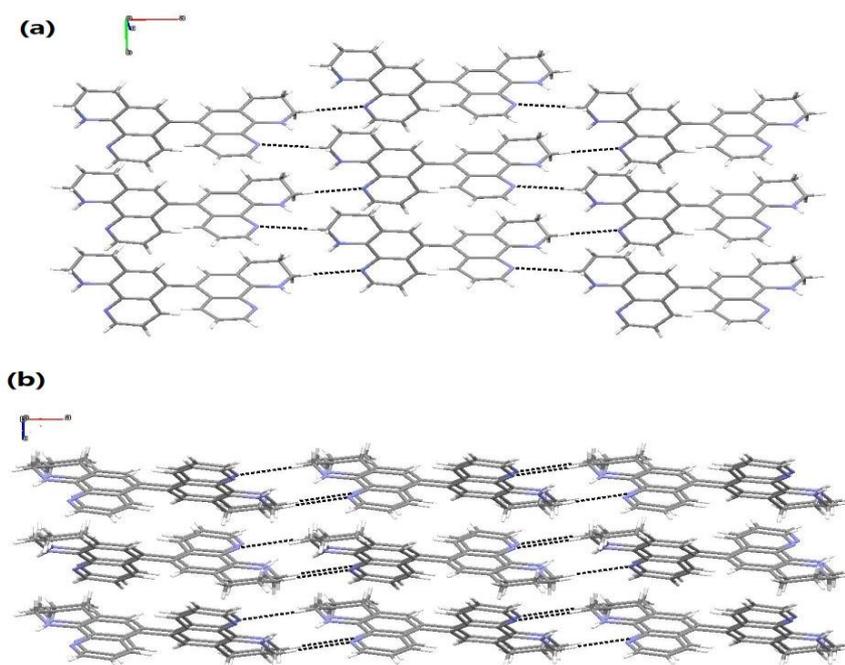


Figure 4 The 2D supramolecular layer (a) and 3D supramolecular structure (b) of compound **1**. Dashed line represents hydrogen bond (b).

Table 1 Crystallographic data and structure refinements for compound **1**

| | |
|---|---|
| Compound | 1 |
| Empirical formula | C ₂₄ H ₂₂ N ₄ |
| Formula weight | 366.46 |
| Crystal system | Monoclinic |
| Space group | C2/c |
| a / Å | 25.745(8) |
| b / Å | 6.706(2) |
| c / Å | 10.834(4) |
| α (deg.) | 90 |
| β (deg.) | 90 |
| γ (deg.) | 90 |
| V / Å ³ | 1870.3(11) |
| Z | 4 |
| μ/mm ⁻¹ | 0.079 |
| F (000) | 776 |
| D _{calc} /g·cm ⁻³ | 1.301 |
| Goodness-of-fit on F ² | 1.147 |
| Final R indices [I > 2σ (I)] | R ₁ = 0.1681, wR ₂ = 0.4866 |
| R indices (all data) | R ₁ = 0.2000, wR ₂ = 0.5028 |
| (Δρ) _{max} (Δρ) _{min} (e/Å ³) | 0.470, -0.525 |
| $R_1 = [\sum(F_o - F_c)] / \sum F_o $; $wR_2 = [\sum[w(F_o ^2 - F_c ^2)^2] / \sum[w(F_o ^2)^2]^{1/2}$, $w = 1 / [\sigma^2 F_o ^2 + (xp)^2 + yp]$; where $p = [F_o ^2 + 2 F_c ^2] / 3$. | |

Table 2. The control experiments of the coupling reaction of *tphen*.

| Order | Reactant A ^a | Reactant B (coupling agent) | Mole ratio of B : A | Reaction temperature, °C | Reaction time, h | Solvent ^b | Isolated yield ^c , % |
|-------|-------------------------|---------------------------------|---------------------|--------------------------|------------------|----------------------|---------------------------------|
| 1 | <i>tphen</i> | Ag ₂ SO ₄ | 0.5 | 100 | 5 | water | 45.8 |
| 2 | <i>tphen</i> | Ag ₂ SO ₄ | 1 | 100 | 5 | water | 45.5 |
| 3 | <i>tphen</i> | Ag ₂ SO ₄ | 2 | 100 | 5 | water | 45.1 |
| 4 | <i>tphen</i> | Ag ₂ SO ₄ | 0.5 | 80 | 5 | water | 39.3 |
| 5 | <i>tphen</i> | Ag ₂ SO ₄ | 0.5 | 100 | 10 | water | 46.3 |
| 6 | <i>tphen</i> | Ag ₂ SO ₄ | 0.5 | 60 | 5 | water | 23.4 |
| 7 | <i>tphen</i> | AgNO ₃ | 1 | 100 | 5 | water | 27.2 |
| 8 | <i>tphen</i> | Ag ₂ SO ₄ | 0.5 | 60 | 5 | 50 wt % | 1.4 |

| | | | | | | | |
|----|--------------|--------------------------------|---|-----|---|---------|----------------|
| | | | | | | ethanol | |
| 9 | <i>tphen</i> | H ₂ SO ₄ | 1 | 100 | 5 | water | 0 ^d |
| 10 | <i>tphen</i> | HNO ₃ | 1 | 100 | 5 | water | 0 ^d |

^a The amounts of reactant A were all 0.23 mmol.

^b The amounts of the solvent were all 10 mL.

^c Base on *tphen*.

^d There was no any new products observed.