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Synthesis of 5,8-Dimethyl-Dibenzo[b,j][1,10]Phenanthroline and Its Ru Complex

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Abstract

A convenient, two-step synthesis of the 5,8-dimethyl-dibenzo[b,j][1,10]phenanthrolines is presented. The first step is a Buchwald-Hartwig amination of 1,2-dibromobenzene and 2'-Aminoacetophenone to produce 1,1'-((1,2-phenylenebis(azanediyl))bis(2,1-phenylene))bis(ethan-1-one), which is converted to the final product via a ring-closing reaction. The overall reaction yield is 63%. The complexation of 5,8-dimethyl-dibenzo[b,j][1,10]phenanthrolines with 2,2'-bipyridine-4,4'-dicarboxylic acid (dc bpy) and Ru Ru(DMSO)₄Cl₂ is also reported and the Ru complex might be used to prepare a nanoscale thin film for dye-sensitized solar cell and other optoelectronic devices.

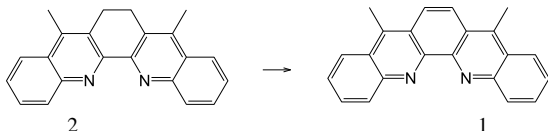
Keywords: Phenanthrolines, Polycyclic Aromatic Hydrocarbons, Synthesis, Dehydrogenation.

Abbreviations: PAHs-Polycyclic Aromatic Hydrocarbons, DSSCs-Dye-Sensitive Solar Cells, DMF-Dimethylformamide, NMR-Nuclear Magnetic Resonance, CI-Chemical Ionization.

Dibenzo[b,j][1,10] phenanthrolines are an interesting group of compounds. They have the potential to combine the properties of Polycyclic Aromatic Hydrocarbons (PAHs) with the flexibility of coordination complexes. The compounds have been used in macrocycles to inhibit telomerases and destabilize DNA, can activate nucleases when used in copper (II) complexes, and have been shown to readily form coordination complexes with ruthenium [1-4].

The ruthenium complex could be used as a sensitizing dye to improve the efficiency of the Dye-Sensitive Solar Cells (DSSCs) and others. However, the current applications of dibenzo[b,j][1,10]phenanthrolines are rather limited, potentially because of the low synthetic yield.

Introduction of two methyl groups on dibenzo[b,j][1,10]phenanthrolines, i.e. synthesis of 5,8-dimethyl-dibenzo[b,j][1,10]phenanthroline (compound 1, **Scheme 1**), is an important step in the applications of this type of chemicals since the methyl can be readily converted to other functional groups, such as -CH₂Cl, -COOH, for the synthesis of dibenzo[b,j][1,10]phenanthrolines derivatives.



Scheme 1: Palladium-catalyzed dehydrogenation to produce 5,8-dimethyl-dibenzo[b,j][1,10]phenanthroline (1).

Several methods have been reported on the synthesis of 1 and its relatives, and the best method appeared to be the one reported by Kempter and Stoss according to the yield. It involved a Friedländer

condensation, followed by a palladium-catalyzed dehydrogenation of the product [5-12].

The Friedländer condensation proceeded with high yields and no difficulty, but yields from literature for the palladium-catalyzed dehydrogenation from 2 (**Scheme 1**) were quite low (10-20%). Conditions for this reaction relied on elevated temperatures (210°C), which have a high potential for unwanted side reactions on a compound of this type, potentially explaining the low yield. No conversion was seen at lower temperatures in methanol, toluene, xylenes, 1,2-dichlorobenzene, acetic acid, and decalin. Decomposition was seen in nitrobenzene, and limited yield (10%) was seen in isocetane. This indicates a high activation energy barrier for the reaction.

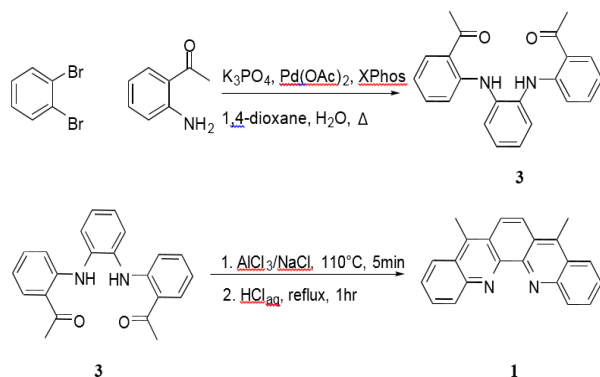
Dehydrogenation to introduce an olefinic bond can be done via oxidation with a number of different standard oxidizing agents. However, all of our attempts on similar systems to generate compound 1 from 2 have failed. Another more effective method of dehydrogenation via bromination/dehydrobromination under mild conditions was pioneered by Barnes in 1948. However, since the benzylic positions at C₆/C₇ and the methyl groups are equally reactive, making 1 directly from 2 via this process was not successful unless the methyl is protected, and subsequent reduction is also effective on the central bond [13-16].

In this work, we report a novel two-step reaction with a total 63% yield starting from 1,2-dibromobenzene and 2'-aminoacetophenone (**Scheme 2**). The first step is a Buchwald-Hartwig amination. Our results show that when 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) was used, reaction yields up to 60% of 3 were achieved, with 2-dicyclohexylphosphino-2,4,6-triisopropylbiphenyl (XPhos) proving far more successful, with yields >80% under the proper conditions. The reaction was optimized using a procedure developed for this ligand in

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Buchwald's lab, using stoichiometric amounts of water to activate the $\text{Pd}(\text{OAc})_2/\text{XPhos}$ precatalyst system [17-19].



Scheme 2: Buchwald-Hartwig amination of 1,2-dibromobenzene with 2'-aminoacetophenone to 3 and 6-exo-trig ring closing reaction of 3 to 1.

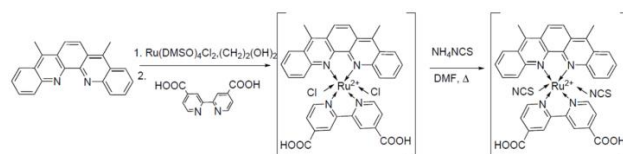
This allowed a 90% yield and the reaction time to be accelerated from 4-6 days using the Ullmann reaction to overnight [20]. NMR analysis of the reaction mixture shows that the individual displacements behave semi-sequentially, with monosubstitution being preferentially followed by monosubstitution of another molecule, rather than disubstitution of the same. It is noteworthy that attempts to use $(\text{tBu})_3\text{P}$ as the ligand failed, as β -arylation proved to be an inescapable byproduct from the reactive acetyl functionalities.

The second step is the ring-closing reaction of 3. A synthesis listed in a paper published in 2012 seemed promising, as it used a targeted Lewis acid (AlCl_3) along with a strong Brønsted acid. In the past, every substrate to date using this combination was a substituted anthraquinone of some kind, which have very different properties from diphenyl ketones or diphenylamines [21-24]. However, this reaction still turned out to be quite successful for the synthesis of 1. The reaction starts with a eutectic mixture of AlCl_3 and NaCl that melts at 110°C . This dissolves the substrate, and can then be carefully diluted with 4M HCl to finish the reaction (Scheme 2). Yields were surprisingly good (70%), and the reaction yielded a clean product without chromatography.

Although many acids have been used to crosslink acetophenone with benzene rings, most of them proved unsuccessful in making 1. Phosphoric acid, sulfuric acid, and Eaton's reagent produced decomposition and a complicated mixture of products. Acetic acid catalyzed by sulfuric acid caused the formation of carboxylic acid byproducts before the desired target could be formed [25-29]. Trifluoroacetic acid formed an unidentified product upon reaction with 3. Weak Lewis acids such as $\text{In}(\text{III})$, $\text{Sn}(\text{II})$, and even $\text{Fe}(\text{III})$ also produced no results. Imidazolium-based ionic liquids and deep eutectic salts, such as that formed between choline chloride and ZnCl_2 , failed to react as well.

Complexation reactions to make a Ruthenium complex are chemically quite straightforward. A metal precursor is chosen with coordinating ligands sufficiently labile to be displaced by the incoming nucleophile. Minimum necessary conditions were tested by mixing one equivalent of 1 with one equivalent of $\text{Ru}(\text{DMSO})_4\text{Cl}_2$ in polar solvent systems with ever increasing boiling points. While 2,2'-bipyridine-4,4'-dicarboxylic acid (dcbpy) would readily coordinate in as mild conditions as refluxing 1,2-dichloroethane, 1 failed to coordinate until refluxing N,N -dimethylformamide (DMF). Even then, coordination was so slow as to take multiple days, so conditions were increased to ethylene glycol. In hot (170°C) ethylene glycol, the coordination takes less than 30 minutes. Therefore, these conditions were used to create

the chloride salt of the final ruthenium complex, with a final reaction in DMF to make the thiocyanate (**Scheme 3**).



Scheme 3: Coordination of 1 to its ruthenium complex.

The DSSC devices based on this Ru complex will be studied and reported in the future. Also, further synthesis could create a library of derivatives that could yield much more insight into this system. This could be used to compare the effect of planarity on the efficiency of the solar cell. By comparing dibenzophenanthroline, dihydridibenzophenanthroline, and biquinoline derivatives, a more complete picture could be drawn as to the interaction of highly aromatic compounds in DSSCs.

Experimental

All reactions were performed under nitrogen unless specified otherwise. All chemicals were purchased from Fisher Scientific and were used as received. Deuterated solvents were purchased from Acros Organics. Nuclear Magnetic Resonance (NMR) spectra were obtained on Varian INOVA 300 MHz and 500 MHz NMR spectrometers. Mass spectrometry (HRMS) experiments were conducted using Micromass AutoSpec M magnetic sector using Chemical Ionization (CI) in methane.

1,1'-((1,2-phenylenebis(azanediyl))bis(2,1-phenylene)) bis(ethan-1-one) (3)

Into a round bottom was added palladium (II) acetate (6.6mg, 29.4 μmol), Xphos (41.7 mg, 87.4 μmol), and potassium phosphate (921 mg, 4.34 mmol), and an inert atmosphere was established. 3 mL of dioxane with 2 μL of water were then added to the round bottom, and the orange solution was heated until the color had deepened to a dark red. The 1,2-dibromobenzene (327.4 mg, 1.39 mmol) and 2-aminoacetophenone (420.6 mg, 3.11 mmol) were then added along with an addition 3 mL of dioxane, and the reaction was heated to reflux overnight. The dioxane was removed in the rotary evaporator, and the reaction mixture was resuspended in dichloromethane with added Celite. This was filtered and washed with an additional 20 mL of dichloromethane.

The dark red solution was then washed with 3 portions of 30 mL 0.8M HCl to remove the excess amine, followed by 2 portions of 30 mL of water. The resulting brownish solution was dried over magnesium sulfate, rotovapped, and chromatographed on silica (30:70 ethyl acetate:hexanes) to yield 428.8 mg of yellow solid (90%). ^1H NMR (499 MHz, Chloroform- d) δ 10.33 (s, 2H), 7.73 (dd, $J=8.1$, 1.6 Hz, 2H), 7.43 (dd, $J=5.9$, 3.6 Hz, 2H), 7.27-7.21 (m, 2H), 7.14 (dd, $J=5.9$, 3.6 Hz, 2H), 7.03 (dd, $J=8.5$, 1.1 Hz, 2H), 6.69 (ddd, $J=8.1$, 7.0, 1.1 Hz, 2H), 2.55 (s, 6H). MS 344.1.

5,8-dimethyldibenzo[b,j][1,10]phenanthroline (1)

A round-bottomed flask was placed in a nitrogen glove box and loaded with 21.245 g of a finely ground 4:1 mixture (by weight) of dried AlCl_3 and NaCl , respectively. This was then heated at 110°C until a clear liquid was formed, and then cooled. 2.043 g (5.94 mmol) of 3 was added, and the mixture was re-heated until a dark brown solution was formed. This was heated for 5 minutes before cooling. Finally, 150mL of 4M HCl was slowly added until the solution was completely neutralized, and it was reheated for 1 hr. The resulting solution was filtered, poured on ice, slowly neutralized with NaHCO_3 , and filtered again to collect the precipitate. The filter cake was washed with water

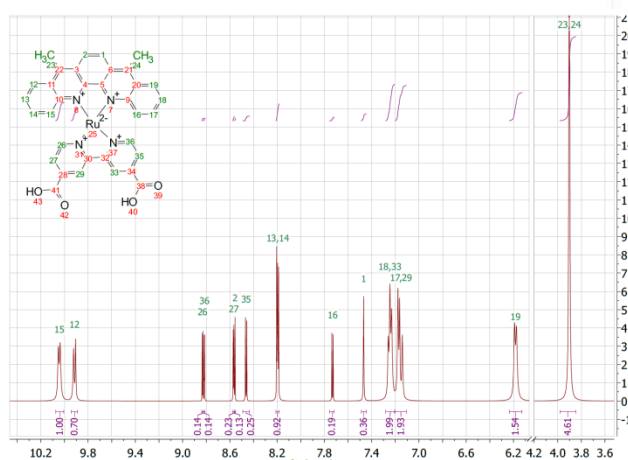


and cold methanol to yield 1.283 mg (4.17 mmol) of yellow solid (70.2%).

This was then recrystallized from $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to yield yellow needles. ^1H NMR (498 MHz, CHCl_3 - d) δ 8.70 (d, $J=8.5$ Hz, 2H), 8.31 (d, $J=8.7$ Hz, 3H), 8.09 (s, 2H), 7.87 (t, $J=7.5$ Hz, 2H), 7.70 (t, $J=7.6$ Hz, 2H), 3.16 (s, 6H). MS 308.1.

Ru(1)(dcbpy)NCS₂

$\text{Ru}(\text{DMSO})_4\text{Cl}_2$ (241.3 mg, 0.499 mmol) was added to a round-bottomed flask, along with 155.2 mg (0.504 mmol) of 1 and 20 mL of dry ethylene glycol. This was heated at 170°C for 30 min. 4,4-dicarboxyl-2,2'-bipyridine (125.3 mg, 0.514 mmol) was then added, and heating continued for another 2 hours. Finally, 253.2 mg (3.33 mmol) of NH_4NCS was added, and heating continued for another 3 hours. Once the reaction was cooled, it was diluted with 0.1 M HNO_3 , and placed at 4°C overnight. The resulting deep red precipitate was filtered, washed with water and acetone, and dissolved in 0.1M Na_2CO_3 . This was then re-precipitated with HNO_3 , filtered, and washed again with water and acetone to yield 174.1 mg of red solid (45%) ^1H -NMR (500 MHz, $\text{DMSO}-d_6$) δ 10.04 (d, $J=7.9$ Hz, 1H), 9.91 (d, $J=8.8$ Hz, 1H), 8.83 (d, $J=3.1$ Hz, 1H), 8.82 (d, $J=1.6$ Hz, 1H), 8.57 (d, $J=3.2$ Hz, 1H), 8.56 (d, $J=0.6$ Hz, 1H), 8.46 (d, $J=5.4$ Hz, 1H), 8.21 - 8.18 (m, 2H), 7.73 (d, $J=5.4$ Hz, 1H), 7.47 (s, 1H), 7.28-7.21 (m, 2H), 7.20-7.11 (m, 2H), 6.18 (d, $J=8.2$ Hz, 1H), 3.90 (s, 6H).



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