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An in Situ Coupling Reaction of Phenolate Promoted by Triphenylborane: A New Synthetic Method for Diphenoquinone Derivates

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Abstract

Organoborane have been recognized to participate in free-radical processes. Herein, the concept of using organoboranes as a radical initiator has been extended to aromatic compounds. Organoborane promoted in situ coupling reaction of phenolate was observed during its reaction with dilithium phenolate, leading to a new synthetic method for the preparation of diphenoquinone derivates in medium to good yields.

Keywords: Organoborane, Coupling reaction, Diphenoquinone derivates, Synthesis

1. Introduction

Since 1967, organoboranes have been recognized to participate in free-radical processes.

This reactivity was initially demonstrated by Davies and Roberts and was first applied to various synthetic reactions by Brown and Suzuki [1-4]. Following the spectacular development of radical chemistry in organic synthesis [5-8], the use of organoboranes has recently led to many novel and useful synthetic applications [9]. For example, organoboranes undergo a wide variety of free radical reactions such as autoxidations which leads to alkyl hydroperoxides [10], 1, 4 additions to α , β -unsaturated derivatives [11-12], additions to disulfides, and oxygen- induced radical coupling reactions. It is evident that organoboranes constitute a versatile source of free radicals and these reactions can be readily controlled to give very clean syntheses. Herein, the concept of using organoboranes as a radical initiator has been extended to aromatic compounds to initiate radical coupling of aromatic compounds to form diphenoquinone derivatives, which has led to a new synthetic method for the preparation of diphenoquinone derivatives [13].

2. Results and Discussion

As shown in Scheme 1, treatment of 2-tert-butyl-6- bromophenol [14] **1a**, **1b**, or **1c** with two equivalents of n-butyllithium in ethyl ether at 0 °C respectively gave the dilithiums of **2a**, **2b**, and **2c** in near quantity yields. The dilithiums of **2a**, **2b**, and **2c** were then treated with one equivalent of triphenylborane in ether at room temperature to give red crystalline compounds of the diphenoquinone derivatives **3a** (70%), and **3b** (64%) and **3c** (51%) in medium to good yields. A small amount of lithium tetraphenylborate was also separated as byproduct (5% yields).

Scheme 1. Synthesis of **3** *via* in situ radical coupling promoted by BPh₃.

It should be noted that this reaction is highly dependent on the solvent used for the reaction. The reaction proceeded smoothly in ethyl ether to give the desired products **3** in the highest yields. When tetrahydrofuran (THF) was used as the solvent, no coupling products **3** were isolated. The R group on the ortho-position also significantly influences the yield of this reaction. When there was a bulky substitution on the ortho position of the phenol, the reaction gave the highest yield (70% when R = t-Bu), whereas if there was no substitution, the reaction yield was medium (51% when R = H). When triphenylborane was replaced with tris(pentafluorophenyl)-borane (a more electro deficient reactant), the reaction gave a deep blue solution and no diphenoquinone derivatives were obtained.

Single crystals of **3a** and **3b** were grown in ethyl ether and were analyzed by X-ray diffraction. The molecular structures of **3a** and **3b** shown in Figure 1 clearly show the coupling of the two carbons through the para-positions of the phenols. The bond distance of C(4)-C(4A) for **3a** (1.396(3) Å) is identical to that of **3b** (1.396(4) Å). The average bond length of C(4)-C(4A) (1.396 Å) is significantly shorter than that of a single bond, indicating the formation of a double bond between C(4) and C(4A). The bond distances of C(2)-C(3) are 1.357(2) Å, and 1.358(3) Å for **3a**, and **3b**, respectively and the bond lengths of C(5)-C(6) are 1.350(2) Å, and 1.345(3) Å, respectively, which are close to C=C double bond lengths. However, the bond distances of C(1)-C(2), C(3)-C(4), C(4)-C(5), and C(1)-C(6) in **3a** are 1.447(2) Å, 1.447(2) Å, 1.442(2) Å, and 1.483(2) Å respectively. The bond distances in **3b** for C(1)-C(2), C(3)-C(4), C(4)-C(5), and C(1)-C(6) are 1.465(3) Å, 1.442(3) Å, 1.436(3) Å, and 1.464(2) Å, respectively. These bond lengths are close to single C-C bond distances. The distance of the C(1)-O(1) bond is 1.253(2) Å for **3a** and 1.252(3) Å for **3b**, indicating the existence of a carbonyl group in both complexes. The torsion angles of C(1)-C(6)-C(5)-C(4) is 3.7(2)° for **3a** and -172.73(19)° for **3b**, indicating that the four atoms in each compound are sited in a plane closely. The distances for B(1)-C(2), B(1)-C(11), B(1)-C(17) and B(1)-C(23)

are identical in both **3a** and **3b**. Each lithium cation is coordinated with two carbons from a phenyl ring, one oxygen atom from the ethyl ether, and another oxygen atom from the carbonyl group, forming a distorted tetrahedral structure.

Fig. 1. Molecular structure of **3a** and **3b** (in 50% thermal ellipsoids) (For clarity, hydrogen atoms are omitted). For bond distances and angles see the supporting information.

This unexpected in situ homocoupling reaction of phenolate during its reaction with triphenylborane prompted us to do more experiments to uncover the reaction mechanism. One equivalent of 4-methoxy-2,2,6,6-tetramethylpiperidiny-1-oxy (TEMPO), a good free radical inhibitor, was added to the reaction system at room temperature and the reaction mixture immediately turned dark and no homocoupling products of the phenolate were isolated after 7 days. The reaction system is highly sensitive to air. When a trace amount of air was leaked into the system, the reaction mixture immediately turned dark blue and the desired product **3** was not obtained from the reaction mixture even at prolonged reaction times. Attempts to trap key intermediates by the stoichiometric reaction of the mixture with N-benzylidene-tert-butyl amine-N-oxide (PBN) failed to reveal any mechanistic implications. These observations clearly point to a free-radical mechanism. Thus, an in situ generated

free-radical coupling reaction by triphenylborane is proposed since organoboranes are known to initiate free radical reactions with electro-rich co-reactants (e.g., the β -alkylation of α, β -unsaturated carbonyl compounds with triorganoboranes [15]). Therefore, a mechanism including the in situ initiation of a free radical coupling process through triphenylborane is proposed and is shown in Scheme 2. When triphenylborane is added to a solution of a dilithium salt **2**, a phenoxy diradical dianion **4** forms in which the cationic Li^+ coordinates to both the B and O atom, and the Li^+ exists as the counter cation. The formed phenoxy radicals are known to be very stable, so they then dimerize to give **5**, which finally transforms to a more stable form of **6** via 1, 3-sigmatropic rearrangement. A diradical intermediate of **7** is formed via LiOH expulsion reaction of **6** in the presence of oxygen which may come from the leaked air. The diradical intermediate of **7** has the quinoid structure **8** as its resonance form. The quinoid structure **8** is then locked in by a B attachment at the *ortho* position to give **3** as the final product.

Scheme 2. Proposed mechanism for the formation of **3**.

The isolation of lithium tetraphenylborate also confirmed the validity of a radical mechanism for this coupling reaction. The initial or dimeric adduct gave the radical anion of lithium triphenylborate through a disproportionation process. The radical anion of lithium triphenylborate is not a stable intermediate and it immediately decomposes to give LiPh and a diphenylboron radical. Interaction of LiPh with triphenylborane finally gives lithium tetraphenylborate finally (see Scheme 3).

Scheme 3. Proposed mechanism for the formation of lithium tetraphenylborate

It should be noted that the diphenoquinone and its derivatives are stable to the air and the four-coordinated borane compounds are excellent charge transistors or acceptors and have been widely applied as organic photoconductor in organic light-emitting devices [16-18]. Traditionally, these compounds have been prepared via oxidation of 2, 6-disubstituted phenols by activated MnO_2 , CrO_3 or other transition metal complexes [19-20]. However, the current method offers new boron substituted derivatives of diphenoquinone which can then be further modified via Suzuki-coupling reaction with other substrates, which is an advantage of this current synthetic method.

3. Conclusions

In summary, a new **method** to prepare boron substituted diphenoquinones via the triphenylboron induced radical coupling of lithium o-lithio-phenolate has been developed. In view of the growing interest in the development of highly efficient electron transport materials for industrial purposes, this new **method** could be applied to the design of a series of diphenoquinone-based compounds, and to other related research areas.

4. Experimental

4.1. General Information

4.1.1. General Procedure for the Preparation of 3: First 2.53 mmol of 2-bromo-6-R-phenol **1** (R = H, Me, or t-Bu) was dissolved in 3.0 mL of ethyl ether in a flask under N₂ gas. The resulting solution was stirred and cooled to -15 °C in an ice-salt bath. To this solution, a solution of n-BuLi in hexanes (2.70 mL, N = 1.85) was added slowly using a syringe to give a light yellow solution. After stirring at -15 °C for 2 h, the mixture was slowly heated to room temperature and kept at room temperature for 2 h. The reaction mixture was then cooled to 0 °C and a solution of triphenylborane in 20 mL of ethyl ether (0.61 g, 2.52 mmol) was added slowly using a syringe. After the addition, the resulting reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture turned red during this time and red crystals of **3** were obtained after slow evaporation of the solvent

4.1.1.1. **3a**

Yield: 70%. ¹H-NMR (400 MHz, d₆-DMSO): δ 1.07 (t, *J* = 7.0 Hz, 12H), 1.34 (s, 18H), 3.35 (dd, *J* = 7.1 Hz, 8H), 6.74 (s, 2H), 6.86 (s, 2H), 6.89-7.41 (m, 30H); ¹³C-NMR (400 MHz, d₆-DMSO): δ 15.9, 30.4, 35.8, 66.4, 117.6, 122.9, 125.8, 127.6, 128.0, 131.9, 133.6, 136.0, 149.3, 192.5; IR (KBr) (ν/ cm⁻¹): 3060, 2971, 2885, 1611, 1555, 1483, 1455, 1427, 1361, 1262, 1185, 1092, 1066, 1032, 916, 888, 848, 737, 708; +ESI *m/z*: 940.67 [*M*]⁺ (calcd 940.76).

4.1.1.2. **3b**

Yield: 64%. ¹H-NMR (400 MHz, d₆-DMSO): δ 1.06 (t, *J* = 6.9 Hz, 12H), 1.70 (s, 6H), 3.39 (dd, *J* = 7.0 Hz, 8H), 6.67 (s, 2H), 6.82 (s, 2H), 6.85-7.42 (m, 30H); ¹³C-NMR (400 MHz, d₆-DMSO): δ 17.5, 30.3, 65.6, 122.1, 122.9, 125.8, 126.1, 128.0, 131.5, 133.5, 136.0, 152.3, 187.3; IR (KBr) (ν/ cm⁻¹): 3058, 2975, 2887, 1712, 1602, 1551, 1480, 1427, 1340,

1245, 1160, 1102, 1065, 1036, 919, 840, 706, 587, 521, 490; +ESI m/z: 854.50 [M]⁺ (calcd 856.50).

4.1.1.3. **3c**

Yield: 51%. ¹H-NMR (400 MHz, d₆-DMSO): δ 1.07 (t, *J* = 6.9 Hz, 12H), 3.40 (q, *J* = 7.0 Hz, 8H), 6.66 (d, *J* = 12.2 Hz, 2H), 6.81 (d, *J* = 12.1 Hz, 2H), 6.83-8.1 (m, 32H); ¹³C-NMR (400 MHz, d₆-DMSO): δ 17.2, 66.4, 121.0, 121.9, 125.4, 125.8, 129.1, 131.9, 134.3, 135.8, 153.4, 186.3; IR (KBr) (ν/ cm⁻¹): 3048, 2973, 2888, 1715, 1608, 1549, 1478, 1431, 1340, 1241, 1163, 1104, 1062, 1035, 917, 843, 709.

4.2. Crystallographic Information

Single crystals of **3a** and **3b** for X-ray diffraction were obtained by slow evaporation of the ethyl ether solvent at 25 °C under N₂. A small amount of lithium tetraphenylborate was also obtained as white crystals during this process. The structures were solved by direct methods (SHELXS-97) and refined by full-matrix least squares (SHELXL-97). All nonhydrogen atoms were refined with anisotropic displacement parameters. Crystallographic data and structural refinements for **3a** and **3b** are summarized in supplementary information.

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Yield: 51 - 70%