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Facile synthesis of diiodinated dihydronaphthalenes and naphthalenes *via* iodine mediated electrophilic cyclization[†]

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A facile, efficient, and general synthetic method for a wide range of 2,3-diiodinated 1,4-dihydrothiophenes and naphthalenes has been developed *via* the electrophilic iodocyclization of various aryl propargyl alcohols. The resulting product 2p can be used for the synthesis of a rubrene intermediate.

Electrophilic iodocyclization of alkyne or allene bound substrates is one of the most powerful methods for the efficient synthesis of a variety of functionalized carboconditions.^{1–7} and heterocycles under mild cvcles Furthermore, the corresponding iodine-containing products can be readily converted to structurally interesting and elaborated compounds through transition metal-catalyzed transformations. Kruglov reported in 1937 an interesting iodocyclization of acetylene glycols, which produced 3,4-diiododihydrofuran derivatives, however, since then the protocol has never been investigated widely.^{6a} Quite recently, Liang and co-workers have successfully extended this chemistry to the construction of various oxygen-containing dihalogenated heterocycles.6b,c In the continuation of our interest in iodocyclization chemistry,7 and in the development of efficient synthetic methods of naphthalene derivatives,⁸ we envisioned that if one of the hydroxyl groups in acetylene glycols is replaced with a suitable aromatic group, 2,3-diiododihydronaphthalene derivatives might be produced via a Friedel–Craft type cyclization. This proved to be the case. Herein, we report a facile and efficient synthetic methodology for a variety of 2,3-diiodinated dihydronaphthalenes 2 and naphthalenes 3 by the electrophilic iodocyclization of various substituted aryl propargyl alcohols 1 (eqn (1)). The resulting dihydronaphthalenes 2 and naphthalene derivatives 3 are potentially useful as precursors for π -electronic organic materials.

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First we investigated the effect of solvents on the iodinemediated electrophilic cyclization of **1a** for the formation of the 2,3-diiodo-1,4-dihydrothiophene **2a** as shown in Table 1. The use of CH₂Cl₂ and CHCl₃ led to good yields of **2a** (~80%), while the use of CH₃CN resulted in moderate yield of **1a** (entries 1–3). It was found that CH₃NO₂ was the best solvent, giving **2a** in 88% isolated yield (entry 4). The decrease of the amount of I₂ (2 equiv.) gave a slightly lower yield of **2a** (entry 5). The use of MeOH and THF as solvents resulted in decomposition of **1a** (entries 6 and 7).

The scope and limitations of iodine mediated electrophilic cyclization of various aryl propargyl alcohols were summaried in Table 2. The reactions of substrates **1b–e** bearing an electron-donating and an electron-withdrawing aromatic group (\mathbb{R}^2) at the propargyl alcoholic carbon produced the corresponding dihydronaphthalenes **2b–e** in good to high yields (entries 1–4). Remarkably, the presence of a double bond in substrate **1f** was also tolerated; the desired dihydronaphthalene **2f** was obtained in 88% yield (entry 5). Not only naphthyl substituent (**1g**), but also heterocycles, such as thienyl (**1h**)

Table 1Optimization of reaction conditions for the formation of $2a^a$

	$\begin{array}{c c} & & & I_2 (3 \text{ equiv}) \\ & & & \\ Ph & & \text{solvent, rt} \end{array} \qquad $		Ph
Entry	Solvent	Time/h	Yield ^b (%)
1	CH ₂ Cl ₂	1	81
2	CHCl ₃	1	80
3	CH ₃ CN	3	68
4	CH_3NO_2	3	91 (88)
5	CH ₃ NO ₂	3	89 ^c
6	MeOH	5	0^d
7	THF	5	0^d

^{*a*} Reaction conditions: **1a** (0.2 mmol), I_2 (0.6 mmol), anhydrous solvents (0.1 M), room temperature. ^{*b*} ¹H NMR yield was determined by using CH₂Br₂ as an internal standard. Isolated yield is shown in parenthesis. ^{*c*} 2 equiv. of I_2 was used. ^{*d*} **1a** was decomposed.

Table 2 Electrophilic iodocyclization of various aryl propargyl alcohols for the formation of 2^a



and tosyl-protected pyrroyl (1i) groups, at R^2 afforded the desired products in high yields (entries 6-8). Subsequently, we examined the effect of substituent at R¹. Similarly, the substrates **1***i*–**i** having electron-donating groups at R¹ underwent the cyclization smoothly to give the product in high yields, while 1m bearing an electron-withdrawing group afforded 2m in moderate yield (entries 9-12). However, in the case of 3-methoxy-substituted substrate 11, the reaction gave a 10:1 mixture of regioisomers (entry 11). When R¹-Ar was a naphthyl group, the reaction proceeded well to give the dihvdrophenanthrene derivative 2n in high yield (entry 13). The reactions also worked well with the substrates 10 and 1p having a methyl or a phenyl group at R³, furnishing the expected tetrasubstituted dihydronaphthalenes 20 and 2p, respectively, as a mixture of two diastereomers (entries 14 and 15). It is noteworthy that when an alkyl substituted substrate **1q** having a β -proton to the propargyl alcohol, such as cyclohexyl group, was employed, the reaction gave the β -proton eliminated substrate 4q as a sole product (eqn (2)).



We further tested this iodocyclization with IBr as an electrophile instead of iodine. Fortunately, in the presence of two equivalents of IBr, **1b** underwent the electrophilic

iodocyclization smoothly to afford the corresponding 3-bromo-2-iodo-dihydronaphthalene 2b' in good yield as a single regioisomer, which was further oxidized with DDQ to produce the naphthalene derivative 3b' quantitatively (eqn (3)).



Based on these observations, a plausible iodocyclization mechanism is proposed as shown in Scheme 1. Presumably, initial activation of the propagyl hydroxyl group of **1a** with a Lewis acidic iodine⁹ leads to the propargyl carbocation intermediate **A** or allene cation **B**¹⁰ along with an unstable hypoiodous acid (HOI) and an iodine anion. Attack of the iodine anion onto the γ -position of **A** or the cation in **B** affords iodoallene **C** which reacts with hypoiodous acid to form an



Scheme 1 A proposed mechanism.

iodonium intermediate **D**.¹¹ Subsequent intramolecular Friedel– Craft type reaction of the aromatic ring with the activated allene^{5/} followed by deprotonation produces **2a** and H₂O.

Interestingly, when alkoxy groups, such as methoxy or ethoxy, were substituted at the propargylic position, the reaction proceeded under an elevated temperature (50 °C), giving the naphthalene derivative **3a** as a major product along with the formation of dihydrofuran **5a**⁶ as a minor product (eqn (4)). However, in the case of the isopropyl group at R,⁴ the reaction produced **5a** as a major product.



Rubrene has been studied widely as an organo-electronic material in the research of field effect transistor, luminescence, and others.¹² We have successfully applied the present method for the synthesis of rubrene intermediate **6p**. The iodocyclization product **2p** was converted to the diiodonaphthalene **3p** under DDQ oxidation, which was treated with *n*-BuLi and diphenyl isobenzofuran, giving the corresponding oxo-bridged adduct **6p** in 83% yield (eqn (5)).



In conclusion, we have developed an efficient and general iodine-mediated electrophilic cyclization for the synthesis of 2,3-diiodo-dihydronaphthalenes from aryl propargyl alcohols. The reaction most probably proceeds through the *in situ* formation of an allene intermediate under Lewis acidic conditions, followed by the Friedel–Craft type reaction. In addition, we found that in the case of alkoxy substituent propargy alcohols, the reaction produced 2,3-diiodonaphthalenes. Furthermore, we have demonstrated that the resulting product can be applicable for the synthesis of an organo-electronic material. Further extension of the present methodology to the construction of heterocycles and application to the synthesis of useful optoelectronic materials are in progress.

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