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Facile synthesis of dihaloheterocycles via electrophilic iodocyclization

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Dedicated to Professor Gilbert Stork on the occasion of his 90th birthday

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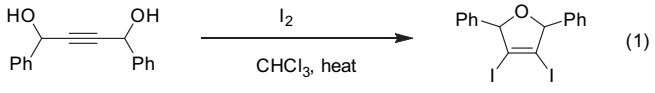
ABSTRACT

An efficient and facile electrophilic iodocyclization for the synthesis of various *O*-, *N*-, and *S*-containing dihaloheterocycles has been developed. A wide range of the substituted propargyl alcohols having −OH, −NTs, and −SAc functional groups reacted with molecular iodine or bromoiodine at ambient temperature to produce the corresponding dihalogenated *O*-, *N*-, and *S*-containing five- and six-membered heterocycles in good to high yields; Under optimized solvent conditions, the reactions of various substituted but-2-yn-1-ones bearing −OH, −NTs, and −SAc functional groups at C4-position, with iodine or bromoiodine at ambient temperature afforded the corresponding 3,4-diiodo- and 3-bromo-4-iodo-substituted furans, pyrroles, and thiophenes in good to high yields. Further transformation of the resulting iodine- or bromine-containing products to polyaromatics potentially of useful as organo-material intermediates has been investigated.

1. Introduction

Polyfunctionalized heterocycles, such as *O*-, *N*-, and *S*-containing five- and six-membered heterocycles, are most important and abundant components in nature.[1] A vast number of biologically active natural and unnatural compounds based on those heterocycles are very useful in the area of pharmaceutical chemistry.[2] Moreover, applications of polysubstituted five-membered aromatic heterocycles have recently been increasing in the field of organic optoelectronic materials, such as field-effect transistors (FETs), light emitting diodes (LEDs), and organic solar cells.[3] For these reasons, many advances have been made in the synthesis of *O*, *N*, and *S*-containing heterocycles for over a century, and a variety of well-established methods have been developed.[1] Except for the most attractive transition metal-catalyzed transformations,[4] the electrophilic iodocyclization of alkyne or allene bound substrates is one of the alternatively powerful methods for the efficient synthesis of a variety of functionalized carbocycles and heterocycles having a mono-iodo-substituent under very mild conditions.[5–11] Furthermore, the corresponding iodine-containing products can be readily converted to structurally interesting and elaborated compounds regioselectively through transition metal-catalyzed coupling reactions.

Electrophilic iodocyclization for the synthesis of dihalogenated heterocycles has been rarely reported, although it provides an opportunity to produce the multi-substituted heterocycles. Kruglov reported in 1937 an interesting iodocyclization of acetylene glycols, which produced 3,4-diiodohydrofuran derivatives, however, since then the protocol has never been investigated widely (Eq. 1).[10a] Recently, Müller and co-workers reported a facile one-pot three-component reaction for the synthesis of 3-chloro-4-iodofurans with moderate yields (Eq. 2).[10b] However, it seems to be difficult to carry out the cross-coupling reaction of the two C-X bond of the resulting furans, since C—Cl bonds generally exhibit low reactivity toward transition metal-catalyzed reactions. Therefore, the development of an efficient and general approach to iodo-or bromo-substituted dihaloheterocycles is desirable. In the continuation of our interest in iodocyclization chemistry,[11] and in the development of efficient synthetic methods of heterocycles,[4a–c] we attempted to synthesize



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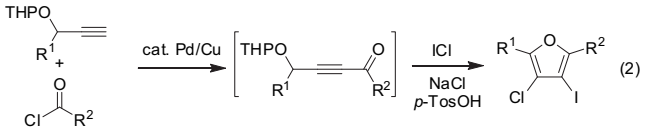

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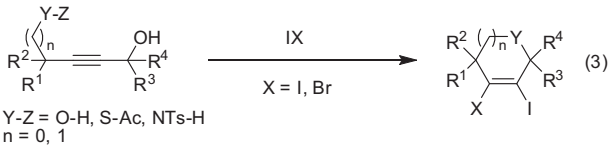
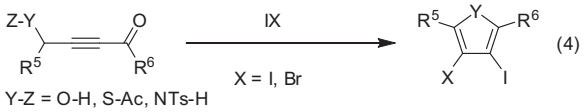
various dihaloheterocycles through a simple iodine-mediated electrophilic cyclization. We found that propargyl alcohols having –OH, –NTs, and –SAc functional groups underwent iodocyclization in the presence of I_2 or IBr, giving various dihalogenated dihydrofurans,[12] dihydropyrans,[12] dihydropyrroles,[12] tetrahydropyridines, dihydrothiophenes,[11e] and dihydrothiopyrans in good to high yield under mild conditions (Eq. 3). Furthermore, the reaction of the substituted but-2-ynyl-1-ones bearing –OH, –NTs, and –SAc functional groups at C4-position with I_2 or IBr afforded the 3,4-dihalogenated furans,[11f] pyrroles, and thiophenes smoothly under different solvent systems (Eq. 4). Herein, we report a detailed investigation of these iodocyclization synthetic methods. It was noted that due to the inconvenient handling, other halogen systems such as bromine were not investigated in this study.



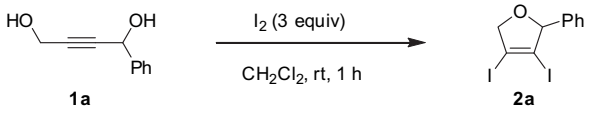


2. Results and discussion

2.1. Synthesis of five- and six-membered dihalogenated dihydroheterocycles via electrophilic iodocyclization

First we investigated the effect of solvents on the iodine-mediated electrophilic cyclization of **1a** for the formation of the 3,4-diiododihydrofurans **2a** as shown in Table 1.The use of aprotic solvents, such as CH_2Cl_2, CH_3NO_2, and CH_3CN led to high yields of **2a** (99–95%), while the use of acetone resulted in a lower yield of **2a** (80%) (entries 1–4). The use of MeOH as a solvent resulted in no reaction (entry 5). The decrease of the amount of I_2 (2 equiv) gave a slightly lower yield of **2a** (entry 6).

Table 1
Optimization of reaction conditions[a]



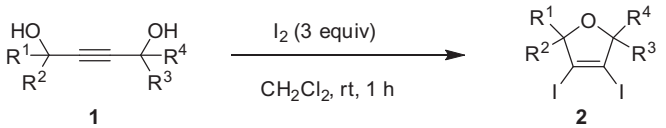
1a **2a**

Entry	Solvents	**2a**[b] (%)
1	CH_2Cl_2	100 (99)
2	CH_3NO_2	97
3	CH_3CN	95
4	Acetone	80
5	MeOH	0
6	CH_2Cl_2 (I_2, 2 equiv)	95

[a] Reaction conditions: **1a** (0.2 mmol), I_2 (0.6 mmol), anhydrous solvent (0.1 M), room temperature, 1 h.
[b] ^1H NMR yield determined using CH_2Br_2 as an internal standard. Isolated yield is shown in parentheses.

The scope and limitations of the iodine-mediated electrophilic cyclization of various but-2-yn-1,4-diols in CH_2Cl_2 were summarized in Table 2. The reactions of substrates bearing an electron-donating (**1b**) and an electron-withdrawing (**1c**) aromatic group at the propargyl alcoholic carbon produced the corresponding dihydrofurans **2b** and **2c** in 99% and 85% yield, respectively; **1c** showed a lower activity than **1b** (entries 1 and 2). Substrates **1d** and **1e** having acyclic tertiary propargyl alcohols afforded the desired products in good to high yields (entries 3 and 4). Similarly, the tertiary propargyl diols **1f**–**j** having five-, six-, seven-, and eight-membered carbocycles underwent the iodocyclization well to give the diiodo-oxaspirocyles **2f**-**j** efficiently (entries 5–9). The reactions also worked well with the substrates **1k** and **1l** having a methyl or a phenyl group at two propargyl alcoholic carbon, furnishing the expected dihydrofurans **2k** and **2l**, respectively, as a mixture of two diastereomers (entries 10 and 11).

Table 2
Synthesis of 3,4-diiododihydrofurans by electrophilic iodocyclization[a]

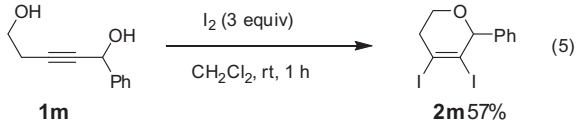


1 **2**

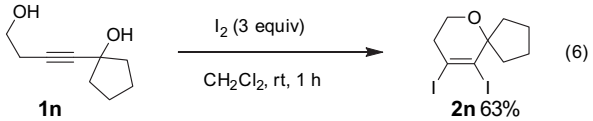
Entry	Substrates	**1**	Products	**2**	Yield[b] (%)
1	R^3=4-MeO–C_6H_4	**1b**		**2b**	99
2	R^3=4-Br–C_6H_4	**1c**		**2c**	85
3	R^3=Ph, R^4=Me	**1d**		**2d**	93
4	R^3=Me, R^4=Me	**1e**		**2e**	83
5	n=1	**1f**		**2f**	92
6	n=2	**1g**		**2g**	85
7	n=3	**1h**		**2h**	81
8	n=4	**1i**		**2i**	75
9		**1j**		**2j**	83
10	R^1=Me, R^3=Ph	**1k**		**2k**	99 (dr=1.1:1)
11	R^1=Ph, R^3=Ph	**1l**		**2l**	86 (dr=1:1)

[a] Reaction conditions: **1** (0.2 mmol), I_2 (0.6 mmol), anhydrous solvent (0.1 M), room temperature, 1 h.
[b] Isolated yield.

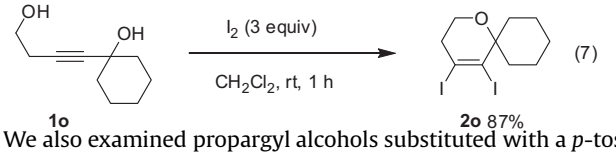
The reaction was further extended to the synthesis of dihydropyrans. When pent-2-yne-1,5-diols **1m**–**o** having a phenyl or a carbocycle at the propargyl alcoholic carbon was used, the reaction proceeded smoothly, furnishing the expected dihydropyran **2m** and oxaspirocycles **2n** and **2o** in good yields (Eqs. 5–7).



1m **2m** 57%

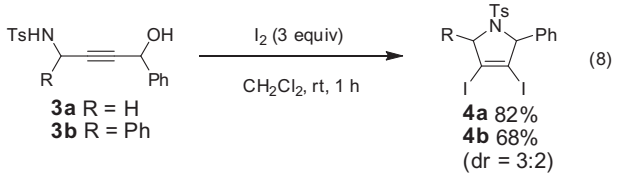


1n **2n** 63%



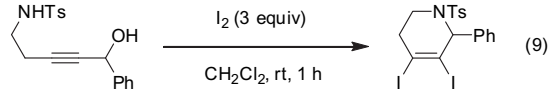
1o **2o** 87%

We also examined propargyl alcohols substituted with a *p*-tosyl (Ts)-protected amine under the standard reaction conditions. When the alkyne-tethered aminoalcohols **3a** or **3b** was treated with I_2 in CH_2Cl_2 at room temperature, 3,4-diiodo-dihydropyrroles **4a** and **4b** were obtained in 82% and 68% yields, respectively, and **4b** was isolated as a 3:2 mixture of two diastereomers (Eq. 8). Similarly, the reaction of pent-2-yne-1-ol **3c** substituted with a tosylamine produced the corresponding diiodotetrahydropyridine **4c** in moderate yield (Eq. 9).



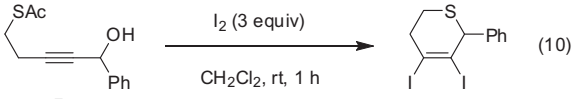
3a R = H
3b R = Ph

4a 82%
4b 68%
(dr = 3:2)



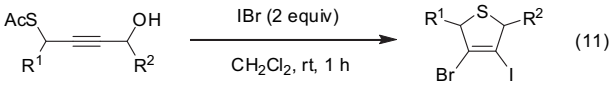
3c **4c** 53%

We further tested this iodocyclization with *S*-hydroxyl-2-butynyl ethanthioates as substrates under the standard conditions to know the generality of the methodology and to know how the method is useful for the synthesis of functionalized 3,4-diiododihydrothiophenes (Table 3). The reactions of substrates **5a**–**c** bearing aromatic rings at the propargyl alcoholic carbon produced the corresponding tri-substituted dihydrothiophenes **6a**–**c** in good to high yields, wherein **5c** having an electron-withdrawing groups on aromatic ring gave a lower yield (entries 1–3). In the case of **5d** having an alkyl substituent at R^2, the corresponding product **6d** was formed in moderate yield (entry 4). Remarkably, the presence of a double bond in substrate was also tolerated; the desired dihydrothiophene **6e** was obtained in 91% yield (entry 5). Substrates **5f**–**h** having heteroaromatic rings, such as thienyl, furanyl, and pyrrolyl, showed a high compatibility with the present reaction conditions, producing **6f**–**h** in high yields (entries 6–8). Interestingly, tertiary alcohols (**5i**–**k**) with a cyclohexyl, cycloheptyl, or cyclooctyl ring were transformed into the expected [4.*n*]thiaspirocycles **6i**–**k** in good yields (entries 9-11). The reaction also worked well with the substrates **5l** and **5m** having two substituents at the both propargylic carbons, furnishing the expected tetra-substituted dihydrothiophenes **6l** and **6m** as a mixture of two diastereomers, respectively (entries 12 and 13). This method also extended to the synthesis of dihydrothiopyran. Thus, when *S*-5-hydroxy-5-phenylpent-3-ynyl ethanethioate **5n** reacted with I_2 under the standard conditions, the expected six-membered product **6n** was obtained in 88% yield (Eq. 10).



5n **6n** 88%

The iodocyclization was also tested with IBr electrophile instead of iodine. In the presence of 2 equiv of IBr, substrates **5a** and **5o** underwent the electrophilic iodocyclization smoothly to afford the corresponding 3-bromo-4-iododihydrothiophenes **6a′** and **6o′** in good yields as a single regioisomer, in which **6o′** was obtained as a 1.6:1 diastereomeric mixture (Eq. 11).

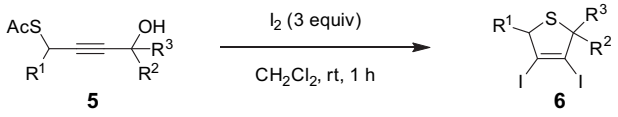


5a R^1 = H, R^2 = Ph
5o R^1 = Ph, R^2 = *p*-tolyl

6a' 76%
6o' 55%
(d.r.= 1.6:1)

Based on these observations, the present iodocyclization mechanism is proposed as shown in Scheme 1. Presumably, initial activation of the propagyl hydroxyl group of substrate (**1**, **3**, **5**) with a Lewis acidic iodine[13] leads to the propargyl carbocation intermediate **A** or allene cation **B**[14] along with an unstable hypoiodous acid (HOI) and an iodine anion. Attack of the iodine anion onto γ-position of **A** or the cation in **B** affords iodoallene **C**, which will react with hypoiodous acid to form an iodonium intermediate **D**.[15] Subsequent intramolecular nucleophilic addition of nucleophiles, such as O, N, or S atom, to the activated allene followed by deprotection of acetyl group produces the corresponding product and acetic acid.

Table 3
Synthesis of 3,4-diiododihydrothiophenes via iodocyclization[a]



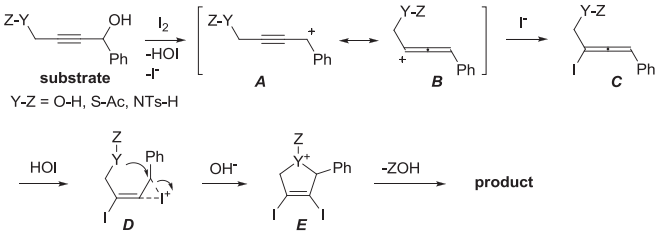
5 **6**

Entry	Substrates	5	Products	6	Yield[b] (%)
	AcS, OH, R_2		S, R^2, I, I		
1	R^2=H	**5a**		**6a**	89
2	R^2=Me	**5b**		**6b**	93
3	R^2=CO_2Me	**5c**		**6c**	71
4	R^2=*n*-C_5H_{11}	**5d**		**6d**	39
5	R^2=(*E*)-CH=CHC_6H_5	**5e**		**6e**	91
	AcS, OH, X		S, X, I, I		
6	X=S	**5f**		**6f**	96
7	X=O	**5g**		**6g**	78
8	X=NTs	**5h**		**6h**	98
	AcS, OH, n		S, n, I, I		
9	*n*=1	**5i**		**6i**	86
10	*n*=2	**5j**		**6j**	89
11	*n*=3	**5k**		**6k**	54

Table 3 (*continued*)

Entry	Substrates	5	Products	6	Yield[b] (%)
12	AcS, OH, Ph, Ph	**5l**	Ph, Ph, I, I	**6l**	76 (dr=1.4:1)
13	AcS, OH, S, S	**5m**	S, S, S, I, I	**6m**	48 (dr=1.3:1)

Ac=acetyl, Ph=phenyl, Me=methyl, Ts=toluenesulfonyl.
[a] Reaction conditions: **5** (0.2 mmol), I_2 (0.6 mmol), CH_2Cl_2 (0.1 M), room temperature, 1 h.
[b] Isolated yield.

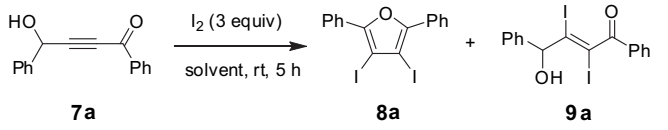


Scheme 1. Proposed reaction mechanism for the formation of dihalogenated dihydroheterocycles.

2.2. Synthesis of five-membered dihalogenated aromatic heterocycles via electrophilic iodocyclization

Encouraged by the success of the synthesis of dihydroheterocycles, we used but-2-yn-1-ones instead of but-2-yn-1-ols as substrates for the iodocyclization. However, when 4-hydroxyl-1,4-diphenylbut-2-yn-1-one **7a** was treated with I_2 under ordinary conditions, a mixture of the corresponding furan **8a** and the diiodinated acyclic olefin **9a** was obtained (Table 4, entry 1). This is not a surprising result, since the addition of I_2 to a triple bond takes place rather readily. Therefore, we screened various organic solvents to improve the yield of **8a**. The use of other aprotic solvent, such as THF, CH_3NO_2, $CHCl_3$, CCl_4, and benzene, did not increase the selectivity (entries 2–6). We were pleased to find that the use of CH_2Cl_2 with MeOH (1.0 equiv) improved the yield of **8a**, but **9a** was still produced in 30% yield (entry 7). This result led us to examine the protic solvents. Fortunately, when MeOH or EtOH was used as a solvent, the yield of **8a** was dramatically increased and formation of **9a** was not detected (entries 10 and 11). These results indicate that the use of protic solvents is indispensable for the selective formation of **8a**.

Table 4
Optimization of solvents[a]

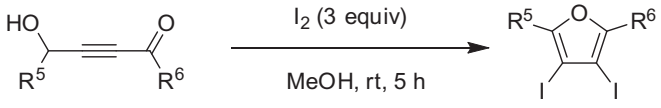


Entry	Solvents	Additive (equiv)	Time (h)	**8a** Yield[b] (%)	**9a**, Yield[b] (%)
1	CH_2Cl_2		0.5	45	50
2	THF		3	21	69
3	CH_3NO_2		3	45	49
4	$CHCl_3$		3	41	58
5	CCl_4		0.25	43	55
6	Benzene		0.3	30	70
7	CH_2Cl_2	MeOH (1.0)	3	65	30
8	MeOH		5	96 (87)	0
9	EtOH		5	96	0

THF=tetrahydrofuran, Tf=trifluoromethanesulfonyl.
[a] Reaction conditions: **7a** (0.2 mmol), I_2 (0.6 mmol), anhydrous solvent (0.1 M), room temperature.
[b] ^1H NMR yield determined using CH_2Br_2 as an internal standard. Isolated yield is shown in parentheses.

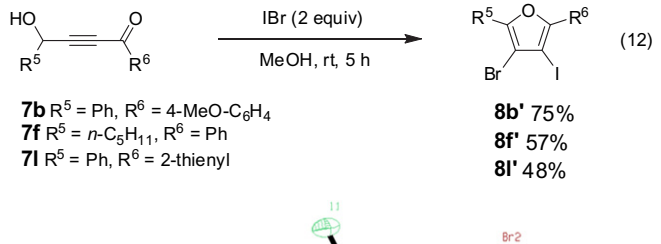
The results of iodocyclization of various 4-hydroxyl-but-2-yn-1-ones with I_2 are summarized in Table 5. The reactions of substrates **7b** and **7c** bearing an electron-donating and an electron-withdrawing aromatic group at R^6 produced the corresponding diiodofurans **8b** and **8c** in high yields, respectively; substrate **7c** having an electron-withdrawing group at R^6 afforded a higher yield (entries 1 and 2). Not only a tosyl-protected pyrroyl substituent (**7d**), but also an alkyl substituent (**7e**) at R^6 afforded the desired tetra-substituted diiodofuran **8d** and **8e** in good yields (entries 3 and 4). Similarly, the reactions also worked well with the substrates **7f**–**i** having various substituted aromatic rings and alkyl group at R^6 and *n*-pentyl group at R^5, furnishing the desired multi-substituted furans in good to high yield (entries 5–8). Substrates **7j** and **7k** having a primary propargyl alcohol moiety were also compatible with the standard reaction conditions, giving the tri-substituted furans **8j** and **8k** in good yields (entries 9 and 10). Next, we investigated the reactivity of IBr electrophile instead of iodine on the present iodocyclization. Substrates **7b**, **7f**, and **7l** underwent the electrophilic cyclization smoothly with 2 equiv of IBr to produce the corresponding 3-bromo-4-iodofurans **8b′**, **8f′**, and **8l′** in good yields (Eq. 12). The structure of **8b′** was unambiguously confirmed by X-ray crystal-structure analysis (Fig. 1).[16]

Table 5
Synthesis of 3,4-diiodofurans by iodocyclization[a]



Entry	Substrates **7**	Products **8**	Yield[b] (%)
1	**7b** R^5=Ph, R^6=4-MeO-C_6H_4	**8b**	83
2	**7c** R^5=Ph, R^6=4-Cl-C_6H_4	**8c**	91
3	**7d** R^5=Ph, R^6=2-(1-tosyl)pyrroyl	**8d**	43
4	**7e** R^5=Ph, R^6=*n*-C_5H_{11}	**8e**	63
5	**7f** R^5=*n*-C_5H_{11}, R^6=Ph	**8f**	89
6	**7g** R^5=*n*-C_5H_{11}, R^6=4-MeO-C_6H_4	**8g**	80
7	**7h** R^5=*n*-C_5H_{11}, R^6=4-Cl-C_6H_4	**8h**	88
8	**7i** R^5=*n*-C_5H_{11}, R^6=*n*-C_5H_{11}	**8i**	68
9	**7j** R^5=H, R^6=Ph	**8j**	85
10	**7k** R^5=H, R^6=*n*-C_5H_{11}	**8k**	60

[a] Reaction conditions: **7** (0.2 mmol), I_2 (0.6 mmol), MeOH (0.1 M), room temperature, 5 h.
[b] Isolated yield.



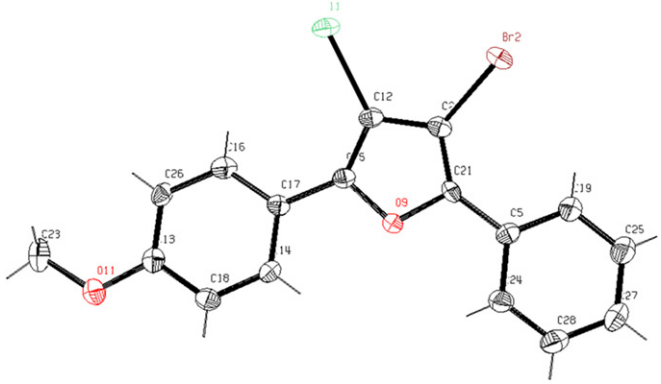
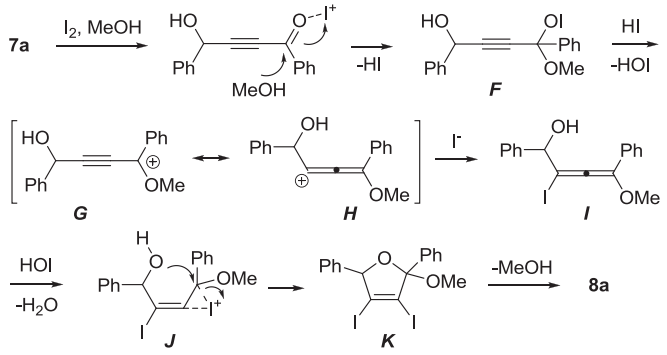


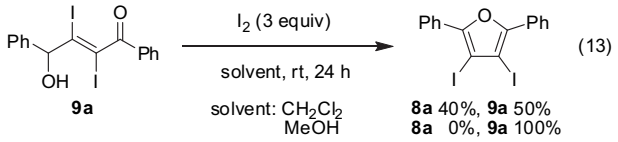
Fig. 1. ORTEP drawing and structure **8b′**.

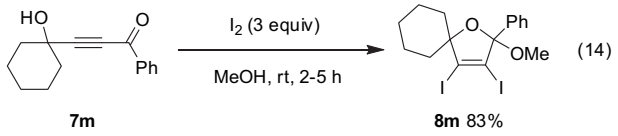
A plausible mechanism for the present iodocyclization is shown in Scheme 2. Initially, butynone **7a** reacts with a Lewis acidic iodine in the presence of MeOH to produce the ketal intermediate **F**. Subsequent dehypoiodination gives propargylic carbocation **G** or allene cation **H** along with an unstable hypoiodous acid (HOI) and iodine anion. Attack of the iodine anion onto the γ-position of **G** or the cation **H** affords iodoallene **I**, which reacts with hypoiodous acid

to form an iodonium intermediate **J**. Subsequent intramolecular nucleophilic addition of an oxygen atom to the activated allene **J** followed by elimination of MeOH produces **8a**. To obtain support for the proposed mechanism, the following experiments were carried out. Treatment of *E*-configured diiodo hydroxyl enone **9a** with I_2 under the standard conditions in CH_2Cl_2 gave **8a** in 40% yield together with the recovered **9a** in 50% yield, indicating that the interconversion of (*E*)- and (*Z*) isomers followed by intramolecular cyclocondensation took place (Eq. 13). This result was in agreement with the previous investigation reported by Obrecht[17] and Müller and co-workers[10b] On the other hand, the reaction of **9a** in MeOH did not produce the corresponding furan **8a** at all. Moreover, when the substrate **7m**, without a proton at the propargylic carbon, was treated with I_2 under the standard conditions, the methoxy incorporated dihydrofuran **8m** was obtained in 83% yield (Eq. 14). These results indicate that the present cyclization must proceed through the formation of the ketal intermediate **F** in the presence of MeOH.



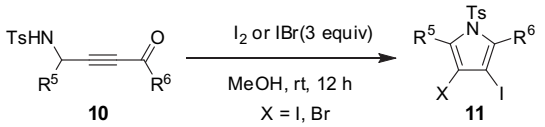
Scheme 2. Proposed mechanism for the formation of diiodofurans.





The success in the synthesis of dihalofurans leads us to investigate the iodocyclization of 4-aminobut-2-yn-1-ones for the synthesis of dihalopyrroles (Table 6). Fortunately, the substrate **10a** having a tosyl-protecting group on amine moiety reacted with I_2 under the standard conditions in MeOH, affording the corresponding pyrrole **11a** in 83% yield without formation of the acyclic diiodinated olefin (entry 1). Surprisingly, when the reaction of **10a** and I_2 was carried out in CH_3NO_2 solvent, **10a** was recovered quantitatively without formation of any products (entry 2). These results suggest that the present pyrrole-formation reaction might proceed through the furan-formation mechanism similar as shown in Scheme 2. We further screened various tosyl-protected aminobut-2-yn-1-ones **10** under the standard conditions. The reaction of substrates **10b** and **10c** bearing aromatic groups at R^6 furnished the desired tri-substituted pyrroles **11b** and **11c** in good yields, irrespective of the electronic nature of the substituents on the aromatic rings (entries 3 and 4). The presence of a double bond in substrate **10d** was also tolerated; the desired pyrrole **11d** was obtained in 53%

Table 6
Synthesis of dihalopyrroles via electrophilic iodocyclization[a]



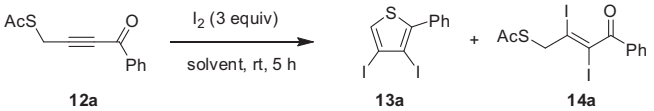
Entry	Substrates **10**	Products **11**	Yield[b] (%)
1	**10a** R^5=H, R^6=C_6H_5	**11a** (X=I)	83
2	**10a** R^5=H, R^6=C_6H_5	**11a** (X=I)	0[c]
3	**10b** R^5=H, R^6=4-Me−C_6H_4	**11b** (X=I)	85
4	**10c** R^5=H, R^6=4-Br−C_6H_4	**11c** (X=I)	77
5	**10d** R^5=H, R^6=(*E*)-CH=CHC_6H_5	**11d** (X=I)	53
6	**10e** R^5=C_6H_5, R^6=C_6H_5	**11e** (X=I)	86
7	**10e** R^5=C_6H_5, R^6=C_6H_5	**11e′** (X=Br)	64[d]

[a] Reaction conditions: **10** (0.2 mmol), I_2 (0.6 mmol), MeOH (0.1 M), room temperature, 12 h.
[b] Isolated yield.
[c] CH_3NO_2 was used instead of MeOH.
[d] IBr (2 equiv) was used instead of I_2.

yield (entry 5). The reaction also worked well with the substrate **10e** having two phenyl groups at R^5 and R^6, respectively, affording the expected tetra-substituted **11e** in high yield (entry 6). Similarly, the reaction of **10e** with IBr electrophiles gave 3-bromo-4-iodo-2,5-diphenylpyrrole **11e′** in 64% yield (entry 7).

This method was further applied to the synthesis of diiodothiophenes **13** using *S*-4-oxo-but-2-ynyl ethanethioates **12** as substrates. When **12a** was treated with I_2 in MeOH solvent, the corresponding diiodothiophenes **13a** was obtained in moderate yield without any formation of the acyclic diiodinated olefin **14a** (Table 7, entry 1). However, in contrast to the reactions for the formation furans and pyrroles, the reaction of **12a** with I_2 in CH_3NO_2 or CH_3CN solvent produced the expected thiophene **13a** in good to high yield (entries 2 and 3). Interestingly, the use of other solvents, such as CH_2Cl_2, THF, and toluene afforded the diiodinated olefin **14a** exclusively without any formation of **13a** (entries 4–6). These results implied that the thiophene-formation reaction should proceed under reaction pathway different from the furan- and pyrrole-formation.

Table 7
Optimization of solvents for the formation of diiodothiophenes[a]

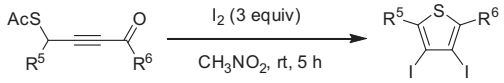


Entry	Solvents	**13a**, Yield[b] (%)	**14a**, Yield[b] (%)
1	MeOH	76 (67)	0
2	CH_3NO_2	96 (83)	0
3	CH_3CN	80 (75)	0
4	CH_2Cl_2	0	91
5	THF	0	95
6	Toluene	0	87

[a] Reaction conditions: **12a** (0.2 mmol), I_2 (0.6 mmol), anhydrous solvent (0.1 M), room temperature, 5 h.
[b] ^1H NMR yield determined using CH_2Br_2 as an internal standard. Isolated yield is shown in parentheses.

Subsequently, various *S*-4-oxo-but-2-ynyl ethanethioates **12** were treated with I_2 in CH_3NO_2 solvent (Table 8). Substrates **12b** and **12c** bearing aromatic groups at R^6 furnished the designed trisubstituted thiophenes **13b** and **13c** in 78% and 85% yield, respectively (entries 1 and 2). The reaction of substrates **12d** and **12e** having a methyl or phenyl substituent at R^5 and R^6, respectively, proceeded smoothly under the standard conditions, affording the

Table 8
Synthesis of 3,4-diiodothiophenes via iodocyclization[a]



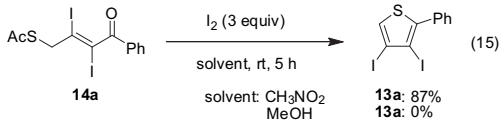
12 13

Entry	Substrates **12**	Products **13**	Yield[b] (%)
1	**12b** R^5=H, R^6=4-Me–C_6H_4	**13b**	78
2	**12c** R^5=H, R^6=4-Cl–C_6H_4	**13c**	85
3	**12d** R^5=Me, R^6=C_6H_5	**13d**	80
4	**12e** R^5=C_6H_5, R^6=C_6H_5	**13e**	82

[a] Reaction conditions: **12** (0.2 mmol), I_2 (0.6 mmol), CH_3NO_2 (0.1 M), room temperature, 5 h.
[b] Isolated yield.

tetra-substituted thiophenes **13d** and **13e** in high yields (entries 3 and 4).

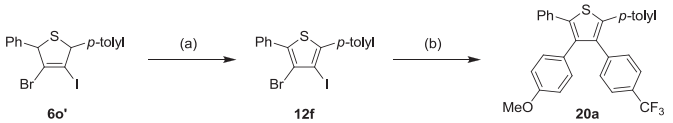
In order to understand the solvent effect on the reaction pathway, we carried out the following reactions. The reaction of the *E*-configured diiodoenone **14a** with I_2 in CH_3NO_2 produced the desired product **13a** in 87% yield, although the reaction in MeOH solvent did not produce **13a**, instead **14a** was recovered quantitatively (Eq. 15). These results indicate that the thiophene-forming cyclization in CH_3NO_2 proceeds through the formation of diiodinated olefin **14a**, followed by isomerization of *E*-configured enone to *Z*-configured enone and the subsequent intramolecular condensation under Lewis acidic I_2 conditions, while the reaction in MeOH undergoes the ketal intermediate-forming pathway similar to the furan- and pyrrole-formation.



2.3. Application of dihaloheterocycle formation methods to the synthesis of useful organic materials

Rubrene has been studied widely as an organic semiconductor; the major application is in organic field-effect transistors (OFETs) and organic light emitting diodes (OLEDs).[18] Especially, rubrene has the highest carrier mobility, which reaches 40 cm^2/V for holes. In general, rubrene is prepared by cycloaddition of isobenzofuran and 2,3-dihalonaphthalene followed by deoxygenation of the resulting oxo-bridged adduct. Various traditional and new methods for synthesizing rubrene intermediates, such as substituted isobenzofurans, were reported.[19] We have successfully applied our current method to the synthesis of isobenzofuran **17a** (Scheme 3). This approach provides an alternative synthetic way to rubrene, and will be useful for synthesizing various functionalized rubrenes. The double Still coupling of the iodocyclization product **8a** with allyltributylstannane produced the 3,4-diallyl-substituted furan **15a**, which was treated with Grubbs(II) catalyst, giving the corresponding dihydroisobenzofuran **16a** in excellent yield. Oxidation of **16a** with Pd/C under refluxing conditions gave the expected isobenzofuran **17a** in 73% yield. Next, **17a** was treated with *n*-BuLi and 3,4-diiodonaphthalene **18a**, which was prepared by our method reported previously,[11g] to produce the oxo-bridged adduct **19a** in 83% yield.

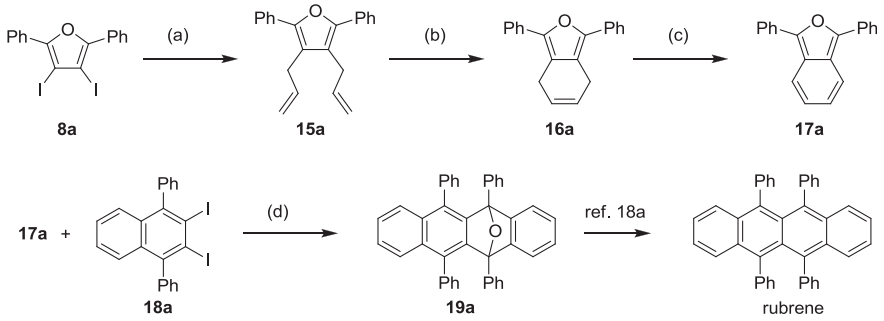
Multi-aryl-substituted thiophenes are useful molecules with interesting optoelectronic and biological properties.[20] The regioselective arylation of C2 and C5 positions of thiophenes is readily accessible, but the controllable arylation of C3 and C4 positions with different aryl groups is not easy. We found that the use of 3-bromo-4-iodo-thiophenes as substrates could provide an efficient and convenient route for the regioselective synthesis of tetraarylthiophenes with different aryl groups. As shown in Scheme 4, the 3-bromo-4-iodo-thiophene **12f** was obtained in 98% yield through the DDQ aromatization of **6o′**. Because of the different reactivity between C–Br and C–I bonds, the double Suzuki coupling reactions proceeded sequentially, furnishing the corresponding unsymmetric tetraaryl-substituted thophene **20a** in good yield and high regioselectivity.[20g]



Scheme 4. Reagents and conditions: (a) DDQ (3 equiv), toluene, reflux, 98%. (b) (i) $Pd(PPh_3)_4$ (3 mol %), PPh_3, K_2CO_3, THF, 4-(trifluoromethyl)phenylboronic acid, 80 °C, 12 h (ii) $Pd(PPh_3)_4$ (6 mol %), K_3PO_4, toluene/dioxane, 4-methoxyphenylboronic acid, 100 °C, 12 h, 66% for 2 steps. DDQ=2,3-dichloro-5,6-dicyano-1,4-benzoquinone.

3. Conclusion

We have developed an efficient and general electrophilic iodocyclization for the synthesis of five- and six-membered dihalogenated heterocycles. The reaction of propargyl alcohols having –OH, –NHTs, and –SAc nucleophilic groups with iodine or bromoiodine afforded the corresponding dihalogenated *O*-, *N*-, and *S*-containing five- and six-membered dihydroheterocycles efficiently. Moreover, various substituted but-2-yn-1-ones bearing –OH, –NHTs, and –SAc nucleophilic groups at C4-position produced the 3,4-diiodo- and 3-bromo-4-iodo-substituted five-membered heteroaromatics, such as furans, pyrroles, and thiophenes in good to high yields, wherein we found that the solvent effect was crucial for the selective formation of the desired products. We have also demonstrated that the resulting dihalogenated heterocyles provided an



Scheme 3. Reagents and conditions: (a) $Pd(PPh_3)_4$ (20 mol %), LiCl, DMF, allyltributylstannane, 100 °C, 83%. (b) Grubbs(II) catalyst (5 mol %), CH_2Cl_2, reflux, 100%. (c) 10% of Pd/C (200 wt %), O_2, MS 4Å, toluene, reflux, 73%. (d) *n*-BuLi (2 equiv), THF, −78 °C to rt, 12 h, 83%. DMF=dimethylforamide, THF=tetrahydrofuran, rt=room temperature, Bu=butyl, MS=molecular sieves.

efficient methodology for the selective synthesis of potentially useful organic electronics. Further applications of the present methods to the synthesis of useful optoelectronic materials are in progress in our laboratory.

4. Experimental section

4.1. General information

^{1}H NMR and ^{13}C NMR spectra were recorded on JEOL JMTC-270/54/SS (JASTEC, 300 MHz, 400 MHz) spectrometers. ^{1}H NMR spectra are reported as follows: chemical shift in parts per million (δ) relative to the chemical shift of $CDCl_3$ at 7.26 ppm, integration, multiplicities (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet and br=broadened), and coupling constants (Hz). ^{13}C NMR spectra reported in ppm (δ) relative to the central line of triplet for $CDCl_3$ at 77 ppm. IR spectra were recorded on JASCO FT/IR-4100 spectrometer; absorptions are reported in cm^{-1}. High-resolution mass spectra were obtained on a BRUKER APEXIII spectrometer and JEOL JMS-700 MStation operator. Column chromatography was carried out employing Silica gel 60 N (spherical, neutral, 40–100 μm, KANTO Chemical Co.). Analytical thin-layer chromatography (TLC) was performed on 0.2 mm precoated plate Kieselgel 60 F_{254} (Merck).

4.2. Materials

Anhydrous dichloromethane, CH_3NO_2, CH_3CN, MeOH, DMF, toluene, CH_2Cl_2 (WAKO), I_2 (TCI), IBr (Aldrich), $Pd(PPh_3)_4$ (Aldrich), $Pd(PPh_3)_2Cl_2$ (TCI), CuI (Aldrich), LiCl (Nakalai), DDQ (Aldrich) were purchased and used as received. Substrates **1**, **3**, **5**, **7**, **10**, and **12** were prepared by modified literature methods (see Supplementary data). The structures of new products were determined by ^{1}H, ^{13}C NMR, and high-resolution mass.

4.3. General procedure for synthesis of 3,4-diiododihydrofurans

I_2 (0.6 mmol, 152 mg) was added to a solution of 1-phenylbut-2-yne-1,4-diol **1a** (0.2 mmol, 32 mg) in dichloromethane (2 mL), and the resulting mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with 10 mL dichloromethane, washed with a saturated sodium thiosulfate. The organic layer was dried over an anhydrous $MgSO_4$. After concentration of the filtrate, the residue was purified by chromatography on silica gel to afford 3,4-diiodo-2-phenyldihydrofuran **2a** (78.7 mg, 99%) as a slight yellow solid.

4.4. General procedure for synthesis of 3,4-diiodofurans

I_2 (0.6 mmol, 152 mg) was added to a solution of 4-hydroxy-1,4-diphenylbut-2-yn-1-one **7a** (0.2 mmol, 48 mg) in MeOH (2 mL), and the resulting mixture was stirred at room temperature for 5 h. The reaction mixture was diluted with 10 mL ether, washed with saturated sodium thiosulfate. The organic layer was dried over an anhydrous $MgSO_4$. After concentration of the filtrate, the residue was purified by chromatography on silica gel to afford 3,4-diiodo-2,5-diphenylfuran **8a** (82.2 mg, 87%) as a white solid.

4.5. Analytical data

*4.5.1. 2-(4-Bromophenyl)-3,4-diiodo-2,5-dihydrofuran (**2c**).* Yellow solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, J=5.4 Hz, 2H), 7.17 (d, J=5.4 Hz, 2H), 5.53 (dd, J=5.7, 3.9 Hz, 1H), 4.81 (dd, J=12.3, 5.7 Hz, 1H), 4.69 (dd, J=12.3, 3.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 83.2, 93.1, 101.4, 106.1, 122.9, 129.1, 131.6, 137.9; IR (neat): 767, 865, 1007, 1041, 1257, 1400, 1600, 2856 cm^{-1}; HRMS (EI) calcd for $C_{10}H_7BrI_2$ (m/z): 475.7770; found, 475.7769.

*4.5.2. 3,4-Diiodo-2,2-dimethyl-2,5-dihydrofuran (**2e**).* Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.53 (d, 2H), 1.38 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.7, 80.7, 92.2, 99.6, 112.9; IR (neat): 793, 820, 911, 1039, 1250, 1336, 1361, 1455, 1599, 2844, 2926, 2973 cm^{-1}; HRMS (EI) calcd for $C_6H_8I_2O$ (m/z), 349.8665; found, 349.8665.

*4.5.3. 3,4-Diiodo-1-oxaspiro[4.7]dodec-3-ene (**2i**).* Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.50 (s, 2H), 1.99–1.89 (m, 2H), 1.82–1.70 (m, 6H), 1.62–1.53 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.9, 23.8, 27.8, 34.9, 80.3, 94.4, 99.6, 113.6; IR (neat): 731, 780, 858, 1040, 1330, 1465, 1596, 2846, 2917 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{16}I_2O$ (m/z): 417.9291; found, 417.9285.

*4.5.4. Compound (**2j**).* Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.00–1.94 (m, 2H), 1.86–1.79 (m, 2H), 1.73–1.55 (m, 11H), 1.45–1.43 (m, 2H), 1.16–1.08 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9, 24.9 (×2), 36.6, 39.9, 91.4, 100.0, 112.6, 114.2; IR (neat): 731, 780, 858, 1040, 1330, 1465, 1596, 2846, 2917 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{18}I_2O$ (m/z): 443.9447; found, 443.9444.

*4.5.5. 3,4-Diiodo-2-methyl-5-phenyl-2,5-dihydrofuran (**2k**).* Brown oil; dr=1.1:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.58–5.52 (m, 1H), 5.03 (dq, J=6.4, 2.0 Hz, 1H) [diastereomeric isomer: 4.88 (dq, J=6.4, 2.0 Hz, 1H)], 1.54 (d, J=6.4 Hz, 3H) [diastereomeric isomer: 1.45 (d, J=6.4 Hz, 3H)]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0 (22.0), 87.8 (88.3), 93.0 (93.4), 107.0 (107.7), 108.7 (109.1), 127.4 (127.8), 128.4 (128.5), 128.7 (128.8), 138.9 (138.9); IR (neat): 824, 894, 1011, 1323, 1444, 1590, 2855, 2928 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{10}I_2O$ (m/z): 411.8821, found: 411.8820.

*4.5.6. 4,5-Diiodo-6-phenyl-3,6-dihydro-2H-pyran (**2m**).* Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.33 (m, 5H), 5.31 (d, J=2.0 Hz, 1H), 3.96–3.91 (m, 1H), 3.83–3.77 (m, 1H), 3.09–3.01 (m, 1H), 2.97–2.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.6, 63.1, 85.0, 107.4, 112.2, 128.3, 128.7 (×2), 139.1; IR (neat): 697, 751, 790, 864, 981, 1069, 1255, 1317, 1448, 2929 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{10}I_2O$ (m/z): 411.8821, found: 411.8818.

*4.5.7. 9,10-Diiodo-6-oxaspiro[4.5]dec-9-ene (**2n**).* Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.75 (t, J=5.4 Hz, 2H), 2.82 (t, J=5.4 Hz, 2H), 2.26–2.16 (m, 2H), 1.93–1.85 (m, 2H), 1.74–1.69 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.7, 39.5, 43.2, 61.2, 91.1, 107.4, 121.5; IR (neat): 793, 954, 1092, 1198, 1262, 1321, 1433, 1579, 2865, 2954 cm^{-1}; HRMS (EI) calcd for $C_9H_{12}I_2O$ (m/z): 389.8978, found: 389.8974.

*4.5.8. 4,5-Diiodo-1-oxaspiro[5.5]undec-4-ene (**2o**).* Brown solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.78 (t, J=5.4 Hz, 2H), 2.83 (t, J=5.4 Hz, 2H), 2.07–1.97 (m, 2H), 1.76–1.72 (m, 2H), 1.65–1.46 (m, 5H), 1.25–1.08 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.5, 24.9, 35.0, 43.6, 59.8, 80.9, 107.8, 122.9; IR (neat): 699, 793, 936, 1091, 1153, 1262, 1321, 1445, 1577, 2851, 2929 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{14}I_2O$ (m/z): 403.9134, found: 403.9129.

*4.5.9. 3,4-Diiodo-2,5-diphenyl-1-tosyl-2,5-dihydro-1H-pyrrole (**4b**).* White solid; dr=3:2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.14 (m, 10H), 6.87–6.76 (m, 4H), 5.68 (s, 2H) [diastereomeric isomer: 5.55 (s, 2H)], 2.26 (s, 3H) [diastereomeric isomer: 2.18 (s, 3H)]; ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 21.4 (21.4), 76.6 (76.9), 107.5 (108.3), 126.7 (126.9), 128.2 (128.3), 128.3 (128.6), 128.6 (128.6), 128.7 (128.9), 136.3 (136.6), 137.6 (137.7), 142.4 (142.8); IR (neat): 677,

763, 1154, 1345, 1738, 2918 cm^{-1}; HRMS (EI) calcd for $C_{23}H_{19}I_2NO_2S$ (*m*/*z*): 626.9226, found: 626.9211.

*4.5.10. 4,5-Diiodo-6-phenyl-1-tosyl-1,2,3,6-tetrahydropyridine (**4c**).* White solid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75–7.72 (m, 2H), 7.41–7.73 (m, 7H), 5.86 (s, 1H), 3.63–3.59 (m, 1H), 3.21–3.13 (m, 1H), 2.58–2.55 (m, 2H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 39.3, 39.9, 67.2, 107.6, 109.4, 127.0, 128.4, 128.5, 128.7, 129.7, 136.3, 137.0, 143.8; IR (neat): 726, 961, 1154, 1345, 1738, 2918 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{17}I_2NO_2S$ (*m*/*z*), 564.9070; found, 564.9077.

*4.5.11. 4,5-Diiodo-6-phenyl-3,6-dihydro-2H-thiopyran (**6n**).* Yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.30 (m, 3H), 7.26–7.24 (m, 2H), 4.88 (s, 1H), 3.27–3.22 (m, 2H), 2.85–2.79 (m, 1H), 2.60–2.55 (m, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 24.8, 44.5, 53.8, 109.78, 114.2, 127.5, 127.7, 128.4, 140.6; IR (neat): 694, 1069, 1450, 1583, 2920 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{10}I_2S$ (*m*/*z*): 427.8593; found, 427.8583.

*4.5.12. 3,4-Diiodo-2-phenyl-1-tosyl-1H-pyrrole (**11a**).* Yellow solid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.38–7.33 (m, 1H), 7.29–7.23 (m, 2H), 7.15–7.05 (m, 4H), 6.99–6.96 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (75.45 MHz, $CDCl_3$) δ 21.6, 78.0, 85.5, 127.0, 127.5, 127.6, 129.3, 129.6, 130.5, 131.9, 134.5, 136.6, 145.5; IR (neat): 695, 661, 765, 1085, 1171, 1366, 3144 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{13}I_2NO_2S$, 548.8649 (*m*/*z*): found, 548.8643.

*4.5.13. 3,4-Diiodo-2-p-tolyl-1-tosyl-1H-pyrrole (**11b**).* White solid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.31–7.12 (m, 6H), 7.00–6.98 (m, 2H), 2.48 (m, 3H), 2.44 (m, 3H); ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 21.5, 21.7, 78.1, 85.5, 126.8, 127.5, 127.5, 128.2, 129.4, 131.6, 134.4, 136.7, 139.2, 145.3; IR (neat): 664, 1174, 1372, 1725, 2918 cm^{-1}; HRMS (EI): calcd for $C_{18}H_{15}I_2NO_2S$ (*m*/*z*): 562.8913; found, 562.8911.

*4.5.14. 2-(4-Bromophenyl)-3,4-diiodo-1-tosyl-1H-pyrrole (**11c**).* White solid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.51 (d, *J*=8.0 Hz, 2H), 7.30–7.20 (m, 4H), 7.96 (d, *J*=8.0 Hz, 2H), 2.45 (s, 3H); ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 21.7, 78.3, 86.0, 123.9, 127.3, 127.5, 129.4, 129.7, 130.8, 133.4, 134.3, 135.2, 145.7; IR (neat): 663, 1169, 1372, 1593, 3134 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{12}BrI_2NO_2S$ (*m*/*z*): 626.7862; found, 626.7858.

*4.5.15. (E)-3,4-Diiodo-2-styryl-1-tosyl-1H-pyrrole (**11d**).* White solid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J*=8.0 Hz, 2H), 7.64 (s, 1H), 7.53 (d, *J*=8.0 Hz, 2H), 7.46–7.35 (m, 3H), 7.30–7.25 (m, 3H), 7.14 (d, *J*=16.0 Hz, 1H); 2.42 (s, 3H); ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 21.7, 81.0, 82.4, 116.1, 126.5, 126.9, 127.4, 128.4, 128.7, 129.9, 133.6, 134.6, 135.9, 136.0, 145.7; IR (neat): 663, 1173, 1378, 1738, 3146 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{15}I_2NO_2S$ (*m*/*z*): 574.8913; found, 574.8917.

*4.5.16. 3,4-Diiodo-2,5-diphenyl-1-tosyl-1H-pyrrole (**11e**).* White solid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.24 (m, 10H), 7.09 (d, *J*=8.0 Hz, 2H), 7.04 (d, *J*=8.0 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 21.7, 87.6, 127.3, 127.4, 128.9, 129.3, 131.5, 132.7, 135.0, 139.1, 145.1; IR (neat): 692, 758, 1172, 1366, 1738, 3023 cm^{-1}; HRMS (EI) calcd for $C_{23}H_{17}I_2NO_2S$ (*m*/*z*): 624.9049; found, 624.9070.

*4.5.17. 3-Bromo-4-iodo-2,5-diphenyl-1-tosyl-1H-pyrrole (**11e'**).* White solid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44–7.37 (m, 10H), 7.10 (d, *J*=8.0 Hz, 2H), 7.04 (d, *J*=8.0 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 21.7, 82.5, 112.4, 127.2, 127.4, 127.5, 128.9, 129.0, 129.2, 130.9, 131.2, 131.4, 132.2, 134.9, 135.2, 138.8, 145.1; IR (neat): 692, 759, 1367, 1738, 3023 cm^{-1}; HRMS (EI) calcd for $C_{23}H_{17}BrINO_2S$ (*m*/*z*): 576.9208; found, 576.9215.

*4.5.18. 3,4-Diiodo-2-phenylthiophene (**13a**).* Slight yellow solid; ^1H NMR (500 MHz, $CDCl_3$) δ 7.62 (1H, s), 7.54–7.52 (2H, m), 7.46–7.39 (3H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 92.7, 93.5, 128.4, 128.9, 129.0, 129.4, 134.8; IR (neat): 692, 764, 862, 1092, 1210, 1270, 1441, 1464, 1597, 1739, 2923 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_6I_2S$ (*m*/*z*): 411.8280, found: 411.8281.

*4.5.19. 3,4-Diiodo-2-p-tolylthiophene (**13b**).* Slight yellow solid; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (1H, s), 7.43 (2H, d, *J*=8.0 Hz), 7.25 (2H, d, *J*=8.0 Hz), 2.42 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3, 92.4, 93.4, 128.76, 129.1, 129.3, 131.9, 138.9, 144.2; IR (neat): 742, 814, 864, 1217, 1367, 1469, 1738, 2919 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_8I_2S$ (*m*/*z*): 425.8436, found: 425.8436.

*4.5.20. 2-(4-Chlorophenyl)-3,4-diiodothiophene (**13c**).* Slight yellow solid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (1H, s), 7.47 (2H, d, *J*=9.0 Hz), 7.41 (2H, d, *J*=9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 93.3, 93.7, 128.7, 129.2, 130.7, 133.2, 135.0, 142.7; IR (neat): 735, 818, 1012, 1093, 1217, 1366, 1463, 1738, 2924 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_5ClI_2S$ (*m*/*z*): 445.7890, found: 445.7893.

*4.5.21. 3,4-Diiodo-2-methyl-5-phenylthiophene (**13d**).* Slight yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54–7.50 (2H, m), 7.46–7.38 (3H, m), 2.60 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.2, 92.3, 96.1, 128.3, 128.6, 129.4, 135.1, 139.7, 141.1; IR (neat): 691, 761, 821, 1031, 1216, 1375, 1599, 1739, 2921 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_8I_2S$ (*m*/*z*): 425.8436, found: 425.8440.

*4.5.22. (E)-S-2,3-Diiodo-4-oxo-4-phenylbut-2-enyl ethanethioate (**14a**).* Brown oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94–7.91 (m, 2H), 7.63–7.59 (m, 1H), 7.50–7.46 (m, 2H), 4.35 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.3, 46.5, 95.0, 96.2, 129.0, 130.3, 131.1, 134.2, 191.3, 193.1; IR (neat): 618, 703, 1124, 1232, 1665, 1693, 1737, 2970 cm^{-1}; HRMS (EI): $[M+H]^+$ calcd for $C_{12}H_{11}I_2O_2S$, 472.8569; found, 472.8553.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.08.084.

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