

RESEARCH ARTICLE

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A concise method to prepare novel fused heteroaromatic diones through double Friedel–Crafts acylation†

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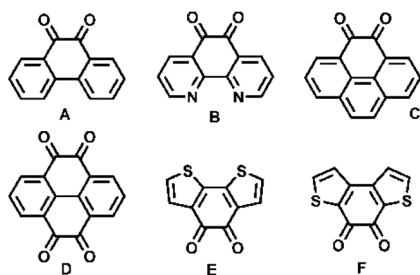
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This paper explored the intramolecular double Friedel–Crafts acylation strategy in approaching different types of novel fused heteroaromatic diones (12 samples using 2,2'-bithiophene, 2,2'-bifuran, 2,2'-bis-elenophene, and 2,2'-bipyrrole as cores) with 16%–85% yield.

Fused aromatic or heteroaromatic diones (Scheme 1) have been demonstrated as powerful building blocks to construct versatile π -conjugated materials ranging from small molecules^{1–6} to conducting polymers,⁷ which can be used in organic solar cells,⁷ organic field-effect transistors,^{5,6b,7d,e,8} lithium-ion batteries,^{3e} sensors,^{2b,3c,6c} phototransistor devices,^{3d} optical waveguides,^{6a} etc. Especially, fused heteroaromatic diones are more attractive because the type, position, and valence of heteroatoms could offer more opportunities to tune the properties and characteristics of new materials constructed from them.⁹ In fact, fused heteroaromatic diones could offer us more opportunities to vary the properties of as-prepared materials through post-modification.¹⁰ Thus, it is a very urgent task to develop the corresponding method for preparing these fused heteroaromatic diones.



Scheme 1 The reported structures of fused aromatic and heteroaromatic diones.

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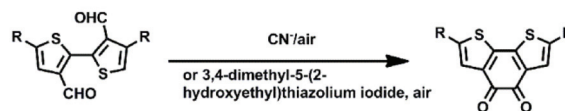
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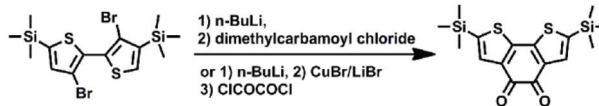
†Electronic supplementary information (ESI) available: Details of experimental procedures, ¹H NMR, ¹³C NMR, HRMS, etc. See DOI: 10.1039/c4qo00032c

There are three main types of methods in the literature to prepare heteroaromatic-fused diones (using the benzo-[2,1-*b*:3,4-*b'*]-dithiophene-4,5-dione (BDTD) core as an example, Scheme 2): (a) dialdehyde undergoes benzoin condensation in the presence of cyanide anions or 3,4-dimethyl-5-(2-hydroxyethyl)thiazolium iodide, followed by air oxidation (Scheme 2a);^{1c,10a} (b) substituted 3,3'-dibromo-2,2'-bithiophene can be converted into diones *via* double lithiation with *n*-butyllithium, followed by reaction with an electrophile (diethyl oxalate or *N,N'*-dimethylpiperazine-2,3-dione) or CuBr/LiBr then oxalyl chloride (Scheme 2b);^{9,10b} (c) diones are formed *via* lithiation of 3-bromo-thiophene with *n*-butyllithium, then reaction with *N,N'*-dimethylpiperazine-2,3-dione or CuBr/LiBr

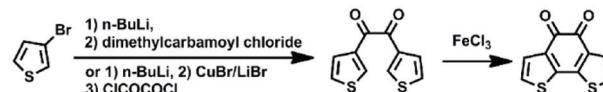
Method A



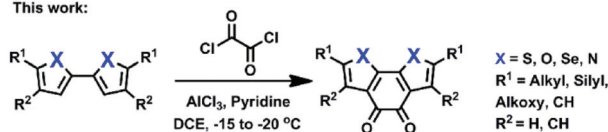
Method B



Method C



This work:



Scheme 2 The synthetic methods to prepare fused heteroaromatic diones.

then oxalyl chloride, followed by intramolecular thiophene–thiophene coupling with FeCl_3 (Scheme 2c).^{10b,11} However, these methods might not become a general method to prepare other important fused heteroaromatic diones such as 2,2'-bifuran, 2,2'-biselenophene, and *N,N'*-dimethyl-2,2'-bipyrrole for the following reasons: (1) some intermediates are not commercially available and need more steps to prepare; (2) some commercial sources are expensive or highly-flammable; and (3) some chemical agents such as cyanide are very toxic and are not environment-friendly. Thus, it should be highly desirable to develop a general, concise and efficient method to address these molecules. In this work, we developed a direct and concise method to synthesize fused heteroaromatic diones ($\text{X} = \text{S}, \text{Se}, \text{O}, \text{N}$) through intramolecular double Friedel–Crafts acylation (Scheme 2).

Although it was in 1911 that Liebermann *et al.*^{11b} demonstrated the possibility of intramolecular double Friedel–Crafts acylation on 4,4'-dimethylbiphenyl, only one recent paper suggested that Friedel–Crafts acylation could be realized on heteroaromatic rings to produce heteroaromatic diones.¹² Nevertheless, in this work,¹² the Friedel–Crafts acylation happened on 2,2'-positions rather than 3,3'-positions, where 2,2'-positions are well known to be more reactive than 3,3'-positions. To the best of our knowledge, there is no report regarding the Friedel–Crafts acylation happening on 3,3'-positions of heteroaromatic rings. Hence, we became interested in examining the possibility of Friedel–Crafts acylation on 3,3'-positions of heteroaromatic rings including 2,2'-bithiophene, 2,2'-bifuran, 2,2'-biselenophene, and *N,N'*-dimethyl-2,2'-bipyrrole.

In order to test our ideas, we used 2,2'-bithiophene as a core and functionalized it with different substituent groups in 5 and 5'-positions (Table 1). The ratios of oxalyl chloride and aluminium chloride to reactants are 1.2 and 3.0, respectively. The effects of different substituent groups (*e.g.*, alkyl groups, electron-donating groups, and electron-withdrawing groups) have been investigated. As shown in Table 1, both alkyl groups and silyl groups underwent intramolecular double Friedel–Crafts acylation in medium yields (25–48%). When the R^1

group becomes more bulky (*e.g.*, using *t*-butyl to replace methyl), the yield increases simultaneously (see entries 1, 2, 4 and 5). The reason for the low yield of compound **1d** (trimethylsilyl group) might be due to the breakage of the C–Si bond, and accordingly, the intermolecular Friedel–Crafts acylation happens (see ESI: S5†). The intramolecular double Friedel–Crafts acylation reaction proceeded very well if a long chain was used (entry 3). Interestingly, when the strong electron-donating group methoxyl was employed, a relatively low yield (25%) was observed. Furthermore, when the electron-withdrawing group (*e.g.* CH_3CO) was introduced in 5 and 5'-positions, no reaction happened due to the lower reactivity of compound **1g** (acetyl group). If R^1 was Br, no target molecule was observed and complex by-products formed. Thus, our results suggest that electron-rich substituents favor the intramolecular double Friedel–Crafts acylation.

Given our success with intramolecular double Friedel–Crafts acylation of 2,2'-bithiophene derivatives, we decided to extend our method to systems containing 2,2'-bifuran, 2,2'-biselenophene, and *N,N'*-dimethyl-2,2'-bipyrrole as cores (Table 2). As shown in Table 2, due to its high reactivity, the target compound (**4a**) for bifuran (**3a**) can only be obtained in 16% yield when the reaction temperature decreases to -50°C . As to 2,2'-biselenophene (**3b**) and *N,N'*-dimethyl-2,2'-bipyrrole (**3c**), the reaction can proceed smoothly with medium yield. It is worth noting that this is the first report of performing intramolecular double Friedel–Crafts acylation on these systems containing 2,2'-bifuran, 2,2'-biselenophene or *N,N'*-dimethyl-2,2'-bipyrrole as the cores.

Further explorations of intramolecular double Friedel–Crafts acylation on more complicated systems (*e.g.* 2,2'-bibenzofuran, 2,2'-bibenzothiophene, and 1,1'-diethyl-1*H*,1'*H'*-2,2'-biindole) have also been demonstrated (Table 3). All reactions gave good yields (35–85%) under similar reaction conditions.

To demonstrate the usefulness of these intermediates, we carried out two derivative reactions (Scheme 3) and our results show that both reactions performed well with high yields. Moreover, the as-prepared products show very good solubility in organic solvents ($>40\text{ mg mL}^{-1}$ in chloroform), which are desirable for device fabrication through spin coating.

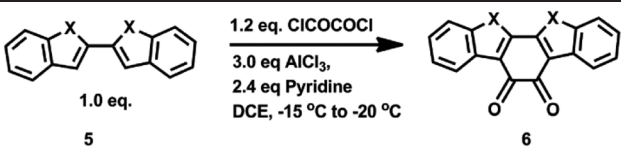
Table 1 Intramolecular double Friedel–Crafts acylation with various bithiophene substrates

Entry	Substrate	R^1	Product	Yield (%)
1	1a	Methyl	2a	32
2	1b	<i>t</i> -Butyl	2b	48
3	1c	<i>n</i> -Hexyl	2c	37
4	1d	Trimethylsilyl	2d	28
5	1e	Tri- <i>i</i> -propylsilyl	2e	45
6	1f	Methoxyl	2f	25
7	1g	Acetyl	2g	No reaction
8	1h	Br	2h	No target molecule

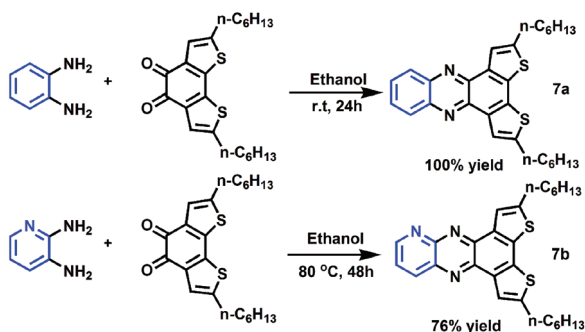
Table 2 Intramolecular double Friedel–Crafts acylation with bifuran, biselenophene and bipyrrole

Entry	Substrate	X	R^1	Product	Yield (%)
1 ^a	3a	O	Trimethylsilyl	4a	16
2	3b	Se	Trimethylsilyl	4b	37
3	3c	N–CH ₃	Methyl	4c	32

^a Reaction temperature is -50°C .

Table 3 Intramolecular double Friedel–Crafts acylation with bibenzofuran, bibenzothiophene and biindole substrates


Entry	Substrate	X	Product	Yield (%)
1	5a	O	6a	35
2	5b	S	6b	58
3	5c	N- <i>n</i> -hexyl	6c	85

**Scheme 3** The derivative reactions based on the 2c.

Conclusions

In conclusion, this communication described our recent progress in the reinvestigation of intramolecular double Friedel–Crafts acylation for preparing fused heteroaromatic diones using 2,2'-bithiophene, 2,2'-bifuran, 2,2'-biselenophene, *N,N'*-dimethyl-2,2'-bipyrrole, 2,2'-bibenzofuran, 2,2'-bibenzothiophene, and 1,1'-dimethyl-1*H*,1'*H'*-2,2'-biindole as starting materials. Our success could offer a more convenient and concise method to create high-performance materials with versatile properties.

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