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Syntheses of 2-aroyl benzofurans through cascade annulation on arynes

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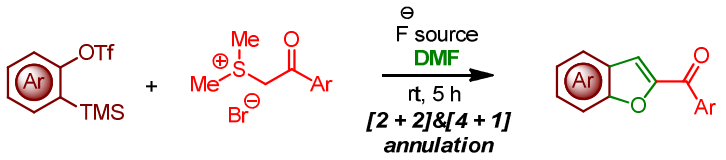


ABSTRACT: The highly efficient, and expedient route for the syntheses of 2-aroyl benzofurans has been developed *via* the cascade [2+2] followed by a [4+1] annulation on arynes. The overall transformation proceeded through the formation of *ortho*-quinone methide by the insertion of transient aryne into *N,N*-dimethylformamide and subsequent trapping with sulfur ylide. Moreover, this transformation has broad range of substrate scope with high functional-group tolerance. This new reaction was successfully utilized in the synthesis of potent CYP19 *Aromatase* inhibitor and late-stage functionalization on the bioactive complex estrone.

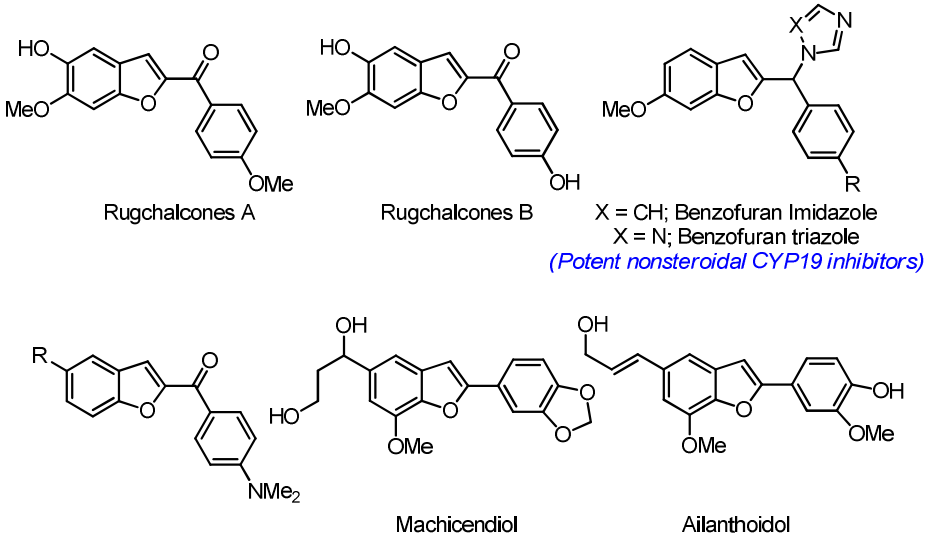
KEYWORDS: domino reaction, ketenimine, copper-catalysis, cycloaddition

INTRODUCTION

The transient reactive intermediates have a pivotal role in organic synthesis to create diverse skeletons of relevance. *ortho*-Quinone methides (*o*-QMs) have gained much importance due to the easy access from phenol derivatives through oxidation, acid promoted *β*-elimination, base promoted *β*-elimination, tautomerization, thermolysis, and photolysis.[1] In addition, the insertion of highly reactive

aryne into carbonyl bond *via* [2 + 2] cycloaddition followed by isomerization gave *o*-QMs which further subjected to nucleophiles to produce multifunctional building blocks in single operation.[2] The recent reviews in this area indicate the volume of contributions to these important functionalities.[3] In 1965, Yaroslavsky *et al.* reported the synthesis of salicylaldehyde from benzyne in 32% yield via *o*-QM, generated from transient benzyne and *N,N*-dimethylformamide (DMF) as carbonyl source.[4] Recently, Miyabe and co-workers described the trapping of these *o*-QMs with active methylene compounds to give 2*H*-chromene derivatives in good yields.[5]

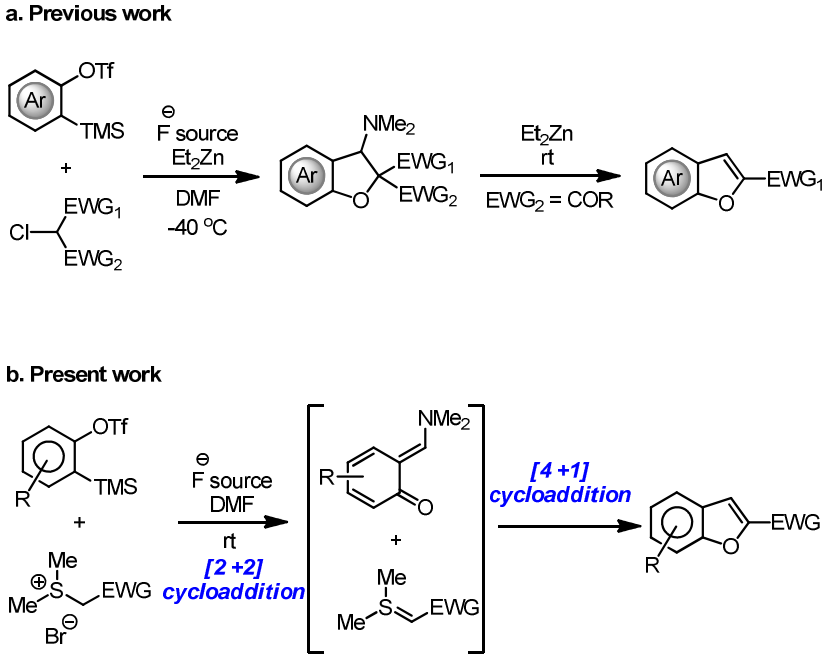
Figure 1. Benzofuran as structural motif in natural products and bioactives.



We have recently taken advantage of the Stolz's contributions in benzyne chemistry[6] for the total synthesis of natural products.[7] Also, we were successful in adding imidate functionality to benzynes to generate disubstituted aryl systems with minimal effort.[8] We were exploring to develop a strategy for easy entry to 2-substituted benzofurans enroute the total synthesis of natural products and bioactive molecules (Figure 1).[9] In 2017, Miyabe *et al.* have recently reported the synthesis of dihydrobenzofurans and benzofurans from arynes wherein *o*-QM reacts with diethyl 2-chloromalonate and diethylzinc at -40 to -60 °C in DMF as a solvent.[10] This method offers advantages in diversity, however it requires low temperature, α-chlorinated methines and use of a highly pyrophoric Et_2Zn in the reaction. Herein, we envisioned that sulfur yilide would be suitable one carbon unit for [4+1] cycloaddition on the *o*-QM for the synthesis of 2-aroyl benzofuran. Sulfur ylides are versatile reagents which can be generated from

easily accessible α-halo carbonyls and dialkyl sulfides. Many research groups elegantly demonstrated the utility of these ylides in cycloaddition reactions.[11] Recently, Xiao *et al*. reported the synthesis of substituted indoles via [4+1] annulation reaction.[12]

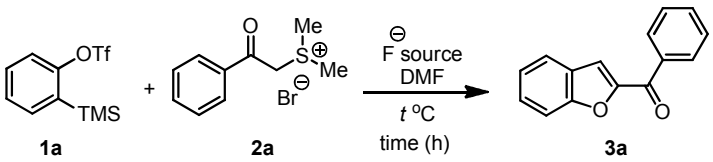
Scheme 1. Previous and present approaches



RESULTS AND DISCUSSION

We initiated our studies with the domino cyclization of *in situ* generated benzyne from **1a**[13] with sulfonium bromide salt **2a** in DMF solvent by applying different fluoride sources at various temperatures (Table 1). To our delight, CsF as base at room temperature led to the formation desired product **3a** in 87% yield. Increasing the reaction temperature did not show any significant variation on yields. Other fluorides, TBAF and KF afforded **3a** in lower yields when compared to CsF. The addition of 18-crown-6 to KF and CsF did not lead to an improvement in the reaction yield. In the case of CsF, decrease in the reaction time was found to have high impact on the efficiency of the reaction.

Table 1. Screening for Optimal Reaction Conditions[a]

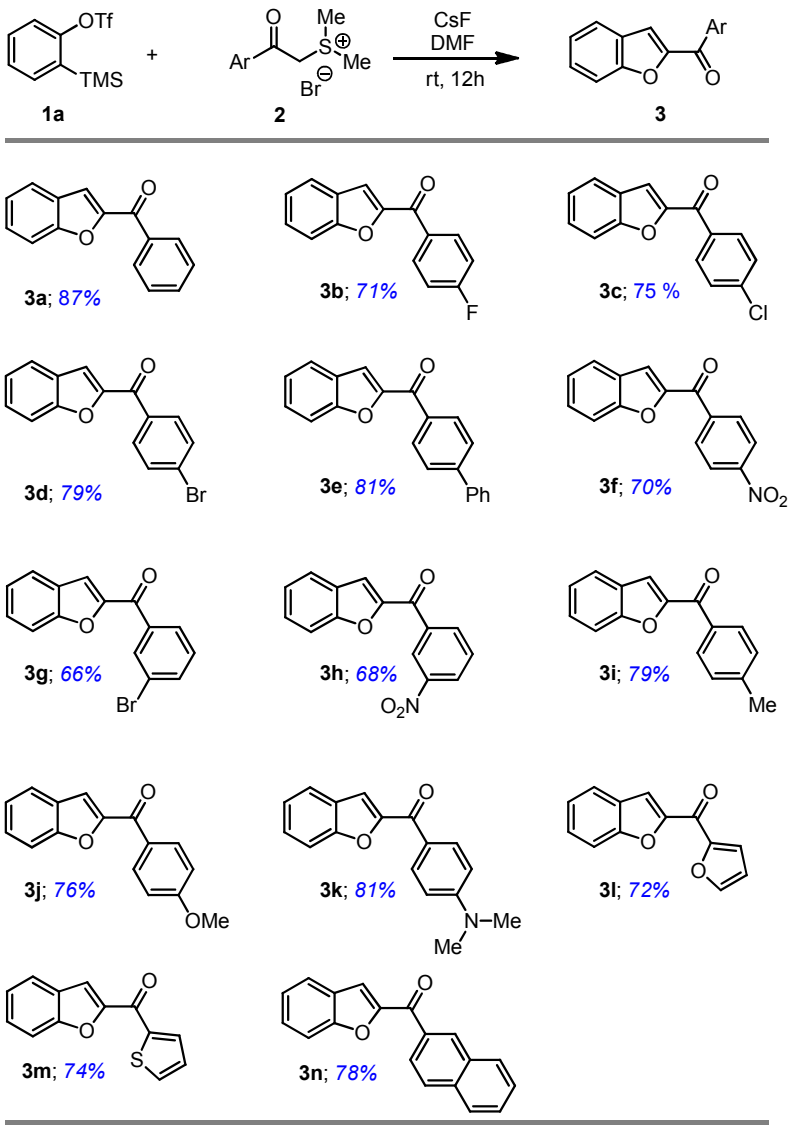


entry	F source	time (h)	*t* (°C)	yield[b]
1	**CsF**	**12**	**rt**	**87**
2	CsF	12	50	87
3	CsF	12	80	88
4[c]	TBAF	12	rt	52
5	KF	12	rt	68
6[c]	CsF/18-*C*-6	12	rt	87
7[c]	KF/18-*C*-6	12	rt	63
8	NaF	1	rt	0
9	CsF	5	rt	30
10[c]	CsF	12	rt	58

[a]Standard reaction conditions: The reaction was carried out with **1a** (1.2 mmol), **2a** (1 mmol), and fluoride source (4 mmol) in solvent (0.1 M). [b]Yield of the isolated product. [c]18-Crown-6 (0.25 mmol) was used.

With the optimal reaction conditions in hand (Table 1, entry 1; 4 equiv of CsF in DMF at rt), the scope of various sulfonium bromide salts **2** were investigated. As summarized in table 2, sulfonium salts having electron-donating or electron-withdrawing substituents on the aromatic ring were well tolerated in this reaction to provide corresponding benzofurans **3a**−**3k** in high yields (66-87%). However, substituents at *meta*-position gave slightly lower yields (Table 2, entries **3g**-**h**). With other sulfonium salts bearing aryl groups such as furan thiophene and naphthyl rings, the reactions proceeded smoothly with good yields (Table 2, entries **3l**−**3n**).

Table 2. Substrate scope for sulphur ylides[a,b]

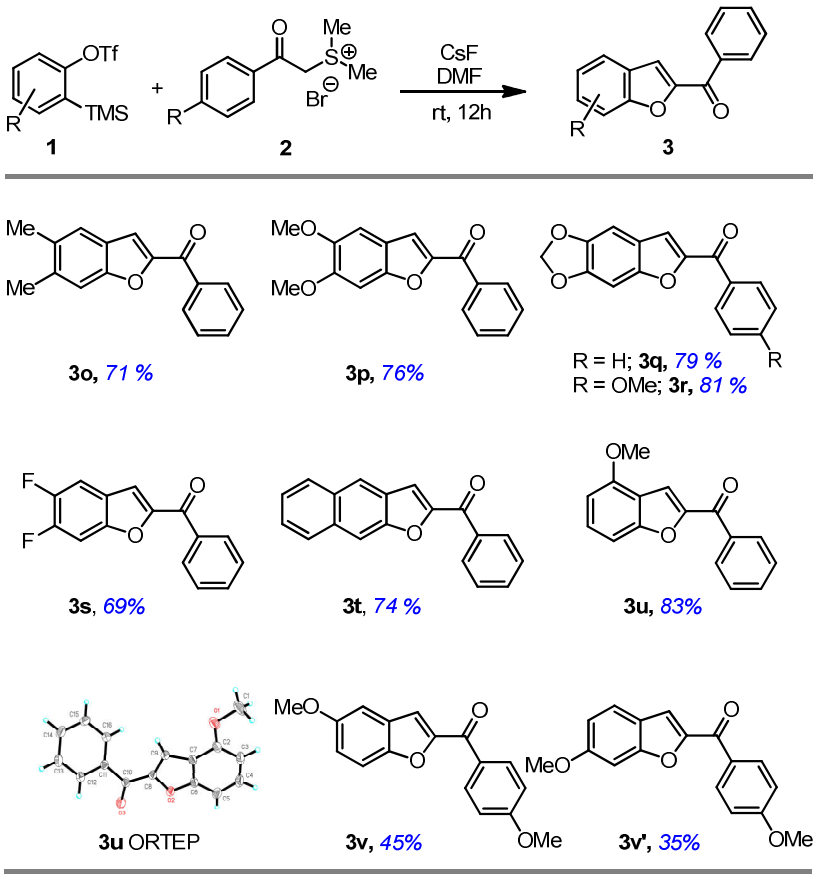


[a]Reaction conditions: The reaction was carried out with **1a** (1.2 mmol), **2** (1 mmol), and fluoride source (4 mmol) in DMF (0.1 M). [b]Yields of products isolated after column chromatography

We next investigated the [2+2] followed by [4+1] cycloaddition reaction of symmetrical and unsymmetrical arynes (Table 3, entries **3o**−**3v**). Regardless of electron-donating or -withdrawing nature of the substituent on the symmetrical aryne precursor **1**, corresponding benzofurans were obtained in good yields (69−83%). It is also noted that the electron-poor aryne gave slightly lower yield (Table 3, entry **3s**). In case of unsymmetrical arynes, 3-methoxytriflate reacted with sulfonium salt **2a** to give **3u** exclusively in 83% yield with complete regiocontrol, which is consistent with previous reports.[14] The

regioselectivity of **3u** was also established single crystal X-ray analysis.[15] However, the annulation of 4-methoxytriflate with **2a** afforded two regioisomers **3v** (45%) and **3v'** (35%) in a 9:7 ratio (isolated by column chromatography).

Table 3. Substrate scope for benzyne[a,b]

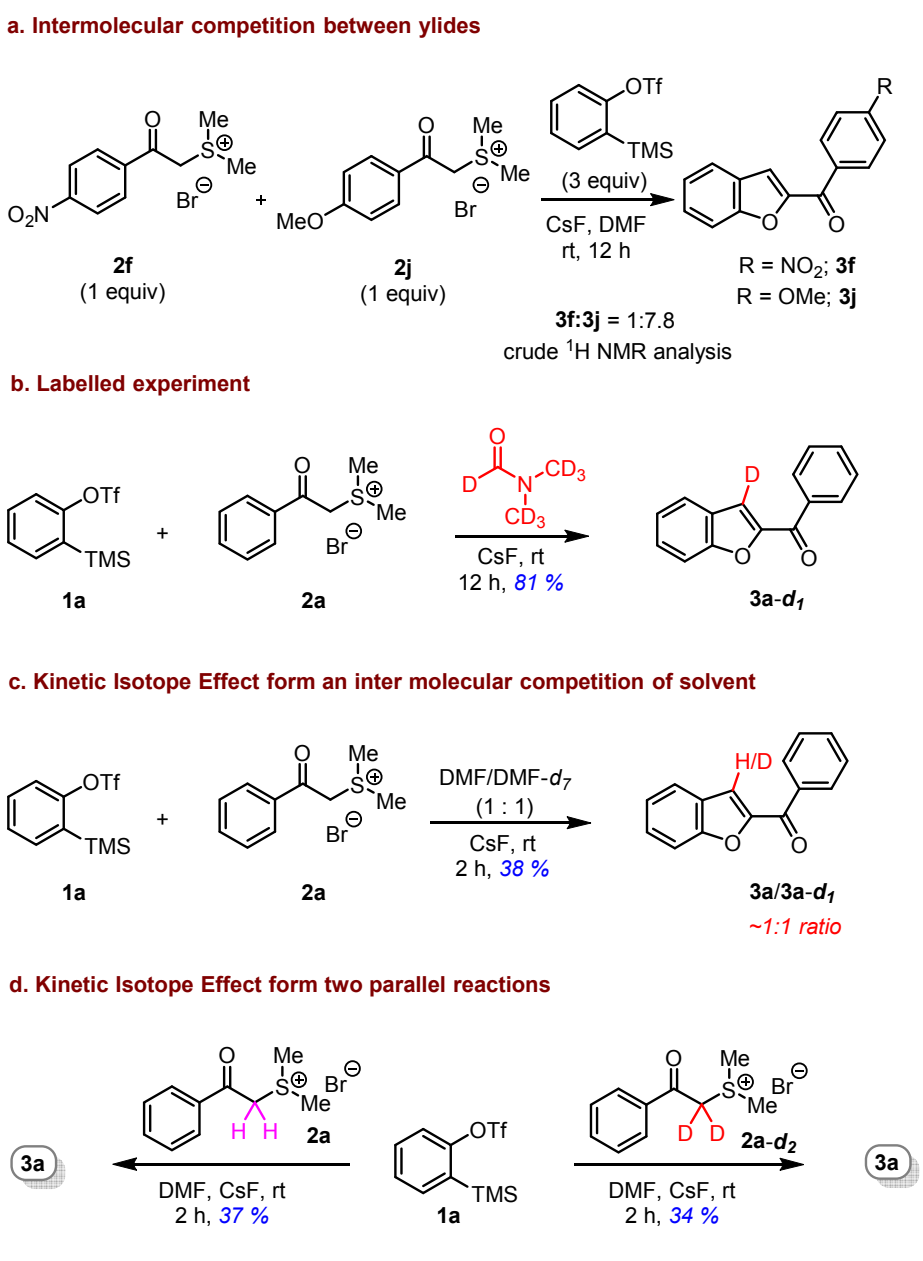


[a]Reaction conditions: The reaction was carried out with **1** (1.2 mmol), **2** (1 mmol), and fluoride source (4 mmol) in DMF (0.1 M). [b]Yields of products isolated after column chromatography

To gain further insights into the mechanism of annulation reaction, a series of competition and labelled experiments were conducted (Scheme 2). The intermolecular competition experiment revealed the formation of product being favored from electron-rich sulfonium salt **2j** than electron-poor substrate **2f**. Next, the reaction between **1a** and **2a** under standard conditions in deuterated DMF-d_7 afforded **3a-*d*$_1$** in 81% yield with exclusive deuterium incorporation at 3 position of benzofuran. This result clearly indicates that the formation of *o*-QM proceeded *via* [2+2] cycloaddition of aryne with DMF solvent. The same reaction in equimolar ratio of DMF/DMF-d_7 solvent afforded ~1:1 ratio of **3a** and **3a-*d*$_1$** in 38%

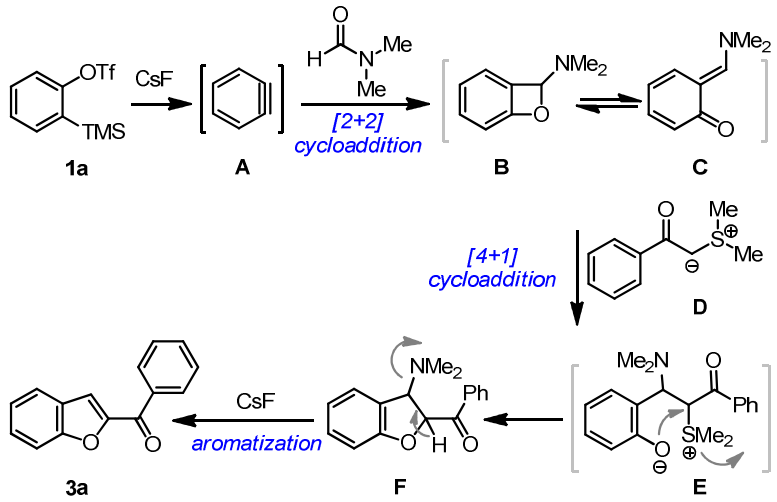
yield. Similarly, two parallel reactions were conducted separately with the non-deuterated substrate **2a** and the deuterated substrate **2a-*d*$_2$** using standard conditions for 2 h, which afforded **3a** in similar yields. Based on these experiments (Scheme 2c & 2d), [2+2] and [4+1] cycloaddition steps as well as aromatization didn't influence the rate of reaction.

Scheme 2. Mechanistic experiments



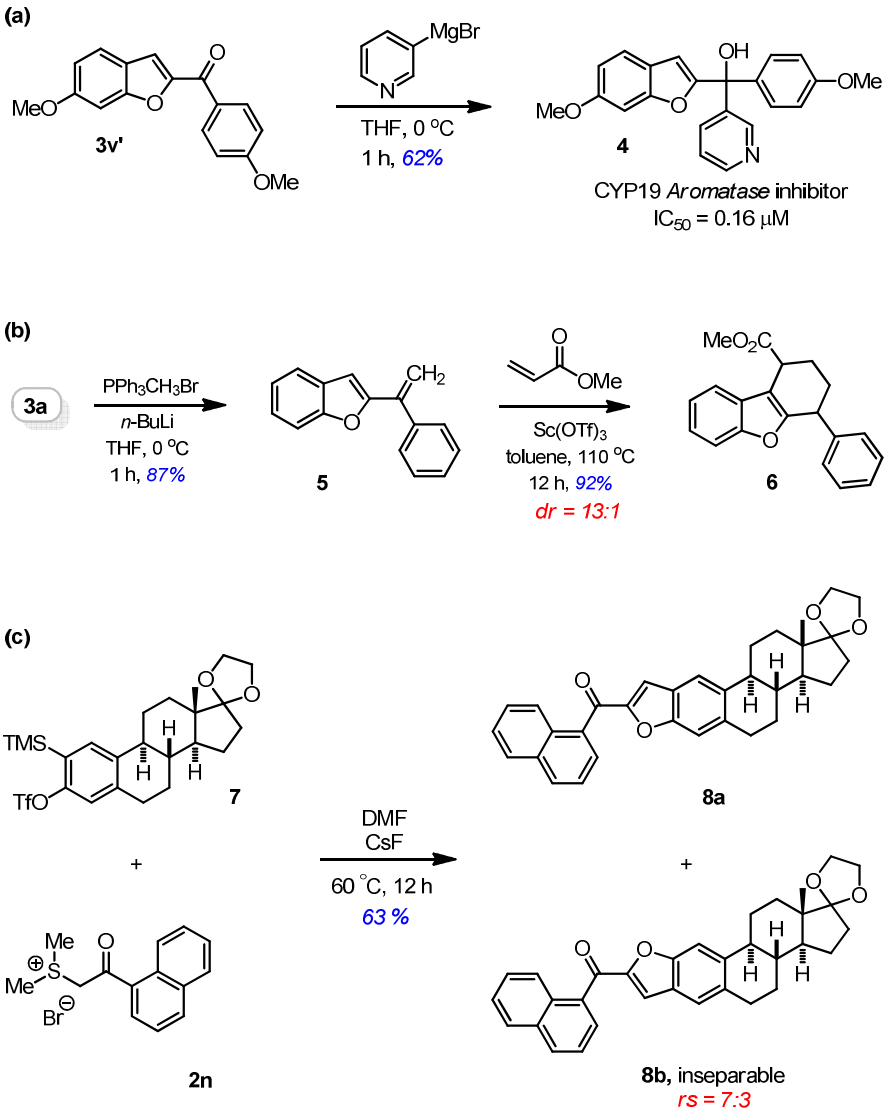
Based on the above experimental outcome and previous reports[3,12], a possible mechanism was proposed in scheme 3. The strained four membered ring intermediate **B** is produced through the C=O group insertion of *N,N*-demethylformamide (DMF) onto transient benzyne **A**, generated *in situ* from aryl triflate **1a** *via* [2+2] cycloaddition. The ring opening of intermediate **B** gives *ortho*-quinone methide **C**, which would further undergo [4+1] cycloaddition with sulfur yilide **D** to afford 2,3-dihydrobenzofuran **F** followed by aromatization leads to the 2-aroyl benzofuran **3a**

Scheme 3. Plausible mechanism



To demonstrate the synthetic utility of this method, 2-aroyl benzofuran **3v'** was treated with pyridine-3-magnesium bromide to generate potent CYP19 *Aromatase* inhibitor **4**[16] in 62% yield (Scheme 4). The C_1-Wittig olefination of **3a** afforded 2-vinylbenzofuran **5** in 87% yield which was further subjected to Diels-Alder reaction[17] using methyl acrylate in the presence of $Sc(OTf)_3$ at 110 °C gave tetrahydrodibenzofuran **6** in 92 % yield with 13:1 ratio of diastereoselectivity. Finally, the present cascade reaction was employed for late-stage functionalization on the complex bioactive steroid estrone. The sterically crowded aryne precursor **7** synthesized from estrone in 5 steps,[18] was subjected to sulfonium salt **2n** under standard reaction conditions at 60 °C to afford the corresponding product as 7:3 ratio of inseparable regiomers **8a** & **8b**.

Scheme 4: Synthetic utility [a,b]



In summary, we have developed a highly practical synthesis of 2-aroyl benzofurans using aryne insertion reaction *via* the formation of *ortho*-quinone methide followed by [4+1] cycloaddition with stable sulfur ylides and subsequent aromatization sequence. Owing the mild reaction conditions and broad range of substrate scope, this method has excellent potential in the natural product synthesis and late-stage functionalization on the complex bioactive molecules.

EXPERIMENTAL SECTION

***General information*:** Unless otherwise noted, all reagents were used as received from commercial suppliers. All reactions were performed under nitrogen atmosphere and in a flame-dried or oven-dried glassware with magnetic stirring. All solvents were dried before use following the standard procedures. Reactions were monitored using thin-layer chromatography (SiO_2). TLC plates were visualized with UV light (254 nm), iodine treatment or using ninhydrin stain. Column chromatography was carried out using silica gel (60-120 mesh & 100-200 mesh) packed in glass columns. NMR spectra were recorded at 300, 400, 500 MHz (H) and at 75, 100, 125 MHz (C), respectively. Chemical shifts (δ) are reported in ppm, using the residual solvent peak in $CDCl_3$ (H: δ = 7.26 and C: δ = 77.16 ppm) as internal standard, and coupling constants (J) are given in Hz. HRMS were recorded using ESI-TOF techniques.

General procedure for the syntheses of 2-aroyl benzofurans through cascade annulation on arynes:

To a stirred solution of triflate **1** (1.2 mmol, 1.2 equiv) in DMF (0.1 M) at room temperature was added CsF (4 mmol, 4 equiv) under N_2 atmosphere and stirred for 10 minutes to generate *o*-QM (ortho quinone methide). Then, sulfonium bromide salt **2** (1 mmol, 1.0 equiv) was added to the reaction mixture and stirred for 12 h. After completion of the reaction, the mixture was poured into ice cold water (10 mL) then extracted with EtOAc (15 mL X 2). The combine organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silical gel (EtOAc/Hexanes) to afford 2-aroyl benzofurans **3**.

Benzofuran-2-yl(phenyl)methanone (3a): White solid (74 mg, 87% yield) R_f = 0.4 (hexanes:EtOAc = 19:1); mp = 88–90 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 – 8.02 (m, 2H), 7.75 – 7.71 (m, 1H), 7.67 – 7.61 (m, 2H), 7.57 – 7.48 (m, 4H), 7.36 – 7.31 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.4, 156.0, 152.2, 137.3, 133.0, 129.5, 128.6, 128.4, 127.0, 124.0, 123.3, 116.6, 112.6; IR (neat): υ_{max} 3063, 1648, 1547, 1299, 972, 749, 722 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{11}O_2$ 223.0759; found: 223.0761.

Benzofuran-2-yl(4-fluorophenyl)methanone (3b): White solid (61 mg, 71% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 133–135 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.17 – 8.09 (m, 2H), 7.73 (d, J = 7.9 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.55 (s, 1H), 7.53 – 7.48 (m, 1H), 7.34 (t, J = 7.5 Hz, 1H), 7.25 – 7.18 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ 182.81, 165.8 (d, J_{CF} = 255.2 Hz), 156.1, 152.3, 133.5 (d, J_{CF} = 2.6 Hz), 132.3 (d, J_{CF} = 9.2 Hz), 128.6, 127.1, 124.2, 123.4, 116.4, 115.9 (d, JCF = 21.9

Hz), 112.7. IR (neat): υ_{max} 3127, 3075, 2929, 1646, 1597, 1502, 1299, 1223, 974, 749 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{10}FO_2$ 241.0665; found: 241.0676.

Benzofuran-2-yl(4-chlorophenyl)methanone (3c): White solid (89 mg, 75% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 150–152 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.55 (s, 1H), 7.51 (t, *J* = 7.3 Hz, 3H), 7.35 (t, *J* = 7.5 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.0, 156.0, 152.1, 139.5, 135.4, 131.0, 128.9, 128.6, 126.9, 124.1, 123.4, 116.5, 112.6; IR (neat): υ_{max} 3123, 2928, 1644, 1550, 1302, 1090, 973, 6983 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{10}ClO_2$ 257.0369; found: 257.0380.

Benzofuran-2-yl4-bromophenyl)methanone (3d): White solid (69 mg, 79% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 170–172 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 – 7.92 (m, 2H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.64 (dd, *J* = 8.4, 0.7 Hz, 1H), 7.55 (d, *J* = 0.8 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.38 – 7.32 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.1, 156.1, 152.1, 135.9, 131.9, 131.0, 128.6, 128.1, 126.9, 124.2, 123.4, 116.6, 112.6; IR (neat): υ_{max} 2925, 2855, 1643, 1549, 1463, 973, 744 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{10}O_2Br$ 300.9864; found: 300.9865.

[1,1'-Biphenyl]-4-yl(benzofuran-2-yl)methanone (3e): White solid (71 mg, 81% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 148–150 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.19 – 8.13 (m, 2H), 7.80 – 7.73 (m, 3H), 7.70 – 7.64 (m, 3H), 7.59 (d, *J* = 0.9 Hz, 1H), 7.54 – 7.47 (m, 3H), 7.45 – 7.40 (m, 1H), 7.35 (ddt, *J* = 7.3, 3.0, 1.9 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 183.9, 156.0, 152.4, 145.8, 139.9, 135.9, 130.2, 129.0, 128.4, 128.3, 127.3, 127.2, 127.1, 124.0, 123.3, 116.3, 112.6; IR (neat): υ_{max} 3056, 2925, 1639, 1551, 1403, 1301, 975, 741 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{15}O_2$ 299.1072; found: 299.1084.

Benzofuran-2-yl(4-nitrophenyl)methanone (3f): Pale yellow solid (61 mg, 70% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 200–202 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.7 Hz, 2H), 8.23 (d, *J* = 8.7 Hz, 2H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.71 – 7.60 (m, 2H), 7.56 (t, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 182.3, 156.3, 151.7, 150.2, 142.1, 130.5, 129.2, 126.8, 124.4, 123.7, 123.6, 117.4, 112.7; IR (neat): υ_{max} 3084, 2934, 1651, 1543, 1351, 1172, 975, 717 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{10}NO_4$ 268.0610; found: 268.0620.

Benzofuran-2-yl(3-bromophenyl)methanone (3g): White solid (58 mg, 66% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 125–127 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 (t, *J* = 1.7 Hz, 1H), 8.03

– 7.95 (m, 1H), 7.81 – 7.72 (m, 2H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.58 – 7.50 (m, 2H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.39 – 7.32 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.75, 156.14, 151.81, 138.93, 135.80, 132.35, 130.15, 128.75, 128.04, 126.90, 124.19, 123.47, 122.79, 116.96, 112.65; IR (neat): υ_{max} 3142, 3060, 1644, 1589, 1550, 1300, 1189, 984, 745 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{10}O_2Br$ 300.9864; found: 300.9865.

Benzofuran-2-yl(3-nitrophenyl)methanone (3h): Pale yellow solid 59 mg, 68% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 134–136 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.96 (t, *J* = 1.9 Hz, 1H), 8.50 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H), 8.48 – 8.38 (m, 1H), 7.83 – 7.74 (m, 2H), 7.67 (d, *J* = 6.3 Hz, 2H), 7.60 – 7.52 (m, 1H), 7.44 – 7.35 (m, 1H); **^{13}C NMR** (75 MHz, CDCl3) δ 181.6, 156.2, 151.6, 148.3, 138.3, 135.1, 129.9, 129.1, 127.2, 126.8, 124.5, 124.4, 123.6, 117.2, 112.7; IR (neat): υ_{max} 3085, 2924, 1654, 1533, 1351, 1304, 1091, 717 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{10}NO_4$ 268.0610; found: 268.0620.

Benzofuran-2-yl(p-tolyl)methanone (3i): White solid (67 mg, 79% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 60–62 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.54 – 7.45 (m, 2H), 7.32 (t, *J* = 7.2 Hz, 3H), 2.46 (s, 3H); **^{13}C NMR** (75 MHz, CDCl3) δ 184.1, 155.9, 152.5, 143.8, 134.6, 129.7, 129.3, 128.2, 127.1, 123.9, 123.3, 116.1, 112.6, 21.7; IR (neat): υ_{max} 2938, 2873, 1419, 1250, 1213, 1143, 918, 843 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{13}O_2$ 237.0916; found: 237.0923.

Benzofuran-2-yl(4-methoxyphenyl)methanone (3j): White solid (65 mg, 76% yield); R_f = 0.5 (hexanes:EtOAc = 9:1); mp = 97–99 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.15 – 8.10 (m, 2H), 7.75 – 7.72 (m, 1H), 7.64 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.53 (d, *J* = 0.9 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.36 – 7.31 (m, 1H), 7.06 – 7.01 (m, 2H), 3.92 (s, 3H); **^{13}C NMR** (400 MHz, $CDCl_3$) δ 182.9, 163.6, 155.8, 152.7, 132.0, 129.9, 128.0, 127.1, 123.9, 123.2, 115.5, 113.9, 112.5, 55.6; IR (neat): υ_{max} 3076, 2936, 1643, 1602, 1260, 1171, 1029, 972, 753 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{13}O_3$ 253.0865; found: 253.0865.

Benzofuran-2-yl(4-(dimethylamino)phenyl)methanone (3k): Yellow solid (70 mg, 81% yield); R_f = 0.5 (hexanes:EtOAc = 9:1); mp = 107–109 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 – 8.10 (m, 2H), 7.71 (d, J = 7.8 Hz, 1H), 7.63 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.49 (d, *J* = 0.9 Hz, 1H), 7.46 (ddd, *J* = 8.4, 5.8, 1.3 Hz, 1H), 7.34 – 7.29 (m, 1H), 6.76 – 6.72 (m, 2H), 3.11 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.1,

155.6, 153.6, 153.5, 132.2, 127.4, 127.3, 124.6, 123.6, 122.9, 114.2, 112.4, 110.8, 40.1; IR (neat): υ_{max} 3509, 3149, 2922, 1631, 1594, 1328, 1173, 970, 754 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{16}NO_2$ 266.1181; found: 266.1191.

Benzofuran-2-yl(furan-2-yl)methanone (3l): Pale yellow solid (60 mg, 72% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 84-86 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 0.9 Hz, 1H), 7.79 – 7.73 (m, 2H), 7.70 (dd, *J* = 3.6, 0.6 Hz, 1H), 7.64 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.50 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.38 – 7.31 (m, 1H), 6.67 (dd, *J* = 3.6, 1.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.1, 155.8, 151.6, 151.5, 147.2, 128.3, 127.2, 124.0, 123.4, 120.4, 115.5, 112.6, 112.4; IR (neat): υ_{max} 3145, 1638, 1565, 1466, 1306, 1022, 983, 751cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{13}H_9O_3$ 213.0552; found: 213.0561.

Benzofuran-2-yl(thiophen-2-yl)methanone (3m): White solid (63 mg, 72% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 66–68 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 3.8, 0.8 Hz, 1H), 7.80 -7.70 (m, 3H), 7.78 -7.61 (m, 1H), 7.55 – 7.46 (m, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.29 – 7.22 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 199.4, 177.6, 175.0, 155.8, 155.4, 152.6, 142.3, 134.6, 134.5, 128.4, 128.2, 127.0, 124.0, 123.2, 114.6, 112.4; IR (neat): υ_{max} 3019, 2979, 1744, 1687, 1389, 1216, 1156, 745, 666 667 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{13}H_9O_2S$ 229.0323; found: 229.0333.

Benzofuran-2-yl(naphthalen-2-yl)methanone (3n): White solid (63 mg, 78% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 100–102 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.06 (dd, *J* = 8.5, 1.4 Hz, 1H), 8.01 – 7.86 (m, 3H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.68 – 7.53 (m, 4H), 7.53 – 7.45 (m, 1H), 7.32 (t, *J* = 7.5 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 184.3, 156.0, 152.4, 135.5, 134.5, 132.4, 131.2, 129.6, 128.6, 128.5, 128.4, 127.9, 127.1, 125.5, 125.2, 124.0, 123.4, 116.5, 112.6; IR (neat): υ_{max} 3059, 1646, 1548, 1296, 1176, 907, 752 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{13}O_2$ 273.0916; found: 273.0928.

(5,6-Dimethylbenzofuran-2-yl)(phenyl)methanone (3o): White solid (68 mg, 71% yield); R_f = 0.4 (hexanes:EtOAc = 20:1); mp = 77–79 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.2 Hz, 2H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 2H), 7.48-7.38 (m, 3H), 3.98 (s, 3H), 3.94 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 184.4, 154.0, 148.8, 138.7, 137.5, 133.1, 132.7, 129.4, 128.5, 125.0, 122.9, 116.7, 112.7, 21.0, 20.0; IR (neat): υ_{max} 3064, 2925, 1648, 1545, 1320, 1235, 970, 721 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}O_2$ 251.1072; found: 251.1082.

(5,6-Dimethoxybenzofuran-2-yl)(phenyl)methanone (3p): Yellow solid (74 mg, 69% yield); R_f = 0.4 (hexanes:EtOAc = 17:3); mp = 127–129 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.2 Hz, 2H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.51 (t, *J* = 7.3 Hz, 2H), 7.45 (s, 1H), 7.10 (s, 1H), 7.06 (s, 1H), 3.96 (s, 3H), 3.93 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 183.6, 152.0, 147.9, 137.6, 132.6, 129.3, 128.5, 119.2, 117.4, 102.8, 95.2, 56.4; cm^{-1}; IR (neat): υ_{max} 300+, 2934, 1642, 1541, 1467, 1298, 1119, 969, 700 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}O_4$ 283.0970; found : 283.0983.

[1,3]Dioxolo[4,5-f]benzofuran-6-yl(phenyl)methanone (3q): Pale yellow solid (81 mg, 79% yield); R_f = 0.5 (hexanes:EtOAc = 17:3); mp = 152–154 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 - 7.97 (m, 2H), 7.64 – 7.57 (m, 1H), 7.55 – 7.48 (m, 2H), 7.40 (s, 1H), 7.06 (s, 1H), 6.99 (d, *J* = 1.3 Hz, 1H), 6.04 (d, *J* = 1.3 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 183.5, 152.5, 152.3, 150.0, 145.9, 137.5, 132.6, 129.3, 128.5, 120.6, 117.6, 102.0, 100.2, 93.9; IR (neat): υ_{max} 2905, 1618, 1458, 1236, 972, 795, 697 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{11}O_4$ 267.0657; found: 267.0668.

[1,3]Dioxolo[4,5-f]benzofuran-6-yl(4-methoxyphenyl)methanone (3r) : Pale yellow solid (82 mg, 81% yield); R_f = 0.5 (hexanes:EtOAc = 8.5:1.5); mp = 164–166 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 – 8.02 (m, 2H), 7.42 (d, J = 0.7 Hz, 1H), 7.07 (s, 1H), 7.04 – 6.98 (m, 3H), 6.05 (s, 2H), 3.91 (s, 3H; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.0, 163.4, 152.8, 152.2, 149.7, 145.8, 131.7, 130.1, 120.7, 116.6, 113.8, 101.9, 100.2, 93.9, 55.5; IR (neat): υ_{max} 2936, 2905, 1618, 1458, 1236, 1171, 972, 795, 697 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{12}O_5Na$ 319.0582; found: 319.0580.

(5,6-Difluorobenzofuran-2-yl)(phenyl)methanone (3s): White solid (68 mg, 69% yield); R_f = 0.4 (hexanes:EtOAc = 19:1); mp = 117–119 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08-8.01 (m, 2H), 7.70 – 7.64 (m, 1H), 7.62 (d, *J* = 0.6 Hz, 1H), 7.71-7.64 (m, 2H), 7.42 – 7.30 (m, 2H); **^{13}C NMR** (101 MHz, CDCl3) δ 183.80, 170.41, 153.40, 152.3 (d, JCF = 6.4 Hz),, 136.63, 133.39, 129.50, 128.74, 117.8 (d, J_{CF} = 22.1 Hz),, 112.3 (d, J_{CF} = 4.1 Hz),, 108.5 (d, J_{CF} = 5.4 Hz),, 108.4 (d, J_{CF} = 5.3 Hz). IR (neat): υ_{max} 2925, 2825, 1658, 1549, 1332, 1122, 722 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_9F_2O_2$ 259.0571; found: 259.0577.

Naphtho[2,3-*b*]furan-2-yl(phenyl)methanone (3t): Pale yellow solid (77 mg, 74% yield); R_f = 0.5 (hexanes:EtOAc = 19:1); mp = 99–101 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 8.12 – 8.07 (m, 2H), 8.05 (s, 1H), 8.01 – 7.95 (m, 2H), 7.70 – 7.62 (m, 2H), 7.60 – 7.43 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.7, 154.1, 154.0, 137.2, 133.6, 133.1, 130.8, 129.6, 128.6, 128.5, 128.1, 127.7, 126.3, 124.7,

122.3, 116.2, 109.0; IR (neat): υ_{max} 3058, 2924, 2855, 640, 1549, 1332, 1122, 972, 722 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{13}O_2$ 273.0916; found: 273.0914.

(4-Methoxybenzofuran-2-yl)(phenyl)methanone (3u): White solid (80 mg, 83% yield); R_f = 0.5 (hexanes:EtOAc = 9:1); mp = 99–101 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.3 Hz, 2H), 7.67 – 7.57 (m, 2H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.42 (t, *J* = 8.2 Hz, 1H), 7.25 (t, *J* = 5.9 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.2, 157.2, 155.1, 151.0, 137.4, 132.7, 129.6, 129.4, 128.5, 118.1, 114.8, 105.3, 103.6, 55.7; IR (neat): υ_{max} 2942, 2843, 1648, 1607, 1541, 1265, 1131, 1087, 972, 731 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]+ Calcd for $C_{16}H_{13}O_3$ 253.0865; found: 253.0871.

(5-Methoxybenzofuran-2-yl)(4-methoxyphenyl)methanone (3v) & (6-Methoxybenzofuran-2-yl)(4-methoxyphenyl)methanone (3v'): Following the general procedure 4-methoxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (135 mg, 0.41 mmol) in DMF at room temperature under N_2 atmosphere, CsF (232.3 mg, 1.5 mmol) was added and the reaction mixture was stirred for 10 minutes then (2-(4-methoxyphenyl)-2-oxoethyl)dimethylsulfonium bromide (100 mg, 0.34 mmol) was added and stirred for 12 h. After completion, the residue was purified by column chromatography on silical gel (8% EtOAc in petroleum ether) to afford product **3v** (43 mg, 45% yield) and **3v'** (33 mg, 35% yield) as yellow solids.

Data for compound 3v: R_f = 0.40 (hexanes:EtOAc = 17:3); mp = 91–93 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 9.9 Hz, 1H), 7.47 (s, 1H), 7.10 (dd, *J* = 7.4, 2.4 Hz, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 3.91 (s, 3H), 3.86 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 182.7, 163.6, 156.6, 153.5, 151.0, 132.0, 129.9, 127.6, 118.1, 115.5, 113.8, 113.1, 103.9, 55.9, 55.5; IR (neat): υ_{max} 2929, 2844, 1643, 1600, 1547, 1262, 1174, 1030, 975, 763 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}O_4$ 283.0975; found: 283.0970.

Data for compound 3v'; R_f = 0.375 (hexanes:EtOAc = 17:3); mp = 136–140 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 – 8.05 (m, 2H), 7.58 (d, *J* = 8.7 Hz, 1H), 7.46 (d, *J* = 0.9 Hz, 1H), 7.11 (d, *J* = 2.1 Hz, 1H), 7.04 – 6.99 (m, 2H), 6.96 (dd, *J* = 8.7, 2.2 Hz, 1H), 3.91 (s, 3H), 3.89 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.5, 163.4, 161.0, 157.4, 152.3, 131.8, 130.1, 123.5, 120.4, 116.3, 114.3, 113.8, 95.7, 55.8, 55.5; IR (neat): υ_{max} 2961, 2929, 2846, 1734, 1639, 1601, 1263, 1170, 1028, 976, 765 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}O_4$ 283.0970; found: 283.0981.

(6-Methoxybenzofuran-2-yl)(4-methoxyphenyl)(pyridin-3-yl)methanol (4): Compound **4** was synthesized using reported procedure[16] from benzofuran **3v'** with 54% yield as a white solid (54%) ; mp = 41–43 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 1.7 Hz, 1H), 8.47 (dd, *J* = 4.7, 1.3 Hz, 1H), 7.69 – 7.66 (m, 1H), 7.30 – 7.27 (m, 1H), 7.22 – 7.15 (m, 4H), 6.89 (d, *J* = 2.1 Hz, 1H), 6.83 – 6.77 (m, 3H), 6.17 (d, *J* = 0.8 Hz, 1H), 3.75 (s, 3H), 3.74 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.9, 159.5, 158.5, 158.3, 156.3, 148.9, 148.8, 139.9, 136.0, 135.6, 135.0, 133.0, 128.7, 122.9, 121.5, 120.9, 113.7, 112.2, 106.5, 96.1, 55.7, 55.3; IR (neat): υ_{max} 2958, 2927, 1510, 1492, 1252, 1030, 830, 756 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{20}NO_4$ 362.1392; found: 362.1402.

2-(1-Phenylvinyl)benzofuran (5): To a solution of methyltriphenylphosphonium bromide (56.2 mg, 0.16 mmol) in anhydrous THF (1.5 mL), at 0 °C, a solution of *n*-BuLi (64 µL of 2.5 M in hexane, 1.6 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 1 h, afterwards a solution of previously synthesized ketone **3a** (25 mg, 0.11 mmol), in anhydrous THF (1.5 mL), was added dropwise at 0 °C. The mixture was allowed to warm to room temperature and stirred for 1 h. The solvent was evaporated in vacuo and the residue was purified by flash column chromatography (silica gel, hexane) to afford the desired olefin **5** (21 mg, 87 %); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 – 7.46 (m, 4H), 7.45 – 7.37 (m, 3H), 7.32 – 7.26 (m, 1H), 7.22 – 7.17 (m, 1H), 6.53 (s, 1H), 6.04 (d, *J* = 1.0 Hz, 1H), 5.43 (d, *J* = 1.2 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.9, 155.0, 139.5, 139.3, 128.9, 128.5, 128.4, 128.2, 124.8, 122.8, 121.1, 115.1, 111.1, 105.9; IR (neat): υ_{max} 2925, 2855, 1454, 1258, 1179, 1067, 971, 749, 702 cm^{-1}; This compound was analysed by GC-MS, observed only one peak in GC-chromatogram at 8.26 rt, this rétention time shows 220 $[M^+]$ peak in the mass spectrum.

Methyl 4-phenyl-1,2,3,4-tetrahydrodibenzo[*b,d*]furan-1-carboxylate (6): A screw-cap vial equipped with stirred bar was charged with a mixture of **5** (10.0 mg, 0.04 mmol, 1 equiv) in toluene and Methyl acrylate (4.5 µL, 0.05 mmol, 1.1 equiv) at room temperature under N_2 atmosphere, $Sc(oTf)_3$ (2.2 mg, 10 mol%) was added and the reaction mixture was stirred for 12 h at 100 °C, after cooling to room temperature solvent was evaporated. To the reaction mixture water was added and extracted with CH_2Cl_2. The organic phase was dried over NaSO4 and the crude product was purified by column chromatography (Hexane) to obtain **6** (12 mg, 92%) with 13 : 1 dr; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56 – 7.52 (m, 1H), 7.38 – 7.35 (m, 1H), 7.33 (ddd, *J* = 13.0, 5.3, 2.3 Hz, 2H), 7.30 – 7.26 (m, 1H), 7.25 – 7.19 (m, 4H), 4.19 – 4.14 (m, 1H), 3.92 (dd, *J* = 7.6, 3.2 Hz, 1H), 3.77 (s, 3H), 2.36 – 2.25 (m, 2H), 2.23 – 2.12 (m, 1H), 2.08 – 1.98 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.1, 155.7, 154.7, 142.1, 128.6, 128.1, 127.7,

126.9, 123.8, 122.6, 119.5, 112.6, 111.3, 52.1, 41.1, 38.4, 31.4, 24.7; IR (neat): υ_{max} 3510, 3389, 2960, 1807, 1737, 1687, 1455, 1172,1068, 755 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd cd for $C_{20}H_{19}O_3$ 307.1334; found: 307.1343.

Compond 8a & 8b: Prepared according to the general procedure as described above at 60 °C in 63% combined yield. It was purified by flash chromatography (12% EtOAc/hexanes; R_f = 0.4) to afford as an inseparable mixture of **8a** and **8b** as a semi solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 5.2 Hz, 1H), 8.07 (dt, *J* = 8.5, 2.1 Hz, 1H), 7.99 (dd, *J* = 14.5, 8.3 Hz, 2H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.67 – 7.55 (m, 3H), 7.54 – 7.48 (m, 1H), 7.45 – 7.35 (m, 1H), 4.04 – 3.86 (m, 4H), 3.10 – 2.94 (m, 2H), 2.49 – 2.35 (m, 2H), 2.12 – 2.00 (m, 1H), 1.96 (dt, *J* = 9.9, 4.4 Hz, 1H), 1.90 – 1.77 (m, 3H), 1.69 – 1.53 (m, 4H), 1.52 – 1.42 (m, 2H), 0.91 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.3, 155.4, 154.9, 152.4, 152.1, 143.0, 139.3, 137.6, 135.4, 134.8, 133.5, 132.4, 131.1, 129.6, 128.4, 127.9, 126.9, 125.3, 124.8, 122.1, 119.3, 119.2, 117.0, 116.4, 111.6, 108.7, 65.3, 64.7, 49.8, 46.1, 44.6, 43.9, 38.8, 38.6, 34.3, 32.0, 30.7, 30.4, 26.9, 26.8, 26.3, 26.1, 22.7, 22.5, 14.3, 14.2; IR (neat): υ_{max} 2228, 2865, 1742, 1646, 1544, 1309, 1108, 909, 766 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{33}H_{33}O_4$ 493.2379; found: 493.2381.

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Supporting Information

Copies of ^{1}H and ^{13}C spectra for all new compounds, deuterium-labelling experiments, and X-ray crystallographic data (CIF file) of compound **3u**. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Recent reviews on *ortho*-quinone methides, see: (a) M. S.; Nagaraju, A.; Anand, N.; Chowdhury, S. Ortho-Quinone Methide (o-QM): A Highly Reactive, Ephemeral and Versatile Intermediate in Organic Synthesis. *RSC Adv.* **2014**, *4*, 55924-55959. (b) Bai, W.-J.; David, J. G.; Feng, Z.-G.; Weaver, M. G.; Wu, K.-L.; Pettus, T. R. R. The Domestication of Ortho-Quinone Methides. *Acc. Chem. Res.* **2014**, *47*,

3655-3664. (c) Van De Water, R. W.; Pettus, T. R. R. o-Quinone Methides: Intermediates Underdeveloped and Underutilized in Organic Synthesis. *Tetrahedron* **2002**, *58*, 5367-5405.

(2) (a) Yoshioka, E. Multi-component Reactions Based on Formal [2+2] Reaction of Benzyne with Formamide. *YAKUGAKU ZASSHI* **2015**, *135*, 1255-1264. (b) Yoshioka, E.; Kohtani, S.; Miyabe, H. Sequential Reaction of Arynes via Insertion into the π-Bond of Amides and Trapping Reaction with Dialkylzincs. *Org. Lett.* **2010**, *12*, 1956-1959. (c) Yoshida, H.; Watanabe, M.; Fukushima, H.; Ohshita, J.; Kunai, A. A 2:1 Coupling Reaction of Arynes with Aldehydes via o-Quinone Methides: Straightforward Synthesis of 9-Arylxanthenes. *Org. Lett.* **2004**, *6*, 4049-4051.

(3) For Recent Reviews See: (a) Miyabe, H. Synthesis of Oxygen Heterocycles via Aromatic C-O Bond Formation Using Arynes. *Molecules* **2015**, *20*, 12558-12575. (b) Yoshioka, E.; Shigeru, K.; Miyabe, H. Three-Component Coupling Reactions of Arynes for the Synthesis of Benzofurans and Coumarins. *Molecules* **2014**, *19*, 863-880.

(4) Yaroslavsky, S. Reaction of Aryldiazonium Salts with Dimethylformamide. *Tetrahedron Lett*. **1965**, *6*, 1503–1507.

(5) (a) Yoshioka, E.; Shigeru K.; Miyabe, H. A Multicomponent Coupling Reaction Induced by Insertion of Arynes into the C=O Bond of Formamide. *Angew. Chem. Int. Ed.* **2011**, *50*, 6638 –6642. For other Recent *o*-QMs Trappings, See: (b) Yoshioka, E.; Kohtani, S.; Miyabe, H. Sequential Reaction of Arynes via Insertion into the π-Bond of Amides and Trapping Reaction with Dialkylzincs. *Org. Lett.* **2010**, *12*, 1956–1959. (c) Yoshioka, E.; Miyabe, H. Insertion of Arynes into the Carbon–Oxygen Double Bond of Amides and Its Application into the Sequential Reactions. *Tetrahedron* **2012**, *68*, 179–189.

(6) For Aryne Insertion Reaction, See: (a) Tambar, U. K.; Stoltz, B. M. The Direct Acyl-Alkylation of Arynes. *J. Am. Chem. Soc*. **2005**, *127*, 5340-5341. (b) Pellissier, H.; Santelli, M. The Use of Arynes in Organic Synthesis. *Tetrahedron* **2003**, *59*, 701-730. (c) Yoshida, H.; Ohshita, J.; Kunai, A. Aryne, Ortho-Quinone Methide, and Ortho-Quinodimethane: Synthesis of Multisubstituted Arenes Using the Aromatic Reactive Intermediates. *Bull. Chem. Soc. Jpn*. **2010**, *83*, 199-219. (d) Bhunia, A.; Yetra, S. R.; Biju, A. T. Recent Advances in Transition-Metal-Free Carbon–Carbon and Carbon–Heteroatom Bond-Forming Reactions Using Arynes. *Chem. Soc. Rev*. **2012**, *41*, 3140-3152. (e) Dubrovskiy, A. V.; Markina, N. A.; Larock, R. C. Use of Benzynes for the Synthesis of Heterocycles. *Org. Biomol. Chem.* **2013**, *11*, 191-

218. (f) Goetz, A. E.; Shah, T. K.; Garg, N. K. Pyridynes and Indolynes as Building Blocks for Functionalized Heterocycles and Natural Products. *Chem. Commun*. **2015**, *51*, 34-45. (g) Caubere, P. Applications of Sodamide-Containing Complex Bases in Organic Synthesis. *Acc. Chem. Res*. **1974**, 7, 301-308. For Application in Natural Product Synthesis, See: (h) Tambar, U. K.; Ebner, D. C.; Stoltz, B. M. A Convergent and Enantioselective Synthesis of (+)-Amurensinine via Selective C−H and C−C Bond Insertion Reactions. *J. Am. Chem. Soc.* **2006**, *128*, 11752-11753. (i) Tadross, P. M.; Virgil, S. C.; Stoltz, B. M. Aryne Acyl-Alkylation in the General and Convergent Synthesis of Benzannulated Macrolactone Natural Products: An Enantioselective Synthesis of (−)-Curvularin. *Org. Lett*. **2010**, *12*, 1612-1614.

(7) Gouthami, P.; Chegondi, R.; Chandrasekhar, S. Formal Total Synthesis of (±)-Cephalotaxine and Congeners via Aryne Insertion Reaction. *Org. Lett.* **2016**, *18*, 2044-2046.

(8) Ramagonolla, K.; Chegondi, R.; Chandrasekhar, S. Insertion of N-Tosylacetimidates/Acetimidamides onto Arynes via [2 + 2] Cycloaddition. *J. Org. Chem*. **2016**, *81*, 2451-2459.

(9) (a) Seo,Y. H.; Damodar, K.; Kim, J.-K.; Jun, J.-G. Synthesis and Biological Evaluation of 2-Aroylbenzofurans, Rugchalcones A, B and their Derivatives as Potent Anti-Inflammatory Agents. *Bio org. Med. Chem. Lett.* **2016**, *26*, 1521-1524. (b) Saberi, M. R.; Vinh, T. K.; Yee, S. W.; Griffiths, B. J. N.; Evans, P. J.; Simons C. Potent CYP19 (Aromatase) 1-[(Benzofuran-2-yl)(phenylmethyl)pyridine, -imidazole, and -triazole Inhibitors: Synthesis and Biological Evaluation. *J. Med. Chem.* **2006**, *49*, 1016-1022. (c) Cui, M.; Ono, M.; Kimura, H.; Liu, B.; Saji, H. Synthesis and Evaluation of Benzofuran-2-yl(phenyl)methanone Derivatives as Ligands for β-Amyloid Plaques. *Bio org. Med. Chem.* **2011**, *19*, 4148-4153. (d) Schneiders, E.G.; R. Stevensonm, R. Synthesis of (+/-)-machicendiol. *J. Org. Chem.* **1979**, *44*, 4710-4711. (e) Sheen, W.S.; Tsai, I. L.; C. M. Teng, C. M.; Chen, I. S. Nor-neolignan and Phenyl Propanoid from Zanthoxylum Ailanthoides. *Phytochemistry* **1994**, *36*, 213-215. (f) Heravi, M. M.; Zadsirjan, V.; Hamidi, H.; Amiri, P. H. T. Total Synthesis of Natural Products Containing Benzofuran Rings. *RSC Adv.* **2017**, *7*, 24470-24521.

(10) Yoshioka, E.; Tanaka, H.; Kohtani, S.; Miyabe, H. Straightforward Synthesis of Dihydrobenzofurans and Benzofurans from Arynes. *Org. Lett.* **2013**, *15*, 3938–3941.

(11) For selected applications on sulfur yilides, see: (a) Corey, E. J.; Chaykovsky, M. Methylsulfinyl Carbanion (CH_3-SO-CH_2-). Formation and Applications to Organic Synthesis. *J. Am. Chem. Soc.* **1965**, *87*, 1353-1364. For selected reviews, see: (b) Trost, B. M.; Melvin, L. S. *Sulfur Ylides,* Academic Press, New York, **1976**. (c) Li, A.-H.; Dai, L.-X.; Aggarwal, V. K. Asymmetric Ylide Reactions: Epoxidation, Cyclopropanation, Aziridination, Olefination, and Rearrangement. *Chem. Rev.* **1997**, *97*, 2341-2372. (d) Aggarwal, V. K.; Winn, C. L. Catalytic, Asymmetric Sulfur Ylide-Mediated Epoxidation of Carbonyl Compounds: Scope, Selectivity, and Applications in Synthesis. *Acc. Chem. Res.* **2004**, *37*, 611-620. (e) McGarrigle, E. M.; Myers, E. L.; Illaa, O.; Shaw, M. A.; Riches, S. L.; Aggarwal, V. K. Chalcogenides as Organocatalysts. *Chem. Rev*. **2007**, *107*, 5841-5883. (f) Sun, X.-L.; Tang, Y. Ylide-Initiated Michael Addition−Cyclization Reactions beyond Cyclopropanes. *Acc. Chem. Res*. **2008**, *41*, 937-948.

(12) (a) Yang, Q.-Q.; Xiao, C.; Lu, L.-Q; An, J.; Tan, F.; Li, B.-J; Xiao, W.-J. Synthesis of Indoles through Highly Efficient Cascade Reactions of Sulfur Ylides and N-(ortho-Chloromethyl)aryl Amides. *Angew. Chem. Int. Ed*. **2012**, *51*, 9137 –9140.

(13) (a) Himishima, Y.; Sonoda, T.; Kobayashi, H. Fluoride-induced 1,2-Elimination of *o*-Trimethylsilylphenyl Triflate to Benzyne under Mild Conditions. *Chem. Lett*. **1983**, 1211. For a modified procedure, see: (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. An Efficient Procedure for the Synthesis of Ortho-Trialkylsilylaryl Triflates: Easy Access to Precursors of Functionalized Arynes. *Synthesis* **2002**, 1454-1458.

(14) (a) Mirzaei, S.; Khosravi, H. Predicting the Regioselectivity of Nucleophilic Addition to Arynes Using Frontier Molecular Orbital Contribution Analysis. *Tetrahedron Lett*. **2017**, 58, 3362–3365. (b) Amandine, C.; Brinet, D.; Florent, J.; Rousselle, P.; Bertounesque, E. Palladium-Catalyzed Direct Arylation of Polysubstituted Benzofurans. *J. Org. Chem*. **2012**, *77*, 1316−1327. (c) Tadross, P. M.; Gilmore, C. D.; Bugga, P.; Virgil, S. C.; Stoltz, B. M. Regioselective Reactions of Highly Substituted Arynes. *Org. Lett*. **2010**, 12, 1224-1227.

(15) CCDC - 1589669 (compound **3t**) contains the supplementary crystallographic data for this paper. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/conts/retrieving.html

(16) Saberi, M. R.; Vinh, T. K.; Yee, S. W.; Griffiths, B. J. N.; Evans, P. J.; Simons C. Potent CYP19 (Aromatase) 1-[(Benzofuran-2-yl)(phenylmethyl)pyridine, -imidazole, and -triazole Inhibitors: Synthesis and Biological Evaluation. *J. Med. Chem.* **2006**, *49,* 1016-1022.

(17) (a) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. The Diels–Alder Reaction in Total Synthesis. *Angew. Chem. Int. Ed.* **2002**, *41*, 1668-1698.

(18) (a) Schön, U.; Messinger, J.; Solodenko, W.; Kirschning, A. Synthetic Approaches towards 4-Functionalized Estrone Derivatives. *Synthesis* **2012**, *44*, 3822. (b) Mesgar M.; Daugulis, O. Synthesis of 1,2-Bis(trifluoromethylthio)arenes via Aryne Intermediates. *Org. Lett.* **2017**, *19*, 4247−4250.