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Article

Formal [4+1] Cycloaddition of *o*-Quinone Methides: Facile Synthesis of Dihydrobenzofurans

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An efficient and straightforward method for the rapid synthesis of 2-substituted dihydrobenzofurans has been developed *via* reaction of sulfur ylides with *o*-quinone methides (*o*-QMs), which were generated under mild conditions. The products could be obtained in excellent yields with various kinds of sulfur ylides.

Introduction

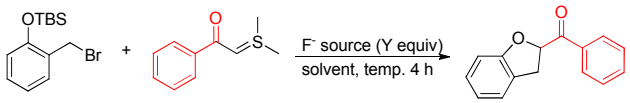
Ortho-quinone methides (*o*-QMs) have been of great interest to the chemical and biological community due to their distinctive properties as Michael acceptors.[1,2] Until now, various methodologies for generation of *o*-QMs *in situ* have been developed, including tautomerization, oxidation, acid or base catalysis, thermolysis, photolysis and olefination of *o*-quinones.[3,4] Moreover, Rokita group reported that O-silylated phenols exposed to fluoride could also produce *o*-QMs under mild reaction condition.[5] In contrast to Rokita's method for generating *o*-QMs, other methods have several disadvantages, such as harsh reaction conditions (e.g. photolysis, high reaction temperature), long reaction time, or using transition metals as oxidants.

o-QMs undergo rapid rearomatization through either Michael addition with nucleophiles, or [4+2] cycloaddition with dienophiles, or oxa-6π-electrocyclisation to give benzopyrans.[3,6] Recently, the Scheidt and Ye groups reported NHC-catalyzed enantioselective formal [4+3] cycloaddition of α,β-unsaturated aldehydes with reactive *o*-QMs to give 2-benzoxopinones, providing a new reaction mode for *o*-QMs.[7] On the other hand, the Zhou and Osyanin groups disclosed that *o*-QMs, which were generated from inaccessible substrates or in the presence of an oxidant, underwent formal [4+1] cycloaddition with sulfur ylides or pyridinium methylides to afford *trans*-2,3-dihydrobenzofurans.[8] Herein, we report an efficient and straightforward method for the rapid synthesis of 2-substituted dihydrobenzofurans, which widely exist in natural products,[9] *via* reaction of sulfur ylides with *o*-QMs.

Results and discussion

Our initial investigation was focused on the model reaction of O-silylated phenol **1a** with sulfur ylide **2a.** The reaction proceeded smoothly to provide the desired product **3a** in 81% yield at 0 °C when TBAF was employed as the fluoride source (entry 1, Table 1). When the equivalent of sulfur ylide **2a** was raised to 1.5 equiv., the product yield increased to 89% (entry 3, Table 1). Considering the crucial role of the fluoride source in triggering the generation of *o*-QMs intermediates, other fluorides such as CsF were examined. We found that CsF displayed the same reactivity with that of TBAF (entry 4, Table 1). Subsequently, the equivalent of fluoride and different temperature were examined, and it was found that the best result could be obtained at room temperature with 2.5 equiv. of TBAF (entry 8, Table 1). Finally, the influence of solvents was examined. In all solvents tested, including CH_2Cl_2, $CHCl_3$, THF, Et_2O, toluene, DMF, MeCN, and MeOH, the desired product was obtained in satisfactory yields (entries 8-16, Table 1), indicating a good solvent tolerance of this reaction. In terms of the product yields and operation convenience, CH_2Cl_2 was chosen as the best solvent.

Table 1. Optimization for the reaction of O-silylated phenol **1a** with sulfur ylide **2a**.[a]



1a **2a** (X equiv) **3a**

entry	F⁻ source	X	Y	solvent	temp. (°C)	yield (%)[b]
1	TBAF	1.0	2.5	DCM	0	81
2	TBAF	1.2	2.5	DCM	0	85
3	TBAF	1.5	2.5	DCM	0	89
4	CsF	1.5	2.5	DCM	0	85
5	TBAF	1.5	1.5	DCM	0	88
6	TBAF	1.5	1.0	DCM	0	82
7	TBAF	1.5	2.5	DCM	-30	36
8	TBAF	1.5	2.5	DCM	rt	89
9	TBAF	1.5	2.5	$CHCl_3$	rt	86
10	TBAF	1.5	2.5	THF	rt	88
12	TBAF	1.5	2.5	Et_2O	rt	86
13	TBAF	1.5	2.5	toluene	rt	74

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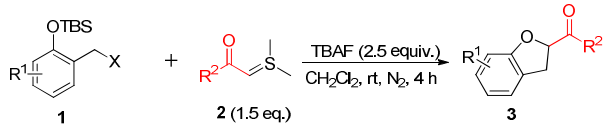
14	TBAF	1.5	2.5	DMF	rt	70
15	TBAF	1.5	2.5	MeCN	rt	77
16	TBAF	1.5	2.5	MeOH	rt	71

[a] **1a** (0.5 mmol), **2a**, solvent (5 mL), room temperature, 12 h. [TBAF (1 M in THF solution)]. [b] Isolated yields.

With the optimized reaction conditions in hand, we explored the reaction scope with using a variety of O-silylated phenols **1** and sulfur ylides **2** (Table 2). Sulfur ylide derivatives bearing electron-donating and withdrawing groups on the phenyl group were well-tolerated (**3a–j**), affording the corresponding products in 83-92% yields. In general, other aromatic substitutes (2-nathyl, 2-furyl, 2-thiazolyl, 2-pyridyl) derived sulfur ylides had little influence on the yields (77-89% yields, entries 12-15, Table 2). Interestingly, ester and amide derived sulfur ylides could be obtained *in situ*, affording the desired products in 42% and 85% yields, respectively (entries 16, 17, Table 2). Furthermore, the 4-Br substituted O-silylated phenols **1b** reacted well with **2a** to afford 2-substituted dihydrobenzofuran (**3q**) in 90% yield (entry 18, Table 2).

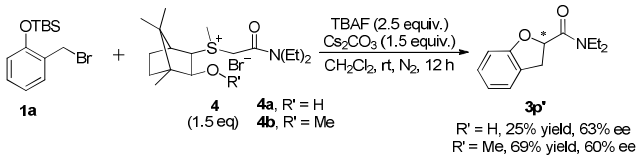
Table 2. Substrate scopes for the reaction of O-silylated phenols **1** and sulfur ylides **2**.[a]



entry	R^1	X	R^2	yield (%)[b]
1	H	Br	Ph	89 (**3a**)
2	H	Cl	Ph	92 (**3a**)
3	H	Br	4-MeC_6H_4	81 (**3b**)
4	H	Br	4-$MeOC_6H_4$	80 (**3c**)
5	H	Br	3-$MeOC_6H_4$	91(**3d**)
6	H	Br	4-FC_6H_4	86 (**3e**)
7	H	Br	2-FC_6H_4	85 (**3f**)
8	H	Br	4-ClC_6H_4	92 (**3g**)
9	H	Br	3-ClC_6H_4	90 (**3h**)
10	H	Br	4-BrC_6H_4	83 (**3i**)
11	H	Br	3-BrC_6H_4	84 (**3j**)
12	H	Br	2-naphthyl	84 (**3k**)
13	H	Br	2-furyl	81 (**3l**)
14	H	Br	2-thiazolyl	95 (**3m**)
15	H	Br	2-pyridyl	77 (**3n**)
16[c]	H	Br	OEt	42 (**3o**)
17[c]	H	Br	NEt_2	85 (**3p**)
18	4-Br	Br	Ph	90 (**3q**)

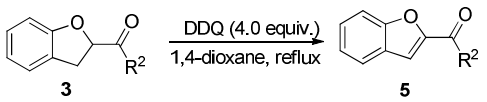
[a] **1** (0.5 mmol), **2** (0.75 mmol), TBAF (2.5 equiv., 1 M in THF solution), CH_2Cl_2 (5 mL), room temperature, 12 h. [b] Isolated yields. [c] Sulfonium salts was used instead of sulfur ylides, using Cs_2CO_3 (1.5 equiv.) as a base.

We further turned our attention to the reaction with chiral sulfonium salts derived from camphor. As shown in Scheme 1, moderate enantioselectivity (63% ee) was observed in reaction of **1a** with chiral sulfonium salt **4a** (R' = H),[10] affording optically active amide **3p'** in only 25% yield. When using the chiral sulfonium salt **4b** (R' = Me),[11] the yield of the desired product could be increased to 69%, but with the similar enantioselectivity (60% ee).



Scheme 1. Reaction of **1a** with chiral sulfonium salt **4**.

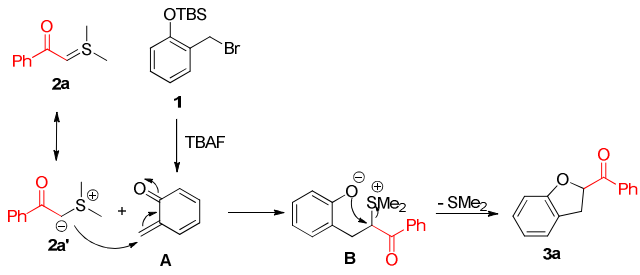
2-Substituted dihydrobenzofurans could be further converted into the corresponding aromatic benzofurans with using DDQ as the oxidizing agent. Thus, 2-benzoyl dihydrobenzofuran **3a** was transformed smoothly to benzofuran **5a** in 81% yield according to the known literature method.[12] When using 2-furoyl dihydrobenzofuran **3l** and 2-picolinyl dihydrobenzofuran **3n** under the same conditions, the desired products **5l** and **5n** were obtained in moderate yields (53-56% yields), Notably, 2-thiazole formyl dihydrobenzofuran **3m** was employed in the reaction, affording the product **5m** with 81% yield When the 2-substituted dihydrobenzofuran **3o** and **3p** was employed, the corresponding benzofuran **5o** and **5p** could be obtained in 75% and 69% yield, respectively (Scheme 2).



5a, R^2 = Ph, 81% yield
5k, R^2 = 2-naphthyl, 83% yield
5l, R^2 = 2-furyl, 56% yield
5m, R^2 = 2-thiazolyl, 81% yield
5n, R^2 = 2-pyridyl, 53% yield
5o, R^2 = OEt, 75% yield
5p, R^2 = NEt_2, 69% yield

Scheme 2. Synthesis of benzofuran **5**.

A plausible mechanism for this formal [4+2] cycloaddition reaction is depicted in Scheme 3. We proposed that the highly reactive *o*-QMs **A** generated through desilylation/elimination reaction. Then sulfur ylides as nucleophiles attacked at the external carbon of *o*-QMs, affording the phenoxide **B**. Finally, the intermediate **B** lost one molecular dimethyl sulfide through nucleophilic attack, providing the 2-substituted dihydrobenzofuran.



Scheme 3. Proposed mechanism.

Experimental section

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General Procedure for the Reaction of O-silylated Phenols and Sulfur Ylides: To a solution of sulfur ylides **2** (0.75 mmol, 1.5 equiv.) in dry CH_2Cl_2 (4 mL), a solution of O-silylated phenol **1** (0.5 mmol, 1.0 equiv.) in dry CH_2Cl_2 (1 mL) was added at room temperature under N_2. Then TBAF (1.0 M in THF, 1.25 mL, 2.5 equiv.) was added dropwise. After the addition, the mixture was stirred at room temperature for 4 h. The reaction was concentrated under reduced pressure and purified by flash chromatography on silica gel (petroleum ether : ethyl acetate = 20:1).

3a,[13] White solid, 89% yield, m.p. 93-95 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.2 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 2H), 7.21 (d, *J* = 7.8 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 6.91 (dd, *J* = 7.4, 4.3 Hz, 2H), 6.02-5.86 (m, 1H), 3.91-3.23 (m, 2H).

3b, Colorless oil, 81% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 6.94-6.82 (m, 2H), 5.90 (m, 1H), 3.60-3.52 (m, 2H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.6, 158.6, 144.2, 131.5, 129.0, 128.8, 127.8, 124.8, 124.4, 120.6, 109.3, 82.1, 32.3, 21.3. HRMS (ESI): Exact mass calcd. for $C_{16}H_{14}O_2Na$ $[M+Na]^+$ 261.0891, found: 261.0883.

3c,[14] White solid, 80% yield, m.p. 108.5-110 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.8 Hz, 2H), 7.19 (d, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 2H), 6.88 (dd, *J* = 7.5, 5.6 Hz, 2H), 5.89 (dd, *J* = 10.2, 7.6 Hz, 1H), 3.89 (s, 3H), 3.61 (dd, *J* = 15.8, 7.7 Hz, 1H), 3.52 (dd, *J* = 15.8, 10.4 Hz, 1H).

3d, White solid, 91% yield, m.p. 94-95.8 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67-7.54 (m, 2H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.20 (d, *J* = 7.3 Hz, 1H), 7.15 (d, *J* = 7.9 Hz, 1H), 6.97-6.84 (m, 2H), 5.95 (t, *J* = 8.9 Hz, 1H), 3.87 (s, 3H), 3.59 (d, *J* = 8.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.3, 159.9, 159.0, 135.7, 129.7, 128.3, 125.1, 124.8, 121.6, 121.1, 120.2, 113.3, 109.8, 82.6, 55.4, 32.8. HRMS (ESI): Exact mass calcd. for $C_{16}H_{14}O_3Na$ $[M+Na]^+$ 277.0841, found: 277.0851.

3e, White solid, 86% yield, m.p. 118.0-120.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 8.6, 5.5 Hz, 2H), 7.21 (dd, *J* = 6.0, 2.7 Hz, 3H), 7.15 (d, *J* = 8.1 Hz, 1H), 6.98-6.84 (m, 2H), 5.89 (dd, *J* = 10.3, 7.3 Hz, 1H), 3.66 (dd, *J* = 15.8, 7.2 Hz, 1H), 3.55 (dd, *J* = 15.8, 10.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.0, 167.7, 164.3, 158.8, 132.0, 131.9, 128.3, 125.1, 124.9, 121.3, 116.0, 115.7, 82.7, 32.2. HRMS (ESI): Exact mass calcd. for $C_{15}H_{11}O_2FNa$ $[M+Na]^+$ 265.0641, found: 265.0634.

3f, Yellow oil, 85% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (t, *J* = 7.4 Hz, 1H), 7.60 (m, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.25-7.12 (m, 3H), 6.92 (d, *J* = 7.7 Hz, 1H), 6.88 (d, *J* = 7.4 Hz, 1H)., 5.99-5.82 (m, 1H), 3.69 (dd, *J* = 15.8, 10.9 Hz, 1H), 3.43 (dd, *J* = 15.9, 5.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.7, 163.3, 160.0, 159.3, 135.3, 135.2, 131.3, 131.3, 128.3, 124.8, 124.8, 124.7, 121.0, 116.7, 116.3, 109.6, 85.0, 84.9, 32.5, 32.5. HRMS (ESI): Exact mass calcd. for $C_{15}H_{11}O_2FNa$ $[M+Na]^+$ 265.0641, found: 265.0634.

3g, White solid, 92% yield, m.p. 113.8-115.6 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.6 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 2H), 7.24-7.06 (m, 2H), 6.91 (d, *J* = 7.4 Hz, 1H), 6.86 (d, *J* = 7.7 Hz, 1H), 5.86 (dd, *J* = 10.3, 7.3 Hz, 1H), 3.64 (dd, *J* = 15.8, 7.2 Hz, 1H), 3.53 (dd, *J* = 15.8, 10.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.0, 158.3, 139.7, 132.4, 130.2, 128.6, 127.9, 124.6, 124.5, 120.8, 109.3, 82.3, 31.8. HRMS (ESI): Exact mass calcd. for $C_{15}H_{11}O_2ClNa$ $[M+Na]^+$ 281.0345, found: 281.0338.

3h, Yellow oil, 90% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.95 (d, *J* = 7.7 Hz, 1H), 7.60 (dd, *J* = 4.9, 4.0 Hz, 1H), 7.47 (t, *J* = 7.9 Hz, 1H), 7.22 (d, *J* = 7.4 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 6.96-6.87 (m, 2H), 5.88 (dd, *J* = 10.2, 7.3 Hz, 1H), 3.65 (dd, *J* = 16.2, 7.7 Hz, 1H), 3.61-3.50 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.9, 158.3, 135.6, 134.6, 133.1, 129.6, 128.7, 127.9, 126.8, 124.5, 124.4, 120.8, 109.3, 82.1, 31.8. HRMS (ESI): Exact mass calcd. for $C_{15}H_{11}O_2ClNa$ $[M+Na]^+$ 281.0345, found: 281.0351.

3i, Yellow solid, 90% yield, m.p. 119.5-120.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.8 Hz, 2H), 7.67 (d, *J* = 7.8 Hz, 2H), 7.26-7.11 (m, 2H), 6.93 (d, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 5.87 (dd, *J* = 9.9, 7.7 Hz, 1H), 3.65 (dd, *J* = 15.8, 7.2 Hz, 1H), 3.54 (dd, *J* = 15.8, 10.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.7, 158.8, 133.3, 132.0, 130.7, 128.9, 128.4, 125.0, 124.9, 121.3, 109.8, 82.7, 32.2. HRMS (ESI):Exact mass calcd. for $C_{15}H_{11}O_2BrNa$ $[M+Na]^+$ 324.9840, found: 324.9851.

3j, Yellow oil, 84% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.99 (d, *J* = 7.5 Hz, 1H), 7.76 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.40 (t, *J* = 7.9 Hz, 1H), 7.22 (d, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 7.9 Hz, 1H), 6.96-6.86 (m, 2H), 5.88 (dd, *J* = 10.2, 7.3 Hz, 1H), 3.64 (dd, *J* = 16.6, 8.0 Hz, 1H), 3.55 (dd, *J* = 16.0, 10.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.8, 158.3, 136.0, 135.8, 131.6, 129.8, 127.9, 127.2, 124.5, 124.5, 122.6, 120.9, 109.3, 82.1, 31.8. HRMS (ESI): Exact mass calcd. for $C_{15}H_{11}O_2BrNa$ $[M+Na]^+$ 324.9840, found: 324.9848.

3k, White solid, 84% yield. m.p. 141.5-143.7 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.10 (dd, *J* = 8.6, 1.5 Hz, 1H), 8.05-7.89 (m, 3H), 7.63 (m, 2H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 7.7 Hz, 1H), 6.92 (dd, *J* = 7.2, 5.7 Hz, 2H), 6.11 (dd, *J* = 10.0, 7.7 Hz, 1H), 3.71 (dd, *J* = 14.3, 6.1 Hz, 1H), 3.63 (dd, *J* = 14.3, 8.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.4, 159.0, 135.8, 132.5, 131.8, 131.1, 129.7, 128.8, 128.6, 128.3, 127.8, 126.9, 125.2, 124.9, 124.4, 121.2, 109.8, 82.6, 32.6. HRMS (ESI): Exact mass calcd. for $C_{19}H_{14}O_2Na$ $[M+Na]^+$ 297.0891, found: 297.0896.

3l, Yellow oil, 81% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.47 (d, *J* = 3.5 Hz, 1H), 7.21 (d, *J* = 6.6 Hz, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 6.99-6.85 (m, 2H), 6.60 (dd, *J* = 3.5, 1.6 Hz, 1H), 5.69 (dd, *J* = 10.3, 7.5 Hz, 1H), 3.63 (dd, *J* = 15.9, 10.4 Hz, 1H), 3.53 (dd, *J* = 16.0, 7.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ

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184.9, 158.5, 149.9, 146.9, 127.9, 124.6, 124.4, 120.8, 119.8, 112.0, 109.2, 82.4, 32.6. HRMS (ESI): Exact mass calcd. for $C_{13}H_{10}O_3Na$ $[M+Na]^+$ 237.0528, found: 237.0519.

3m, Yellow oil, 95% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 3.8 Hz, 1H), 7.73 (d, *J* = 4.9 Hz, 1H), 7.25-7.15 (m, 3H), 6.92 (t, *J* = 7.2 Hz, 2H), 5.68 (t, *J* = 8.5 Hz, 1H), 3.61 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.7, 158.4, 140.0, 134.5, 133.7, 127.9, 127.8, 124.6, 124.5, 120.9, 109.3, 83.5, 32.9. HRMS (ESI): Exact mass calcd. for $C_{13}H_{10}O_2SNa$ $[M+Na]^+$ 253.0299, found: 253.0305.

3n, White solid, 77% yield. m.p. 118.5-120.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.1 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.90 (dt, *J* = 7.7, 1.6 Hz, 1H), 7.54 (dd, *J* = 7.0, 5.4 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 2H), 6.97 (d, *J* = 8.1 Hz, 1H), 6.88 (t, *J* = 7.4 Hz, 1H), 6.49 (dd, *J* = 10.9, 7.6 Hz, 1H), 3.85 (dd, *J* = 16.0, 10.9 Hz, 1H), 3.31 (dd, *J* = 16.1, 7.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.3, 159.7, 151.6, 149.1, 137.1, 128.2, 127.6, 125.2, 124.7, 123.0, 120.8, 109.8, 82.3, 34.0. HRMS (ESI): Exact mass calcd. for $C_{14}H_{11}NO_2Na$ $[M+Na]^+$ 248.0687, found: 248.0680.

3q,[15] White solid, 90% yield, m.p. 138.5-140 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07-8.00 (m, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.32-7.20 (m, 2H), 6.76 (t, *J* = 9.8 Hz, 1H), 5.96 (dd, *J* = 10.1, 7.4 Hz, 1H), 3.61 (dd, *J* = 16.1, 7.4 Hz, 1H), 3.57-3.47 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.8, 158.2, 134.2, 133.8, 131.1, 129.1, 128.8, 127.8, 127.7, 113.0, 111.2, 82.9, 32.2.

General Procedure for Synthesis of 3o, 3p: A mixture of O-silylated phenol **1** (0.5 mmol, 1.0 equiv.), sulfonium salt **2** (0.75 mmol, 1.5 equiv.) and Cs_2CO_3 (0.75 mmol, 1.5 equiv.) in dry CH_2Cl_2 (5 mL) was stirred at room temperature under N_2. Then TBAF (1.0 M in THF, 1.25 mL, 2.5 equiv.) was added dropwise. After the addition, the mixture was stirred at room temperature for 24 h. The reaction was concentrated under reduced pressure and purified by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10:1-5:1).

3o,[16] Yellow oil, 42% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 10.8, 7.8 Hz, 2H), 6.90 (t, *J* = 7.3 Hz, 2H), 5.20 (dd, *J* = 10.4, 7.1 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.58 (dd, *J* = 15.8, 10.6 Hz, 1H), 3.39 (dd, *J* = 15.8, 7.0 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H).

3p,[17] Colorless oil, 85% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 7.3 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 6.86 (t, *J* = 7.4 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 5.36 (dd, *J* = 9.8, 7.7 Hz, 1H), 3.73 (dd, *J* = 15.6, 7.6 Hz, 1H), 3.57-3.39 (m, 4H), 3.32 (dd, *J* = 15.5, 9.9 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H).

Conclusions

In summary, we have developed a straightforward and efficient approach to 2-substitiuted dihydrobenzofurans through reaction of sulfur ylides with *o*-quinone methides that could be generated under mild conditions. In addition, chiral sulfonium salts could also be employed in this reaction, affording the desired product with moderate enantioselectivity. The products 2-substitiuted dihydrobenzofurans could be conveniently converted to 2-substituted benzofurans with using DDQ as the oxidant. Applications of this [4+1] cycloaddition reaction to other substrates and to the construction of biologically relevant compounds are ongoing in our laboratory.

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