Synthesis of 2-(Diarylmethylene)-3-benzofuranones Promoted via Palladium-Catalyzed Reactions of Aryl iodides with 3-Aryl-1-(2- *tert*-butyldimethylsilyloxy)phenyl-2-propyn-1-ones

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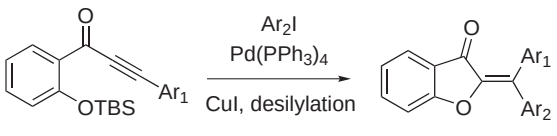
Abstract: 3-Substituted-1-(2-*tert*-butyldimethylsilyloxy)phenyl-2-propyn-1-ones were coupled with aryl iodides by using palladium as a catalyst in ambient MeOH solution and gave 2-(diarylmethylene)-3-benzofuranones in moderate to good yields.

Key words: palladium, coupling, cyclizations

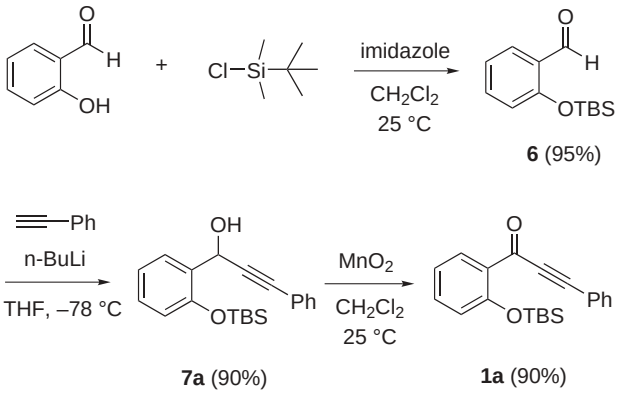
2-Methylene-3-benzofuranones, a series of naturally generated components with special constructions and widely spread in species of higher plants,[1] have a major impact on biological activities, especially in reducing cancer risk by preventing the oxidative damage to intracellular organs.[2] and by providing antiprotozoan activity for those receiving immunosuppressive drugs or infected with HIV.[3] Recently, chemical profiles of palladium metal catalyzed reactions have begun to surface, including heterocycles formed from the intramolecular cyclization of the complex intermediates offered between the acetylene subunit and aryl iodides, initiated by various nucleophiles.[4–6] It is considered that active π-electron-rich acetylenes are required for the palladium-catalyzed reactions and the relating reactivity of them are usually reduced in the presence of electron-withdrawing groups, which probably resulted the negative response in proceeding such reactions. However, the role of palladium-catalyzed reactions in generating heterocyclic compounds by using a α,β-unsaturated acetylenic subunits coupling with aryl iodides is still under investigation, and to date there have been no related reports. As the main force to establish a rational generating method for such compounds, a novel route to 2-(diarylmethylene)-3-benzofuranone **2** by the palladium-catalyzed coupling reaction of compound **1** with aryl iodides (Equation 1) is presented in this work.



1 **2**

Equation 1

The synthesis of 1-(2-*tert*-butyldimethylsilyloxy)phenyl-3-phenyl-2-propyn-1-one (**1a**)[7] is summarized in Scheme 1. The first attempt for the generation of our proposed target molecule **2aa** was carried out by treatment of **1a** with iodobenzene in the presence of catalytic amount of $Pd(PPh_3)_4$ and CuI, K_2CO_3 as a base in refluxing MeOH to give the uncoupled products benzylidene **3a** and flavone **4a** in 40% and 45% yields, respectively (Equation 2). The consideration for the blockage of coupling factor of iodobenzene was probably due to the faster desilylcyclization and protonation during heating state. Hence, a mild ambient reaction status was processed and the desired 2-(diphenylmethylene)benzofuranone (**2aa**) was obtained in 92% yield. The reaction processes were described in experimental section. The structure of **2aa** was unambiguously determined by X-ray crystallography (Figure 1).



Scheme 1

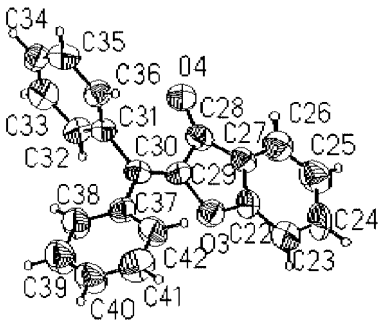


Figure 1 X-ray spectrum of compound **2aa**

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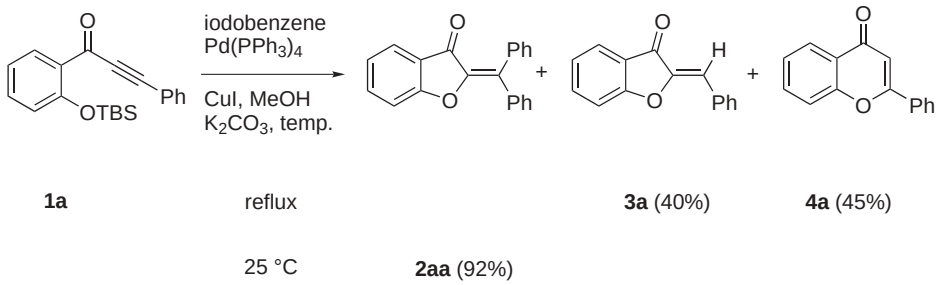
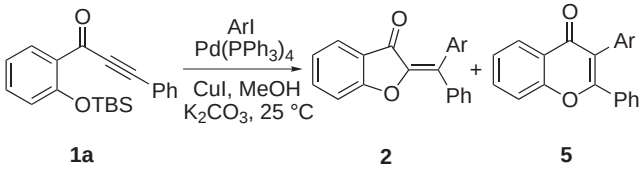


Equation 2

Various aryl iodides bearing electron-donating or electron-withdrawing groups on the phenyl ring, including the heterocycle, 4-iodopyridine, were introduced to this palladium-catalyzed coupling reaction of **1a** to give the desired 2-(diarylmethylene)-3-benzofuranones **2ab**–**af** in good chemical yield (reaction details see experimental section). The results are summarized in Table 1. Only the reaction of **1a** with 2-iodothiophene gave 2-thienyl-1-phenylmethylene-3-benzofuranone (**2af**) in 35% yield, along with 2-phenyl-3-thienylbenzopyran-4-one (**5af**) in 52% yield. We propose that the possible reason for such phenomenon is that thiophene is less steric hindrance when compared to phenyl group, thereby allowing the formation of the benzopyranone structure.

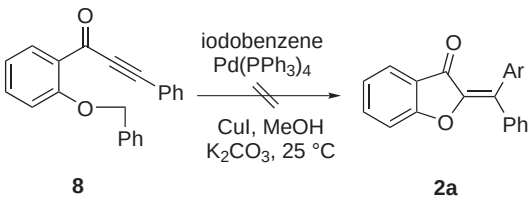
Table 1 The results of Coupling of Compound **1a** with Various Aryl Iodides



Entry	Isolated yield (%)	
ArI = 4-iodoanisole	**2ab** (85%)	
ArI = 4-iodotoluene	**2ac** (89%)	
ArI = 4-iodobenzonitrile	**2ad** (87%)	
ArI = 4-iodobenzotrifluoride	**2ae** (76%)	
ArI = 2-iodothiophene	**2af** (35%)	**5af** (52%)

In a further exploration of the substituent effect on the alkyne terminus on compound **1**, derivatives **1b**–**e** were prepared according to the procedure described above. Reaction of **1b** with aryl iodides as the conditions of **1a** offered the 2-diarylmethylene-3-benzofuranones **2ba**,**bb, 2bd** and **2bg** in good yields (Table 2). However, reaction of **1c** with aryl iodides gave 3-benzofuranones **2ca**,**cb** in lower yields together with the uncoupled benzofuranones **3c** in 22% and 37% yields, respectively. Moreover, reaction of **1d** with 4-iodobenzene gave the uncoupled product **3d**, as the only isolated product in 85% yield. Compound **1e** was also explored in this reaction, and product **4ea** was obtained in 54% yield. The above profiles suggested that the phenyl ring on the alkyne terminus carried an electron-withdrawing group, deactivating the formation of the complex between aryl palladium and the acetylene. At the same time, it accelerated the rate of the cyclization reaction to form the uncoupled benzofuranones. A remarkable point raised in this report is: the presence of the deactivating groups on phenyl ring reduced the reactivity of the palladium-π-electron complex greatly and resulted the uncoupled products, although the α,β-unsaturated acetylene had a carbonyl group.

The benzyl phenyl ether **8** was also synthesized to test the generality of the palladium-catalyzed reaction under mild reaction conditions. Treatment of **8** with iodobenzene under the same reaction conditions gave a complex product mixture, but no desired product was given. (Equation 3)



Equation 3

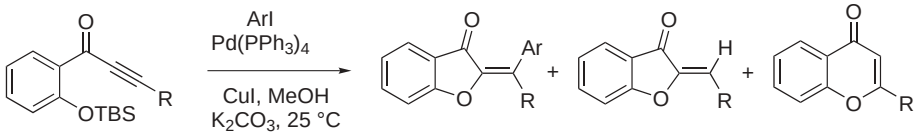
In conclusion, we have establish a novel route to synthesize 2-(diarylmethylene)-3-benzofuranones by palladium-catalyzed cyclization of 3-aryl-1-(2-*tert*-butyldimethylsilyloxy)phenyl-2-propyn-1-ones. The yields are from moderate to good.

General Procedure of the Coupling Reaction of 3-Substituted-1-(2-*tert*-butyldimethylsilyloxy)phenyl-2-propyn-1-ones with Aryl Iodides: A degassed solution of 3-substituted-1-(2-*tert*-butyldimethylsilyloxy)phenyl-2-propyn-1-ones (1 mmol) in anhyd MeOH (10 mL) containing aryl iodide (2 mmol), $Pd(PPh_3)_4$ (0.05 mmol) and CuI (0.1 mmol), K_2CO_3 (3 mmol) was added to the solution. The resulting solution was stirred for 2 h at 25 °C, MeOH was removed and then quenched with sat. aq NH_4Cl solutions and extracted with EtOAc. The organic layer was separated and dried over $MgSO_4$. After filtration, the solvent was evaporated in vacuo. The residue was purified by flash chromatography to give the products.

1-(2-*tert*-Butyldimethylsilyloxy)phenyl-3-phenyl-2-propyn-1-one (1a)

Compound **1a** was obtained in 99% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.03 (dd, *J* = 7.8, 1.8 Hz, 1 H), 7.64–7.60 (m, 2 H), 7.47–7.33 (m, 4 H), 7.10–7.01 (m, 1 H), 6.94–6.89 (m, 1 H), 1.00 (s, 9 H), 0.24 (s, 6 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 155.7, 134.1,

Table 2 Results of Reaction of 2-(1-Substituted Propynonyl)-1-*tert*-butyldimethylsilyl Phenyl Ethers **1** with Aryl Iodides



1 **2** **3** **4**

Entry	ArI	Isolated yield (%)		
1b R = *p*-$C_6H_4OCH_3$	4-iodobenzene	**2ba** (92%)		
	4-iodoanisole	**2bb** (85%)		
	4-iodobenzonitrile	**2bd** (91%)		
	2-iodopyridine	**2bg** (99%)		
1c R = *p*-$C_6H_4CF_3$	4-iodobenzene	**2ca** (36%)	**3c** (22%)	
	4-iodoanisole	**2cb** (28%)	**3c** (37%)	
1d R = *p*-C_6H_4CN	4-iodobenzene		**3d**[a] (85%)	
1e R = $(CH_3)_4CH_3$	4-iodobenzene			**4e** (54%)

[a] Compound **3d** was an uncoupled product: 2-(1-methylbenzoylmethylenyl)benzofuranone.

132.7, 132.6, 130.4, 130.3, 129.5, 128.6, 128.5, 121.5, 120.9, 120.6, 96.8, 91.4, 88.8, 25.9, 25.8, 25.7, 18.4, –4.2, –4.1.

MS (EI): *m*/*z* = 336 (44) [M^+], 331 (35), 324 (44), 316 (61).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{24}O_2Si$: 336.1546; found: 336.1529.

1-(2-*tert*-Butyldimethylsilyloxy)phenyl-3-anisolyl-2-propyn-1-one (1b)

Compound **1b** was obtained in 79% yield. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.96 (dd, *J* = 7.8, 2.0 Hz, 1 H), 7.61–7.54 (m, 2 H), 7.45–7.37 (m, 1 H), 7.04 (td, *J* = 8.6, 1.0 Hz, 1 H), 6.93–6.86 (m, 3 H), 3.84 (s, 3 H), 1.00 (m, 9 H), 0.23 (m, 6 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 161.4, 155.5, 134.9, 134.8, 133.8, 132.4, 129.8, 121.5, 120.9, 114.3, 114.2, 112.4, 92.5, 88.7, 55.3, 25.9, 25.8, 25.7, 18.4, –4.2, –4.1.

MS (EI): *m*/z = 366 (46) [M^+], 362 (22), 354 (60).

HRMS (EI): *m*/z calcd for $C_{22}H_{26}O_3$: 366.1652; found: 366.1579.

1-(2-*tert*-Butyldimethylsilyloxy)phenyl-3-toluenyl-2-propyn-1-one (1c)

Compound **1c** was obtained in 90% yield. ^1H NMR (200 MHz, $CDCl_3$): δ = 8.01 (dd, *J* = 7.8, 2.0 Hz, 1 H), 7.75–7.63 (m, 4 H), 7.50–7.41 (m, 1 H), 7.11–6.91 (m, 2 H), 1.00 (s, 9 H), 0.24 (s, 6 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 177.3, 156.1, 134.7, 133.2, 133.1, 132.7, 131.7, 129.2, 126.4, 125.7, 125.6, 124.6, 121.6, 121.2, 90.2, 89.1, 25.9, 25.8, 25.7, 18.6, –4.0, –3.9.

MS (EI): *m*/z = 404 (50) [M^+], 390 (100), 374 (65).

HRMS (EI): *m*/z calcd for $C_{22}H_8O_2SiF_3$ 404.1419; found: 404.1415.

1-(2-*tert*-Butyldimethylsilyloxy)phenyl-3-benzonitrilyl-2-propyn-1-one (1d)

Compound **1d** was obtained in 88% yield. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.98 (dd, *J* = 7.8, 1.8 Hz, 1 H), 7.68 (s, 4 H), 7.49–7.41 (m, 1 H), 7.10–7.02 (m, 1 H), 6.94–6.89 (m, 1 H), 0.99 (s, 9 H), 0.23 (s, 6 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 176.8, 156.0, 134.7, 133.0, 132.5, 132.1, 128.9, 125.4, 121.4, 121.0, 117.9, 113.6, 96.8, 91.4, 88.1, 29.6, 25.8, 25.7, 25.6, 18.4, –4.2, –4.1.

MS (EI): *m*/*z* = 361 (20) [M^+], 359 (56), 348 (28).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{23}NO_2Si$ 361.1499; found: 361.1477.

1-(2-*tert*-Butyldimethylsilyloxy)phenyl-2-heptyn-1-one (1e)

Compound **1e** was obtained in 70% yield. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.93 (dd, *J* = 7.6, 1.8 Hz, 1 H), 7.42–7.34 (m, 1 H), 7.05–7.00 (m, 1 H), 6.97–6.85 (m, 1 H), 2.43 (t, *J* = 7.0 Hz, 2 H), 1.65–1.25 (m, 7 H), 1.03–0.89 (m, 11 H), 0.22 (s, 6 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 155.5, 133.8, 132.6, 129.6,121.5,121.4, 120.8, 95.1, 81.5, 29.8, 25.9, 25.8, 25.7, 22.0, 18.9, 18.4, 13.4, –4.3, –4.2

MS (EI): *m*/*z* = 316 (81) [M^+], 259 (100), 229 (26).

HRMS (EI): *m*/*z* calcd for for $C_{19}H_{28}O_2Si$: 316.1859; found: 316.1851.

2-(1-Anisolyl-1-phenylmethylenyl) Benzofuranone (2ab)

Compound **2ab** was obtained in 85% yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 0.4 Hz, 1 H), 7.61–7.59 (m, 2 H), 7.58–7.51 (m, 2 H), 7.50–7.40 (m, 3 H), 7.39–7.13 (m, 3 H), 6.95 (d, *J* = 9.2 Hz, 2 H), 3.86 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 183.0, 164.9, 160.4, 143.7, 138.1, 136.2, 136.1, 133.3, 132.3, 131.4, 130.4, 129.1, 128.7, 128.3, 128.1, 127.8, 124.5, 122.8, 113.7, 113.6, 112.7, 55.3.

MS (EI): *m*/*z* = 328 (99) [M^+], 327 (100), 297 (17), 284 (12).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{16}O_3$: 328.1099; found: 328.1104.

2-(1-Phenyl-1-tolunylmethylenyl) Benzofuranone (2ac)

Compound **2ac** was obtained in 89% yield. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.75–7.27 (m, 13 H), 2.45 (m, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 183.1, 164.9, 139.6, 138.9, 137.8, 136.2, 135.9, 134.6, 132.4, 131.5, 131.3, 130.5, 130.4, 129.1, 128.9, 128.7, 128.1, 128.0, 124.4, 122.8, 112.6, 21.4.

MS (EI): *m*/*z* = 312 (75) [M^+], 311 (100), 297 (47), 221 (26).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{16}O_2$: 312.1151; found: 312.1138.

2-(1-Benzonitrilyl-1-phenylmethylenyl) Benzofuranone (2ad)
Compound **2ad** was obtained in 87% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.87–7.60 (m, 4 H), 7.54–7.29 (m, 6 H), 7.25–7.15 (m, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 183.3, 165.3, 143.8, 140.8, 137.7, 136.9, 136.3, 132.0, 131.8 131.6, 131.2, 131.0, 130.3, 129.6, 129.4, 128.4, 124.6, 123.4, 122.5, 118.7, 112.8, 112.4.

MS (EI): *m*/*z* = 323 (59) (M^+), 322 (100), 190 (10).

HRMS(EI): *m*/*z* calcd for $C_{22}H_{13}NO_2$: 323.0947; found: 323.0941.

2-(1-Phenyl-1-trifluorobenzylmethylenyl) Benzofuranone (2ae)
Compound **2ae** was obtained in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.61 (m, 4 H), 7.55–7.53 (m, 2 H), 7.47–7.28 (m, 5 H), 7.21–7.17 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.7, 131.5, 131.3, 131.1, 130.8, 130.3, 129.4, 129.1, 128.8, 128.4, 128.3, 125.3, 125.2, 125.1, 125.1, 125.0, 124.6, 124.5, 123.4, 123.2, 112.7, 112.6.

MS (EI): *m*/*z* = 366 (57) (M^+), 365 (100), 297 (13), 221 (35).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{13}O_2F_3$: 366.0868; found: 366.0842.

2-(1-Thienyl-1-phenylmethylenyl) Benzofuranone (2af)
Compound **2af** was obtained in 35% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.67–7.60 (m, 3 H), 7.59–7.48 (m, 3 H), 7.39–7.35 (m, 3 H), 7.25–7.08 (m, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 182.5, 164.5, 140.5, 136.1, 134.5, 133.6, 132.0, 130.3, 129.7, 129.6, 128.6, 128.4, 128.0, 127.4, 125.2, 124.3, 123.3, 123.2, 112.7.

MS (EI): *m*/*z* = 304 (65) (M^+), 303 (100), 184 (19).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{12}SO_2$: 304.0559; found: 304.0546.

2-(1-Anisolyl-1-phenylmethylenyl) Benzofuranone (2ba)
Compound **2ba** was obtained in 92% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 0.4 Hz, 1 H), 7.61–7.59 (m, 2 H), 7.58–7.51 (m, 2 H), 7.50& ndash;7.40 (m, 3 H), 7.39–7.13 (m, 3 H), 6.95 (d, *J* = 9.2 Hz, 2 H), 3.86 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 183.0, 164.8, 160.4, 138.0, 135.9, 133.2, 132.3, 131.3, 130.3, 129.7, 129.1, 128.6, 128.2, 128.0, 124.5, 124.4, 123.3, 122.7, 113.6, 113.5, 112.5, 55.3.

MS (EI): *m*/*z* = 328 (99) (M^+), 327 (100), 297 (17), 284 (12).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{16}O_3$: 328.1099; found: 328.1104.

2-(1,1-Dianisolylmethylenyl) Benzofuranone (2bb)
Compound **2bb** was obtained in 85% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.72–7.69 (m, 1 H), 7.68–7.48 (m, 3 H), 7.31–7.11 (m, 4 H), 6.98–6.91 (m, 4 H), 3.87 (d, *J* = 2.2 Hz, 6 H). ^{13}C NMR (50 MHZ, $CDCl_3$): δ = 183.0, 164.8, 160.6, 160.5, 143.3, 136.1, 133.7, 133.6, 133.5, 132.4, 132.3, 130.3, 128.1, 124.5, 123.7, 122.8, 113.8, 113.7, 113.6, 112.7, 55.5, 55.4.

MS (EI): *m*/*z* = 358 (100) (M^+), 357 (67), 327 (21), 238 (8).

HRMS (EI): *m*/*z* calcd for $C_{23}H_{18}O_4$: 358.1205; found: 358.1205.

2-(1-Anisolyl-1-benzonitrilylmethylenyl) Benzofuranone (2bd)
Compound **2bd** was obtained in 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 8.4, 2.0 Hz, 2 H), 7.68–7.61 (m, 2 H), 7.50 (dd, *J* = 6.8, 2.0 Hz, 2 H), 7.43 (dd, *J* = 6.4, 2.0 Hz, 2 H), 7.30 (dd, *J* = 8.4, 0.8 Hz, 2 H), 7.20–7.16 (m, 1 H), 6.95 (dd, *J* = 6.8, 2.0 Hz, 2 H), 3.86 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.0, 160.7, 143.0, 141.1, 136.6, 133.0, 132.1, 132.0, 131.7, 131.3, 131.2, 129.3, 128.4, 124.5, 123.2, 122.7, 118.7, 114.1, 114.0, 112.7, 112.2, 55.3, 31.9.

MS (EI): *m*/*z* = 353 (91) (M^+), 352 (100), 338 (15), 322 (35), 190 (11)

HRMS (EI): *m*/*z* calcd for $C_{23}H_{15}NO_3$: 353.1053; found: 353.1053.

2-(1-Anisolyl-1-pyridinylmethylenyl) Benzofuranone (2bg)
Compound **2bg** was obtained in 99%. ^{1}H NMR (200 MHz, $CDCl_3$, 200 MHz): δ = 8.76 (d, *J* = 4.0 Hz, 1 H), 7.83–7.75 (m, 1 H), 7.65–7.56 (m, 4 H), 7.41–7.27 (m, 3 H), 7.14 (t, *J* = 7.4 Hz, 1 H), 6.95 (d, *J* = 8.8 Hz, 2 H), 3.83 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 183.5, 165.2, 160.5, 155.1, 149.8, 143.9, 136.4, 136.3, 132.8, 132.1, 127.9, 125.6, 124.3, 123.0, 122.9, 122.6, 113.9, 113.8, 113.5, 112.6, 55.2.

MS (EI): *m*/*z* = 313 (58) (M^+), 298 (100), 201 (80).175 (44).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{15}NO_3$: 313.1104; found: 313.1065.

2-(1-Phenyl-1-trfluorobenzylmethylenyl) Benzofuranone (2ca)
Compound **2ca** and **3ca** were obtained in 58% yield and they could not be separated by liquid chromatography. The ^{1}H NMR spectrum showed a mixture of **2ca** (36%) and **3ca** (22%). The following spectrum belongs to **2ca**. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (td, *J* = 8.4, 0.8 Hz, 1 H), 7.18 (td, *J* = 7.6, 0.8 Hz 1 H), the other peaks of aromatic could not be separated from those of **3ca**.

2-(1-Anisolyl-1-trifluorobenzylmethylenyl) Benzofuranone (2cb)
Compound **2cb** was obtained in 28% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74–7.59 (m, 5 H), 7.41–7.29 (m, 2 H), 7.28–7.16 (m, 3 H), 6.96 (d, *J* = 6.8, 2.4 Hz, 2 H), 3.87 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.8, 160.6, 136.6, 134.1, 132.3, 131.5, 130.8, 130.6,130.3, 128.4, 128.3, 127.0, 125.3, 125.0, 124.9, 124.7,124.6, 123.7, 123.1, 113.7, 112.9, 112.6.

MS (EI): *m*/*z* = 396 (100) (M^+), 395 (91), 367 (25), 262 (17).

HRMS (EI): *m*/*z* calcd for $C_{23}H_{15}O_3F_3$: 396.0974; found: 396.0978.

2-(1-Methylenyl-1-trifluorobenzyl) Benzofuranone (3c)
Compound **3c** were obtained in 22% and 37% yields, respectively; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (dd, *J* = 8.0, 0.4 MHz, 1 H), 8.23–8.04 (m, 2 H), 7.81–7.72 (m, 3 H), 7.61 (d, *J* = 1.2 Hz, 1 H), 7.59–7.43 (m, 1 H), 6.87 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.6, 166.3, 147.8, 137.3, 135.7, 131.4, 130.8, 125.8, 125.7, 125.6, 124.8, 123.8, 121.3, 112.9, 112.6, 110.6.

MS (EI): *m*/*z* = 290 (80) (M^+), 289 (100), 221 (71).

HRMS (EI): *m*/*z* calcd for $C_{16}H_9O_2F_3$: 290.0555; found: 290.0552.

2-(1-Methylbenzoylmethylenyl) Benzofuranone (3d)
Compound **3d** was obtained in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25–8.20 (m, 3 H), 8.19–8.00 (m, 2 H), 7.99–7.71 (m, 1 H), 7.61–7.59 (m, 1 H), 7.47–7.42 (m, 1 H), 6.89 (s, 1 H), 3.97 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.2, 166.1, 162.0, 156.2, 135.7, 134.0, 132.6, 130.1, 126.2, 126.1, 125.7, 125.4, 123.9, 118.1, 108.7, 52.4, 29.6.

MS (EI): *m*/*z* = 280 (20) (M^+), 247 (100), 220 (15), 189 (18).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{12}O_4$: 280.0735; found: 280.0736.

3-Thienyl Flavone (5af)
Compound **5af** was obtained in 52% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 0.6 Hz, 1 H), 7.63–7.43 (m, 8 H), 7.21–7.10 (m, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 182.5, 164.5, 140.5, 137.9, 136.2, 134.5, 133.5, 132.0, 131.5, 130.3, 129.7, 128.9, 128.6, 128.4, 128.0, 124.4, 123.3, 122.8, 112.6.

MS (EI): *m*/*z* = 304 (66) (M^+), 303(100), 184(16).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{12}SO_2$: 304.0559; found: 304.0546.

2-(1-Phenyl-propanonyl)-1-methylphenyl Ether (8)
Compound **8** was obtained in 93% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.07 (dd, *J* = 8.0, 1.8 Hz, 1 H), 7.55–7.27 (m, 11 H), 7.10–7.02 (m, 2 H), 5.24 (s, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 176.8, 158.7, 136.2, 134.7, 132.9, 132.8, 132.1, 130.1, 128.6, 128.5,

128.4, 128.3, 127.8, 127.4, 127.1, 127.0, 126.9, 120.6, 113.5, 89.5, 70.6, 30.8.

MS (EI): *m*/*z* = 312 (79) (M^+), 311(67), 233(30), 165(46).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{16}O_2$: 312.1151; found: 312.1138

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References

(1) (a) Westenburg, H. E.; Lee, K. J.; Lee, S. K.; Fong, H. H. S.; von Breeman, R. B.; Pezzuto, J. M.; Kinghorn, A. D. *J. Nat. Prod.* **2000**, *63*, 1696. (b) Budzikiewicz, H.; Laufenderg, G.; Clark, C.; Proksch, P. *Phytochemistry* **1984**, *23*, 2625. (c) Bohlmann, F.; Grenz, M.; Gupta, R. K.; Dhar, A. K.; Ahmed, M.; King, R. B.; Robinson, H. *Phytochemistry* **1980**, *19*, 2391.

(2) (a) Lee, B. M.; Lee, S. K.; Kim, H. S. *Cancer Lett.* **1998**, *132*, 219. (b) Kinghorn, A. D.; Fong, H. H. S.; Farnsworth, N. R.; Mehta, R. G.; Moon, R. C.; Moriarty, R. M.; Pezzuto, J. M. *Curr. Org. Chem.* **1998**, *2*, 597.

(3) (a) Kayser, O.; Waters, W. R.; Woods, K. M.; Upton, S. J.; Keithly, J. S.; Kiderlen, A. F. *Planta Med.* **2001**, *67*, 722. (b) Sepuvelda, B. S.; Cassels, B. K. *Planta Med.* **1999**, *20*, 199. (c) Kayser, O.; Kiderlen, A. F.; Folkens, U.; Kolodziej, H. *Planta Med.* **1999**, *65*, 316. (d) Kayser, O.; Kiderlen, A. F.; Brun, R. *Planta Med.* **2001**, *67*, 718.

(4) (a) Larock, R. C.; Yum, E. K.; Doty, M. J.; Sham, K. K. C. *J. Org. Chem.* **1995**, *60*, 3270. (b) Arcadi, A.; Cacchi, S.; Del Rosario, M.; Fabrizi, G.; Marinelli, F. *J. Org. Chem.* **1996**, *61*, 9280. (c) Saulinier, M. G.; Frenneson, D. B.; Deshpande, M. S.; Vyas, D. M. *Tetrahedron Lett.* **1995**, *36*, 7841.

(5) (a) Bouyssi, D.; Gore, J.; Balme, G.; Louis, D.; Wallach, J. *Tetrahedron Lett.* **1993**, *34*, 3129. (b) Cavicchioli, M.; Bouyssi, D.; Gore, J.; Balme, G. *Tetrahedron Lett.* **1996**, *37*, 1429. (c) Arcadi, A.; Burini, A.; Cacchi, S.; Delmastro, M.; Marinelli, F.; Pietroni, B. R. *J. Org. Chem.* **1993**, *57*, 976.

(6) (a) Portscheller, J. C.; Malinakova, H. C. *Org. Lett.* **2002**, *21*, 3679. (b) Roesch, K. R.; Zhang, H.; Larock, R. C. *J. Org. Chem.* **2001**, *66*, 8042. (c) Wei, L. M.; Lin, C. F.; Wu, M. J. *Tetrahedron Lett.* **2000**, *41*, 1215. (d) Bruyere, D.; Gaignard, G.; Balme, G.; Lancelin, J. M. *Tetrahedron Lett.* **1997**, *38*, 827. (e) Fournet, G.; Balme, G.; Van Hemebryck, B.; Gore, J. *Tetrahedron Lett.* **1990**, *31*, 5147.

(7) Treatment of 2-hydroxybenzaldehyde with TBDMSCl and imidazole gave compound **6** in 95% yield. Applying phenylacetylene with *n*-BuLi in THF resulted a respective lithium salt. Subsequent exposure the aldehyde **6** to the lithium salt provided the alcohol **7a** in 90% yield. The α,β-unsaturated ketone **1a** was obtained by oxidation of **7a** with MnO_2 in 90% yield.