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Access to 2,3-Disubstituted Benzofurans through One-Pot Acid-Catalyzed Nucleophilic Substitution/TBAF-Mediated Oxacycloisomerization

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An efficient synthetic strategy for the synthesis of diversely 2,3-disubstituted benzofurans is described. This method is based on the use of propargylic alcohols generated from TBS-protected *ortho*-hydroxy benzaldehydes as starting materials and allows a library of 2,3-disubstituted benzofurans to be built. The procedure consists of one-pot nucleophilic substitution, TBS-deprotection, and *exo-dig* cycloisomerization.

Introduction

Substituted benzofurans are an important class of heterocycles that display diverse pharmacological activities.[1] Among these, 2,3-disubstituted benzofurans have garnered considerable attention as synthetic targets due to the presence of their skeleton as an integral part of various biologically active natural products as well as pharmaceutical compounds.[2] For example (Figure 1), (1) the tetracyclic meroterpenoid natural product (+)-liphagal (**I**),[2g] a selective inhibitor of phosphatidylinositol 3-kinase (PI3K), isolated from the Caribbean sponge *Aka coralliphaga*; (2) amiodarone (**II**),[2a,2f] a clinically used drug for controlling intractable cardiac arrhythmias; (3) a phenolic compound (**III**),[2d] which is an inhibitor of testosterone 5α-reductase, isolated from the stems of *Dalbergia cochinchinensis*. In addition, numerous 2,3-disubstituted benzofurans have been reported to possess antifungal, antiviral, antidiabetic, and antiparasitic activities etc.[3] As a result, several methods have been developed for the synthesis of 2,3-disubstituted benzofurans.[4] The majority of the reactions involved intramolecular cyclization of *o*-alkynylphenols or *o*-alkynylphenyl ethers through carbon–oxygen bond formation.[5]

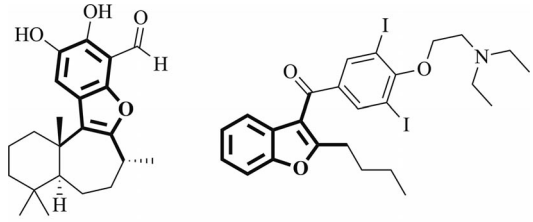

Figure 1. Structures of selected benzofuran-based molecules.

Although these methods offer some advantages, typically they require the use of transition metals either in the cyclization reaction or for the preparation of substrates. Therefore, there is still scope for the development of new methods, especially those that do not require the use of metal catalyst.

π-Activated (benzylic, allylic, and propargylic) alcohols have attracted considerable attention in the direction of green and atom-economy chemistry, because they generate only water as a byproduct in the reaction.[6] Furthermore, their availability and ease of preparation also makes them as an attractive source. The efficacy of π-activated alcohols

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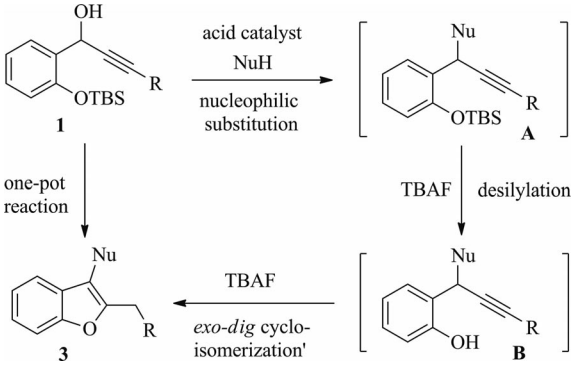
in direct nucleophilic S_N1-type reactions towards carbon–carbon, carbon–nitrogen, and carbon–oxygen bond formation has been demonstrated under different reaction conditions, in particular, in the presence of Lewis or Brønsted acids.[7] Our recent studies have also been focused in this direction for the synthesis of heterocyclic compounds.[8] For instance, C^3-alkylation of 4-hydroxycoumarin to give furanocoumarins,[8a] through *N*-alkylation of tosylhydrazones towards pyrazoles,[8b] alkylation of 1,3-dicarbonyl compounds for various oxygenated heterocycles,[8c] and *O*-alkylation of hydroximides to 2,5-dihydroisoxazoles,[8d] have been successfully demonstrated. In a continuation of this work, we were prompted to explore the use of propargylic alcohols for the synthesis of 2,3-disubstituted benzofurans.

A search of the literature showed that a few methods have been developed to access substituted benzofurans from hydroxyphenylpropargylic alcohols.[9] The first example of benzofuran formation from 1-(2-hydroxyphenyl)-2-yn-1-ol was observed during the deprotection of methylthiomethyl (MTM) ether with $HgCl_2$ in acetonitrile/water under reflux conditions.[9a] Bartolo and co-workers have reported tandem Pd^0-catalyzed carbonylative deallylation/Pd^{II}-catalyzed heterocyclization leading to 2,3-disubstituted benzofurans from 1-(2-allyloxyphenyl)-2-yn-1-ols.[9b–9e] Tian et al. have demonstrated a single example of the one-pot synthesis of benzofuran from 2-(1,3-diphenylprop-2-yn-1-yl)phenol using $ZnCl_2$ (10 mol-%) and TMSCl (50 mol-%) at 70 °C in dichloroethane.[10] Xiaobing Xu et al. have observed the formation of benzofurans/naphthofurans under the action of 10 mol-% $FeCl_3$ and Na_2CO_3 at 135 °C, in their study.[11] However, all these reactions require metal catalysts and, furthermore, they do not easily allow the generation of diversely substituted benzofurans. Herein, we describe a mild and general protocol for the synthesis of diversely 2,3-disubstituted benzofurans through a one-pot reaction under metal-free conditions.

Based on the knowledge that our group has gained in the use of π-activated alcohols and on literature reports on benzofuran synthesis, we envisioned that 2,3-disubstituted benzofurans could be accessible from 1-[(*tert*-butyldimethylsilyloxy)phenyl]-2-yn-1-ol derivatives in a one-pot operation. It was expected that, in the first step, S_N1-nucleophilic substitution of **1** with various nucleophiles in the presence of an acid catalyst would generate intermediate **A**. In a second step, desilylation with tetrabutylammonium fluoride (TBAF) to give intermediate **B** followed by subsequent *exo-dig* oxacycloisomerization would lead to 2,3-disubstituted benzofurans **3** (Scheme 1).



Scheme 1. Proposed strategy for 2,3-disubstituted benzofurans.

Results and Discussion

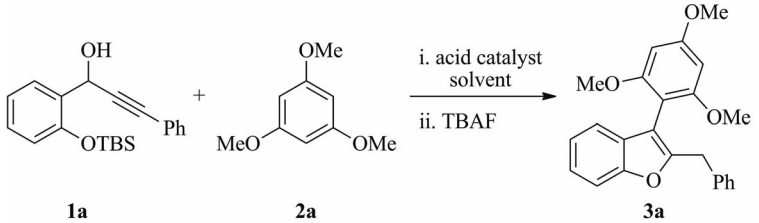
To verify the proposed strategy, we chose to use TBS-protected alkynol **1a**, derived from TBS-protected salicylaldehyde and phenylacetylene using a known procedure,[12] as a model substrate and 1,3,5-trimethoxybenzene (**2a**) as the nucleophile for optimization of reaction conditions (Table 1). Thus, compound **1a** was treated with **2a** in the presence of $BF_3{\cdot}Et_2O$ (5 mol-%) in acetonitrile at room temperature.[13]

After the consumption of both starting materials **1a** and **2a** (reaction monitored by TLC), TBAF in tetrahydrofuran (THF) was added and stirring was continued for 12 h at room temperature, however, the reaction did not provide the expected benzofuran **3a**, instead the isolated product was identified as uncyclized intermediate **3a′**, which was obtained in 97% yield. Thus, the same reaction was conducted by increasing the reaction temperature to reflux after the addition of TBAF; to our delight, the desired cyclized product, benzofuran **3a**, was obtained in 94% yield (Table 1, entry 2). Subsequently, different solvents such as CH_3NO_2 and CH_2Cl_2 were explored for the above one-pot reaction and it was found that acetonitrile was optimal (Table 1, entries 3 and 4). As shown in Table 1, other acid catalysts such as $B(C_6F_5)_3$, *p*TSA, and 10-camphorsulfonic acid (CSA) were also tested for initial nucleophilic substitution and, in all cases, the reaction proceeded to provide the benzofuran **3a** in reasonably good yields (Table 1, entries 5–7). It is important to mention that both the nucleophilic substitution and TBAF-promoted *tert*-butyldimethylsilyl deprotection progressed at room temperature, whereas *exo-dig* oxa-cycloisomerization (benzofuran formation) required heating to reflux temperature. Furthermore, control experiments confirmed that the presence of TBAF was essential for the oxacycloisomerization reaction.[14] Although a few TBAF-mediated heterocyclization reactions are known, to the best of our knowledge, this is the first example for the synthesis of benzofuran formation.[15]

With the standard reaction conditions in hand, we then examined the scope and generality of the method by synthesizing a library of 2,3-disubstituted benzofurans using a range of propargylic alcohols **1a–d** and carbon nucleophiles **2a–d**; the results are summarized in Table 2.

We first explored the use of different nucleophiles for substitution followed by oxacycloisomerization. The reactions of **1a** with electron-rich aromatic nucleophiles, anisole (**2b**) and indole (**2c**), under the established conditions proceeded to give the corresponding 3-aryl-2-benzylbenzofurans **3b** and **3c** in 92 and 88% yields, respectively

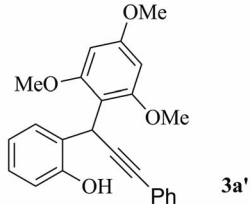
Table 1. Optimization of reaction conditions.



1a **2a** **3a**

Entry[a]	Nucleophilic substitution			TBS-deprotection[b] & *exo-dig* cyclization (2 equiv. 1M TBAF in THF)		
	Catalyst (5 mol-%)	Solvent	Temp. /time (h)	Temp.[b] /time (h)	Product	Yield (%)[c]
1	$BF_3{\cdot}Et_2O$	CH_3CN	r.t. / 0.25	r.t. / 12 h	**3a'**	97
2	**$BF_3{\cdot}Et_2O$**	**CH_3CN**	**r.t. / 0.25**	**reflux / 8 h**	**3a**	**94**
3	$BF_3{\cdot}Et_2O$	CH_3NO_2	r.t. / 0.25	reflux / 12 h	**3a**	86
4	$BF_3{\cdot}Et_2O$	CH_2Cl_2	r.t. / 2	reflux / 8 h	**3a**	90
5	$B(C_6F_5)_3$	CH_3CN	r.t. / 6	reflux / 8 h	**3a**	78
6	*p*TSA	CH_3CN	r.t. / 1	reflux / 8 h	**3a**	75
7	CSA	CH_3CN	r.t. / 1	reflux / 8 h	**3a**	80

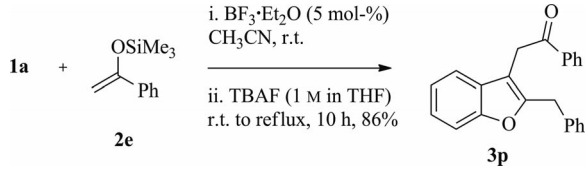
[a]Reactions were carried out under N_2 atmosphere. [b]Reactions were stirred at r.t. for 15 min prior to reflux. [c]Isolated yields after column chromatography.



3a'

(Table 2). Interestingly, the aliphatic nucleophile, allyltrimethylsilane (**2d**), also participated well in the reaction with **1a**, providing the corresponding 3-allyl-2-benzylbenzofuran **3d** in 81% yield. This reaction allowed the synthesis of benzofuran with an sp^3-carbon substituent at the 3-position, which is a significant advantage of the present method (product **3d**; Table 2, entry 1). Subsequently, various propargylic alcohols were explored to obtain the corresponding 2,3-disubstituted benzofurans (Table 2). Accordingly, substrate **1b**, derived from the reaction of 5-bromo-2-hydroxybenzaldehyde with phenylacetylene, was treated with nucleophiles **2a**–**d** to furnish the corresponding benzofurans **3e**–**h** in good yields (Table 2, entry 2). Similarly, propargylic alcohols **1c** and **1d** also effectively participated in the reaction with **2a**–**d** under the described reaction conditions to give 2,3-disubstituted benzofurans **3i**–**o** (Table 2, entries 3 and 4), except for the reaction of **1c** with **2c**, which gave an inseparable mixture of unidentified products. It should be mentioned that, in the case of propargylic alcohol **1c**, the *exo-dig* oxacycloisomerization proceeded at room temperature, which may be due to the presence of electron-withdrawing ester functionality on the alkyne.

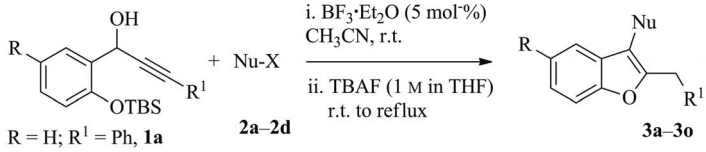
Later, the reactivity of silylenol ether **2e** with **1a** was also tested under the present one-pot reaction conditions and, to our delight, the reaction provided the corresponding benzofuran **3p** in 86% yield (Scheme 2).



Scheme 2. Synthesis of **3p**.

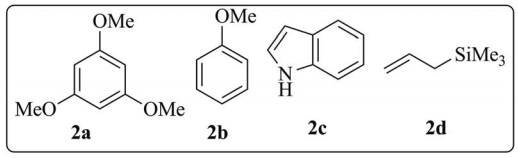
In subsequent studies, we also investigated the reactivity of propargylic alcohols **1e** and **1f**, obtained from the reaction of TBS-protected salicylaldehyde with alkynes derived from Boc-protected prolinol and Garner's aldehyde, with allyltrimethylsilane (**2d**). From these reactions, the corresponding 3-allylbenzofurans **3q** and **3r** were obtained in 74 and 61% yields, respectively (Scheme 3). The reaction of **1e** with **2d** proceeded under the described reaction conditions [Equation (1), Scheme 3], whereas in the case of **1f**, we found that 5 mol-% $B(C_6F_5)_3$ was a suitable acid catalyst for the nucleophilic substitution reaction; see Equation (2) in Scheme 3), because the acid-labile acetonide group was not stable in the presence of $BF_3{\cdot}Et_2O$.

Table 2. One-pot synthesis of 2,3-disubstituted benzofurans.



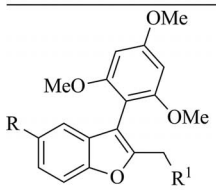
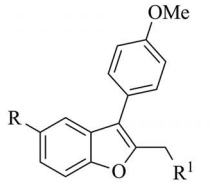
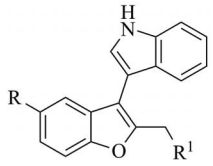
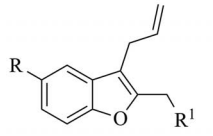
R = H; R^1 = Ph, **1a**
R = Br; R^1 = Ph, **1b**
R = H; R^1 = COOEt, **1c**
R = Br, R^1 = CH_2CH_2OBn, **1d**

2a–2d **3a–3o**

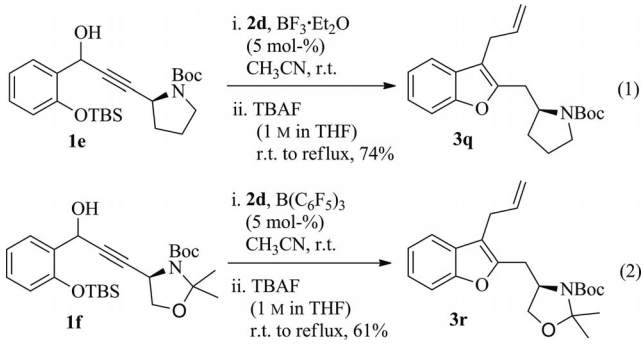


2a **2b** **2c** **2d**

Product[a] / reaction time / yield[b]

	entry 1 (from **1a**)	entry 2 (from **1b**)	entry 3 (from **1c**)	entry 4 (from **1d**)
	R = H R^1 = Ph **3a**, 8 h, 94%	R = Br R^1 = Ph **3e**, 14 h, 86%	R = H R^1 = COOEt **3i**, 12 h, 78%	R = Br R^1 = CH_2CH_2OBn **3l**, 15 h, 83%
	R = H R^1 = Ph **3b**, 12 h, 92%	R = Br R^1 = Ph **3f**, 16 h, 91%	R = H R^1 = COOEt **3j**, 12 h, 92%	R = Br R^1 = CH_2CH_2OBn **3m**, 12 h, 89%
	R = H R^1 = Ph **3c**, 12 h, 88%	R = Br R^1 = Ph **3g**, 14 h, 84%	inseparable mixture of products	R = Br R^1 = CH_2CH_2OBn **3n**, 16 h, 81%
	R = H R^1 = Ph **3d**, 10 h, 81%	R = Br R^1 = Ph **3h**, 10 h, 93%	R = H R^1 = COOEt **3k**, 10 h, 82%	R = Br R^1 = CH_2CH_2OBn **3o**, 10 h, 86%

[a]All the products were characterized by IR, ^{1}H, ^{13}C NMR and MS. [b]Isolated yields after column chromatography.



Scheme 3. Synthesis of **3q** and **3r**.

Conclusions

We have demonstrated a mild and efficient approach for the synthesis of 2,3-disubstituted benzofurans starting from easily accessible 1-[(*tert*-butyldimethylsilyloxy)pheyl]-2-yn-1-ol derivatives. The developed strategy is metal free and proceeds in a one-pot manner involving nucleophilic substitution, TBS-deprotection, followed by *exo-dig* oxacycloisomerization reactions. This approach to diversely 2,3-disubstituted benzofurans complements existing routes and allows the synthesis of new benzofuran derivatives with structural complexity. Importantly sp^3-carbon substitution at the C^3 position of the benzofuran can also be achieved.

Experimental Section

General: ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with 300, 500 or 75 MHz spectrometers. Chemical shifts (δ) are reported in ppm downfield from TMS as internal standard; signal patterns are indicated as follows: s, singlet; d, doublet; dd, doublet of doublet; t, triplet; m, multiplet; br. s, broad singlet. Coupling constants (J) are given in Hz. FTIR spectra were recorded either as KBr thin films or neat. For MS and HRMS, m/z ratios are reported as atomic mass units. All the reagents and solvents were reagent grade and used without further purification unless specified otherwise. Technical grade ethyl acetate and petroleum ether used for column chromatography were distilled prior to use. Column chromatography was carried out by using silica gel (60–120 mesh) packed in glass columns. All the reactions were performed under nitrogen in flame- or oven-dried glassware with magnetic stirring.

General Procedure for the Preparation of TBS-protected Alkynol: To a solution of phenylacetylene (1 mmol) in anhydrous THF (5 mL) was slowly added *n*BuLi (1.6 M in THF, 1.5 mmol) at –78 °C. The reaction mixture was stirred for 45 min, then a solution of the corresponding TBS protected salicylaldehyde (1 mmol) in THF (5 mL) was added to the reaction mixture, which was then stirred at –78 °C for 4 h. After completion of the reaction (monitored by TLC), it was quenched by addition of aq. saturated NH_4Cl (50 mL). The aqueous layer was extracted with ethyl acetate (2 × 50 mL). The combined organic layer was washed with brine (20 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography.

1-[2-(*tert*-Butyldimethylsilyloxy)phenyl]-3-phenylprop-2-yn-1-ol (1a): Colourless liquid. IR (KBr): $\tilde{\nu}_{max}$ = 3428, 2931, 1598, 1488, 1258, 1027, 916, 835, 759, 691 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.60 (d, J = 8.1 Hz, 1 H, Ar), 7.44–7.13 (m, 6 H, Ar), 6.97 (t, J = 7.5 Hz, 1 H, Ar), 6.80 (d, J = 7.5 Hz, 1 H, Ar), 5.84 (d, J = 6.0 Hz, 1 H, CH-O), 2.61 (d, J = 6.0 Hz, 1 H, OH), 1.05 (s, 9 H, *t*Bu-Si), 0.30 [d, J = 2.2 Hz, 6 H, Si-$(CH_3)_2$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.0, 131.6, 131.0, 129.3, 128.3, 128.1, 122.7, 121.4, 88.7, 86.0, 61.3, 29.6, 25.7, –4.1 ppm. MS (ESI): m/z = 361 [M + Na]$^+$. $C_{21}H_{26}O_2Si$ (338.27): calcd. C 74.55, H 7.69; found C 74.67, H 7.58.

1-[5-Bromo-2-(*tert*-butyldimethylsilyloxy)phenyl]-3-phenylprop-2-yn-1-ol (1b): Colourless liquid. IR (KBr): $\tilde{\nu}_{max}$ = 3427, 2931, 1591, 1480, 1270, 1030, 914, 842, 690 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89–7.28 (m, 7 H, Ar), 6.72 (d, J = 8.0 Hz, 1 H, Ar), 5.87 (s, 1 H, CH-O), 1.03 (s, 9 H, *t*Bu-Si), 0.28 [d, J = 5.9 Hz, 6 H, Si-$(CH_3)_2$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.0, 133.2, 132.0, 131.7, 130.8, 128.5, 128.2, 122.3, 120.1, 113.6, 88.0, 86.3, 60.5, 25.7, 18.2, –4.1 ppm. MS (ESI): m/z = 439 [M + Na]$^+$. $C_{21}H_{25}BrO_2Si$ (417.42): calcd. C 60.57, H 6.00; found C 60.49, H 5.96.

Ethyl 4-[2-(*tert*-Butyldimethylsilyloxy)phenyl]-4-hydroxybut-2-ynoate (1c): Colourless liquid. IR (KBr): $\tilde{\nu}_{max}$ = 3481, 2933, 2235, 1713, 1489, 1254, 1019, 919, 839, 756 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47 (d, J = 7.9 Hz, 1 H, Ar), 7.23 (t, J = 7.9 Hz, 1 H, Ar), 6.99 (d, J = 6.9 Hz, 1 H, Ar), 6.85 (d, J = 7.9 Hz, 1 H, Ar), 5.74 (s, 1 H, C*H*-OH), 4.22 (q, J = 6.2, J = 13.8 Hz, 2 H, CH_2-O), 1.29 (t, J = 6.2 Hz, 3 H, CH_3-CH_2), 1.04 (s, 9 H, *t*Bu-Si), 0.31 [s, 6 H, Si-$(CH_3)_2$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.3, 153.0, 129.9, 129.0, 128.1, 121.4, 118.4, 86.3, 61.9, 60.9, 25.7, 18.2, 13.9, –4.0 ppm. MS (ESI): m/z = 361 [M + Na]$^+$. $C_{18}H_{26}O_4Si$ (334.49): calcd. C 64.67, H 7.78; found C 64.71, H 7.69.

5-(Benzyloxy)-1-[5-bromo-2-(*tert*-butyldimethylsilyloxy)phenyl]pent-2-yn-1-ol (1d): Colourless liquid. IR (KBr): $\tilde{\nu}_{max}$ = 3411, 2932, 1590, 1478, 1269, 1107, 1012, 918, 843, 699 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.66 (d, J = 2.4 Hz, 1 H, Ar), 7.33 (m, 5 H, Ar), 6.65 (d, J = 8.6 Hz, 1 H, Ar), 5.50 (s, 1 H, CH_2-O), 4.53 (s, 2 H, CH_2Ar), 3.57 (t, J = 7.1 Hz, 2 H, CH_2-OBn), 2.55 (t, J = 6.7 Hz, 2 H, CH_2-C), 1.02 (s, 9 H, *t*Bu-Si), 0.25 [d, J = 3.9 Hz, 6 H, Si-$(CH_3)_2$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.9, 137.9, 133.5, 131.8, 130.8, 128.3, 127.6, 125.7, 120.0, 113.5, 83.9, 80.2, 72.9, 68.1, 60.0, 28.5, 25.6, 20.2, –4.2, –4.2 ppm. MS (ESI): m/z = 361 [M + Na]$^+$. $C_{24}H_{31}BrO_3Si$ (475.50): calcd. C 60.75, H 6.54; found C 60.82, H 6.63.

(2*S*)-*tert*-Butyl 2-{3-[2-(*tert*-Butyldimethylsilyloxy)phenyl]-3-hydroxyprop-1-ynyl}pyrrolidine-1-carboxylate (1e): Colourless liquid. $[\alpha]_D^{20}$ = –41.2 (c = 1.06, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3406, 2931, 2859, 1677, 1400, 1257 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70–7.53 (br. s, 1 H, Ar), 7.19 (t, J = 7.5 Hz, 1 H, Ar), 6.96 (t, J = 7.5 Hz, 1 H, Ar), 6.81 (d, J = 7.9 Hz, 1 H, Ar), 5.74 (s, 1 H, CH-O), 4.68–4.44 (m, 1 H, CH-N), 3.52–3.24 (m, 2 H, CH_2-N), 2.75–2.63 (br. s, 1 H, OH), 2.12–2.00 (m, 2 H, CH_2-CH_2), 1.94–1.65 (m, 2 H, CH_2-CH_2), 1.43 (s, 9 H, Boc), 1.02 (s, 9 H, *t*Bu-Si), 0.29 (s, 3 H, Si-CH_3), 0.26 (s, 3 H, Si-CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.9, 152.7, 131.2, 129.0, 128.0, 121.2, 118.2, 86.3, 81.0, 79.5, 60.2, 48.1, 45.5, 33.5, 28.3, 25.6, 23.6, 18.0, –4.2, –4.3 ppm. HRMS (ESI): calcd. for $C_{24}H_{37}NO_4SiNa$ [M + Na]$^+$ 454.2384; found 454.2376.

(4*R*)-*tert*-Butyl 4-{3-[2-(*tert*-Butyldimethylsilyloxy)phenyl]-3-hydroxyprop-1-ynyl}-2,2-dimethyloxazolidine-3-carboxylate: (1f): Colourless liquid. $[\alpha]_D^{20}$ = –1.1 (c = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3447, 2932, 2859, 1701, 1601, 1373, 1378, 1256 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64–7.51 (br. s, 1 H, Ar), 7.15 (t, J = 7.5 Hz, 1 H, Ar), 6.94 (t, J = 7.5 Hz, 1 H, Ar), 6.77 (d, J = 7.5 Hz, 1 H, Ar), 5.69 (s, 1 H, CH-O), 4.72–4.50 (m, 1 H, CH-N), 4.08–3.96 (m, 2 H, CH_2-O), 2.54–2.41 (br. s, 1 H, OH), 1.68–1.38 [m, 15 H, Boc, $(CH_3)_2C$], 1.04 (s, 9 H, *t*Bu-Si), 0.28 (s, 3 H, Si-CH_3), 0.27 (s, 3 H, Si-CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.9, 151.4, 131.0, 129.3, 128.0, 121.3, 121.3, 118.4, 94.3, 84.9, 80.2, 68.6, 60.3, 48.6, 28.3, 25.7, 18.1, 14.1, –4.1, –4.2 ppm. HRMS (ESI): calcd. for $C_{25}H_{39}NO_5SiNa$ [M + Na]$^+$ 484.2490; found 484.2458.

2-[3-Phenyl-1-(2,4,6-trimethoxyphenyl)prop-2-ynyl]phenol (3a′): Colourless liquid. IR (KBr): $\tilde{\nu}_{max}$ = 3429, 2939, 1598, 1488, 1217, 1112, 955, 692 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54 (dd, J = 7.5, 7.4 Hz, 1 H, Ar), 7.44–7.21 (m, 6 H, Ar), 7.05 (t, J = 7.3 Hz, 2 H, Ar), 6.77 (q, J = 7.5, 13.2 Hz, 2 H, Ar), 6.12 (s, 1 H, Ar), 5.71 (s, 1 H, CH-C=), 3.90 [s, 6 H, $(OCH_3)_2$Ar] 3.76 (s, 3 H, (OCH_3)-Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.5, 157.7, 154.1, 131.6, 130.1, 128.1, 128.0, 127.6, 125.6, 123.9, 119.6, 116.3, 109.3, 91.8, 89.4, 81.6, 56.0, 55.3, 27.9 ppm. HRMS (ESI): calcd. for $C_{24}H_{23}O_4$ [M + H]$^+$ 375.1591; found 375.1565.

General Procedure for the Preparation of 2,3-Disubstituted Benzofurans: Nucleophile **2a**–**d** (1 mmol) was added to a solution of TBS-protected propargylic alcohols **1a**–**d** (1 mmol) in CH_3CN (10 mL), followed by $BF_3{\cdot}Et_2O$ (5 mol-%). The resulting mixture was stirred at room temperature. After disappearance of both starting materials (reaction monitored by TLC), TBAF (1 M in THF, 2 mmol) was added. The resulting mixture was stirred at room temperature for 15 min, then the temperature was raised to reflux and stirring was continued for the given time (Table 2). After completion of the reaction, the solvent was evaporated in vacuo and the crude product was purified by column chromatography on silica gel (EtOAc/hexanes) to afford the corresponding benzofuran **3a**–**o**.

2-Benzyl-3-(2,4,6-trimethoxyphenyl)benzofuran (3a): White solid; m.p. 106–108 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2929, 2850, 1596, 1454, 1335, 1226, 1142, 1126, 975, 749 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36 (d, J = 8.1 Hz, 1 H, Ar), 7.24–7.03 (m, 8 H, Ar), 6.17 (s, 2 H,

Ar), 3.94 (s, 2 H, CH_2Ar), 3.85 (s, 3 H, OCH_3Ar), 3.64 [s, 6 H, $(OCH_3)_2Ar$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.2, 159.3, 154.3, 153.9, 138.1, 129.8, 128.7, 128.1, 126.0, 122.9, 121.9, 120.4, 110.8, 109.9, 101.6, 90.6, 55.5, 55.3, 33.5 ppm. HRMS (ESI): calcd. for $C_{24}H_{23}O_4$ $[M + H]^+$ 375.1591; found 375.1565.

2-Benzyl-3-(4-methoxyphenyl)benzofuran (3b): White solid; m.p. 131–133 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2836, 1600, 1512, 1454, 1246, 1028, 835, 728, 715, 580 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.51 (dd, J = 6.6, 1.8 Hz, 1 H, Ar), 7.42–7.13 (m, 10 H, Ar), 6.96 (dd, J = 6.7, 2.0 Hz, 2 H, Ar), 4.16 (s, 2 H, CH_2Ar), 3.38 (s, 3 H, OCH_3Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8, 154.2, 152.1, 130.1, 128.5, 128.4, 126.5, 123.8, 122.5, 119.6, 114.2, 111.0 ppm. MS (ESI): m/z = 315 $[M + H]^+$. $C_{22}H_{18}O_2$ (314.38): calcd. C 84.03, H 5.73; found C 84.68, H 5.65.

3-(2-Benzylbenzofuran-3-yl)-1*H*-indole (3c): Brick-red solid; m.p. 124–126 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3397, 2922, 1717, 1598, 1448, 1263, 1084, 924, 805, 736, 580, 507 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.17 (s, 1 H, NH), 7.14 (d, J = 7.5 Hz, 1 H, Ar), 7.48–7.37 (m, 3 H, Ar), 7.28–7.06 (m, 10 H, Ar), 4.17 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.4, 152.8, 138.2, 136.2, 128.5, 126.4, 123.6, 123.0, 122.3, 120.4, 120.3, 119.9, 111.3, 111.0, 107.5, 33.0 ppm. MS (ESI): m/z = 324 $[M + H]^+$. $C_{23}H_{17}NO$ (323.39): calcd. C 85.44, H 5.26, N 4.33; found C 85.33, H 5.23, N 4.64.

3-Allyl-2-benzylbenzofuran (3d): Pale-yellow liquid. IR (KBr): $\tilde{\nu}_{max}$ = 2136, 1639, 1454, 1256, 1089, 913, 745, 708 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.11 (m, 9 H, Ar), 6.01–5.36 (m, 1 H, CH=CH_2), 5.13–5.02 (m, 2 H, CH_2=CH), 4.07 (s, 2 H, CH_2Ar), 3.00 (dd, J = 6.0, 1.5 Hz, 2 H, CH_2-C) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.1, 152.7, 137.7, 135.5, 129.4, 129.3, 126.4, 123.4, 122.0, 119.3, 115.8, 112.8, 110.8, 32.5, 27.9 ppm. MS (ESI): m/z = 247 $[M - H]^-$. $C_{18}H_{16}O$ (248.32): calcd. C 87.09, H 6.45; found C 87.14, H 6.49.

2-Benzyl-5-bromo-3-(2,4,6-trimethoxyphenyl)benzofuran (3e): Yellow solid; m.p. 136–138 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2932, 2838, 1736, 1593, 1453, 1337, 1219, 1130, 1041, 969, 805, 701, 618 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.15 (m, 8 H, Ar), 6.23 (s, 2 H, Ar), 3.96 (s, 2 H, CH_2Ar), 3.87 (s, 3 H, OCH_3Ar), 3.66 [s, 6 H, $(OCH_3)_2Ar$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.5, 159.2, 155.5, 153.1, 137.6, 131.9, 128.6, 128.1, 126.2, 125.7, 123.1, 115.1, 112.2, 109.7, 100.8, 90.7, 55.5, 55.3, 33.5 ppm. HRMS (ESI): calcd. for $C_{24}H_{22}BrO_4$ $[M + H]^+$ 453.0696; found 453.0688.

2-Benzyl-5-bromo-3-(4-methoxyphenyl)benzofuran (3f): Colourless liquid. IR (KBr): $\tilde{\nu}_{max}$ = 2924, 2852, 1596, 1511, 1450, 1250, 1171, 717 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.62 (d, J = 1.5 Hz, 1 H, Ar), 7.38–7.17 (m, 9 H, Ar), 6.97 (d, J = 9.1 Hz, 2 H, Ar), 4.14 (s, 2 H, CH_2Ar), 3.85 (s, 3 H, OCH_3Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 153.5, 153.0, 137.5, 130.9, 130.1, 128.6, 128.4, 126.6, 123.8, 122.4, 117.5, 115.7, 114.4, 112.5, 55.3, 32.8 ppm. MS (ESI): m/z = 391 $[M - H]^-$. $C_{22}H_{17}BrO_2$ (393.28): calcd. C 67.34, H 4.33; found C 67.54, H 4.78.

3-(2-Benzyl-5-bromobenzofuran-3-yl)-1*H*-indole (3g): Red solid; m.p. 152–154 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3405, 2923, 2856, 1722, 1617, 1446, 1332, 1262, 1085, 927, 800, 734 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.21 (s, 1 H, NH), 7.56 (s, 1 H, Ar), 7.50 (d, J = 7.7 Hz, 1 H, Ar), 7.40 (d, J = 8.1 Hz, 1 H, Ar), 7.31 (s, 2 H, Ar), 7.29–7.09 (m, 8 H, Ar), 4.15 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.4, 153.1, 137.8, 136.1, 131.6, 128.5, 128.4, 126.5, 123.1, 122.9, 122.5, 120.2, 119.9, 105.5, 112.4, 11.3, 106.7, 33.0 ppm. HRMS (ESI): calcd. for $C_{23}H_{15}BrNO$ $[M - H]^-$ 400.0343; found 400.0341.

3-Allyl-2-benzyl-5-bromobenzofuran (3h): Yellow liquid. IR (KBr): $\tilde{\nu}_{max}$ = 2922, 1602, 1454, 1256, 1089, 913, 746, 707 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.30 (m, 2 H, Ar), 7.28–7.08 (m, 6 H, Ar), 6.00–5.85 (m, 1 H, CH=CH_2), 5.13–5.01 (m, 2 H, CH=CH_2), 4.06 (s, 2 H, CH_2Ar), 3.42 (d, J = 6.0 Hz, 2 H, CH_2-CH=CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.1, 152.6, 137.7, 135.5, 129.3, 128.5, 126.5, 123.4, 122.0, 119.3, 115.8, 112.8, 110.8, 32.6, 27.9 ppm. MS (ESI): m/z = 325 $[M - H]^-$.

Ethyl 2-[3-(2,4,6-Trimethoxyphenyl)benzofuran-2-yl]acetate (3i): Colourless liquid. IR (KBr): $\tilde{\nu}_{max}$ = 2939, 2840, 1741, 1601, 1454, 1227, 1204, 1155, 1033, 813, 748, 639 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.45 (d, J = 7.7 Hz, 1 H, Ar), 7.30–7.07 (m, 3 H, Ar), 6.21 (s, 2 H, Ar), 4.16 (q, J = 6.9, 14.1 Hz, 2 H, CH_2-O), 3.89 (s, 3 H, OCH_3Ar), 3.73 [s, 6 H, $(OCH_3)_2Ar$], 3.66 (s, 2 H, CH_2C=O), 1.30 (t, J = 6.9 Hz, 3 H, CH_3CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2, 161.3, 159.0, 154.3, 148.1, 129.2, 123.2, 122.9,120.9, 110.9, 101.0, 90.7, 60.8, 55.5, 55.2, 33.8, 14.0 ppm. HRMS (ESI): calcd. for $C_{21}H_{23}O_6$ $[M + H]^+$ 371.1489; found 371.1481.

Ethyl 2-[3-(4-Methoxyphenyl)benzofuran-2-yl]acetate (3j): Colourless liquid. IR (KBr): $\tilde{\nu}_{max}$ = 2922, 2852, 1512, 1453, 1247, 1029, 772, 746 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.21–7.15 (dd, J = 1.7, 7.7 Hz, 1 H), 7.11–7.05 (m, 2 H, Ar), 7.00–6.95 (m, 1 H, Ar), 6.83–6.78 (m, 1 H, Ar), 6.70–6.62 (m, 3 H, Ar), 4.08 (q, J = 7.1, 14.1 Hz, 2 H, CH_2-O), 3.85 (s, 3 H, OCH_3Ar), 3.78 (s, 2 H, CH_2C=O), 1.19 (t, J = 6.98 Hz, 3 H, CH_3CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2, 146.3, 131.4, 130.1, 129.1, 124.2, 122.7, 120.7, 120.5, 119.8, 111.7, 61.4, 55.3, 33.8, 33.4, 29.6, 14.1 ppm. HRMS (ESI): calcd. for $C_{19}H_{18}NaO_4$ $[M + Na]^+$ 333.1097; found 333.1123.

Ethyl 2-(3-Allylbenzofuran-2-yl)acetate (3k): Colourless liquid. IR (KBr): $\tilde{\nu}_{max}$ = 2925, 1741, 1454, 1248, 1186, 1030, 746 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.40 (dd, J = 14.6, 7.8 Hz, 2 H, Ar), 7.25–7.10 (m, 2 H, Ar), 5.94 (m, 1 H, HC=C), 5.16–5.02 (m, 2 H, CH_2C=C), 4.16 (q, J = 7.5, 14.3 Hz, 2 H, CH_2C=), 3.71 (s, 2 H, CH_2C=O), 3.42 (d, J = 6.0 Hz, 2 H, CH_2-O), 1.27 (t, J = 7.5 Hz, 3 H, CH_3CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9, 154.2, 146.7, 135.1, 129.0, 123.8, 122.2, 119.4, 115.9, 114.7, 110.9, 61.2, 32.8, 27.7, 14.0 ppm. HRMS (ESI): calcd. for $C_{15}H_{16}O_3$ $[M + Na]^+$ 267.0992; found 267.0986.

2-[3-(Benzyloxy)propyl]-5-bromo-3-(2,4,6-trimethoxyphenyl)benzofuran (3l): Green solid; m.p. 152–154 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2941, 2838, 1729, 1598, 1502, 1453, 1352, 1228, 1153, 1126, 1097, 967, 805, 748, 699, 623, 523 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.29–7.18 (m, 8 H, Ar), 6.17 (s, 2 H, Ar), 4.38 (s, 2 H, CH_2Ar), 3.85 (s, 3 H, OCH_3Ar), 8.70 [s, 6 H, $(OCH_3)_2Ar$], 3.45 (t, J = 6.9 Hz, 2 H, CH_2=CH_2), 2.71 (t, J = 6.9 Hz, 2 H, CH_2Ar), 1.99 (m, 2 H, CH_2-CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.3, 159.0, 157.3, 141.0, 138.5, 128.2, 127.4, 127.3, 125.3, 122.9, 115.0, 112.0, 90.6, 72.7, 69.5, 55.5, 55.3, 27.4, 24.2 ppm. HRMS (ESI): calcd. for $C_{27}H_{27}NaBrO_5$ $[M + Na]^+$ 533.0939; found 533.0950.

2-[2-(Benzyloxy)ethyl]-5-bromo-3-(4methoxyphenyl)benzofuran (3m): Yellow liquid. IR (KBr): $\tilde{\nu}_{max}$ = 2925, 1725, 1596, 1511, 1452, 1248, 1174, 1105, 765 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.59 (d, J = 1.5 Hz, 1 H, Ar), 7.36–7.17 (m, 9 H, Ar), 6.91 (dd, J = 6.7, 2.2 Hz, 2 H, Ar), 4.39 (s, 2 H, CH_2Ar), 3.82 (s, 3 H, OCH_3Ar), 3.47 (t, J = 6.0 Hz, 2 H, CH_2-O), 2.96 (t, J = 7.5 Hz, 2 H, CH_2-CH), 2.06 (m, 2 H, CH_2-CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.9, 155.4, 152.7, 138.3, 131.1, 130.0, 128.2, 127.5, 126.3, 124.0, 122.1, 116.5, 115.6, 114.3, 112.2, 72.8, 69.0, 55.2, 28.1, 23.4 ppm. MS (ESI): m/z = 473 $[M + Na]^+$. $C_{25}H_{23}BrO_3$ (451.36): calcd. C 66.66, H 5.11; found C 66.73, H 5.13.

3-{2-[3-(Benzyloxy)propyl]-5-bromobenzofuran-3-yl}-1*H*-indole (3n): Dark-brown liquid. IR (KBr):$\tilde{\nu}_{max}$ = 3446, 2924, 2854, 1729, 1459,

1378, 1271, 1122, 1072, 741 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.31 (s, 1 H, NH), 7.54 (s, 2 H, Ar), 7.48 (d, J = 7.7 Hz, 1 H, Ar), 7.37 (d, J = 8.3 Hz, 1 H, Ar), 7.31 (s, 2 H, Ar), 7.28–7.06 (m, 7 H, Ar), 4.13 (s, 2 H, CH_2Ar), 3.44 (t, J = 5.8 Hz, 2 H, CH_2-CH=CH_2), 2.97 (t, J = 7.1 Hz, 2 H, CH_2Ar), 2.05 (m, 2 H, CH_2-CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.2, 153.0, 138.3, 136.2, 131.9, 128.2, 127.5, 127.4, 126.1, 123.1, 122.7, 122.5, 120.1, 120.0, 115.4, 112.2, 111.3, 72.7, 69.1, 28.2, 29.6 ppm. MS (ESI): m/z = 460 $[M + H]^+$. $C_{26}H_{22}BrNO_2$ (460.37): calcd. C 67.97, H 4.79, N 3.05; found C 67.54, H 4.78, N 3.03.

3-Allyl-2-(benzyloxymethyl)-5-bromobenzofuran (3o): Colorless liquid. IR (KBr): $\tilde{\nu}_{max}$ = 2924, 2851, 1720, 1637, 1602, 1451, 1360, 1266, 1198, 1102, 916, 801, 738 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.50 (d, J = 1.9 Hz, 1 H, Ar), 7.32–7.2 (m, 7 H, Ar), 5.94–5.85 (m, 1 H, CH_2=CH_2), 5.10–5.04 (m, 2 H, CH_2=CH_2), 4.47 (s, 2 H, CH_2Ar), 3.46 (t, J = 5.9 Hz, 2 H, CH_2Ar), 3.32 (d, J = 5.9 Hz, 2 H, CH_2-CH=), 2.85 (t, J = 6.9 Hz, 2 H, CH_2-CH=), 2.01 (m, 2 H, CH_2-CH_2) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 155.8, 152.7, 138.3, 135.2, 131.5, 128.3, 127.6, 127.5, 125.9, 121.9, 115.9, 115.1, 112.0, 111.8, 72.9, 69.0, 29.6, 28.1, 27.6, 22.9 ppm. MS (ESI): m/z = 407 $[M + Na]^+$.

2-(2-Benzylbenzofuran-3-yl)-1-phenylethanone (3p): White solid; m.p. 110–113 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2925, 2863, 1724, 1676, 1589, 1444, 1332, 1208, 1093, 985, 877, 744, 685, 581 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.74 (dd, J = 6.7, 1.5 Hz, 2 H, Ar), 7.55–7.33 (m, 5 H, Ar), 7.28–7.10 (m, 7 H, Ar), 4.20 (s, 2 H, CH_2C=O), 4.41 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.2, 154.1, 153.8, 137.0, 136.3, 133.2, 128.6, 128.5, 128.2, 126.6, 123.6, 122.4, 119.1, 110.9, 110.0, 33.9, 32.9 ppm. HRMS (ESI): calcd. for $C_{23}H_{18}NaO_2$ $[M + Na]^+$ 349.1199; found 349.1207.

(*S*)-*tert*-Butyl 2-[(3-Allylbenzofuran-2-yl)methyl]pyrrolidine-1-carboxylate (3q): Colorless liquid. $[\alpha]_D^{20}$ = –19.5 (c = 2.0, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2929, 1692, 1640, 1935 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.46 (d, J = 6.6 Hz, 1 H, Ar), 7.39 (d, J = 7.6 Hz, 1 H, Ar), 7.25–7.14 (m, 2 H, Ar), 6.00–5.91 (m, 1 H, HC=C), 5.15–5.03 (m, 2 H, C=CH_2), 4.23–4.08 (m, 1 H, CH-N), 3.45–3.09 (m, 5 H, CH_2-N, CH_2-C=C, N-CH-CH_2-Ar), 2.97–2.71 (m, 1 H, N-CH-CH_2-Ar), 1.91–1.57 (m, 4 H, CH_2-CH_2), 1.47 (s, 9 H, Boc) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.4, 154.1, 151.9, 135.6, 129.3, 123.3, 122.0, 119.3, 115.7, 113.4, 110.7, 79.4, 56.5, 46.2, 29.6, 28.5, 27.9, 22.6 ppm. MS (ESI): m/z = 364 $[M + Na]^+$.

(*R*)-*tert*-Butyl 4-[(3-Allylbenzofuran-2-yl)methyl]-2,2-dimethyloxazolidine-3-carboxylate (3r): Colorless liquid. $[\alpha]_D^{20}$ = –25.0 (c = 1.1, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2927, 1697, 1638, 1385 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.46 (d, J = 7.9 Hz, 1 H, Ar), 7.39 (d, J = 7.9 Hz, 1 H, Ar), 7.25–7.14 (m, 2 H, Ar), 6.03–5.91 (m, 1 H, HC=C), 5.15–5.04 (m, 2 H, C=CH_2), 4.32–4.13 (m, 1 H, CH-N), 3.95–3.84 (m, 2 H, CH_2-O), 3.47–3.39 (m, 2 H, CH_2-C=), 3.22 (m, 1 H, N-CH-CH_2-Ar), 2.98–2.88 (m, 1 H, N-CH-CH_2-Ar), 1.68–1.44 [m, 15 H, (Boc), $(CH_3)_2C$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.2, 151.3, 151.1*, 135.6, 135.4*, 129.1, 123.5, 123.4*, 122.1, 122.0*, 119.4, 115.8, 115.7*, 113.8, 113.7*, 110.8, 80.2, 79.9*, 66.7, 66.4*, 56.8, 56.5*, 29.6, 29.3*, 28.4, 27.8*, 27.5, 26.9*, 24.4, 23.2* ppm (*asterisk denotes conformer peaks). MS (ESI): m/z = 394 $[M + Na]^+$.

Supporting Information (see footnote on the first page of this article): Copies of ^1H and ^{13}C NMR spectra for all compounds.

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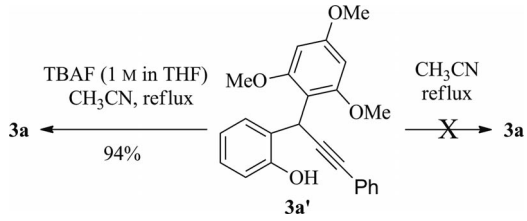
[14] The control experiment was carried out using **3a′** as the starting material. In the presence of TBAF the desired benzofuran **3a** was obtained in 94% yield, whereas in the absence of TBAF no reaction took place.



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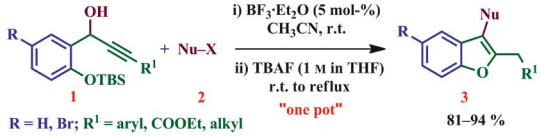

A one-pot method for the synthesis of diversely 2,3-disubstituted benzofurans from propargylic alcohols is described. The strategy involves acid-catalyzed nucleophilic substitution followed by TBAF-mediated desilylative *exo-dig*-oxacycloisomerization.

Keywords: Synthetic methods / Combinatorial chemistry / Cyclization / Nucleophilic substitution / Oxygen heterocycles / Alkynes

