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ONE-POT SYNTHESIS OF (*Z*)-*N*-SUBSTITUTED ISOBENZOFURAN-1(3*H*)-IMINES FROM SECONDARY BENZOTHIOAMIDES AND CARBONYL COMPOUNDS

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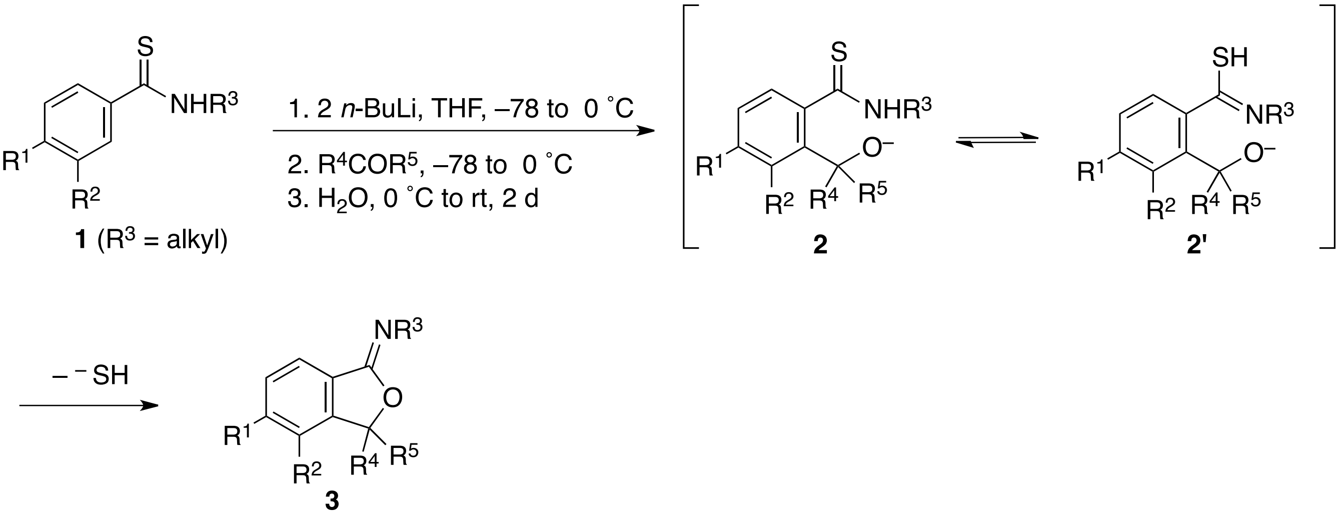
Abstract – An efficient one-pot methodology for the synthesis of (*Z*)-*N*-substituted isobenzofuran-1(3*H*)-imines starting from secondary benzothioamides has been developed. The reaction of the starting materials with two equivalents of butyllithium generated 2,*N*-dilithio-*N*-alkyl(or aryl)benzothioamides, which were then allowed to react with carbonyl compounds to give, after aqueous treatment, the desired products in satisfactory yields.

Isobenzofuran-1(3*H*)-imine derivatives attract respectable attention of synthetic organic and medicinal chemists, because some of these derivatives have been reported to exhibit biological activities.[1] To date, a number of methods for the general preparation of this class of heterocycles have been reported. In 1984, Dordor *et al.* reported the synthesis of *N*-(2-hydroxy-1,1-dimethylethyl)isobenzofuran-1(3*H*)-imines by the reaction of 2-(2-lithiophenyl)-4,4-dimethyloxazolines with carbonyl compounds.[2] Several elegant methods have also been developed recently.[3]

We previously reported the reaction of *N*-alkyl-2,*N*-dilithiobenzothioamides, generated by the treatment of *N*-alkylbenzothioamides with two equivalents of butyllithium, with aldehydes afforded *N*-alkyl-2-(1-hydroxyalkyl)benzothioamides. In this previous work, we demonstrated that these hydroxy-benzothioamides can be transformed into (*Z*)-*N*-alkylbenzo[*c*]thiophen-1(3*H*)-imines or 2-alkyl-2,3-dihydro-1*H*-isoindole-1-thiones upon exposure to methanesulfonyl chloride/triethylamine or sodium hydride/phenyl chloroformate, respectively.[4] We, therefore, became interested in developing a new and concise method for the preparation of isobenzofuran-1(3*H*)-imines through formation of this type of hydroxy-benzothioamides. In this paper, we wish to report the results of our investigation, which offer an efficient methodology for the synthesis of (*Z*)-*N*-substituted isobenzofuran-1(3*H*)-imines (**3**) and (**5**), which involves a one-pot reaction starting from *N*-substituted benzothioamides (**1**) and (**4**), respectively. The one-pot synthesis of (*Z*)-*N*-alkylisobenzofuran-1(3*H*)-imines (**3**) from *N*-alkylbenzothioamides (**1**) was achieved as illustrated in Scheme 1. Thus, *N*-alkyl-2,*N*-dilithiobenzothioamides, generated by the reaction of **1** with two equivalents of butyllithium at –78 to 0 °C (1.5 h), were allowed to react with carbonyl compounds at –78 to 0 °C as described previuously,[4] and a small quantity of water was added. The resulting mixtures stood for two days at rt under stirring to afford, after aqueous workup and the subsequent purification of the crude products by column chromatography on silica gel or recrystallization, (*Z*)-*N*-alkylisobenzofuran-1(3*H*)-imines (**3**). After treatment of the reaction mixture with water, the alkoxides of the resulting 2-(1-hydroxyalkyl)benzothioamides (**2**) are thought to cyclize through the tautomeric intermediates (**2'**) accompanying elimination of lithium hydrogensulfide.



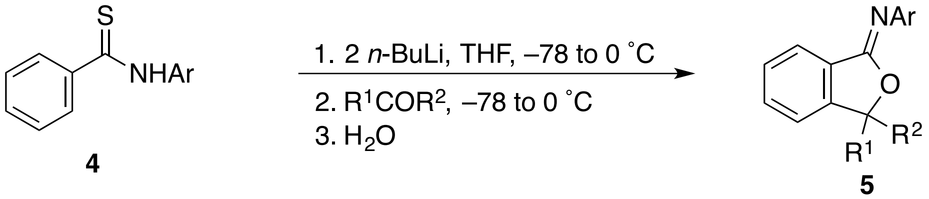
Scheme 1

Table 1. Preparation of (*Z*)-*N*-alkylisobenzofuran-1(3*H*)-imines (**3**)

Entry	**1**	R^1	R^2	R^3	R^4COR^5	**3**	Yield/%[a]
1	**1a**	H	H	Et	PhCHO	**3a**	83
2	**1a**	H	H	Et	4-ClC_6H_4CHO	**3b**	83
3	**1a**	H	H	Et	4-MeOC_6H_4CHO	**3c**	82
4	**1a**	H	H	Et	EtCHO	**3d**	43
5	**1a**	H	H	Et	Ph_2CO	**3e**	74
6	**1b**	H	H	*n*-Bu	PhCHO	**3f**	60
7	**1b**	H	H	*n*-Bu	pyridine-3-carboxaldehyde	**3g**	52
8	**1c**	Cl	H	Et	PhCHO	**3h**	71
9	**1d**	OMe	H	Et	PhCHO	**3i**	72
10	**1e**	H	OMe	Et	PhCHO	**3j**	51

[a] Yields of isolated products.

The results are summarized in Table 1. As can be seen from it, the yields of the products are generally fair to good. Benzophenone and pyridine-3-carboxaldehyde were usable in the present reaction to give the corresponding desired products (**3e**) and (**3g**) in somewhat decreased yields (Entries 5 and 7, respectively). Propanal proved to be also usable, though the yield of the corresponding product (**3d**) is rather lower (Entry 4). However, ketones carrying α-hydrogen(s), such as cyclohexanone and acetophenone, did not work well in the reactions with the dilithium compound from **1a**; no expected product was obtained at all in each case. This could be attributed to the complete deprotonation of α-hydrogen of these ketones with the dilithium compound. These results are not shown in Table 1. In some cases, the cyclization did not complete in the period, and small quantities of the corresponding 2-(1-hydroxyalkyl)benzothioamides were obtained (Entries 6, 7, and 10). When *N*-ethyl-3-methoxybenzothioamide (**1e**) was used, the corresponding desired products (**3j**) was produced with highly regioselectivity; no another possible regioisomeric product was detected in the mixture of this reaction (Entry 10). These results indicate that lithiation took place only at the 2-position of the amide, due to the adjacent orientating methoxy group. The geometry of the 1-*N*-alkylimino moiety of **3** was assumed to be Z on the basis of NOESY analyses. For example, no interaction between the methylene protons of the *N*-ethyl group (δ 3.59) and the proton at the 7-position (δ 7.88) of **3a** could be observed.



Scheme 2

Table 2. Preparation of (*Z*)-*N*-arylisobenzofuran-1(3*H*)-imines (**5**)

Entry	4	Ar	R^1COR^2	5	Yield/%[a]
1	**4a**	Ph	PhCHO	**5a**	63
2	**4a**	Ph	4-ClC_6H_4CHO	**5b**	60
3	**4a**	Ph	4-$MeOC_6H_4CHO$	**5c**	60
4	**4a**	Ph	naphthalene-2-carboxaldehyde	**5d**	58
5	**4a**	Ph	thiophene-3-carboxaldehyde	**5e**	49
6	**4a**	Ph	(*E*)-PhCH=CHCHO	**5f**	46
7	**4a**	Ph	EtCHO	**5g**	40
8	**4a**	Ph	PhCOMe	**5h**	35
9	**4a**	Ph	xanthen-9-one	**5i**	50
10	**4a**	Ph	cyclohexanone	**5j**	32
11	**4b**	4-ClC_6H_4	PhCHO	**5k**	32
12	**4c**	3-$MeOC_6H_4$	PhCHO	**5l**	33

[a] Yields of isolated products.

Next, we were interested in investigating the usability of *N*-arylbenzothioamides (**4**) in the synthesis of (*Z*)-*N*-arylisobenzofuran-1(3*H*)-imines (**5**), and found that the preparation of **5** could be accomplished more conveniently as shown in Scheme 2. Thus, treatment of **4** with butyllithium and carbonyl compounds was carried out as described above and the reaction mixtures were worked up using water as usual. The cyclization occurred spontaneously during work up to give **5**. The yields of **5** are compiled in Table 2. The reaction of 2,*N*-dilithio-*N*-phenylbenzothioamide, generated from *N*-phenylbenzothioamide (**4a**), with an α,β-unsaturated aldehyde, such as cinnamaldehyde, afforded the corresponding products (**5f**) in moderate yield (Entry 6). Apart from the reaction with *N*-ethyl-2,*N*-dilithiobenzothioamide (**1a**), acetophenone and cyclohexanone were successfully used in the reaction with 2,*N*-dilithio-*N*-phenylbenzothioamides to give the corresponding products (**5h**) and (**5j**) albeit in lower yields (Entries 8 and 10, respectively). The lower yields relative to *N*-alkyl derivatives (**3**) can be ascribed to incomplete dilithiation; some quantities of **4** were recovered.

In conclusion, we have demonstrated an efficient one-pot procedure for the preparation of (*Z*)-*N*-substituted isobenzofuran-1(3*H*)-imines from *N*-substituted benzothioamides and carbonyl compounds. The present method may find usefulness in the ready availability of the starting materials as well as the simplicity of the operations.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer Spectrum 65 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 and 125 MHz, respectively. High-resolution MS spectra were measured by a Thermo Scientific Exactive spectrometer (ESI and DART, positive) or a JEOL JMS-T100GCV (EI, TOF; 70eV) spectrometer. Elemental analyses were performed with an Elementar Vario EL II instrument. TLC was carried out on Merck Kieselgel 60 PF_{254}. Column chromatography was performed using WAKO GEL C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

Starting Materials. *N*-Alkylbenzothioamides (**1a–e**) were prepared according to the procedure reported previously by us.[4] *n*-BuLi was supplied by Asia Lithium Corporation. All other chemicals used in this study were commercially available.

***N*-Arylbenzothioamides (4).** These compounds were prepared from PhLi and ArNCS according to the procedure for the preparation of **1a–e**.[4]

***N*-Phenylbenzothioamide (4a):**[5] yield: 75%; a yellow solid; mp 99–101 °C (hexane/CH_2Cl_2) (lit.,[6] 101–102 °C). The ^{1}H and ^{13}C NMR data for this compound was identical to those reported previously.[7]

***N*-(4-Chlorophenyl)benzothioamide (4b):**[8] yield: 73%; a yellow solid; mp 150–153 °C (hexane/CH_2Cl_2) (lit.,[9] 152.5–153.5 °C). The ^{1}H and ^{13}C NMR data for this compound was identical to those reported previously.[9]

***N*-(3-Methoxyphenyl)benzothioamide (4c):**[10] yield: 95%; a yellow solid; mp 90–92 °C (hexane/CH_2Cl_2) (lit.,[11] 92.5–93.5 °C). The ^{1}H and ^{13}C NMR data for this compound was identical to those reported previously.[11]

Typical Procedure for the Preparation of (*Z*)-*N*-Alkylisobenzofuran-1(3*H*)-imines (3). (*Z*)-*N*-Ethyl-3-phenylisobenzofuran-1(3*H*)-imine (3a). To a stirred solution of **1a** (0.17 g, 1.0 mmol) in THF (4 mL) at –78 °C was added *n*-BuLi (1.6 M in hexane; 2.0 mmol) dropwise and the mixture was gradually warmed to 0 °C. After 1.5 h stirring at the same temperature, it was cooled to –78 °C and treated with PhCHO (0.11 g, 1.0 mmol), then temperature was gradually raised to 0 °C and H_2O (0.2 mL) was added. Stirring of the resulting mixture was continued for 2 d at rt before addition of saturated aqueous NH_4Cl (20 mL). The reaction mixture was extracted with AcOEt (3 × 10 mL). The combined extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 to give **3a** (0.20 g, 83%); a white solid; mp 105–107 °C; IR (KBr) 1689, 1610 cm^{-1}; ^{1}H NMR δ 1.30 (t, *J* = 7.4 Hz, 3H), 3.59 (q, *J* = 7.4 Hz, 2H), 6.38 (s, 1H), 7.18 (dd, *J* = 8.0, 2.3 Hz, 1H), 7.27 (d, *J* = 7.4 Hz, 2H), 7.35–7.39 (m, 3H), 7.42–7.46 (m, 2H), 7.88 (dd, *J* = 8.0, 2.9 Hz, 1H); ^{13}C NMR δ 16.0, 41.9, 84.7, 122.2, 123.07, 123.08, 126.8, 128.7, 128.8, 130.2, 131.4, 138.7, 146.4, 158.9. HR-MS (EI). Calcd for $C_{16}H_{15}NO$ (M): 237.1154. Found: *m/z* 237.1147.

3-(4-Chlorophenyl)-(*Z*)-*N*-ethylisobenzofuran-1(3*H*)-imine (3b): a pale-yellow oil; R_f 0.26 (AcOEt/hexane 1:3); IR (neat) 1697, 1613 cm^{-1}; ^{1}H NMR δ 1.28 (t, *J* = 7.4 Hz, 3H), 3.57 (q, *J* = 7.4 Hz, 2H), 6.34 (s, 1H), 7.15 (dd, *J* = 8.0, 2.8 Hz, 1H), 7.21 (d, *J* = 9.2 Hz, 2H), 7.35 (d, *J* = 9.2 Hz, 2H), 7.43–7.47 (m, 2H), 7.87 (dd, *J* = 8.6, 2.7 Hz, 1H); ^{13}C NMR δ 15.9, 41.9, 83.9, 122.1, 123.3, 128.2, 129.0, 129.1, 130.2, 131.5, 134.8, 137.2, 145.9, 158.6. HR-MS (EI). Calcd for $C_{16}H_{14}ClNO$ (M): 271.0764. Found: *m/z* 271.0757.

(*Z*)-*N*-Ethyl-3-(4-methoxyphenyl)isobenzofuran-1(3*H*)-imine (3c): a yellow solid; mp 70–72 °C (hexane/CH_2Cl_2); IR (KBr) 1693, 1611 cm^{-1}; ^{1}H NMR δ 1.28 (t, *J* = 7.4 Hz, 3H), 3.56 (q, *J* = 7.4 Hz, 2H), 3.80 (s, 3H), 6.34 (s, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 7.14–7.18 (m, 3H), 7.42–7.46 (m, 2H), 7.88 (dd, *J* = 7.4, 2.3 Hz, 1H); ^{13}C NMR δ 16.0, 41.8, 55.3, 84.7, 114.2, 122.3, 123.0, 128.6, 128.7, 130.5, 130.7, 131.3, 146.4, 158.9, 160.1. HR-MS (EI). Calcd for $C_{17}H_{17}NO_2$ (M): 267.1259. Found: *m/z* 267.1251.

3,(*Z*)-*N*-Diethylisobenzofuran-1(3*H*)-imine (3d): a yellow oil; R_f 0.20 (AcOEt/hexane 1:3); IR (neat) 1693 cm^{-1}; ^{1}H NMR δ 0.95 (t, *J* = 7.4 Hz, 3H), 1.28 (t, *J* = 7.4 Hz, 3H), 1.74–1.83 (m, 1H), 2.02–2.10 (m, 1H), 3.50–3.61 (m, 2H), 5.44 (t, *J* = 6.3 Hz, 1H), 7.29 (d, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.48 (td, *J* = 7.4, 1.1 Hz, 1H), 7.82 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR δ 8.6, 15.9, 28.3, 41.6, 84.0, 121.1, 123.1, 128.4, 130.96, 131.00, 146.2, 159.4. HR-MS (EI). Calcd for $C_{12}H_{15}NO$ (M): 189.1154. Found: *m/z*

189.1151.

(*Z*)-*N*-Ethyl-3,3-diphenylisobenzofuran-1(3*H*)-imine (3e): a yellow solid; mp 104–106 °C (hexane); IR (KBr) 1698 cm^{-1}; ^{1}H NMR δ 1.31 (t, *J* = 7.4 Hz, 3H), 3.66 (q, *J* = 7.4 Hz, 2H), 7.28–7.34 (m, 11H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.52 (td, *J* = 7.4, 1.1 Hz, 1H), 7.86 (dd, *J* = 7.4, 1.1 Hz, 1H); ^{13}C NMR δ 16.0, 42.0, 92.8, 123.4, 123.7, 127.0, 128.0, 128.3 (2 overlapped Cs), 130.2, 131.2, 142.5, 148.3, 158.0. HR-MS (EI). Calcd for $C_{22}H_{19}NO$ (M): 313.1467. Found: *m/z* 313.1467. Anal. Calcd for $C_{22}H_{19}NO$: C, 84.31; H, 6.11; N, 4.47. Found: C, 86.14; H, 6.05; N, 4.32.

(*Z*)-*N*-Butyl-3-phenylisobenzofuran-1(3*H*)-imine (3f): a yellow solid; mp 80–82 °C (hexane); IR (KBr) 1688, 1612 cm^{-1}; ^{1}H NMR δ 0.94 (t, *J* = 7.4 Hz, 3H), 1.37–1.49 (m, 2H), 1.64–1.70 (m, 2H), 3.55 (t, *J* = 7.4 Hz, 2H), 6.37 (s, 1H), 7.17 (dd, *J* = 6.3, 2.8 Hz, 1H), 7.27 (dd, *J* = 8.0, 1.7 Hz, 2H), 7.33–7.39 (m, 3H), 7.40–7.46 (m, 2H), 7.87 (dd, *J* = 6.3, 2.3 Hz, 1H); ^{13}C NMR δ 14.0, 20.7, 30.1, 47.2, 84.6, 122.2, 123.1 (2 overlapped Cs), 126.8, 128.7, 128.8, 130.2, 131.3, 138.7, 146.4, 158.9. HR-MS (EI). Calcd for $C_{18}H_{19}NO$ (M): 265.1467. Found: *m/z* 265.1475. Anal. Calcd for $C_{18}H_{19}NO$: C, 81.47; H, 7.22; N, 5.28. Found: C, 81.21; H, 7.15; N, 5.29.

(*Z*)-*N*-Butyl-3-(pyridin-3-yl)isobenzofuran-1(3*H*)-imine (3g): a white solid; mp 72–74 °C (hexane); IR (KBr) 1697 cm^{-1}; ^{1}H NMR δ 0.94 (t, *J* = 7.4 Hz, 3H), 1.38–1.44 (m, 2H), 1.64–1.70 (m, 2H), 3.54 (t, *J* = 7.4 Hz, 2H), 6.40 (s, 1H), 7.18 (dd, *J* = 8.0, 2.9 Hz, 1H), 7.29 (dd, *J* = 8.0, 2.9 Hz, 1H), 7.46–7.51 (m, 3H), 7.90 (dd, *J* = 5.2, 3.4 Hz, 1H), 8.60 (d, *J* = 5.2 Hz, 1H), 8.63 (s, 1H); ^{13}C NMR δ 13.9, 20.6, 33.0, 47.2, 82.1, 122.1, 123.3, 123.8, 129.1, 130.2, 131.5, 134.3, 134.5, 145.3, 148.2, 150.2, 158.2. HR-MS (EI). Calcd for $C_{17}H_{18}N_2O$ (M): 266.1419. Found: *m/z* 266.1406. Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.51; H, 6.78; N, 10.50.

5-Chloro-(*Z*)-*N*-ethyl-3-phenylisobenzofuran-1(3*H*)-imine (3h): a white solid; mp 85–87 °C (hexane/CH_2Cl_2); IR (KBr) 1687 cm^{-1}; ^{1}H NMR δ 1.29 (t, *J* = 7.4 Hz, 3H), 3.52–3.62 (m, 2H), 6.33 (s, 1H), 7.15 (d, *J* = 1.1 Hz, 1H), 7.24–7.27 (m, 2H), 7.36–7.42 (m, 4H), 7.79 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR δ 15.9, 42.0, 84.1, 122.6, 124.3, 126.8, 128.8, 129.0, 129.1, 129.4, 137.5, 138.0, 148.0, 157.7. HR-MS (EI). Calcd for $C_{16}H_{14}ClNO$ (M): 271.0764. Found: *m/z* 271.0759. Anal. Calcd for $C_{16}H_{14}ClNO$: C, 70.72; H, 5.19; N, 5.15. Found: C, 70.46; H, 5.14; N, 5.04.

(*Z*)-*N*-Ethyl-5-methoxy-3-phenylisobenzofuran-1(3*H*)-imine (3i): a white solid; mp 138–140 °C (hexane); IR (KBr) 1689, 1606 cm^{-1}; ^{1}H NMR δ 1.28 (t, *J* = 7.4 Hz, 3H), 3.55 (q, *J* = 7.4 Hz, 2H), 3.77 (s, 3H), 6.30 (s, 1H), 6.61 (s, 1H), 6.96 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.27 (d, *J* = 7.4 Hz, 2H), 7.34–7.40 (m, 3H), 7.78 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR δ 16.1, 41.7, 55.6, 84.3, 106.3, 115.9, 122.6, 124.3, 126.9, 128.82, 128.84, 138.6, 148.5, 158.7, 162.6. HR-MS (EI). Calcd for $C_{17}H_{17}NO_2$ (M): 267.1259. Found: *m/z* 267.1261. Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.21; H, 6.49; N, 5.12.

(*Z*)-*N*-Ethyl-4-methoxy-3-phenylisobenzofuran-1(3*H*)-imine (3j): a pale-yellow solid; mp 86–88 °C (hexane/CH_2Cl_2); IR (KBr) 1688, 1605 cm^{-1}; ^1H NMR δ 1.28 (t, *J* = 7.4 Hz, 3H), 3.52–3.59 (m, 2H), 3.69 (s, 3H), 6.39 (s, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 7.26–7.28 (m, 2H), 7.31–7.35 (m, 3H), 7.41 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.46 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR δ 16.0, 41.9, 55.4, 83.7, 112.7, 114.9, 127.2, 128.3, 128.5, 130.7, 132.2, 134.0, 138.0, 154.3, 159.1. HR-MS (EI). Calcd for $C_{17}H_{17}NO_2$ (M): 267.1259. Found: *m*/*z* 267.1260. Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.11; H, 6.41; N, 5.14.

Typical Procedure for the Preparation of (*Z*)-*N*-Arylisobenzofuran-1(3*H*)-imines (5). 3,(*Z*)-*N*-Diphenylisobenzofuran-1(3*H*)-imine (5a). To a stirred solution of **4a** (0.43 g, 2.0 mmol) in THF (7 mL) at –78 °C was added *n*-BuLi (1.6 M in hexane; 4.0 mmol) dropwise and the solution was gradually warmed to 0 °C and stirring was continued for 2 h. Then, the mixture was cooled to –78 °C and PhCHO (0.21 g, 2.0 mmol) was added dropwise. The temperature was again raised to 0 °C and H_2O (20 mL) was added. The mixture was extracted with AcOEt (3 × 10 mL), and the combined extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residual solid was recrystallized from hexane/CH_2Cl_2 to afford **5a** (0.36 g, 63%); a pale-yellow solid; mp 144–146 °C; IR (KBr) 1686 cm^{-1}; ^1H NMR δ 6.45 (s, 1H), 7.08 (t, *J* = 6.9 Hz, 1H), 7.21–7.36 (m, 10H), 7.51 (dd, *J* = 8.0, 2.9 Hz, 2H), 8.02 (dd, *J* = 8.0, 3.4 Hz, 1H); ^{13}C NMR δ 85.8, 122.2, 123.6, 123.9, 124.1, 126.9, 128.6, 128.9, 128.97, 129.00, 130.5, 132.1, 138.0, 146.4, 146.5, 158.2. HR-MS (EI). Calcd for $C_{20}H_{15}NO$ (M): 285.1154. Found: *m*/*z* 285.1140. Anal. Calcd for $C_{20}H_{15}NO$: C, 84.19; H, 5.30; N, 4.91. Found: C, 83.87; H, 5.31; N, 4.83.

3-(4-Chlorophenyl)-(*Z*)-*N*-phenylisobenzofuran-1(3*H*)-imine (5b): a pale-yellow solid; mp 79–81 °C (hexane); IR (KBr) 1682 cm^{-1}; ^1H NMR δ 6.42 (s, 1H), 7.06–7.12 (m, 1H), 7.19–7.23 (m, 3H), 7.30–7.35 (m, 6H), 7.51–7.54 (m, 2H), 8.00–8.04 (m, 1H); ^{13}C NMR δ 85.0, 122.2, 123.5, 124.0, 124.2, 128.4, 128.7, 129.1, 129.2, 130.5, 132.2, 135.0, 136.5, 146.0, 146.2, 157.8. HR-MS (EI). Calcd for $C_{20}H_{14}ClNO$ (M): 319.0764. Found: *m*/*z* 319.0749. Anal. Calcd for $C_{20}H_{14}ClNO$: C, 75.12; H, 4.41; N, 4.38. Found: C, 74.90; H, 4.55; N, 4.37.

3-(4-Methoxyphenyl)-(*Z*)-*N*-phenylisobenzofuran-1(3*H*)-imine (5c): a pale-yellow solid; mp 133–135 °C (hexane/CH_2Cl_2); IR (KBr) 1669, 1611 cm^{-1}; ^1H NMR δ 3.79 (s, 3H), 6.42 (s, 1H), 6.88 (d, *J* = 8.6 Hz, 2H), 7.07 (t, *J* = 6.9 Hz, 1H), 7.17–7.21 (m, 3H), 7.28–7.33 (m, 4H), 7.49–7.53 (m, 2H), 8.01 (dd, *J* = 8.6, 3.4 Hz, 1H); ^{13}C NMR δ 55.3, 88.8, 114.2, 122.3, 123.6, 123.8, 124.0, 128.6, 128.7, 128.9, 129.9, 130.8, 132.1, 146.4, 146.6, 158.3, 160.2. MR-MS (EI). Calcd for $C_{21}H_{17}NO_2$ (M): 315.1259. Found: *m*/*z* 315.1245. Anal. Calcd for $C_{21}H_{17}NO_2$: C, 79.98; H, 5.43; N, 4.44. Found: C, 79.74; H, 5.48; N, 4.40.

3-(Naphthalen-2-yl)-(*Z*)-*N*-phenylisobenzofuran-1(3*H*)-imine (5d): a pale-yellow solid; mp 131–133 °C (hexane/CH_2Cl_2); IR (KBr) 1670 cm^{-1}; ^1H NMR δ 6.62 (s, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 7.23–7.26 (m, 2H), 7.31 (dd, J = 8.0, 7.4 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.50–7.58 (m, 4H), 7.81–7.85 (m, 4H), 8.07 (dd, J = 8.0, 1.7 Hz, 1H); ^{13}C NMR δ 86.1, 122.4, 123.6, 123.97, 124.01, 124.1, 126.6, 126.66, 126.71, 127.8, 128.1, 128.6, 129.0, 129.1, 130.7, 132.2, 133.1, 133.5, 135.2, 146.4, 146.5, 158.3. MR-MS (DART). Calcd for $C_{24}H_{18}NO$ (M+H): 336.1388. Found: *m/z* 336.1375. Anal. Calcd for $C_{24}H_{17}NO$: C, 85.94; H, 5.11; N, 4.18. Found: C, 85.82; H, 5.17; N, 4.07.

(*Z*)-*N*-Phenyl-3-(thiophen-3-yl)isobenzofuran-1(3*H*)-imine (5e): a white solid; mp 124–126 ˚C (hexane/CH_2Cl_2); IR (KBr) 1671, 1612 cm^{-1}; ^{1}H NMR δ 6.55 (s, 1H), 6.91 (dd, J = 4.6, 1.1 Hz, 1H), 7.06–7.10 (m, 1H), 7.28–7.35 (m, 7H), 7.50–7.55 (m, 2H), 8.01 (dd, J = 8.0, 1.7 Hz, 1H); ^{13}C NMR δ 81.4, 122.2, 123.5, 123.9, 124.0, 124.1, 125.9, 126.9, 128.6, 129.1, 130.7, 132.0, 138.7, 145.7, 146.3, 157.9. MR-MS (DART). Calcd for $C_{18}H_{14}NOS$ (M+H): 292.0796. Found: *m/z* 292.0782. Anal. Calcd for $C_{18}H_{13}NOS$: C, 74.20; H, 4.50; N, 4.81. Found: C, 74.06; H, 4.64; N, 4.75.

(*Z*)-*N*-Phenyl-3-((*E*)-2-phenylethenyl)isobenzofuran-1(3*H*)-imine (5f): a yellow viscous oil; R_f 0.20 (AcOEt/hexane 1:9); IR (neat) 1688 cm^{-1}; ^{1}H NMR δ 6.07 (d, J = 8.0 Hz, 1H), 6.15 (dd, J = 15.5, 8.0 Hz, 1H), 6.82 (d, J = 15.5 Hz, 1H), 7.08–7.12 (m, 1H), 7.24–7.44 (m, 10H), 7.51 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.4 Hz, 1H), 8.00 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 85.3, 122.1, 123.4, 124.0, 124.1, 125.1, 126.9, 128.5, 128.65, 128.70, 129.1, 130.8, 132.0, 134.6, 135.6, 145.4, 146.4, 158.1. MR-MS (ESI). Calcd for $C_{22}H_{18}NO$ (M+H): 312.1388. Found: *m/z* 312.1376.

3-Ethyl-(*Z*)-*N*-phenylisobenzofuran-1(3*H*)-imine (5g): a yellow oil; R_f 0.28 (AcOEt/hexane 1:10); IR (neat) 1678 cm^{-1}; ^{1}H NMR δ 0.95 (t, J = 7.4 Hz, 3H), 1.81–1.89 (m, 1H), 2.04–2.13 (m, 1H), 5.54 (dd, J = 6.3, 4.6 Hz, 1H), 7.09–7.12 (m, 1H), 7.32–7.36 (m, 5H), 7.48 (t, J = 7.4 Hz, 1H), 7.55 (td, J = 7.4, 1.1 Hz, 1H), 7.96 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 8.6, 28.0, 85.1, 121.1, 123.5, 123.8, 123.9, 128.6, 128.7, 131.3, 131.8, 146.3, 146.7, 158.7. HR-MS (EI). Calcd for $C_{16}H_{15}NO$ (M): 237.1154. Found: *m/z* 237.1158.

3-Methyl-3,(*Z*)-*N*-diphenylisobenzofuran-1(3*H*)-imine (5h): a pale-yellow oil; R_f 0.30 (AcOEt/hexane 1:10); IR (neat) 1687 cm^{-1}; ^{1}H NMR δ 2.01 (s, 3H), 7.11 (t, J = 7.4 Hz, 1H), 7.28 (t, J = 7.4 Hz, 1H), 7.32–7.36 (m, 5H), 7.39–7.44 (m, 4H), 7.47 (t, J = 7.4 Hz, 1H), 7.52 (ddd, J = 8.0, 7.4, 1.1 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H); ^{13}C NMR δ 27.4, 90.3, 121.6, 123.8, 124.0, 124.1, 125.1, 128.0, 128.58, 128.60, 128.8, 130.0, 132.1, 142.0, 146.5, 150.8, 157.6. HR-MS (EI). Calcd for $C_{21}H_{17}NO$ (M): 299.1310. Found: *m/z* 299.1309.

(*Z*)-*N*-Phenyl-3*H*-spiro[isobenzofuran-1,9'-xanthene]-3-imine (5i): a pale-yellow solid; mp 242–244 ˚C (hexane/CH_2Cl_2); IR (KBr) 1692 cm^{-1}; ^{1}H NMR δ 6.67–6.71 (m, 1H), 6.89 (dd, J = 8.0, 1.1 Hz, 2H), 7.00 (ddd, J = 8.0, 6.9, 1.1 Hz, 2H), 7.06–7.15 (m, 7H), 7.29 (ddd, J = 8.0, 6.9, 1.1 Hz, 2H), 7.53–7.58 (m, 2H), 8.06–8.08 (m, 1H); ^{13}C NMR δ 65.9, 117.0, 119.3, 123.3, 123.9, 124.1, 126.4, 126.9, 128.0, 128.6, 129.2, 129.5, 130.2, 133.8, 136.2, 150.5, 152.6, 166.8. MR-MS (DART). Calcd for $C_{26}H_{18}NO_2$ (M+H):

376.1337. Found: *m/z* 376.1323. Anal. Calcd for $C_{26}H_{17}NO_2$: C, 83.18; H, 4.56; N, 3.73. Found: C, 82.53; H, 4.62; N, 3.69.

(*Z*)-*N*-Phenyl-3'*H*-spiro[cyclohexane-1,1'-isobenzofuran]-3'-imine (5j): a yellow oil; R_f 0.39 (AcOEt/hexane 1:10); IR (neat) 1678 cm^{-1}; ^{1}H NMR δ 1.70–1.89 (m, 10H), 7.11 (t, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.35 (dd, *J* = 8.0, 7.4 Hz, 2H), 7.44–7.47 (m, 3H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.94 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR δ 22.6, 24.9, 36.7, 89.6, 120.5, 123.8, 124.1, 124.2, 128.5, 128.6, 130.6, 131.6, 146.6, 151.3, 157.8. MR-MS (DART). Calcd for $C_{19}H_{20}NO$ (M+H): 278.1545. Found: *m/z* 278.1533.

(*Z*)-*N*-(4-Chlorophenyl)-3-phenylisobenzofuran-1(3*H*)-imine (5k): a pale-yellow solid; mp 160–162 °C (hexane/CH_2Cl_2); IR (KBr) 1700 cm^{-1}; ^{1}H NMR δ 6.47 (s, 1H), 7.22–7.27 (m, 5H), 7.30 (d, *J* = 9.2 Hz, 2H), 7.34–7.39 (m, 3H), 7.50–7.55 (m, 2H), 8.00 (dd, *J* = 8.0, 2.3 Hz, 1H); ^{13}C NMR δ 86.1, 122.3, 123.9, 125.1, 127.0, 128.7, 128.9, 129.10, 129.12, 129.3, 130.4, 132.3, 137.7, 144.9, 146.5, 158.7. MR-MS (DART). Calcd for $C_{20}H_{15}ClNO$ (M+H): 320.0842. Found: *m/z* 320.0828. Anal. Calcd for $C_{20}H_{14}ClNO$: C, 75.12; H, 4.41; N, 4.38. Found: C, 74.87; H, 4.54; N, 4.31.

(*Z*)-*N*-(3-Methoxyphenyl)-3-phenylisobenzofuran-1(3*H*)-imine (5l): a yellow viscous oil; R_f 0.39 (AcOEt/hexane 1:3); IR (neat) 1687 cm^{-1}; ^{1}H NMR δ 3.78 (s, 3H), 6.46 (s, 1H), 6.65 (ddd, *J* = 7.4, 2.3, 1.7 Hz, 1H), 6.90 (t, *J* = 2.3 Hz, 1H), 6.95 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.20–7.29 (m, 4H), 7.32–7.38 (m, 3H), 7.49–7.53 (m, 2H), 8.02 (dd, *J* = 6.9, 2.3 Hz, 1H); ^{13}C NMR δ 55.2, 85.9, 109.1, 110.0, 115.9, 122.3, 123.9, 126.9, 128.9, 128.97, 129.01, 129.3, 130.4, 132.2, 137.8, 146.6, 147.7, 158.5, 159.9. MR-MS (DART). Calcd for $C_{21}H_{18}NO_2$ (M+H): 316.1337. Found: *m/z* 316.1322.

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