Synthesis of (*Z*)-2-[(*Z*)-3-Alkylideneisobenzofuran-1(3*H*)-ylidene]acetic Acid Derivatives by Sequential Coupling–Cyclization between 3-(2-Iodophenyl)-3-oxopropanoic Acid Derivatives and Terminal Alkynes

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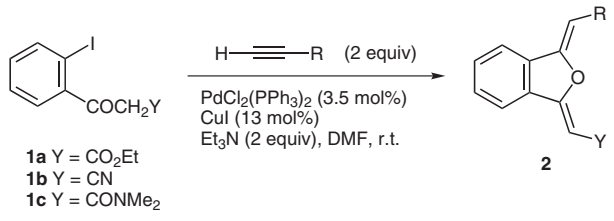
Abstract: 3-(2-Iodophenyl)-3-oxopropanoic acid derivatives reacted efficiently with various terminal alkynes in the presence of catalytic amounts of dichlorobis(triphenylphosphine)palladium and copper(I) iodide and two molar amounts of triethylamine in *N*,*N*-dimethylformamide at room temperature to afford the corresponding (*Z*)-2-[(*Z*)-3-alkylideneisobenzofuran-1(3*H*)-ylidene]acetic acid derivatives in reasonable yields.

Key words: alkynes, coupling, furans, palladium, ring closure

The transition-metal-catalyzed coupling–cyclization sequence between aryl halides carrying an appropriate functional group at the *o*-position and terminal alkynes has been successfully employed for the synthesis of a variety of benzene-fused heterocyclic compounds.[1] We found that ethyl 3-(2-iodophenyl)-3-oxopropanoate (**1a**) and 3-(2-iodophenyl)-3-oxopropanenitrile (**1b**) underwent coupling with terminal alkynes, followed by ring closure, in the presence of catalytic amounts of palladium and copper catalysts to afford the corresponding 3-substituted ethyl (*Z*)-2-[(*Z*)-3-alkylideneisobenzofuran-1(3*H*)-ylidene]acetates and (*Z*)-2-[(*Z*)-3-alkylideneisobenzofuran-1(3*H*)-ylidene]acetonitriles **2**, respectively. 3-Alkylideneisobenzofuran-1(3*H*)-one derivatives have held considerable interest not only for organic chemists, but also for medicinal chemists, because of their biological activity.[2] Accordingly, a number of efficient methods for the preparation of this class of molecules have recently been reported.[3] We now show the results of our investigation, which provide access to vinylogous analogues of 3-alkylideneisobenzofuran-1(3*H*)-one derivatives; these compounds may be biologically interesting, but are not easily available by other routes.



1a Y = CO_2Et
1b Y = CN
1c Y = $CONMe_2$

Scheme 1

For the preparation of (*Z*)-2-[(*Z*)-3-alkylideneisobenzofuran-1(3*H*)-ylidene]acetic acid derivatives **2**, commercially available ethyl 3-(2-iodophenyl)-3-oxopropanoate (**1a**) and 3-(2-iodophenyl)-3-oxopropanenitrile (**1b**), which was easily prepared from commercially available ethyl 2-iodobenzoate and acetonitrile, were allowed to react with terminal alkynes as illustrated in Scheme 1; the results are summarized in Table 1. We first examined the reaction of **1a** with propargyl alcohol under the conditions previously reported by Kundu et al. for the preparation of benzofurans from 2-iodophenol and various terminal alkynes.[4] Thus, a solution of **1a** and propargyl alcohol in *N*,*N*-dimethylformamide containing catalytic amounts of dichlorobis(triphenylphosphine)palladium and copper(I) iodide, and two molar amounts of triethylamine was stirred for 2.5 hours at room temperature. The product, ethyl (*Z*)-2-[(*Z*)-3-(2-hydroxyethylene)isobenzofuran-1(3*H*)-ylidene]acetate (**2a**), was obtained in fair yield after the usual aqueous workup followed by purification of the crude product using preparative TLC on silica gel (Table 1, entry 1). The isobenzofuran structure of this product was confirmed on the basis of its ^{1}H NMR spectrum, which exhibits the signal assignable to the vinyl proton adjacent to the hydroxymethyl group as a triplet (J = 6.4 Hz). This excludes the possibility of the benzopyran structure; the coupling constant between H4 and the methylene of the hydroxymethyl group should be much smaller. The stereochemistry of this compound was determined on the basis of NOE experiments. Thus, an enhancement (9.5%) of the signal at δ = 7.59 assignable to H7 of the isobenzofuran ring was observed on irradiation of the signal at δ = 5.60 assignable to the vinyl proton adjacent to the ethoxycarbonyl group. Irradiation of the signal at δ = 5.68 assignable to the vinyl proton adjacent to the hydroxymethyl group resulted in an enhancement (6.7%) of the signal at δ = 7.61 assignable to H4 of the isobenzofuran ring.

In order to explore the scope of the present palladium-catalyzed sequence, we next examined the reactions of **1a** with a variety of terminal alkynes. When propargyl alcohol derivatives were used as the coupling partner of **1a**, the reactions proceeded more cleanly to afford the corresponding products **2b** and **2c** in good yields (entries 2 and 3). The corresponding products **2d**, **2f**, and **2g** were obtained in moderate to fair yields by using a propargyl ether or propargyl amines (entries 4, 6, and 7, respectively). We may ascribe the lower yield of **2e** by using propargyl ben-

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Table 1 (*Z*)-2-[(*Z*)-3-Alkylideneisobenzofuran-1(3*H*)-ylidene]acetic Acid Derivatives **2**

Entry	Substrates		Time	Product	Yield[a] (%)
	1	R			
1	**1a**	CH_2OH	2.5 h	**2a**	73
2	**1a**	$C(Me)_2OH$	1 d	**2b**	82
3	**1a**	1-hydroxycyclohexyl	40 h	**2c**	75
4	**1a**	CH_2OMe	1 h	**2d**	63
5	**1a**	CH_2OBz	4.5 h	**2e**	34
6	**1a**	CH_2NMe_2	2 h	**2f**	59
7	**1a**	CH_2NMePh	19 h	**2g**	64
8	**1a**	CH_2SPh	3 h	**2h**	44
9	**1a**	[(4,6-dimethylpyrimidin-2-yl)sulfanyl]methyl	19 h	**2i**	48
10	**1a**	Bu	2 d	**2j**	60
11	**1a**	Ph	2 h	**2k**	68
12	**1b**	CH_2OH	1 d	**2l**	47
13	**1b**	1-hydroxycyclohexyl	2 d	**2m**	47
14	**1b**	CH_2OMe	18 h	**2n**	44
15	**1b**	Ph	10 h	**2o**	52
16	**1c**	Ph	20 h	**2p**	0[b]

[a] Isolated yields.
[b] An intractable mixture of products was obtained.

zoate to the leaving-group ability of the benzoyloxy group (entry 5). The reactions using propargyl sulfides were conducted under the same conditions to give the corresponding products **2h** and **2i**, but in somewhat lower yields (entries 8 and 9). Although an aliphatic alkyne, such as hex-1-yne, was sluggish in this coupling–cyclization sequence under the same conditions, the reaction afforded a fair yield of the desired product **2j** (entry 10). Phenylacetylene also worked well in this reaction to give the corresponding products **2k** in fair yield (entry 11). The structure determination of most of these products was achieved in a manner similar to that described for **2a**. Although the structure of the products **2b**, **2c**, and **2k** could not be determined in a similar manner, reasonable chemical shifts of the signals assigned to the vinyl protons of the 3-alkylidene groups supported the isobenzofuran structure.[3h,5] The signals for H4 of the corresponding (2-benzopyran-1-ylidene)acetic acid derivatives would appear at a much lower magnetic field.[3h,5] A limitation of the present method was indicated by the reactions of **1a** with propargyl bromide and methyl acetylenecarboxylate, which gave only intractable mixtures of products.

In order to evaluate the generality of the present isobenzofuran formation, we then examined the palladium-catalyzed reaction of 3-(2-iodophenyl)-3-oxopropanenitrile (**1b**). We found that when compound **1b** was treated with propargyl alcohol, 1-ethynylcyclohexanol, methyl propargyl ether, and ethynylbenzene under the above-mentioned conditions, the corresponding (*Z*)-2-[(*Z*)-3-alkylideneisobenzofuran-1(3*H*)-ylidene]acetonitriles **2l–o** were formed in moderate yields (entries 12–15). Unfortunately, however, the reaction of 3-(2-iodophenyl)-*N*,*N*-dimethyl-3-oxopropanamide (**1c**) with ethynylbenzene under the same reaction conditions resulted in the formation of an intractable mixture of products, from which no more than a trace of the desired products **2p** was isolated (entry 16); we do not have any explanation for this result.

The exclusive formation of the 5-*exo* cyclization products **3** may be ascribed to the basic conditions in the present reactions, because Uchiyama et al. have reported that 2-(2-phenylethynyl)benzoic acid underwent 5-*exo* cyclization under basic conditions to provide 3-benzylideneisobenzofuran-1(3*H*)-one while it underwent 6-*endo* cyclization under acidic conditions to provide 3-phenyl-2-benzopyran-1-one.[5]

In conclusion, we have shown that a palladium-catalyzed coupling–cyclization sequence between 3-(2-iodophenyl)-3-oxopropanoic acid derivatives and terminal alkynes provides an efficient method for the preparation of (*Z*)-2-[(*Z*)-3-alkylideneisobenzofuran-1(3*H*)-ylidene]acetic acid derivatives. Since the method employs readily available starting materials and is experimentally

simple, it may prove useful in organic synthesis. We are now exploring the applicability of the present procedure to the synthesis of related heterocycles.

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were determined with a Shimadzu FTIR-8300 spectrophotometer. ^{1}H NMR spectra were determined in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz. ^{13}C NMR spectra were determined in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz. LR-MS spectra (EI, 70 eV) were measured by a JEOL JMS-AX505 HA spectrometer. TLC was carried out on a Merck Kieselgel 60 PF_{254}. Column chromatography was performed using Merck Kieselgel 60 (0.063–0.200 mm). All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

N-Methyl-*N*-(prop-2-ynyl)aniline was prepared by the reported procedure.[6] All other chemicals used in this study were commercially available.

3-(2-Iodophenyl)-3-oxopropanenitrile (1b)
This compound was obtained by treating ethyl 2-iodobenzoate with an equimolar molar amount of 2-lithioacetonitrile (generated by the action of BuLi upon MeCN in THF at –78 °C) for 15 min as a white solid; yield: 57%; mp 86–88 °C (hexane–CH_2Cl_2).

IR (KBr): 2260, 1690 cm^{-1}.

^{1}H NMR: δ = 4.06 (s, 2 H), 7.23 (ddd, *J* = 8.2, 7.3, 2.3 Hz, 1 H), 7.44–7.55 (m, 2 H), 8.00 (dd, *J* = 8.2, 0.9 Hz, 1 H).

Anal. Calcd for C_9H_6INO: C, 39.88; H, 2.23; N, 5.17. Found: C, 39.76; H, 2.34; N, 5.15.

3-(2-Iodophenyl)-*N*,*N*-dimethyl-3-oxopropanamide (1c)
This compound was obtained by treating ethyl 2-iodobenzoate with *N*,*N*-dimethylacetamide in the presence of NaH in THF at reflux temperature for 2.5 h as a yellow oil as a tautomeric mixture with the corresponding enol amide (ca. 3:7); yield: 47%; R_f = 0.30 (THF–hexane, 1:3).

IR (neat): 3200–2600, 1705, 1628, 1605 cm^{-1}.

^{1}H NMR: δ = 3.00 (s, 1.8 H), 3.06 (s, 4.2 H), 4.10 (s, 0.6 H), 5.51 (s, 0.7 H), 7.07 (ddd, *J* = 7.8, 7.3, 1.4 Hz, 0.7 H), 7.15 (ddd, *J* = 7.8, 7.3, 1.4 Hz, 0.3 H), 7.38 (ddd, *J* = 7.8, 7.3, 1.4 Hz, 0.7 H), 7.43–7.51 (m, 1 H), 7.64 (dd, *J* = 7.8, 1.4 Hz, 0.3 H), 7.91 (dd, *J* = 7.8, 1.4 Hz, 0.7 H), 7.94 (dd, *J* = 7.8, 1.4 Hz, 0.3 H), 8.2–8.9 (br, 0.7 H).

Anal. Calcd for $C_{11}H_{12}INO_2$: C, 41.66; H, 3.81; N, 4.42. Found: C, 41.54; H, 3.82; N, 4.39.

4,6-Dimethyl-2-(prop-2-ynylsulfanyl)pyrimidine
Treatment of 4,6-dimethylpyrimidine-2-thiol with an equimolar amount of propargyl bromide in the presence of an equimolar amount of Et_3N in THF at r.t. for 2 h gave the title compound as a white solid; yield: 71%; mp 29–31 °C (hexane–Et_2O).

IR (KBr): 3211, 2114 cm^{-1}.

^{1}H NMR: δ = 2.17 (t, *J* = 2.7 Hz, 1 H), 2.41 (s, 6 H), 3.96 (d, *J* = 2.7 Hz, 2 H), 6.72 (s, 1 H).

Anal. Calcd for $C_9H_{10}N_2S$: C, 60.64; H, 5.65; N, 15.72. Found: C, 60.53; H, 5.40; N, 15.63.

Ethyl (*Z*)-2-[(*Z*)-3-(2-Hydroxyethylidene)isobenzofuran-1(3*H*)-ylidene]acetate (2a); Typical Procedure
A mixture of ethyl 3-(2-iodophenyl)-3-oxopropanoate (**1a**, 0.23 g, 0.71 mmol), propargyl alcohol (78 mg, 1.4 mmol), and Et_3N (0.14 g, 1.4 mmol) in DMF (2 mL) containing $PdCl_2(PPh_3)_2$ (18 mg, 0.025 mmol) and CuI (18 mg, 0.092 mmol) was stirred at r.t. for 2.5 h. CH_2Cl_2 and H_2O (10 mL each) were added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic layers were washed with 5% aq NaOH (3 × 10 mL) and dried (anhyd $MgSO_4$). After evaporation of the solvent, the residue was separated by column chromatography (silica gel, THF–hexane, 1:10) to give **2a** as a white solid; yield: 0.13 g (73%); mp 99–101 °C (hexane–CH_2Cl_2).

IR (KBr): 3466, 1697, 1684, 1643, 1612 cm^{-1}.

^{1}H NMR: δ = 1.35 (t, *J* = 7.3 Hz, 3 H), 2.24 (t, *J* = 6.0 Hz, 1 H), 4.26 (q, *J* = 7.3 Hz, 2 H,), 4.65 (dd, *J* = 6.4, 6.0 Hz, 2 H), 5.60 (s, 1 H), 5.68 (t, *J* = 6.4 Hz, 1 H), 7.45 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.52 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.59 (d, *J* = 7.8 Hz, 1 H), 7.61 (d, *J* = 7.8 Hz, 1 H).

^{13}C NMR: δ = 14.36, 57.27, 60.03, 88.31, 103.03, 120.23, 121.12, 129.71, 131.55, 132.71, 133.93, 152.46, 161.61, 165.56.

MS: *m*/*z* (%) = 246 (33) [M$^+$], 217 (100).

Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 67.96; H, 5.69.

Ethyl (*Z*)-2-[(*Z*)-3-(2-Hydroxy-2-methylpropylidene)isobenzofuran-1(3*H*)-ylidene]acetate (2b)
White solid; mp 61–64 °C (hexane–Et_2O).

IR (KBr): 3408, 1693, 1681, 1643 cm^{-1}.

^{1}H NMR: δ = 1.36 (t, *J* = 7.3 Hz, 3 H), 1.60 (s, 6 H,), 3.55 (s, 1 H), 4.28 (q, *J* = 7.3 Hz, 2 H), 5.60 (s, 1 H), 5.66 (s, 1 H), 7.45 (ddd, *J* = 7.8, 7.3, 1.4 Hz, 1 H), 7.52 (ddd, *J* = 7.8, 7.3, 0.9 Hz, 1 H), 7.55 (d, *J* = 7.8 Hz, 1 H), 7.60 (d, *J* = 7.8 Hz, 1 H).

MS: *m*/*z* (%) = 274 (15) [M$^+$], 259 (46), 213 (100).

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 69.70; H, 6.82.

Ethyl (*Z*)-2-{(*Z*)-3-[(1-Hydroxycyclohexyl)methylene]isobenzofuran-1(3*H*)-ylidene}acetate (2c)
White solid; mp 100–101 °C (hexane–Et_2O).

IR (KBr): 3396, 3350, 1715, 1692, 1670, 1643 cm^{-1}.

^{1}H NMR: δ = 1.21–1.98 (m, 13 H), 3.61 (s, 1 H), 4.28 (q, *J* = 7.3 Hz, 2 H), 5.59 (s, 1 H), 5.65 (s, 1 H), 7.45 (ddd, *J* = 7.8, 7.3, 0.9 Hz, 1 H), 7.52 (ddd, *J* = 7.8, 7.3, 0.9 Hz, 1 H), 7.57 (d, *J* = 7.8 Hz, 1 H), 7.61 (d, *J* = 7.8 Hz, 1 H).

MS: *m*/*z* (%) = 314 (42) [M$^+$], 267 (81), 225 (100).

Anal. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.40; H, 7.10.

Ethyl (*Z*)-2-[(*Z*)-3-(2-Methoxyethylidene)isobenzofuran-1(3*H*)-ylidene]acetate (2d)
White solid; mp 42–45 °C (hexane–Et_2O).

IR (KBr): 1705, 1688, 1639 cm^{-1}.

^{1}H NMR: δ = 1.37 (t, *J* = 7.3 Hz, 3 H), 3.44 (s, 3 H), 4.27 (q, *J* = 7.3 Hz, 2 H), 4.47 (d, *J* = 7.3 Hz, 2 H), 5.59 (t, *J* = 7.3 Hz, 1 H), 5.61 (s, 1 H), 7.46 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.53 (ddd, *J* = 7.8, 7.3, 1.4 Hz, 1 H), 7.61 (d, *J* = 7.8 Hz, 2 H).

MS: *m*/*z* (%) = 260 (7.2) [M$^+$], 229 (16), 173 (100).

Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20. Found: C, 69.14; H, 6.16.

Ethyl (*Z*)-2-[(*Z*)-3-(2-Benzoyloxyethylidene)isobenzofuran-1(3*H*)-ylidene]acetate (2e)
Pale-yellow solid; mp 95–98 °C (hexane–Et_2O).

IR (KBr): 1701, 1687, 1636 cm^{-1}.

^1H NMR: δ = 1.38 (t, *J* = 7.3 Hz, 3 H), 4.28 (q, *J* = 7.3 Hz, 2 H), 5.34 (d, *J* = 7.3 Hz, 2 H), 5.64 (s, 1 H), 5.75 (t, *J* = 7.3 Hz, 1 H), 7.44 (t, *J* = 7.8 Hz, 2 H), 7.48 (t, *J* = 7.8 Hz, 1 H), 7.53–7.58 (m, 2 H), 7.63 (d, *J* = 7.8 Hz, 2 H), 8.09 (d, *J* = 7.3 Hz, 2 H).

^{13}C NMR: δ = 14.42, 59.37, 60.10, 89.14, 97.69, 120.55, 121.19, 128.34, 129.70, 130.14, 130.17, 131.57, 132.96, 133.33, 133.63, 154.20, 161.26, 165.36, 166.57.

MS: *m*/*z* (%) = 350 (28) [M^+], 245 (76), 199 (100).

Anal. Calcd for $C_{21}H_{18}O_5$: C, 71.99; H, 5.18. Found: C, 72.00; H, 5.06.

Ethyl (*Z*)-2-{(*Z*)-3-[2-(Dimethylamino)ethylidene]isobenzofuran-1(3*H*)-ylidene}acetate (2f)
Yellow oil; R_f = 0.10 (THF–acetone, 1:1).

IR (neat): 1705, 1690, 1647 cm^{-1}.

^1H NMR: δ = 1.37 (t, *J* = 7.3 Hz, 3 H), 2.35 (s, 6 H), 3.46 (d, *J* = 6.9 Hz, 2 H), 4.27 (q, *J* = 7.3 Hz, 2 H), 5.56 (t, *J* = 6.9 Hz, 1 H), 5.58 (s, 1 H), 7.44 (dd, *J* = 8.2, 7.3 Hz, 1 H), 7.52 (ddd, *J* = 8.2, 7.3, 0.9 Hz, 1 H), 7.60 (d, *J* = 8.2 Hz, 2 H).

MS: *m*/*z* (%) = 273 (12) [M^+], 230 (100).

Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.16; H, 6.96; N, 5.04.

Ethyl (*Z*)-2-[(*Z*)-3-{2-[Methyl(phenyl)amino]ethylidene}isobenzofuran-1(3*H*)-ylidene]acetate (2g)
Pale-yellow solid; mp 95–98 °C (hexane–Et_2O).

IR (KBr): 1711, 1688, 1645 cm^{-1}.

^1H NMR: δ = 1.38 (t, *J* = 7.3 Hz, 3 H), 3.03 (s, 3 H), 4.29 (q, *J* = 7.3 Hz, 2 H), 4.47 (d, *J* = 6.9 Hz, 2 H), 5.54 (t, *J* = 6.9 Hz, 1 H), 5.61 (s, 1 H), 6.74 (t, *J* = 7.3 Hz, 1 H), 6.86 (d, *J* = 8.2 Hz, 2 H), 7.25 (dd, *J* = 8.2, 7.3 Hz, 2 H), 7.43 (ddd, *J* = 7.8, 6.9, 0.9 Hz, 1 H), 7.49 (dd, *J* = 7.8, 6.9 Hz, 1 H), 7.52 (d, *J* = 7.8 Hz, 1 H), 7.61 (d, *J* = 7.8 Hz, 1 H).

MS: *m*/*z* (%) = 335 (22) [M^+], 229 (100).

Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 74.84; H, 6.34; N, 4.06.

Ethyl (*Z*)-2-{(*Z*)-3-[3-(Phenylsulfanyl)ethylidene]isobenzofuran-1(3*H*)-ylidene}acetate (2h)
Yellow viscous oil; R_f = 0.33 (THF–hexane, 1:10).

IR (neat): 1709, 1688, 1651 cm^{-1}.

^1H NMR: δ = 1.37 (t, *J* = 7.3 Hz, 3 H), 4.08 (d, *J* = 8.2 Hz, 2 H), 4.29 (q, *J* = 7.3 Hz, 2 H), 5.52 (t, *J* = 8.2 Hz, 1 H), 5.58 (s, 1 H), 7.13 (tt, *J* = 7.3, 1.4 Hz, 1 H), 7.23 (dd, *J* = 8.2, 7.3 Hz, 2 H), 7.40–7.46 (m, 3 H), 7.48 (ddd, *J* = 7.8, 7.3, 0.9 Hz, 1 H), 7.53 (d, *J* = 7.8 Hz, 1 H), 7.57 (d, *J* = 7.8 Hz, 1 H).

MS: *m*/*z* (%) = 338 (4.5) [M^+], 229 (100).

Anal. Calcd for $C_{20}H_{18}O_3S$: C, 70.98; H, 5.36. Found: C, 70.71; H, 5.50.

Ethyl (*Z*)-2-[(*Z*)-3-{2-[(4,6-Dimethylpyrimidin-2-yl)sulfanyl]ethylidene}isobenzofuran-1(3*H*)-ylidene]acetate (2i)
White solid; mp 86–87 °C (hexane–Et_2O).

IR (KBr): 1713, 1686, 1655 cm^{-1}.

^1H NMR: δ = 1.36 (t, *J* = 7.3 Hz, 3 H), 2.41 (s, 6 H), 4.27 (q, *J* = 7.3 Hz, 2 H), 4.30 (d, *J* = 7.8 Hz, 2 H), 5.60 (s, 1 H), 5.73 (t, *J* = 7.8 Hz, 1 H), 6.70 (s, 1 H), 7.42 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.49 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.55 (d, *J* = 7.8 Hz, 1 H), 7.60 (d, *J* = 7.8 Hz, 1 H).

^{13}C NMR: δ = 14.43, 23.85, 26.69, 59.93, 88.13, 100.88, 115.66, 120.15, 121.13, 129.43, 131.36, 133.00, 134.11, 152.63, 161.73, 165.58, 167.06, 170.74.

MS: *m*/*z* (%) = 368 (48) [M^+], 229 (100).

Anal. Calcd for $C_{20}H_{20}N_2O_3S$: C, 65.20; H, 5.47; N, 7.60. Found: C, 64.87; H, 5.72; N, 7.47.

Ethyl (*Z*)-2-[(*Z*)-3-Pentylideneisobenzofuran-1(3*H*)-ylidene]acetate (2j)
Pale-yellow viscous oil; R_f = 0.23 (THF–hexane, 1:20).

IR (neat): 1713, 1686, 1645 cm^{-1}.

^1H NMR: δ = 0.95 (t, *J* = 7.3 Hz, 3 H), 1.36 (t, *J* = 7.3 Hz, 3 H), 1.43 (sextet, *J* = 7.3 Hz, 2 H), 1.53 (quint, *J* = 7.3 Hz, 2 H), 2.55 (dt, *J* = 7.8, 7.3 Hz, 2 H), 4.25 (q, *J* = 7.3 Hz, 2 H), 5.47 (t, *J* = 7.8 Hz, 1 H), 5.55 (s, 1 H), 7.39 (ddd, *J* = 7.8, 7.3, 0.9 Hz, 1 H), 7.49 (ddd, *J* = 7.8, 7.3, 0.9 Hz, 1 H), 7.55 (d, *J* = 7.8 Hz, 1 H), 7.58 (d, *J* = 7.8 Hz, 1 H).

MS: *m*/*z* (%) = 272 (100) [M^+].

Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.72; H, 7.52.

Ethyl (*Z*)-2-[(*Z*)-3-Benzylideneisobenzofuran-1(3*H*)-ylidene]acetate (2k)
Pale-yellow solid; mp 94–95 °C (hexane–Et_2O).

IR (KBr): 1678, 1639 cm^{-1}.

^1H NMR: δ = 1.45 (t, *J* = 7.3 Hz, 3 H), 4.36 (q, *J* = 7.3 Hz, 2 H), 5.69 (s, 1 H), 6.33 (s, 1 H), 7.29 (t, *J* = 7.3 Hz, 1 H), 7.43–7.47 (m, 3 H), 7.56 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.66 (d, *J* = 8.2 Hz, 1 H), 7.71 (d, *J* = 7.8 Hz, 1 H), 8.02 (d, *J* = 7.3 Hz, 2 H).

MS: *m*/*z* (%) = 292 (92) [M^+], 220 (100).

Anal. Calcd for $C_{19}H_{16}O_3$: C, 78.06; H, 5.52. Found: C, 77.89; H, 5.54.

(*Z*)-2-[(*Z*)-3-(2-Hydroxyethylidene)isobenzofuran-1(3*H*)-ylidene]acetonitrile (2l)
Pale-yellow solid; mp 148–149 °C (hexane–CH_2Cl_2).

IR (KBr): 3450, 3384, 2208, 1641 cm^{-1}.

^1H NMR: δ = 1.69 (s, 1 H), 4.65 (d, *J* = 6.9 Hz, 2 H), 5.00 (s, 1 H), 5.72 (t, *J* = 6.9 Hz, 1 H), 7.49 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.58 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.60 (d, *J* = 7.8 Hz, 1 H), 7.64 (d, *J* = 7.8 Hz, 1 H).

MS: *m*/*z* (%) = 199 (32) [M^+], 170 (100).

Anal. Calcd for $C_{12}H_9NO_2$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.34; H, 4.51; N, 6.91.

(*Z*)-2-{(*Z*)-3-[(1-Hydroxycyclohexyl)methylene]isobenzofuran-1(3*H*)-ylidene}acetonitrile (2m)
Pale-yellow solid; mp 88–92 °C (hexane–Et_2O).

IR (KBr): 3420, 2210, 1641, 1614 cm^{-1}.

^1H NMR: δ = 1.39–1.98 (m, 10 H), 2.48 (s, 1 H), 4.99 (s, 1 H), 5.66 (s, 1 H), 7.47 (ddd, *J* = 7.8, 6.9, 1.8 Hz, 1 H), 7.55–7.60 (m, 3 H).

MS: *m*/*z* (%) = 267 (61) [M^+], 224 (100).

Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.39; H, 6.68; N, 5.19.

(*Z*)-2-[(*Z*)-3-(2-Methoxyethylidene)isobenzofuran-1(3*H*)-ylidene]acetonitrile (2n)
Pale-yellow solid; mp 77–79 °C (hexane–CH_2Cl_2).

IR (KBr): 2210, 1645 cm^{-1}.

^{1}H NMR: δ = 3.44 (s, 3 H), 4.42 (d, *J* = 7.3 Hz, 2 H), 4.99 (s, 1 H), 5.64 (t, *J* = 7.3 Hz, 1 H), 7.49 (t, *J* = 7.8 Hz, 1 H), 7.58 (t, *J* = 7.8 Hz, 1 H), 7.60 (d, *J* = 7.8 Hz, 1 H), 7.63 (d, *J* = 7.8 Hz, 1 H).

MS: *m*/*z* (%) = 213 (58) [M$^+$], 182 (100).

Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.23; H, 5.20; N, 6.57. Found: C, 73.18; H, 5.10; N, 6.48.

(*Z*)-2-[(*Z*)-3-Benzylideneisobenzofuran-1(3*H*)-ylidene]acetonitrile (2o)

Pale-yellow solid; mp 97–99 °C (hexane–Et_2O).

IR (KBr): 2205, 1637, 1614 cm^{-1}.

^{1}H NMR: δ = 5.07 (s, 1 H), 6.36 (s, 1 H), 7.31 (t, *J* = 7.3 Hz, 1 H), 7.45 (t, *J* = 7.3 Hz, 2 H), 7.49 (ddd, *J* = 7.8, 7.3, 0.9 Hz, 1 H), 7.61 (ddd, *J* = 7.8, 7.3, 0.9 Hz, 1 H), 7.64 (d, *J* = 7.8 Hz, 1 H), 7.72 (d, *J* = 7.8 Hz, 1 H), 7.88 (d, *J* = 7.3 Hz, 2 H).

^{13}C NMR: δ = 66.05, 104.77, 116.01, 120.10, 121.20, 128.02, 128.88, 129.59 (two overlapped C's), 129.79, 132.27, 133.31, 135.89, 149.68, 167.01.

MS: *m*/*z* (%) = 245 (100) [M$^+$].

Anal. Calcd for $C_{17}H_{11}NO$: C, 83.25; H, 4.52; N, 5.71. Found: C, 83.09; H, 4.54; N, 5.69.

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