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Palladium-Catalyzed Regioselective 5-*exo*-*O*-Cyclization/Oxidative Heck Cascades from *o*-Alkynylbenzamides and Electron-Deficient Alkenes

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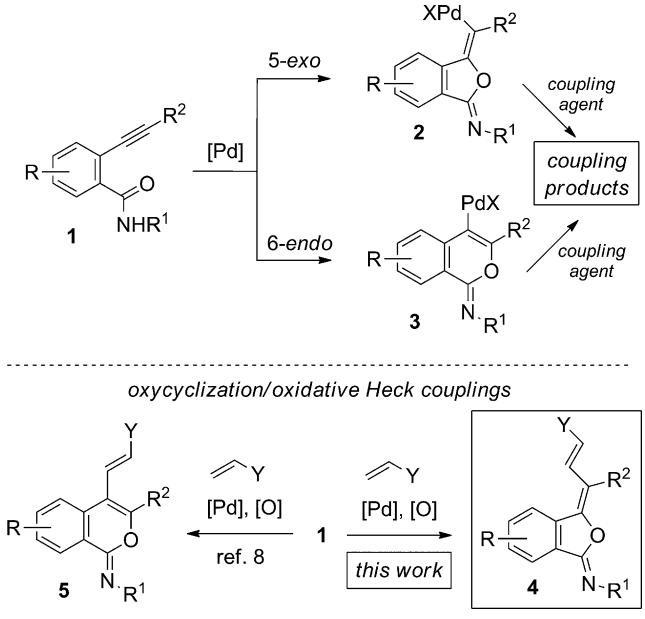
Dedicated to the memory of Professor Alan R. Katritzky

Keywords: Homogeneous catalysis / Palladium / Cyclization / Cross-coupling / Regioselectivity / Oxygen heterocycles

A Pd-catalyzed 5-*exo*-selective oxycyclization/oxidative Heck coupling cascade is described, starting from readily available *ortho*-alkynylbenzamides and functionalized olefins. The key to a high regioselectivity in the cyclization step is the choice of catalyst and/or additives. Thus, $Pd(OAc)_2$ provides the desired 5-*exo* products predominantly, whereas with $PdCl_2$ or $Pd(TFA)_2$, the corresponding 6-*endo* products prevail. The subsequent oxidative Heck-type coupling takes place stereoselectively with the very predominant formation of *E* isomers, leading to an effective preparation of structurally diverse carbonyl-substituted allylideneisobenzofuranimines.

Introduction

Metal-catalyzed intramolecular additions of heteroatom-based nucleophiles onto C–C triple bonds have found widespread application in the synthesis of a variety of heterocyclic derivatives that often have useful properties, or at least are related to products with known practical applications.[1] The merits of this type of strategy in the construction of complex molecules are even more evident when the metal-promoted cyclization is followed by an additional coupling to an external reagent.[2] Further interest stems from the possibility of gaining access to different families of products, using the same starting materials, by exercising efficient control over the regiochemistry (*exo*/*endo*) of the cyclization.[3] Thus, for substrates of the *o*-alkynylbenzamide type (**1** in Scheme 1), the formation of isofuranimine- and isochromenimine-derived products has been reported, presumably arising from the corresponding intermediate palladium complexes **2** and **3** as a result of 5-*exo*- and 6-*endo*-*O*-cyclizations, respectively. In fact, such palladium-catalyzed heterocyclization/coupling cascade reactions of substrates **1** have been shown to be very regioselective. For example, products derived from the 5-*exo*-heterocyclization mode were obtained with aryl halide coupling agents.[4] Similarly, oxidative dimerization[5] and oxidative coupling to an *o*-alkynylaniline[6] or carbon monoxide[7] are also 5-*exo*-selective reactions. On the other hand, the corresponding oxidative coupling reactions of *o*-alkynylbenzamides with electron-deficient alkenes have provided products **5** derived from 6-*endo*-cyclizations.[8–10] Significantly, no example of a re-



Scheme 1. Palladium-catalyzed oxycyclization/coupling reactions of *o*-alkynylbenzamides.

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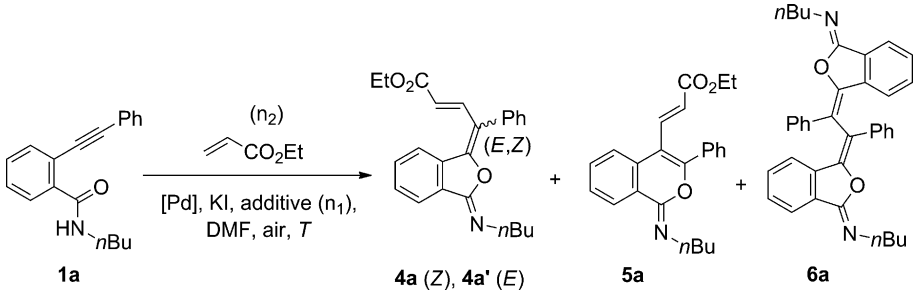
gioselectivity switch between the two modes (*exo*/*endo*) of cyclization has been described in the literature for a particular type of coupling agent starting from *o*-alkynylbenzamides.

In this paper, we describe a palladium-catalyzed 5-*exo*-*dig*-selective *O*-cyclization/oxidative-Heck cascade from *o*-alkynylbenzamides and electron-deficient alkenes, leading to the formation of products **4**, whose isobenzofuranimine core structure has been the subject of significant synthetic attention in recent years.[4–7,11] These results complement previous related work where, under modified conditions, the regiochemistry of cyclization was 6-*endo*.[8–10] Remarkably, the regioselectivity change from *endo* to *exo* is triggered by the presence of carboxylate or carbonate anions in the reaction medium. Finally, in selected cases, hydrolysis of the imino functionality of products **4** has been undertaken to demonstrate the potential of the method to also provide a route to the corresponding lactone derivatives.

Results and Discussion

A survey of reaction conditions was conducted with a representative substrate **1a** (Table 1). Standard conditions for regioselective 6-*endo*-*O*-cyclization/intermolecular Heck-coupling cascades involve treatment of a substrate **1** with a catalytic amount of $PdCl_2(PPh_3)_2$ (5 mol-%), KI (0.5 equiv.), and excess ethyl acrylate in DMF at 80 °C under an air atmosphere. As shown in Table 1, entry 1, isochromenimine **5a** was obtained exclusively under those conditions.[8] In related work where the Heck-type coupling was intramolecular, the formation of regioisomeric side-products was noticed when the coupling reactions were carried out in the presence of Et_3N.[9] Therefore, the conditions of Table 1, entry 1 were modified by adding one equivalent of Et_3N. This resulted in the formation of a small amount of a 5-*exo*-cyclization-derived product **4a**, accompanying the major product **5a** (Table 1, entry 2). Increasing the amount of Et_3N fivefold had only a modest effect on the amount of **4a** produced (Table 1, entry 3), whereas the alternative use of the stronger amine base DBN (1,5-diazabicyclo[4.3.0]-non-5-ene) resulted in cycloisomerization of the starting **1a** and formation of an isoindolone-type product **7a** (Table 1, entry 4, Figure 1). A control experiment revealed that this *N*-cyclization was not catalyzed by Pd^{II}, and that cycloisomerization was probably promoted by a Brönsted base/Brönsted acid couple.[12] On the other hand, the addition of a small amount (10%) of other additives (KOBz, NaOAc, K_2CO_3) produced a more pronounced increase in the relative amounts of 5-*exo*-cyclization-derived products (Table 1, entries 5–7). The best overall *exo*/*endo* ratio was obtained with K_2CO_3 (Table 1, entry 7), but this reaction was complicated by competing cycloisomerization, and also gave a relatively low *Z*/*E* ratio at the exocyclic C=C bond. In those three reactions, the formation of oxidative dimerization

Table 1. Representative experiments in the optimization of the reaction conditions.[a]



1a **4a** (*Z*), **4a'** (*E*) **5a** **6a**

	[Pd]	additive (n_1)	n_2	T	**4a**,**4a′**[b]	**5a**	**6a**
1	$PdCl_2(PPh_3)_2$	–	6	80	–	82[c]	–
2	$PdCl_2(PPh_3)_2$	Et_3N (1)	6	80	8 (80:20)	86[c]	2
3	$PdCl_2(PPh_3)_2$	Et_3N (5)	6	80	12 (82:18)	82	[d]
4	$PdCl_2(PPh_3)_2$	DBN (5)	6	80	[e]	–	–
5	$PdCl_2(PPh_3)_2$	KOBz (0.1)	6	80	40 (77:23)	53	5
6	$PdCl_2(PPh_3)_2$	NaOAc (0.1)	6	80	49 (87:13)	34	13
7	$PdCl_2(PPh_3)_2$	K_2CO_3 (0.1)	6	80	67 (78:22)[e]	15[e]	10[e]
8	$Pd(OAc)_2/PPh_3$	–	6	80	52 (89:11)	8	34
9	$Pd(TFA)_2/PPh_3$	–	6	80	1.5 (*Z*)	91	–
10	$Pd(OAc)_2/PPh_3$	DMAP (0.05)	10	80	67 (91:9)	9	22
11	$Pd(OAc)_2/PPh_3$	DMAP (0.01)	20	35	75 (97:3)	6	18

[a] Reaction conditions: A solution of **1a**, palladium complex [Pd] (5 mol-% relative to **1a**), PPh_3 (where appropriate, 10 mol-%), KI (0.5 equiv.), an additive (where appropriate, n_1 = number of equivalents), and ethyl acrylate (n_2 = number of equivalents) in DMF (8.5 mL/mmol) was heated at the indicated temperature (T) [°C] under an air atmosphere. Unless otherwise indicated, the yields [%] were determined by ^{1}H NMR spectroscopy using an internal standard. [b] Combined yield of **4a** and **4a′**. In parentheses, **4a**/**4a′** ratio. [c] Isolated yield. Where indicated, the values for the other products were estimated using this yield in combination with the crude ratios measured by ^{1}H NMR spectroscopy. [d] Detected by ^{1}H NMR spectroscopy in the crude product but not quantified. [e] Isoindolone **7a**[13] was obtained (69% in entry 4, 7% in entry 7).

product **6a** was also observed. The preparation of products of type **6** from *o*-alkynylbenzamides **1** has recently been reported in the literature under the combined action of catalytic Pd^{II} and Cu^{II}.[5] Not surprisingly, $Pd(OAc)_2/PPh_3$, without added acetate anion, triggered a very predominant 5-*exo*-cyclization (Table 1, entry 8), with an overall *exo*/*endo* ratio of 91:9 (including the formation of **6a**). However, similar use of $Pd(TFA)_2/PPh_3$ (TFA = trifluoroacetate) gave almost no change relative to $PdCl_2(PPh_3)_2$ (Table 1, entry 9, *exo*/*endo* = 2:98). It was found that the use of small amounts of DMAP (4-dimethylaminopyridine) improved the **4a**/**5a** ratio and, in combination with an increase in the amount of alkene, also resulted in the formation of smaller amounts of dimer **6a** (Table 1, entry 10). Finally, a reasonable compromise between the different selectivities at play was reached by using 20 equiv. of alkene with just 1 mol-% of DMAP at 35 °C (Table 1, entry 11). Under these conditions, **4a** was isolated in 73% yield (see also Table 2, entry 1).

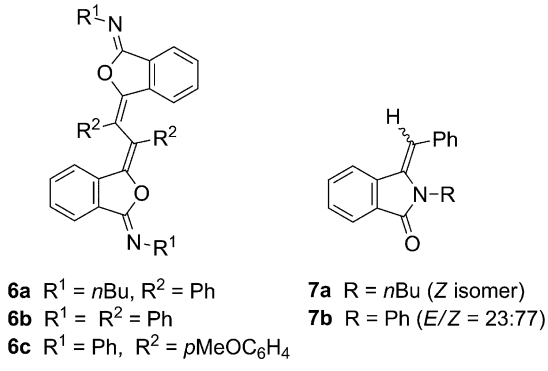
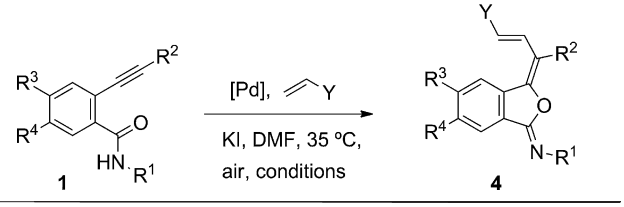


Figure 1. Cycloisomerization and oxidative dimerization products obtained in the reactions of **1**.

Next, the generality of the 5-*exo*-*O*-cyclization/Heck coupling cascade was studied with a representative set of *o*-alkynylbenzamides **1** and electron-deficient alkenes, using the conditions of Table 1, entry 11 as standard. These results are collected in Table 2. The effect of the structure of substrate **1** was probed by introducing all of the four possible combinations of alkyl- and aryl-type substituents at R^1 and R^2, located at the carboxamide amino group and the terminal alkyne position, respectively (Table 2, entries 1–3, 7–8, and 10–13). Additional substitution with either electron-donating (OMe) or electron-withdrawing (Cl) groups was made on the benzamide aryl ring of substrates **1** (Table 2, entries 5 and 6). Besides ethyl acrylate, the use of methyl vinyl ketone as the alkene partner is also illustrated (Table 2, entries 4 and 9). Interestingly, the two reactions with methyl vinyl ketone took place without complications arising from competing hydroarylation processes.[8] In all cases, the expected products **4** were obtained in preparatively useful isolated yields with high regio- and stereoselectivities. Thus, the indicated diene stereoisomer was formed almost exclusively, with traces of other isomers being observed in the crude product but not isolated. The alternative 6-*endo* regioisomers **5** were usually obtained as minor (≤10%) side-products, and the oxidative dimerization products related to **6** were absent in most cases. The standard conditions were found to be efficient, with just two exceptions that needed some degree of adjustment. One was the case of alkyl/alkyl substitution at R^1 and R^2 (substrate **1b**), which gave a comparatively low regioselectivity. Thus, under the standard conditions, a 61:39 **4b**/**5b** ratio was obtained. However, this improved to 83:17 when K_2CO_3 (10 mol-%) was used as additive with a $PdCl_2(PPh_3)_2$ precatalyst (Table 2, entry 2). A different problem was found with Ph/Ph substituted analog **1i**, which showed a high tendency towards cycloisomerization under the standard conditions. As a result, **4i** was produced in only 27% yield, and an isoindolone **7b**[14] (Figure 1) was obtained as the major product (57%, *E*/*Z* = 23:77). In this case, the competing cycloisomerization was completely suppressed by using KOBz (10 mol-%) in combination with $PdCl_2(PPh_3)_2$, and the desired product (i.e., **4i**) was obtained in 71% yield (Table 2, entry 11). The same conditions were also used with substrate **1j**, with a similar result (Table 2, entry 12).

Table 2. 5-*exo*-Selective oxidative oxycyclization/coupling reactions of *o*-alkynylbenzamides and electron-deficient alkenes.[a]



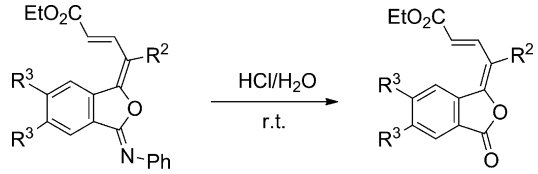
1 4

Entry	**1**	R^1, R^2, R^3, R^4	Y	*t* [h]	**4**, yield [%][b]	*exo*/*endo* ratio[c]
1	**1a**	*n*Bu, Ph, H, H	CO_2Et	29	**4a**, 73	94:6[d]
2[e]	**1b**	*n*Bu, *n*Hex, H, H	CO_2Et	20	**4b**, 77	83:17
3	**1c**	Ph, *n*Hex, H, H	CO_2Et	21	**4ca**, 80	94:6
4	**1c**	Ph, *n*Hex, H, H	COMe	17	**4cb**, 87	92:8
5	**1d**	Ph, *n*Hex, Cl, H	CO_2Et	23	**4d**, 68	90:10
6	**1e**	Ph, *n*Hex, MeO, MeO	CO_2Et	19	**4e**, 80	89:11
7	**1f**	*p*ClC_6H_4, *n*Hex, H, H	CO_2Et	19	**4f**, 84	94:6
8	**1g**	*p*$MeOC_6H_4$, *n*Hex, H, H	CO_2Et	21	**4ga**, 89	93:7
9	**1g**	*p*$MeOC_6H_4$, *n*Hex, H, H	COMe	17	**4gb**, 80	90:10
10	**1h**	*p*CNC_6H_4, *n*Hex, H, H	CO_2Et	24	**4h**, 85	91:9
11[f]	**1i**	Ph, Ph, H, H	CO_2Et	29	**4i**, 71	[g]
12[f]	**1j**	*p*$MeOC_6H_4$, Ph, H, H	CO_2Et	24	**4j**, 69	97:3[h]
13	**1k**	Ph, *p*$MeOC_6H_4$, H, H	CO_2Et	26	**4k**, 70	93:7

[a] Reaction conditions: Unless otherwise indicated, a solution of **1**, $Pd(OAc)_2$ (5 mol-% relative to **1**), PPh_3 (10 mol-%), KI (0.5 equiv.), DMAP (1 mol-%), and ethyl acrylate (20 equiv.) in DMF (8.5 mL/mmol) was heated at 35 °C for the given time (*t*) [h] under an air atmosphere. [b] Yield [%] of purified product. [c] Ratio measured in the crude product. [d] Dimeric product **6a** obtained in 18% yield. [e] Reaction run with $PdCl_2(PPh_3)_2$ as catalyst and K_2CO_3 (10 mol-%) instead of DMAP. [f] Reaction run with $PdCl_2(PPh_3)_2$ as catalyst and KOBz (10 mol-%) instead of DMAP. [g] No *endo* product was found. Dimeric product **6b**[5] obtained in 8% yield. [h] Dimeric product **6c**[5] obtained in 8% yield.

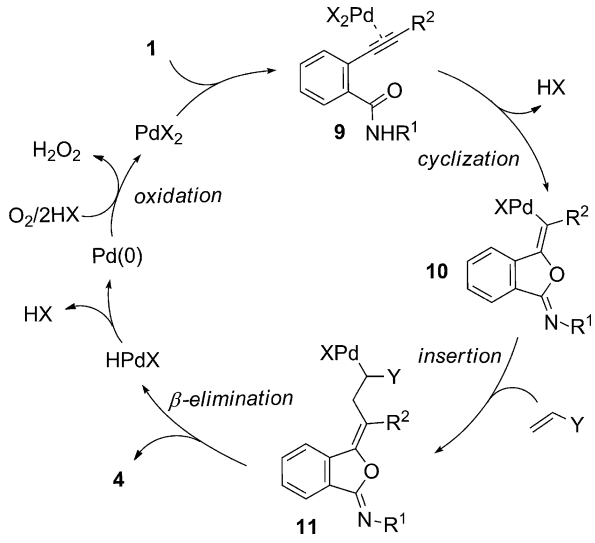
The imino functionality of imidates **4** can be hydrolyzed under acidic conditions,[5,15] as exemplified by the conversion of **4e** and **4i** into the corresponding lactones **8** in high yields (Scheme 2). As a result, a two-step route to 3-

allylideneisobenzofuranones appears to be established, using *o*-alkynylbenzamides as starting materials. The preparation of related derivatives has been described using rather more elaborate routes involving, for example, a metal-mediated cycloisomerization of appropriately *o*-substituted benzoic acids,[16] or, alternatively, metal-catalyzed cross-coupling reactions of 3-(3-tributylstannylmethylene)isobenzofuran-1(3*H*)-ones.[17,18]



Scheme 2. Hydrolysis of imidates **4**.

The synthesis of cyclic imidate derivatives related to **4** has been reported only in the case where Y = Ar. In that instance, a two-step parallel synthesis was used, where *o*-alkynylbenzamides were first subjected to iodocyclization, and then the resulting 3-iodomethylene-type products underwent a Heck coupling with styrenes.[19] In comparison, the method reported here for the preparation of products **4** featuring a carbonyl-type Y substituent takes place directly in a one-pot cascade process, starting from *o*-alkynylbenzamides and electron-deficient alkenes. Interestingly, the success of this new reaction relies on an appropriate choice of catalyst and/or additives. Thus, comparison between Table 1, entries 1 and 5–8 indicates that the very strong preference of the $PdCl_2(PPh_3)_2$ catalyst for a 6-*endo*- vs. a 5-*exo*-cyclization is reversed either by adding 10 mol-% of NaOAc or K_2CO_3 (Table 1, entries 6 and 7) or simply by changing the Pd counterion from Cl to OAc (Table 1, entry 8). However, the reasons for this change in the regiochemistry of the cyclization remain elusive. Upon addition of KOBz, NaOAc, or K_2CO_3 (Table 1, entries 5–7) to the *endo*-selective catalyst $PdCl_2(PPh_3)_2$, the *exo*/*endo* ratio increases in the order KOBz < NaOAc < K_2CO_3. This, together with a comparison between the effect of $Pd(OAc)_2$ (Table 1, entry 8) and the *endo*-selective $Pd(TFA)_2$ (Table 1, entry 9), seem to point towards the basicity of the anion as a determining factor for the regiochemistry. In any case, the oxidative cascade is likely to proceed through the same catalytic cycle as other related palladium-catalyzed heterocyclization/Heck-type coupling cascades, comprising Pd^{II}-promoted *O*-cyclization, carbopalladation, β-H elimination, and Pd^0 to Pd^{II} oxidation (Scheme 3).[8] In this general scheme, a base could conceivably participate in the cyclization step through an interaction with the N–H bond[20] or, alternatively, have an effect on the equilibrium positions of the various steps of the catalytic cycle involving release of acid. Whatever the actual reasons, this kind of catalyst-controlled regiochemical change, while still relatively uncommon in metal-catalyzed reactions,[21] is nevertheless a desirable tool, as it provides new synthetic options for structure diversification from a common set of starting materials.



Scheme 3. Expected catalytic cycle for the oxycyclization/oxidative Heck coupling.

Conclusions

A regioselectivity switch between 6-*endo*- and 5-*exo*-*dig*-cyclization in palladium-catalyzed oxidative cyclization/Heck-type coupling cascades of *o*-alkynylbenzamides and electron-deficient alkenes is triggered by a change in the palladium catalyst or by the addition of a suitable base (acetate, benzoate, or carbonate). Reaction conditions have been found that allow the efficient preparation of 3-methyleneisobenzofuran-1(3*H*)-imine derivatives incorporating the electron-deficient alkene carbon unit as additional substituent. The conversion into the corresponding isobenzofuranones by selective hydrolysis of the imino functionality has been demonstrated in selected cases.

Experimental Section

General Methods: All reactions involving air- and moisture-sensitive materials were carried out under an atmosphere of dry Ar. Triethylamine and toluene were distilled from CaH_2 and purged with Ar. Commercially sourced DMF (≥99.8%) was kept over molecular sieves (4 Å). Flash column chromatography was carried out using silica gel (230–400 mesh). Routine NMR spectra were obtained at 25 °C with a Bruker AV-300 spectrometer (300 MHz for ^1H, and 75.4 MHz for ^{13}C) or a Bruker AV-500 spectrometer (500 MHz for ^1H, and 125.7 MHz for ^{13}C), using $CDCl_3$ or [D_6]-acetone as solvent and internal reference ($CDCl_3$ δ = 7.26 ppm for ^1H, and δ = 77.0 ppm for ^{13}C; [D_6]acetone δ = 2.05 ppm for ^1H, and δ = 29.84 ppm for ^{13}C). Coupling constants (*J*) are given in Hertz (Hz). The DEPT sequence was routinely used for ^{13}C multiplicity assignment. Infrared spectra (IR) data were obtained from a thin film deposited onto a NaCl plate, and were measured with a Jasco FTIR 4100 instrument in the interval between 4000 and 600 cm^{-1} with a 4 cm^{-1} resolution; only characteristic absorptions are listed. Electron impact (EI) mass spectra were obtained with a

Hewlett–Packard HP59970 instrument operating at 70 eV. Chemical ionization mass spectra were acquired with an Agilent 6890N gas chromatograph coupled to a mass spectrometer with a Micromass GCT time of flight (TOF) analyzer. Melting points were measured with a Büchi B-540 apparatus in open capillary tubes. New compounds were fully characterized by their ^{1}H and ^{13}C NMR, IR, and HRMS spectral properties. Additionally, for products **4**, the use of 2D NMR correlations (COSY, HSQC, HMBC, and NOESY) allowed us to differentiate between the different regioisomeric possibilities. Structural assignments were confirmed by X-Ray analysis of product **4f** (Figure S1, Supporting Information).[22]

Representative Procedure for 5-*exo*-Heterocyclization/Intermolecular Heck Coupling Cascades: A solution of **1** (0.235 mmol), $Pd(OAc)_2$ (2.6 mg, 12 μmol), PPh_3 (6.2 mg, 23 μmol), KI (19 mg, 0.12 mmol), DMAP (290 μg, 2.3 μmol), and an electron-deficient alkene (4.70 mmol) in DMF (2 mL) was stirred at 35 °C for the time indicated in Table 2. The mixture was cooled to 25 °C, then saturated $NaHCO_3$ solution (4 mL) was added. The mixture was extracted with EtOAc (3 × 8 mL), the combined organic layers were dried (Na_2SO_4), and the solvent was removed. The residue was purified by flash chromatography (silica gel saturated with Et_3N, mixtures of hexanes/EtOAc/Et_3N) to give the products indicated in Table 2. Additional preparation and characterization details are given below.

Ethyl (*E*)-4-[(1*Z*,3*Z*)-3-(Butylimino)isobenzofuran-1(3*H*)-ylidene]-4-phenylbut-2-enoate (4a), Ethyl (*E*)-4-[(1*E*,3Z)-3-(Butylimino)isobenzofuran-1(3*H*)-ylidene]-4-phenylbut-2-enoate (4a′), and (1*Z*,1′*Z*,3*E*,3′*E*)-3,3′-(1,2-Diphenylethane-1,2-diylidene)bis[*N*-butylisobenzofuran-1(3*H*)-imine] (6a): Prepared from **1a**[23] (65 mg, 0.23 mmol) and ethyl acrylate (510 μL, 4.68 mmol). The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 98:1:1 to 84:15:1) to give **5a**[8] (4.4 mg, 5%), **4a** (64 mg, 73%), and **6a** (11.7 mg, 18%). Compound **4a′** was also detected in the crude product.

Data for **4a**: Yellow solid, m.p. 59–61 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, *J* = 7.3 Hz, 3 H), 1.22–1.33 (m, 5 H), 1.49–1.59 (m, 2 H), 3.37 (t, *J* = 7.1 Hz, 2 H), 4.24 (q, *J* = 7.1 Hz, 2 H), 5.80 (d, *J* = 15.2 Hz, 1 H), 7.32–7.46 (m, 5 H), 7.55 (t, *J* = 7.4 Hz, 1 H), 7.63–7.68 (m, 1 H), 7.91 (d, *J* = 7.5 Hz, 1 H), 8.10 (d, *J* = 7.9 Hz, 1 H), 8.47 (d, *J* = 15.2 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.7 (CH_3), 14.3 (CH_3), 20.5 (CH_2), 32.7 (CH_2), 47.8 (CH_2), 60.4 (CH_2), 118.4 (C), 121.6 (CH), 123.4 (CH), 124.5 (CH), 127.8 (CH), 128.2 (2 CH), 130.0 (2 CH), 130.4 (CH), 131.9 (C), 132.0 (CH), 135.0 (C), 135.1 (C), 140.5 (CH), 150.9 (C), 153.6 (C), 167.3 (C) ppm. IR (film): $\tilde{\nu}$ = 1704 (s), 1611 (s), 1597 (m) cm^{-1}. MS (CI): *m*/*z* (%) = 376 (100) [M + H]$^+$, 375 (20). HRMS (CI): calcd. for $C_{24}H_{26}NO_3$ [M + H]$^+$ 376.1913; found 376.1904.

Data for **4a′** (obtained as a by-product in the reactions of **1a**; see Table 1): White solid, m.p. 100–102 °C. ^{1}H NMR (300 MHz, [D_6]-acetone): δ = 1.01 (t, *J* = 7.3 Hz, 3 H), 1.23 (t, *J* = 7.1 Hz, 3 H), 1.45–1.57 (m, 2 H), 1.69–1.78 (m, 2 H), 3.77 (t, *J* = 6.7 Hz, 2 H), 4.15 (q, *J* = 7.0 Hz, 2 H), 5.40 (d, *J* = 15.5 Hz, 1 H), 6.22 (d, *J* = 7.9 Hz, 1 H), 7.32 (t, *J* = 7.5 Hz, 1 H), 7.35–7.42 (m, 2 H), 7.49–7.54 (m, 1 H), 7.57–7.65 (m, 3 H), 7.82 (d, *J* = 7.5 Hz, 1 H), 8.47 (d, *J* = 15.5 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, [D_6]acetone): δ = 14.2 (CH_3), 14.5 (CH_3), 21.3 (CH_2), 33.8 (CH_2), 48.2 (CH_2), 60.7 (CH_2), 117.2 (C), 121.0 (CH), 123.7 (CH), 124.6 (CH), 129.7 (CH), 130.4 (2 CH), 131.3 (2 CH), 131.6 (CH), 132.3 (CH), 132.6 (C), 135.0 (C), 135.9 (C), 141.0 (CH), 151.1 (C), 153.0 (C), 166.9 (C) ppm. IR (film): $\tilde{\nu}$ = 1706 (s), 1613 (s), 1595 (m) cm^{-1}. MS (CI): *m*/*z* (%) = 376 (100) [M + H]$^+$, 375 (42), 374 (11). HRMS (CI): calcd. for $C_{24}H_{26}NO_3$ [M + H]$^+$ 376.1913; found 376.1909.

Data for **6a**: Yellow solid, m.p. 129–131 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 7.3 Hz, 3 H), 1.49–1.61 (m, 2 H), 1.76–1.86 (m, 2 H), 3.74–3.89 (m, 2 H), 7.22–7.38 (m, 5 H), 7.55 (t, *J* = 7.7 Hz, 1 H), 7.83 (d, *J* = 7.5 Hz, 1 H), 7.91 (d, *J* = 7.5 Hz, 2 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0 (CH_3), 20.8 (CH_2), 33.0 (CH_2), 48.3 (CH_2), 113.2 (C), 122.8 (CH), 123.5 (CH), 127.7 (CH), 128.5 (2 CH), 129.3 (2 CH), 129.7 (CH), 130.5 (C), 131.9 (CH), 135.8 (C), 136.3 (C), 148.5 (C), 154.5 (C) ppm. IR (film): $\tilde{\nu}$ = 1702 (s), 1610 (m) cm^{-1}. MS (CI): *m*/*z* (%) = 553 (100) [M + H]$^+$, 552 (58), 551 (13). HRMS (CI): calcd. for $C_{38}H_{37}N_2O_2$ [M + H]$^+$ 553.2855; found 553.2845.

Ethyl (*E*)-4-[(1*E*,3*Z*)-3-(Butylimino)isobenzofuran-1(3*H*)-ylidene]-dec-2-enoate (4b): Prepared from **1b** (33.5 mg, 0.117 mmol) and ethyl acrylate (255 μL, 2.34 mmol), using $PdCl_2(PPh_3)_2$ (5 mol-%) as catalyst, and K_2CO_3 (10 mol-%) instead of DMAP. The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 98:1:1 to 95:4:1) to give **5b**[10] (7.3 mg, 16%) and **4b** (34.4 mg, 77%).

Data for **4b**: Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86–0.90 (m, 3 H), 0.96 (t, *J* = 7.3 Hz, 3 H), 1.25–1.48 (m, 11 H), 1.51–1.60 (m, 2 H), 1.65–1.75 (m, 2 H), 2.56–2.62 (m, 2 H), 3.66 (t, *J* = 7.1 Hz, 2 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 6.11 (d, *J* = 15.4 Hz, 1 H), 7.47 (t, *J* = 7.5 Hz, 1 H), 7.55–7.60 (m, 1 H), 7.88 (d, *J* = 7.6 Hz, 1 H), 7.97 (d, *J* = 8.0 Hz, 1 H), 8.28 (d, *J* = 15.4 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.9 (CH_3), 14.0 (CH_3), 14.3 (CH_3), 20.7 (CH_2), 22.6 (CH_2), 27.3 (CH_2), 28.6 (CH_2), 29.4 (CH_2), 31.6 (CH_2), 32.9 (CH_2), 47.8 (CH_2), 60.4 (CH_2), 118.0 (CH, C), 123.3 (CH), 124.2 (CH), 129.7 (CH), 131.7 (C), 131.9 (CH), 134.8 (C), 139.8 (CH), 151.7 (C), 153.7 (C), 167.4 (C) ppm. IR (film): $\tilde{\nu}$ = 1704 (s), 1613 (s) cm^{-1}. MS (CI): *m*/*z* (%) = 384 (100) [M + H]$^+$, 383 (20), 382 (23), 340 (11), 338 (10), 312 (12), 300 (15), 299 (67). HRMS (CI): calcd. for $C_{24}H_{34}NO_3$ [M + H]$^+$ 384.2539; found 384.2524.

Ethyl (*E*)-4-[(1*E*,3*Z*)-3-(Phenylimino)isobenzofuran-1(3*H*)-ylidene]-dec-2-enoate (4ca): Prepared from **1c**[24] (72 mg, 0.24 mmol) and ethyl acrylate (515 μL, 4.72 mmol). The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 98:1:1 to 93:6:1) to give **5ca**[8] (5 mg, 5%) and **4ca** (77 mg, 80%).

Data for **4ca**: Yellow solid, m.p. 70–72 °C. ^{1}H NMR (300 MHz, [D_6]acetone): δ = 0.90 (t, *J* = 6.9 Hz, 3 H), 1.32–1.46 (m, 9 H), 1.56–1.66 (m, 2 H), 2.61–2.66 (m, 2 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 6.25 (d, *J* = 15.4 Hz, 1 H), 7.20–7.25 (m, 1 H), 7.41–7.51 (m, 4 H), 7.69–7.75 (m, 1 H), 7.83–7.88 (m, 1 H), 8.06 (d, *J* = 8.4 Hz, 2 H), 8.29 (d, *J* = 15.4 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0 (CH_3), 14.3 (CH_3), 22.6 (CH_2), 27.6 (CH_2), 28.9 (CH_2), 29.5 (CH_2), 31.5 (CH_2), 60.5 (CH_2), 118.9 (CH), 119.6 (C), 124.0 (CH), 124.1 (CH), 124.2 (2 CH), 125.0 (CH), 128.7 (2 CH), 129.9 (CH), 132.0 (C), 132.5 (CH), 134.5 (C), 139.3 (CH), 145.2 (C), 151.7 (C), 152.5 (C), 167.3 (C) ppm. IR (film): $\tilde{\nu}$ = 1704 (s), 1685 (s), 1610 (s), 1591 (s) cm^{-1}. MS (CI): *m*/*z* (%) = 404 (100) [M + H]$^+$, 403 (21), 358 (10), 320 (11), 319 (40), 246 (16). HRMS (CI): calcd. for $C_{26}H_{30}NO_3$ [M + H]$^+$ 404.2226; found 404.2206.

(*E*)-5-[(1*E*,3*Z*)-3-(Phenylimino)isobenzofuran-1(3*H*)-ylidene]undec-3-en-2-one (4cb) and (*E*)-4-[(*Z*)-3-Hexyl-1-(phenylimino)-1*H*-isochromen-4-yl]but-3-en-2-one (5cb): Prepared from **1c**[24] (72 mg, 0.24 mmol) and methyl vinyl ketone (383 μL, 4.72 mmol). The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 95:4:1 to 79:20:1) to give **5cb** (6.2 mg, 7%) and **4cb** (77 mg, 87%).

Data for **4cb**: Yellow-brown solid, m.p. 54–56 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86–0.91 (m, 3 H), 1.26–1.41 (m, 6 H), 1.49–1.59 (m, 2 H), 2.39 (s, 3 H), 2.53–2.58 (m, 2 H), 6.47 (d, J = 15.5 Hz, 1 H), 7.16–7.21 (m, 1 H), 7.36–7.46 (m, 4 H), 7.58 (t, J = 7.5 Hz, 1 H), 7.65–7.70 (m, 1 H), 7.99 (d, J = 8.0 Hz, 1 H), 8.07 (d, J = 7.6 Hz, 1 H), 8.16 (d, J = 15.5 Hz, 1 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.6 (CH_2), 27.6 (CH_2), 28.6 (CH_3), 28.9 (CH_2), 29.5 (CH_2), 31.5 (CH_2), 119.9 (C), 124.1 (2 CH), 124.2 (2 CH), 125.1 (CH), 127.1 (CH), 128.7 (2 CH), 130.1 (CH), 132.1 (C), 132.6 (CH), 134.4 (C), 137.8 (CH), 145.2 (C), 152.3 (C), 152.4 (C), 197.5 (C) ppm. IR (film): $\tilde{\nu}$ = 1683 (s), 1667 (s), 1608 (m), 1577 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 373 (27) $[M]^+$, 302 (32), 289 (16), 288 (100), 274 (11), 272 (13), 260 (23), 259 (12), 258 (22), 248 (17), 246 (34), 245 (11), 234 (17), 232 (24), 230 (18), 217 (13), 197 (17), 179 (15), 77 (12). HRMS (EI): calcd. for $C_{25}H_{27}NO_2$ $[M]^+$ 373.2042; found 373.2044.

Data for **5cb**: Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84–0.89 (m, 3 H), 1.17–1.30 (m, 6 H), 1.48–1.55 (m, 2 H), 2.40 (s, 3 H), 2.50 (t, J = 7.4 Hz, 2 H), 6.46 (d, J = 16.2 Hz, 1 H), 7.08–7.16 (m, 3 H), 7.32–7.37 (m, 2 H), 7.41–7.59 (m, 4 H), 8.41 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.4 (CH_2), 27.3 (CH_2), 28.0 (CH_3), 28.6 (CH_2), 31.1 (CH_2), 31.4 (CH_2), 109.5 (C), 122.5 (2 CH), 122.9 (CH), 123.3 (C), 123.7 (CH), 127.8 (CH), 128.0 (CH), 128.6 (2 CH), 132.4 (CH), 132.6 (C), 132.8 (CH), 136.7 (CH), 146.3 (C), 148.7 (C), 156.1 (C), 197.6 (C) ppm. IR (film): $\tilde{\nu}$ = 1654 (s), 1591 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 373 (6) $[M]^+$, 330 (14), 289 (14), 288 (100), 278 (13), 277 (83), 276 (26), 260 (19), 246 (25), 235 (29), 234 (84), 233 (47), 232 (83), 218 (12), 217 (17), 204 (19), 185 (10). HRMS (EI): calcd. for $C_{25}H_{27}NO_2$ $[M]^+$ 373.2042; found 373.2039.

Ethyl (*E*)-4-[(1*E*,3*Z*)-6-Chloro-3-(phenylimino)isobenzofuran-1(3*H*)-ylidene]dec-2-enoate (4d): Prepared from **1d** (80 mg, 0.235 mmol) and ethyl acrylate (513 μL, 4.70 mmol). The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 98:1:1 to 97:2:1) to give **5d**[10] (9.5 mg, 9%) and **4d** (70 mg, 68%).

Data for **4d**: Yellow solid, m.p. 92–93 °C. ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 0.91 (t, J = 6.9 Hz, 3 H), 1.34–1.47 (m, 9 H), 1.57–1.66 (m, 2 H), 2.63–2.69 (m, 2 H), 4.29 (q, J = 7.1 Hz, 2 H), 6.30 (d, J = 15.4 Hz, 1 H), 7.22–7.29 (m, 1 H), 7.42–7.51 (m, 4 H), 7.75 (dd, J = 8.3, 1.6 Hz, 1 H), 8.01 (s, 1 H), 8.06 (d, J = 8.3 Hz, 1 H), 8.18 (d, J = 15.4 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 14.4 (CH_3), 14.6 (CH_3), 23.4 (CH_2), 28.3 (CH_2), 29.6 (CH_2), 30.2 (CH_2), 32.3 (CH_2), 61.0 (CH_2), 121.0 (CH), 121.6 (C), 124.6 (CH), 125.3 (2 CH), 126.2 (2 CH), 129.6 (2 CH), 131.4 (CH), 131.6 (C), 136.7 (C), 138.9 (CH), 139.2 (C), 146.0 (C), 151.0 (C), 151.8 (C), 167.1 (C) ppm. IR (film): $\tilde{\nu}$ = 1710 (s), 1685 (s), 1611 (s), 1590 (m) cm^{-1}. MS (EI): *m*/*z* (%) = 439 (1) [^{37}Cl M]$^+$, 437 (4) [^{35}Cl M]$^+$, 353 (24), 320 (11), 308 (23), 307 (17), 306 (14), 294 (10), 292 (17), 282 (31), 281 (29), 280 (100), 279 (31), 278 (11), 268 (26), 266 (21). HRMS (EI): calcd. for $C_{26}H_{28}{}^{35}ClNO_3$ $[M]^+$ 437.1758; found 437.1766. HRMS (EI): calcd. for $C_{26}H_{28}{}^{37}ClNO_3$ $[M]^+$ 439.1728; found 439.1748.

Ethyl (*E*)-4-[(1*E*,3*Z*)-5,6-Dimethoxy-3-(phenylimino)isobenzofuran-1(3*H*)-ylidene]dec-2-enoate (4e): Prepared from **1e** (86 mg, 0.235 mmol) and ethyl acrylate (513 μL, 4.68 mmol). The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 96:3:1 to 49:50:1), to give **5e**[10] (11 mg, 10%) and **4e** (87 mg, 80%).

Data for **4e**: Yellow solid, m.p. 149–150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85–0.90 (m, 3 H), 1.28–1.36 (m, 9 H), 1.48–1.58 (m, 2 H), 2.49–2.54 (m, 2 H), 4.02 (s, 3 H), 4.05 (s, 3 H), 4.26 (q, J = 7.1 Hz, 2 H), 6.10 (d, J = 15.4 Hz, 1 H), 7.16 (tt, J = 7.0, 1.6 Hz, 1 H), 7.34–7.43 (m, 6 H), 8.22 (d, J = 15.4 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0 (CH_3), 14.3 (CH_3), 22.6 (CH_2), 27.4 (CH_2), 28.9 (CH_2), 29.5 (CH_2), 31.5 (CH_2), 56.2 (CH_3), 56.4 (CH_3), 60.4 (CH_2), 104.5 (CH), 105.1 (CH), 117.9 (C), 118.0 (CH), 124.2 (2 CH), 124.8 (CH), 125.5 (C), 128.2 (C), 128.6 (2 CH), 139.6 (CH), 145.4 (C), 151.5 (C), 151.8 (C), 152.8 (C), 153.2 (C), 167.3 (C) ppm. IR (film): $\tilde{\nu}$ = 1738 (m), 1705 (s), 1679 (s), 1597 (s), 1500 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 463 (8) $[M]^+$, 380 (22), 379 (100), 346 (12), 334 (39), 333 (26), 332 (14), 318 (14), 307 (30), 306 (74), 305 (20), 295 (10), 294 (39), 292 (17), 290 (18). HRMS (EI): calcd. for $C_{28}H_{33}NO_5$ $[M]^+$ 463.2359; found 463.2358.

Ethyl (*E*)-4-{(1*E*,3*Z*)-3-[(4-Chlorophenyl)imino]isobenzofuran-1(3*H*)-ylidene}dec-2-enoate (4f): Prepared from **1f** (80 mg, 0.235 mmol) and ethyl acrylate (513 μL, 4.70 mmol). The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 97:2:1 to 91:8:1) to give **5f**[10] (8 mg, 8%) and **4f** (87 mg, 84%).

Data for **4f**: Yellow solid, m.p. 110–112 °C. ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 0.91 (t, J = 6.9 Hz, 3 H), 1.30–1.47 (m, 9 H), 1.56–1.66 (m, 2 H), 2.63–2.68 (m, 2 H), 4.28 (q, J = 7.1 Hz, 2 H), 6.28 (d, J = 15.4 Hz, 1 H), 7.43–7.51 (m, 4 H), 7.74 (t, J = 7.6 Hz, 1 H), 7.86–7.91 (m, 1 H), 8.05–8.09 (m, 2 H), 8.29 (d, J = 15.4 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 14.4 (CH_3), 14.6 (CH_3), 23.4 (CH_2), 28.1 (CH_2), 29.6 (CH_2), 30.2 (CH_2), 32.3 (CH_2), 61.0 (CH_2), 120.5 (CH), 120.7 (C), 124.9 (2 CH), 126.7 (2 CH), 129.6 (2 CH), 130.6 (C), 131.3 (CH), 132.6 (C), 134.2 (CH), 135.4 (C), 139.4 (CH), 145.3 (C), 152.2 (C), 153.7 (C), 167.2 (C) ppm. IR (film): $\tilde{\nu}$ = 1711 (s), 1678 (s), 1610 (s), 1579 (m) cm^{-1}. MS (EI): *m*/*z* (%) = 439 (2) [^{37}Cl M]$^+$, 437 (6) [^{35}Cl M]$^+$, 366 (15), 355 (10), 353 (34), 320 (13), 309 (14), 308 (31), 307 (35), 306 (14), 292 (15), 282 (24), 281 (21), 280 (100), 279 (22), 278 (13), 268 (23), 266 (18), 264 (37). HRMS (EI): calcd. for $C_{26}H_{28}{}^{35}ClNO_3$ $[M]^+$ 437.1758; found 437.1763. HRMS (EI): calcd. for $C_{26}H_{28}{}^{37}ClNO_3$ $[M]^+$ 439.1728; found 439.1749. The structural assignment was additionally confirmed by X-Ray analysis (Figure S1, Supporting Information).

Ethyl (*E*)-4-{(1*E*,3*Z*)-3-[(4-Methoxyphenyl)imino]isobenzofuran-1(3*H*)-ylidene}dec-2-enoate (4ga) and Ethyl (*E*)-3-{(*Z*)-3-Hexyl-1-[(4-methoxyphenyl)imino]-1*H*-isochromen-4-yl}acrylate (5ga): Prepared from **1g**[24] (79 mg, 0.235 mmol) and ethyl acrylate (513 μL, 4.70 mmol). The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 97:2:1 to 87:12:1) to give **5ga** (7 mg, 7%) and **4ga** (91 mg, 89%).

Data for **4ga**: Yellow solid, m.p. 79–80 °C. ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 0.86–0.91 (m, 3 H), 1.28–1.38 (m, 7 H), 1.42–1.51 (m, 2 H), 1.57–1.66 (m, 2 H), 2.64–2.69 (m, 2 H), 3.82 (s, 3 H), 4.24 (q, J = 7.1 Hz, 2 H), 6.21 (d, J = 15.4 Hz, 1 H), 6.97 (d, J = 9.0 Hz, 2 H), 7.53 (d, J = 9.0 Hz, 2 H), 7.66 (t, J = 7.3 Hz, 1 H), 7.76–7.82 (m, 1 H), 7.98–8.03 (m, 2 H), 8.27 (d, J = 15.4 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 14.4 (CH_3), 14.7 (CH_3), 23.4 (CH_2), 28.3 (CH_2), 29.5 (CH_2), 30.3 (CH_2), 32.3 (CH_2), 55.7 (CH_3), 60.9 (CH_2), 114.7 (2 CH), 119.7 (C, CH), 124.4 (CH), 124.7 (CH), 127.4 (2 CH), 131.0 (CH), 133.3 (C), 133.4 (CH), 134.8 (C), 138.9 (C), 139.6 (CH), 151.2 (C), 152.6 (C), 158.5 (C), 167.3 (C) ppm. IR (film): $\tilde{\nu}$ = 1705 (s), 1682 (s), 1603 (s), 1505 (s) cm^{-1}. MS (CI): *m*/*z* (%) = 434 (100) $[M + H]^+$, 433 (64), 349 (47). HRMS (CI): calcd. for $C_{27}H_{32}NO_4$ $[M + H]^+$ 434.2331; found 434.2317.

Data for **5ga**: Yellow oil. ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 0.84–0.88 (m, 3 H), 1.24–1.37 (m, 9 H), 1.63–1.71 (m, 2 H), 2.64–2.69 (m, 2 H), 3.80 (s, 3 H), 4.25 (q, J = 7.1 Hz, 2 H), 6.22 (d, J = 16.0 Hz, 1 H), 6.92 (d, J = 8.9 Hz, 2 H), 7.25 (d, J = 8.9 Hz, 2 H),

7.46–7.52 (m, 2 H), 7.62–7.71 (m, 2 H), 8.34 (d, J = 7.1 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 14.3 (CH_3), 14.6 (CH_3), 23.1 (CH_2), 28.0 (CH_2), 29.3 (CH_2), 31.7 (CH_2), 32.1 (CH_2), 55.6 (CH_3), 61.1 (CH_2), 110.3 (C), 114.6 (2 CH), 124.0 (CH), 124.5 (C), 125.3 (2 CH), 125.6 (CH), 128.2 (CH), 128.8 (CH), 133.2 (CH), 133.5 (C), 138.5 (CH), 140.0 (C), 148.4 (C), 156.6 (C), 157.4 (C), 166.5 (C) ppm. IR (film): $\tilde{\nu}$ = 1715 (s), 1652 (s), 1636 (s) cm^{-1}. MS (CI): *m*/*z* (%) = 434 (90) [M + H]$^+$, 433 (100). HRMS (CI): calcd. for $C_{27}H_{32}NO_4$ [M + H]$^+$ 434.2331; found 434.2318.

(*E*)-5-{(1*E*,3*Z*)-3-[(4-Methoxyphenyl)imino]isobenzofuran-1(3*H*)-ylidene}undec-3-en-2-one (4gb) and (*E*)-4-[(*Z*)-3-Hexyl-1-(4-methoxyphenylimino)-1*H*-isochromen-4-yl]but-3-en-2-one (5gb): Prepared from **1g**[24] (79 mg, 0.235 mmol) and methyl vinyl ketone (381 μL, 4.70 mmol). The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 94:5:1 to 74:25:1) to give **5gb** (6.6 mg, 7%) and **4gb** (76 mg, 80%).

Data for **4gb**: Yellow-orange solid, m.p. 102–104 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88–0.92 (m, 3 H), 1.32–1.44 (m, 6 H), 1.56–1.63 (m, 2 H), 2.40 (s, 3 H), 2.59–2.64 (m, 2 H), 3.85 (s, 3 H), 6.47 (d, J = 15.5 Hz, 1 H), 6.93 (d, J = 9.0 Hz, 2 H), 7.52–7.58 (m, 3 H), 7.65 (t, J = 7.5 Hz, 1 H), 7.98 (d, J = 8.0 Hz, 1 H), 8.03 (d, J = 7.6 Hz, 1 H), 8.17 (d, J = 15.5 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.7 (CH_2), 27.8 (CH_2), 28.6 (CH_3), 28.9 (CH_2), 29.6 (CH_2), 31.6 (CH_2), 55.4 (CH_3), 113.9 (2 CH), 119.4 (C), 123.9 (CH), 124.0 (CH), 126.4 (2 CH), 126.9 (CH), 130.0 (CH), 132.2 (CH), 132.6 (C), 134.1 (C), 138.0 (CH), 151.0 (C), 152.7 (C), 157.4 (C), 197.6 (C) ppm. IR (film): $\tilde{\nu}$ = 1681 (m), 1600 (m), 1573 (s), 1504 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 403 (54) [M]$^+$, 388 (21), 362 (11), 361 (32), 360 (77), 347 (12), 346 (24), 333 (11), 332 (43), 319 (28), 318 (100), 304 (14), 302 (16), 290 (30), 289 (17), 288 (28), 277 (14), 276 (66), 275 (22), 274 (17), 264 (18), 263 (13), 262 (44), 261 (15), 260 (16), 258 (12), 253 (14), 247 (14), 246 (20), 245 (10), 238 (39), 233 (11), 232 (17), 217 (13), 197 (40), HRMS (EI): calcd. for $C_{26}H_{29}NO_3$ [M]$^+$ 403.2147; found 403.2146.

Data for **5gb**: Yellow solid, m.p. 64–66 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84–0.90 (m, 3 H), 1.20–1.33 (m, 6 H), 1.52–1.62 (m, 2 H), 2.40 (s, 3 H), 2.53 (t, J = 7.5 Hz, 2 H), 3.83 (s, 3 H), 6.46 (d, J = 16.2 Hz, 1 H), 6.90 (d, J = 8.8 Hz, 2 H), 7.21 (d, J = 8.8 Hz, 2 H), 7.39–7.44 (m, 2 H), 7.50–7.56 (m, 2 H), 8.39 (d, J = 7.7 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.4 (CH_2), 27.4 (CH_2), 27.9 (CH_3), 28.6 (CH_2), 31.2 (CH_2), 31.4 (CH_2), 55.4 (CH_3), 109.5 (C), 113.8 (2 CH), 122.8 (CH), 123.7 (C), 124.3 (2 CH), 127.6 (CH), 127.9 (CH), 132.0 (CH), 132.3 (C), 132.6 (CH), 136.8 (CH), 139.0 (C), 147.9 (C), 156.1 (C), 156.2 (C), 197.6 (C) ppm. IR (film): $\tilde{\nu}$ = 1693 (m), 1650 (s), 1607 (m), 1504 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 403 (10) [M]$^+$, 360 (15), 319 (15), 318 (100), 290 (16), 276 (16), HRMS (EI): calcd. for $C_{26}H_{29}NO_3$ [M]$^+$ 403.2147; found 403.2144.

Ethyl (*E*)-4-{(1*E*,3*Z*)-3-[(4-Cyanophenyl)imino]isobenzofuran-1(3*H*)-ylidene}dec-2-enoate (4h) and Ethyl (*E*)-3-{(*Z*)-1-[(4-Cyanophenyl)imino]-3-hexyl-1*H*-isochromen-4-yl}acrylate (5h): Prepared from **1h** (77 mg, 0.233 mmol) and ethyl acrylate (508 μL, 4.66 mmol). The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 96:3:1 to 87:12:1) to give **5h** (8 mg, 8%) and **4h** (85 mg, 85%).

Data for **4h**: Yellow solid, m.p. 120–122 °C. ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 0.84–0.88 (m, 3 H), 1.26–1.41 (m, 9 H), 1.49–1.59 (m, 2 H), 2.55–2.60 (m, 2 H), 4.24 (q, J = 7.1 Hz, 2 H), 6.26 (d, J = 15.5 Hz, 1 H), 7.53 (d, J = 8.4 Hz, 2 H), 7.73 (t, J = 7.5 Hz, 1 H), 7.79 (d, J = 8.4 Hz, 2 H), 7.88 (t, J = 7.7 Hz, 1 H), 8.06 (d, J = 8.2 Hz, 2 H), 8.23 (d, J = 15.5 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 14.3 (CH_3), 14.4 (CH_3), 23.3 (CH_2), 28.0 (CH_2), 29.6 (CH_2), 30.1 (CH_2), 32.2 (CH_2), 61.0 (CH_2), 108.6 (C), 119.6 (C), 121.0 (CH), 121.4 (C), 124.9 (CH), 125.1 (CH), 125.3 (2 CH), 131.4 (CH), 132.0 (C), 133.8 (2 CH), 134.6 (CH), 135.6 (C), 139.1 (CH), 151.2 (C), 151.9 (C), 155.0 (C), 167.2 (C) ppm. IR (film): $\tilde{\nu}$ = 2224 (w), 1703 (s), 1681 (s), 1613 (s), 1594 (s) cm^{-1}. MS (CI): *m*/*z* (%) = 429 (100) [M + H]$^+$, 428 (25), 344 (29). HRMS (CI): calcd. for $C_{27}H_{29}N_2O_3$ [M + H]$^+$ 429.2178; found 429.2164.

Data for **5h**: Brown oil. ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 0.83–0.87 (m, 3 H), 1.23–1.37 (m, 9 H), 1.50–1.57 (m, 2 H), 2.58 (t, J = 7.3 Hz, 2 H), 4.25 (q, J = 7.1 Hz, 2 H), 6.23 (d, J = 16.0 Hz, 1 H), 7.32 (d, J = 7.8 Hz, 2 H), 7.57 (d, J = 7.8 Hz, 2 H), 7.65–7.77 (m, 4 H), 8.36 (d, J = 7.4 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 14.3 (CH_3), 14.6 (CH_3), 23.0 (CH_2), 27.8 (CH_2), 29.2 (CH_2), 31.5 (CH_2), 32.1 (CH_2), 61.1 (CH_2), 107.3 (C), 110.8 (C), 119.9 (C), 123.3 (C), 124.2 (CH), 124.3 (CH), 126.3 (CH), 128.6 (CH), 129.1 (CH), 133.8 (2 CH), 134.0 (C), 134.2 (CH), 138.1 (CH), 151.1 (C), 152.6 (C), 156.2 (C), 166.3 (C) ppm. IR (film): $\tilde{\nu}$ = 2224 (w), 1715 (s), 1652 (s), 1593 (s) cm^{-1}. MS (CI): *m*/*z* (%) = 429 (100) [M + H]$^+$, 428 (53). HRMS (CI): calcd. for $C_{27}H_{29}N_2O_3$ [M + H]$^+$ 429.2178; found 429.2159.

Ethyl (*E*)-4-Phenyl-4-[(1*Z*,3*Z*)-3-(phenylimino)isobenzofuran-1(3*H*)-ylidene]but-2-enoate (4i): Prepared from **1i** (70 mg, 0.235 mmol) and ethyl acrylate (513 μL, 4.7 mmol), using $PdCl_2(PPh_3)_2$ (5 mol-%) as catalyst, and KOBz (10 mol-%) instead of DMAP. The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 97:2:1 to 80:19:1), to give **4i** (66 mg, 71%) and **6b**[5] (5.7 mg, 8%).

Data for **4i**: Yellow solid, m.p. 143–145 °C. ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 1.27 (t, J = 7.1 Hz, 3 H), 4.21 (q, J = 7.1 Hz, 2 H), 5.77 (d, J = 15.3 Hz, 1 H), 7.07 (t, J = 7.2 Hz, 1 H), 7.17–7.22 (m, 2 H), 7.28 (d, J = 7.9 Hz, 2 H), 7.42–7.54 (m, 5 H), 7.78 (t, J = 7.5 Hz, 1 H), 7.92 (t, J = 7.5 Hz, 1 H), 8.07 (d, J = 7.8 Hz, 1 H), 8.21 (d, J = 7.9 Hz, 1 H), 8.49 (d, J = 15.3 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 14.6 (CH_3), 61.0 (CH_2), 120.5 (C), 123.2 (CH), 124.8 (CH), 125.2 (CH), 125.9 (2 CH), 126.1 (CH), 128.9 (CH), 129.2 (2 CH), 129.3 (2 CH), 131.0 (2 CH), 131.9 (CH), 133.2 (C), 134.0 (CH), 135.2 (C), 135.9 (C), 140.4 (CH), 145.6 (C), 151.9 (C), 152.5 (C), 167.0 (C) ppm. IR (film): $\tilde{\nu}$ = 1704 (s), 1681 (s), 1609 (s), 1593 (s) cm^{-1}. MS (CI): *m*/*z* (%) = 396 (100) [M + H]$^+$, 395 (71), 350 (10), 322 (27), 321 (17). HRMS (CI): calcd. for $C_{26}H_{22}NO_3$ [M + H]$^+$ 396.1600; found 396.1581.

Ethyl (*E*)-4-{(1*Z*,3*Z*)-3-[(4-Methoxyphenyl)imino]isobenzofuran-1(3*H*)-ylidene}-4-phenylbut-2-enoate (4j): Prepared from **1j** (77.0 mg, 0.235 mmol) and ethyl acrylate (513 μL, 4.7 mmol), using $PdCl_2(PPh_3)_2$ (5 mol-%) as catalyst, and KOBz (10 mol-%) instead of DMAP. The crude was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 95:4:1 to 60:39:1), to give **4j** (72 mg), **5j**[8] (2 mg, 2%), and **6c**[5] (5.7 mg, 8%). Product **4j** was further purified by stirring for 16 h at room temperature in hexanes (5 mL). The solvent was then decanted to give pure **4j** (69 mg, 69%).

Data for **4j**: Yellow-orange solid, m.p. 149–151 °C. ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 1.27 (t, J = 6.9 Hz, 3 H), 3.76 (s, 3 H), 4.21 (q, J = 6.9 Hz, 2 H), 5.76 (d, J = 15.1 Hz, 1 H), 6.74 (d, J = 8.3 Hz, 2 H), 7.29 (d, J = 8.5 Hz, 2 H), 7.47–7.56 (m, 5 H), 7.74 (t, J = 7.3 Hz, 1 H), 7.88 (t, J = 7.4 Hz, 1 H), 8.02 (d, J = 7.4 Hz, 1 H), 8.18 (d, J = 7.6 Hz, 1 H), 8.49 (d, J = 15.1 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 14.6 (CH_3), 55.6 (CH_3), 60.9 (CH_2), 114.5 (2 CH), 120.1 (C), 122.8 (CH), 124.6 (CH), 125.1 (CH), 127.9 (2 CH), 128.9 (CH), 129.3 (2 CH), 131.0

(2 CH), 131.9 (CH), 133.6 (CH), 134.8 (C), 136.1 (C), 138.4 (C), 140.5 (CH), 150.9 (C), 152.2 (C), 158.7 (C), 167.0 (C) ppm. IR (film): $\tilde{\nu}$ = 1704 (s), 1680 (s), 1605 (s), 1594 (s) cm^{-1}. MS (CI): *m*/*z* (%) = 426 (100) $[M + H]^+$, 425 (93), 380 (20), 352 (31), 351 (13). HRMS (CI): calcd. for $C_{27}H_{24}NO_4$ $[M + H]^+$ 426.1705; found 426.1692.

Ethyl (2*E*,4*Z*)-4-[(*Z*)-(4-Methoxyphenyl)-4-(3-phenylimino-3*H*-isobenzofuran-1-ylidene)]but-2-enoate (4k): Prepared from **1k** (77 mg, 0.235 mmol) and ethyl acrylate (513 μL, 4.70 mmol). The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 90:9:1 to 70:29:1) to give **5k**[10] (4 mg, 4%) and **4k** (70 mg, 70%).

Data for **4k**: Yellow solid, m.p. 139–141 °C. ^1H NMR (300 MHz, [D$_6$]acetone): δ = 1.31 (t, *J* = 7.1 Hz, 3 H), 3.92 (s, 3 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 5.87 (d, *J* = 15.2 Hz, 1 H), 7.08–7.18 (m, 3 H), 7.24–7.29 (m, 2 H), 7.34–7.37 (m, 2 H), 7.43 (d, *J* = 8.8 Hz, 2 H), 7.78 (t, *J* = 7.5 Hz, 1 H), 7.90–7.95 (m, 1 H), 8.09 (d, *J* = 7.7 Hz, 1 H), 8.19 (d, *J* = 8.0 Hz, 1 H), 8.49 (d, *J* = 15.2 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 14.6 (CH_3), 55.7 (CH_3), 60.9 (CH_2), 114.5 (2 CH), 120.3 (C), 123.3 (CH), 124.8 (CH), 125.1 (CH), 125.8 (2 CH), 126.1 (CH), 127.8 (C), 129.3 (2 CH), 131.7 (CH), 132.4 (2 CH), 133.1 (C), 133.9 (CH), 135.4 (C), 140.8 (CH), 145.7 (C), 151.7 (C), 152.7 (C), 160.6 (C), 167.0 (C) ppm. IR (film) $\tilde{\nu}$ 1694 (s), 1679 (s), 1602 (s), 1587 (s), 1509 (s) cm^{-1}. MS (CI): *m*/*z* (%) = 426 (100) $[M + H]^+$, 425 (61), 352 (11). HRMS (CI): calcd. for $C_{27}H_{24}NO_4$ $[M + H]^+$ 426.1705; found 426.1689.

Ethyl (*E*)-4-[(*E*)-5,6-Dimethoxy-3-oxoisobenzofuran-1(3*H*)-ylidene]-dec-2-enoate (8a): HCl (37% aq.; 12 μL, 0.145 mmol) was added to a solution of **4e** (27.0 mg, 0.058 mmol) in THF (1.2 mL), and the mixture was stirred for 2 h at room temperature. The mixture was diluted with brine (5 mL), and extracted with CH_2Cl_2 (3 × 4 mL). The combined organic extracts were washed with saturated $NaHCO_3$ solution (1 mL) and water (1 mL), and dried (Na_2SO_4). The crude mixture was purified by flash chromatography (silica gel saturated with Et_3N, hexanes/EtOAc/Et_3N, 94:5:1 to 84:15:1), to give **8a** (20.3 mg, 90%) as a yellow solid, m.p. 136–137 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 6.6 Hz, 3 H), 1.25–1.41 (m, 9 H), 1.50–1.60 (m, 2 H), 2.60–2.65 (m, 2 H), 3.98 (s, 3 H), 4.07 (s, 3 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 6.21 (d, *J* = 15.5 Hz, 1 H), 7.32 (s, 1 H), 7.41 (s, 1 H), 8.18 (d, *J* = 15.5 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.1 (CH_3), 14.3 (CH_3), 22.6 (CH_2), 27.6 (CH_2), 29.0 (CH_2), 29.4 (CH_2), 31.7 (CH_2), 56.4 (2 CH_3), 60.7 (CH_2), 105.5 (CH), 106.0 (CH), 119.0 (C), 120.4 (CH), 121.6 (C), 131.9 (C), 139.0 (CH), 148.2 (C), 151.5 (C), 154.9 (C), 166.2 (C), 167.0 (C) ppm. IR (film): $\tilde{\nu}$ = 1770 (s), 1703 (s), 1602 (m) cm^{-1}. MS (CI): *m*/*z* (%) = 389 (98) $[M + H]^+$, 388 (100), 387 (13), 343 (65), 342 (30), 272 (16). HRMS (CI): calcd. for $C_{22}H_{29}O_6$ $[M + H]^+$ 389.1964; found 389.1956.

Ethyl (*E*)-4-[(*Z*)-3-Oxoisobenzofuran-1(3*H*)-ylidene]-4-phenylbut-2-enoate (8b): The hydrolysis procedure described above for the synthesis of **8a** was followed, starting from **4i** (35.0 mg, 0.0885 mmol), and running the reaction for 1 h. The crude mixture was purified by flash chromatography (silica gel, hexanes/EtOAc, 85:15 to 80:20), to give **8b** (23.0 mg, 81%) as a yellow solid, m.p. 145–147 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.1 Hz, 3 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 5.89 (d, *J* = 15.3 Hz, 1 H), 7.32–7.34 (m, 2 H), 7.37–7.48 (m, 3 H), 7.65 (t, *J* = 7.5 Hz, 1 H), 7.84 (t, *J* = 7.8 Hz, 1 H), 7.99 (d, *J* = 7.6 Hz, 1 H), 8.17 (d, *J* = 8.1 Hz, 1 H), 8.44 (d, *J* = 15.3 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 14.5 (CH_3), 61.1 (CH_2), 123.3 (C), 125.3 (CH), 125.6 (CH), 126.8 (CH), 129.2 (CH), 129.3 (2 CH), 130.9 (2 CH), 132.1 (CH), 135.5 (C), 136.3 (CH), 138.2 (C), 140.2 (CH), 148.4 (C), 166.0 (C), 166.7 (C) ppm. IR (film): $\tilde{\nu}$ = 1777 (s), 1707 (s), 1612 (m) cm^{-1}. MS (CI): *m*/*z* (%) = 321 (100) $[M + H]^+$, 320 (71), 276 (15), 275 (73), 274 (15), 247 (20), 246 (12). HRMS (CI): calcd. for $C_{20}H_{17}O_4$ $[M + H]^+$ 321.1127; found 321.1114.

Supporting Information (see footnote on the first page of this article): Preparation and characterization details for compounds **1b**, **1d**, **1e**, **1f**, **1h**, and **1k**; ORTEP diagram of **4f**; copies of ^1H and ^{13}C NMR spectra for all new compounds.

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[1] a) B. Godoi, R. F. Schumacher, G. Zeni, *Chem. Rev.* **2011**, *111*, 2937–2980; b) X. M. Zeng, *Chem. Rev.* **2013**, *113*, 6864–6900.
[2] H. V. Adcock, P. W. Davies, *Synthesis* **2012**, *44*, 3401–3420.
[3] K. Gilmore, I. V. Alabugin, *Chem. Rev.* **2011**, *111*, 6513–6556.
[4] Z. Y. Yan, C. M. Tan, X. Wang, F. Li, G. L. Gao, X. M. Chen, W. S. Wu, J. J. Wang, *Synlett* **2011**, 1863–1870.
[5] B. Yao, C. Jaccoud, Q. Wang, J. Zhu, *Chem. Eur. J.* **2012**, *18*, 5864–5868.
[6] B. Yao, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2013**, *52*, 12992–12996; *Angew. Chem.* **2013**, *125*, 13230–13234.
[7] R. Mancuso, I. Ziccarelli, D. Armentano, N. Marino, S. V. Giofrè, B. Gabriele, *J. Org. Chem.* **2014**, *79*, 3506–3518.
[8] a) R. Álvarez, C. Martínez, Y. Madich, J. G. Denis, J. M. Aurrecoechea, Á. R. de Lera, *Chem. Eur. J.* **2010**, *16*, 12746–12753; b) R. Álvarez, C. Martínez, Y. Madich, J. G. Denis, J. M. Aurrecoechea, Á. R. de Lera, *Chem. Eur. J.* **2012**, *18*, 13894–13896.
[9] a) C. Martínez, J. M. Aurrecoechea, Y. Madich, J. G. Denis, Á. R. de Lera, R. Álvarez, *Eur. J. Org. Chem.* **2012**, 99–106; b) C. Martínez, J. M. Aurrecoechea, Y. Madich, J. G. Denis, A. R. de Lera, R. Álvarez, *Eur. J. Org. Chem.* **2012**, 6291–6292.
[10] Y. Madich, J. G. Denis, A. Ortega, C. Martinez, A. Matrane, L. Belachemi, A. R. de Lera, R. Álvarez, J. M. Aurrecoechea, *Synthesis* **2013**, *45*, 2009–2017.
[11] a) C. Schlemmer, L. Andernach, D. Schollmeyer, B. F. Straub, T. Opatz, *J. Org. Chem.* **2012**, *77*, 10118–10124; b) S. Mehta, T. Yao, R. C. Larock, *J. Org. Chem.* **2012**, *77*, 10938–10944; c) K. Bert, T. Noel, W. Kimpe, J. L. Goeman, J. Van der Eycken, *Org. Biomol. Chem.* **2012**, *10*, 8539–8550.
[12] a) C. Kanazawa, M. Terada, *Tetrahedron Lett.* **2007**, *48*, 933–935; b) A one-pot Sonogashira/cycloisomerization sequence performed in the presence of DBU also leads to *N*-cyclization. It is likely that this cyclization is also a Brönsted-base/Brönsted-acid-promoted process: S. Sarkar, S. Dutta, R. Dey, S. Naskar, *Tetrahedron Lett.* **2012**, *53*, 6789–6792.
[13] a) L. Li, M. Wang, X. J. Zhang, Y. W. Jiang, D. W. Ma, *Org. Lett.* **2009**, *11*, 1309–1312; b) M. Hellal, G. D. Cuny, *Tetrahedron Lett.* **2011**, *52*, 5508–5511.
[14] C. Kanazawa, M. Terada, *Chem. Asian J.* **2009**, *4*, 1668–1672.
[15] X. Liu, X. Xin, D. X. Xiang, Y. J. Liang, X. Q. Xin, W. L. Li, D. W. Dong, *RSC Adv.* **2013**, *3*, 1346–1349.
[16] F. Bellina, D. Ciucci, P. Vergamini, R. Rossi, *Tetrahedron* **2000**, *56*, 2533–2545.
[17] A. Duchene, J. Thibonnet, J. L. Parrain, E. Anselmi, M. Abarbri, *Synthesis* **2007**, 597–607.
[18] The corresponding six-membered lactones, analogous to **8**, are available by hydrolysis of the 6-*endo*-cyclization products **5**,[10] and have also been prepared by oxycyclization/oxidative Heck cascades from 2-alkynylbenzoate esters: P. Zhao, D. Chen, G. Song, K. Han, X. Li, *J. Org. Chem.* **2012**, *77*, 1579–1584.

[19] S. Mehta, J. P. Waldo, B. Neuenswander, G. H. Lushington, R. C. Larock, *ACS Comb. Sci.* **2013**, *15*, 247–254.
[20] The interaction of a base with a sulfonamide N–H has been calculated to have an effect on the regioselectivity of Cu-catalyzed *N*-nucleophile additions to alkynes: N. T. Patil, A. Nijamudheen, A. Datta, *J. Org. Chem.* **2012**, *77*, 6179–6185.
[21] a) S. Y. Tang, Q. X. Guo, Y. Fu, *Chem. Eur. J.* **2011**, *17*, 13866–13876; b) B. Li, Y. Park, S. Chang, *J. Am. Chem. Soc.* **2014**, *136*, 1125–1131; c) D. Fujino, H. Yorimitsu, A. Osuka, *J. Am. Chem. Soc.* **2014**, *136*, 6255–6258, and references cited therein.
[22] CCDC-994241 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[23] H. Sashida, A. Kawamukai, *Synthesis* **1999**, 1145–1148.
[24] G. N. Liu, Y. Zhou, D. J. Ye, D. Y. Zhang, X. Ding, H. L. Jiang, H. Liu, *Adv. Synth. Catal.* **2009**, *351*, 2605–2610.

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