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N-Acylsaccharins as Amide-Based Arylating Reagents via Chemoselective N−C Cleavage: Pd-Catalyzed Decarbonylative Heck Reaction

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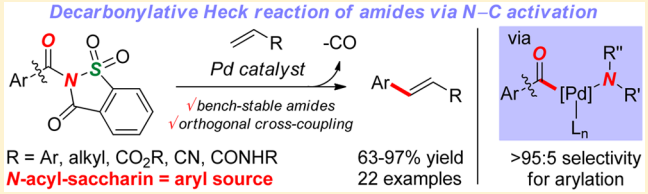
Supporting Information

ABSTRACT: Palladium-catalyzed decarbonylative Heck reaction of amides by chemoselective N−C activation using *N*-acylsaccharins as coupling partners has been accomplished. These studies represent only the second example of amide-Heck reactions reported to date. A broad range of electronically diverse amide and olefin coupling partners is amenable to this transformation. Orthogonal site-selective Heck cross-couplings by C−Br/N−C cleavage and mechanistic studies are reported. This report introduces readily available, bench-stable, cheap, and benign *N*-acylsaccharins as aryl transfer reagents to access versatile aryl-metal intermediates.



The ability to perform selective functionalization reactions represents an enabling approach in organic synthesis. Since the first report in 1968, the Heck reaction has been established as one of the most powerful, chemoselective transition-metal-catalyzed transformations in organic synthesis.[1,2] The classic Heck reaction furnishes functionalized olefins that are essential structural motifs for the synthesis of pharmaceuticals, organic materials, agrochemicals, and complex natural products in both academic and industrial settings.[3] In particular, the use of feedstock alkenes as nucleophilic coupling partners has become a central tool for industrial manufacturing due to lowering the cost associated with olefin prefunctionalization.[4] Methods have been reported for the cross-coupling of aryl halides,[5a−d] triflates,[5e] pseudohalides,[5f] and diazonium salts.[5g,h] While oxidative Heck reactions of carboxylic acids,[6a] phosphonic acids,[6b] and hydrocarbons[6c] have been developed, these methods require stoichiometric oxidants, proceed with limited scope or control of regioselectivity.[2]

In contrast, decarbonylative Heck reactions of stable aroyl electrophiles, such as esters and amides, remain a significant challenge (Figure 1).[7] The advantages of using esters and amides in comparison with typical cross-coupling partners include (i) low cost; (ii) high stability; (iii) ready availability; and (iv) unprecedented potential for unconventional cross-couplings with orthogonal selectivity controlled by the facility of metal insertion into the C−O or C−N bond, which is not possible with unstable aroyl halides and anhydrides. Mechanistically, metal insertion into a weak C(CO)−X bond (X = O, N) enables the use of orthogonal coupling partners to aryl(aroyl) halides by decarbonylation of the initially formed acyl-metal species.[8] However, despite the significant progress in the development of ester electrophiles for Heck reactions,[7c,d] the potential of amides as electrophilic coupling partners remains to be explored.[2f,9] The chief challenge in activating the amide

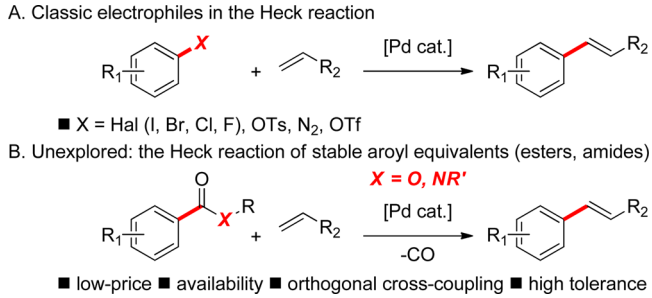


Figure 1. Classic and aroyl electrophiles in the Heck reaction.

bond toward metal insertion is the amide $n_N \rightarrow \pi^*_{C=O}$ resonance (planar amides, ca. 15−20 kcal/mol).[10] A general use of amides as coupling partners in the Heck reaction would have a potential to extend to the functionalization of biomolecules and large scale industrial olefinations using bench-stable, chemoselective, low-cost acid amide reagents.

We have recently established the first decarbonylative Heck reaction of amides using *N*-glutarimides as coupling partners by steric distortion (Figure 2A).[11] The first decarbonylative Suzuki and direct decarbonylative C−H activation of *N*-glutarimide amides using Ni and Rh catalysis have been developed.[12] Recently, Ni-catalyzed decarbonylative borylation of amides by N−C cleavage has been accomplished.[13,14] These reactions proceed via selective N−C insertion/decarbonylation, in which the facility of metal insertion is controlled by amide destabilization.[15] Extensive studies on amide geometry provide additional evidence for the distortion of amides undergoing metal insertion.[16] To expand the generality of decarbonylative

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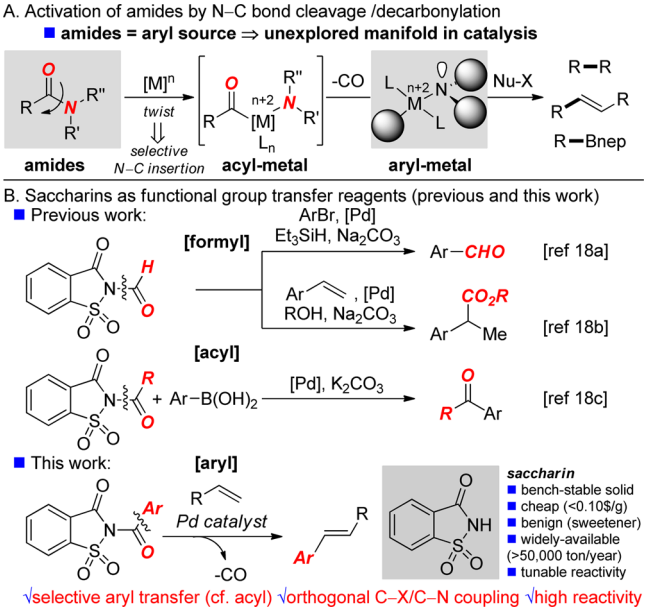


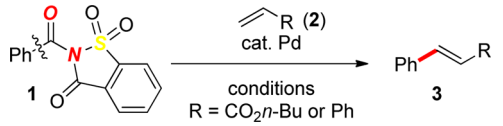
Figure 2. (a) Decarbonylative N−C cleavage in amides. (b) Saccharins as electrophilic functional group transfer reagents.

Heck reactions by N−C cleavage, we considered *N*-acylsaccharins as bench-stable, amide-based, electrophilic coupling partners.[17] Recently, *N*-acylsaccharins have emerged as efficient functional group transfer reagents in metal-catalyzed formylation[18a] and alkoxycarbonylation.[18b] We have developed conditions for the Suzuki-Miyaura cross-coupling of *N*-acylsaccharins to yield ketones with exclusive RC(O)−coupling selectivity (acyl transfer, Figure 2B).[18c]

Herein, we report for the first time the Pd-catalyzed decarbonylative Heck reaction of *N*-acylsaccharins as electrophilic coupling partners by highly chemoselective N−C bond cleavage/decarbonylation. The following features of our findings are noteworthy: (i) low-price, availability, benign nature of saccharin; (ii) bench-stability and ease of crystallization of *N*-acylsaccharins, which allows to avoid sensitive intermediates during cross-couplings; (iii) excellent functional group tolerance and wide range of electronically diverse amide and olefin coupling partners that undergo this transformation; (iv) operationally simple, base-free, ligand-free conditions; (v) the first iterative Heck cross-couplings using carbonyl electrophiles by site-selective C−N/C−Br cleavage; (vi) most importantly, this report introduces readily available, bench-stable, cheap *N*-acylsaccharins as aryl transfer reagents for metal-catalyzed transformations via metal-insertion/decarbonylation to access versatile aryl metal intermediates. Our studies demonstrate the highest reactivity of *N*-acylsaccharins in amide N−C cleavage discovered to date.[18c]

The Heck cross-coupling of *N*-benzoylsaccharin (**1**) with *n*-butyl acrylate (**2**) was investigated as a model reaction to identify the most active catalyst system. Selected key optimization results obtained during the optimization studies are summarized in Table 1. Under our standard conditions, **1** underwent the decarbonylative N−C coupling in excellent 98% yield (entry 1). Notably, we found that the presence of halide salts had a negative impact on the reaction efficiency (entries 2−15).[19] Similarly, the use of external nucleophiles[7] (entries 4 and 13) and other solvents (entries 5−6 and 11−12) resulted in a diminished yield of the arylation product. We hypothesize that these effects are consistent with high electrophilicity of *N*-

Table 1. Optimization of Pd-Catalyzed Decarbonylative Heck Reaction of *N*-Acylsaccharins by N−C Cleavage[a]



entry	catalyst	ligand	solvent	yield (%)
1	$PdCl_2$		NMP	98
2	$PdCl_2$	LiBr	NMP	63
3[b]	$PdCl_2$	LiBr	NMP	41
4[c]	$PdCl_2$	LiBr	NMP	<5
5	$PdCl_2$	LiBr	toluene	<5
6	$PdCl_2$	LiBr	dioxane	19
7[d]	$PdCl_2$	LiBr	NMP	43
8[e]	$PdCl_2$	LiBr	NMP	28
9[f]	$PdCl_2$	LiBr	NMP	<5
10[b]	$PdCl_2$		NMP	53
11	$PdCl_2$		toluene	26
12	$PdCl_2$		dioxane	36
13[c]	$PdCl_2$		NMP	25
14[d]	$PdCl_2$		NMP	50
15[e]	$PdCl_2$		NMP	40
16[g]	$PdCl_2$	LiBr	NMP	<5
17[g,h,i]	$PdCl_2$		NMP	75
18[g,i,j]	$PdCl_2$		NMP	92

[a]Conditions: **1** (0.20 mmol), R-CH=CH_2 (2.0 equiv), catalyst (3 mol %), ligand (9 mol%), 160 °C, 18 h. R = CO_2n-Bu. [b]R-CH=CH_2 (1.2 equiv). [c]Isoquinoline (0.10 equiv). [d]120 °C. [e]80 °C. [f]Ligand (1 equiv). [g]R = Ph. [h]180 °C. [i]Catalyst (5 mol%). [j]R-CH=CH_2 (3 equiv).

acylsaccharins and competing nucleophilic addition. Mechanistically, the reaction ensues at 80 °C with complete aryl- vs acyl-selectivity (entries 8−9 and 14−15), consistent with the high propensity of the N−C bond in *N*-acylsaccharins for metal insertion/decarbonylation.[18a−c] Furthermore, we were pleased to find that after small adjustment of the reaction conditions, the process could be extended to valuable styrene nucleophiles (entries 16−18). The use of other Pd precursors, including $Pd(OAc)_2$, $PdBr_2$, and PdI_2 resulted in low reaction efficiency (not shown). Importantly, under the optimized conditions, products resulting from the acyl-transfer (cf. arylation) were not observed,[18c] demonstrating efficient decarbonylation under these conditions.[8] Furthermore, cleavage of the alternative C−SO_2 bond was not observed.[20] Overall, the optimized conditions compare favorably with other methods for the decarbonylative Heck reactions in terms of operational simplicity and reaction efficiency (vide infra).[7,11]

With the optimized conditions in hand, the substrate scope was next investigated (Table 2). As shown, a wide range of electronically varied substrates containing diverse functional groups underwent the cross-coupling in high yields and with generally excellent regioselectivity (entries 1−21). Neutral (**3a**), electron-rich (**3b**), electron-poor (**3c**), fluoro- (**3d**), chloro- (**3e**), bromo- (**3f**), ester- (**3g**), and nitro-containing substrates (**3h**) were perfectly tolerated, affording the corresponding olefins in 63−82% yields. Debromination was not observed. Moreover, ortho-substituted *N*-acylsaccharins (**3i**, **3j**) coupled in high yields. The scope of the reaction with respect to the olefin component is also broad and encompasses *α*,*β*-unsaturated esters (**3k**, **3o**), amides (**3l**), and nitriles (**3m**). Disubstituted olefins are suitable coupling partners (**3n**).[21a] Aliphatic alkenes can also be used (**3p**); however, these

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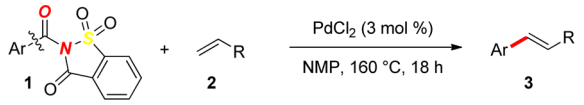
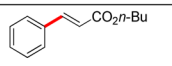
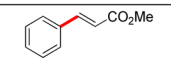
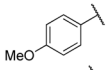
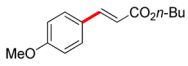
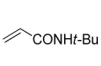
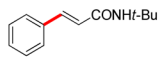
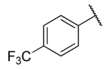
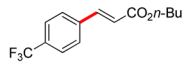
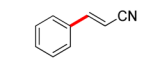
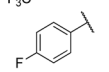
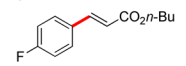
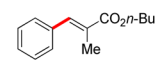
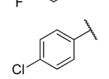
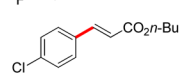
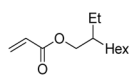
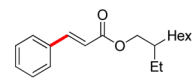
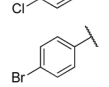
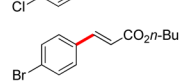
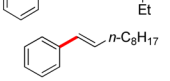
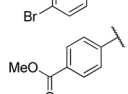
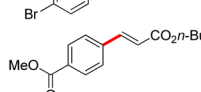
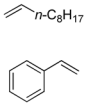
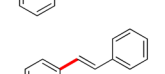
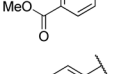
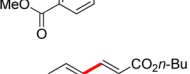
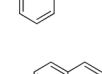
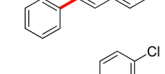
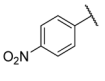
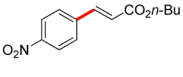
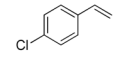
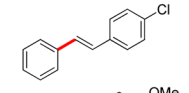
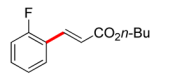
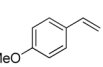
Table 2. Pd-Catalyzed Decarbonylative Heck Cross-Coupling of *N*-Acylsaccharins by N−C Cleavage: Substrate Scope[a]



entry	3	amide	product (3)	yield (%)	entry	3	olefin	product (3)	yield (%)
1	**3a**			82	11	**3k**			81
2	**3b**			73	12	**3l**			80
3	**3c**			78	13	**3m**			95
4	**3d**			69	14[b]	**3n**			78
5	**3e**			72	15	**3o**			75
6	**3f**			63	16[c]	**3p**			84
7	**3g**			65	17[d]	**3q**			85
8	**3h**			77	18[d]	**3r**			89
9	**3i**			91	19[d]	**3s**			79
10	**3j**			97	20[d] 21[d]	**3s** **3t**			70 71

R = MeO (**3s**)
R = CF_3 (**3t**)

[a]**1** (0.20 mmol), R-CH=CH_2 (2.0 equiv), $PdCl_2$ (3 mol%), NMP, 160 °C, selectivity >20:1. [b]Selectivity: 5.80:2.20:1.00. [c]Isomers (8.44:2.72:5.99:1.00). [d]**1** (1.0 equiv), R-CH=CH_2 (3.0 equiv), $PdCl_2$ (5 mol%). 2,1/1,2:91:9 (**3q**), 95:5 (**3r**), 81:19 (**3s**), 75:25 (**3s′**), 92:8 (**3t**).

substrates afford mixture of isomers, as expected.[21b,7c] Finally, electronically diverse styrenes underwent coupling in good yields and with high regioselectivity. For these substrates a higher catalyst loading (5 mol%) was used to obtain optimum results. Only monoarylation products were observed in all examples examined.[7d,e] In all cases, exclusive formation of *E* isomers was found. At this stage, saccharin recovery has not been performed as recovery from highly polar solvents is not straightforward. The reaction enables synthesis of olefins with diverse electrophilic functional handles for further manipulation. Of note is the synthesis of a common UV−B sunscreen produced industrially (**3o**).[4a] While the reaction requires NMP as a polar solvent to achieve optimum yields, the reaction does not require expensive oxidants and the scope of the reaction is not limited to *ortho*-substituted substrates as is the case with oxidative Heck reactions.[6−8] To assess the utility of the process, the coupling was performed on a 2.0 mmol scale using *n*-butyl acrylate and styrene, and gave **3a** and **3q** in 79% (>20:1 selectivity) and 87% (92:8 selectivity) isolated yields, respectively, attesting to the synthetic utility of the method.

Intrigued by the high reactivity of *N*-acylsaccharins (twisted amide bond: τ = 23.0°, χ_N = 12.5°),[18c] we conducted preliminary studies to gain insight into the reaction mechanism (Scheme 1).[22] (1) Intermolecular competition experiments between differently substituted *N*-acylsaccharins indicated that electron-deficient substrates react preferentially (Scheme 1A). (2) Experiments with different olefins established the following reactivity order: H_2C=CH−CO_2n-Bu ≈ H_2C=CH-Ph > H_2C=C-MeCO_2n-Bu (Scheme 1B). (3) Experiments with aroyl electrophiles revealed the following order of reactivity: *N*-acylsaccharins > *N*-glutarimides ≈ $(Ar-CO)_2O$ ≫ Ar−CO_2R (Scheme 1C). (4) Electronic effects observed in the regioselectivity of the arylation with styrenes (styrene: ρ-value of 1.21, R^2 = 0.99; amide: ρ^+-value of 0.46, R^2 = 0.90) indicate an increase in the arylation regioselectivity of electron-deficient

Scheme 1. Mechanistic Studies

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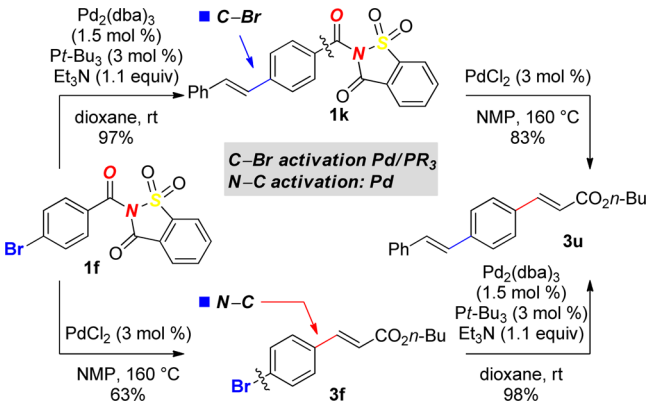
olefins and electron-deficient amides. These preliminary studies are consistent with the initial metal insertion into the amide N−C bond;[9] olefin insertion might be a kinetically relevant step in the reaction.[22b] The high reactivity of *N*-acylsaccharins (cf. glutarimides)[11] bodes well for further applications in decarbonylative cross-couplings by amide N−C cleavage.

We highlighted the synthetic utility of *N*-acylsaccharins as orthogonal cross-coupling partners in iterative site-specific C−N/C−Br cross-coupling (Scheme 2).[23] The Heck cross-coupling of aryl bromides can be achieved by Pd/P*t*-Bu$_3$-catalysis,[5d,22c] leaving the amide bond in *N*-acylsaccharins intact (Scheme 2, top). Alternatively, the amide N−C cross-coupling can be followed by the C−Br cleavage (Scheme 2, bottom). To our knowledge, this is the first sequential cross-coupling involving decarbonylative Heck reactions.[2,3,7] The iterative cross-coupling is facilitated by the high reactivity of *N*-acylsaccharins[18] and the ease of purification of intermediates by recrystallization.[17]

Scheme 2. Iterative Heck Cross-Coupling of *N*-Acylsaccharins: C−N vs C−Br Cleavage



In summary, we have reported the first Pd-catalyzed decarbonylative Heck cross-coupling of *N*-acylsaccharins by chemoselective N−C cleavage. A variety of amide and olefin substrates is suitable for this reaction. The sequential Heck coupling of C−Br and C−N bonds has been demonstrated for the first time. *N*-Acylsaccharins are air-stable, crystalline solids that show comparable reactivity to *N*-glutarimide amides. The discovery that *N*-acylsaccharins serve as selective bench-stable aryl transfer reagents may enable the development of a broad range of novel metal-catalyzed transformations.

EXPERIMENTAL SECTION

General Methods. All starting materials reported in the manuscript have been prepared according to the method reported previously.[24] All compounds reported in this manuscript have been previously reported or are commercially available unless noted otherwise. Spectroscopic data matched literature values. General methods have been published.[18c]

General Procedure for Amide Synthesis. An oven-dried flask (25 mL) equipped with a stir bar was charged with amine (typically, 3.0 mmol, 1.0 equiv), triethylamine (typically, 1.0 equiv), and *N*,*N*-dimethylacetamide (DMAc, typically, 0.75 M), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. Acyl chloride (typically, 1.0 equiv) was added dropwise to the reaction mixture with vigorous stirring at 0 °C, and the reaction mixture was stirred for 1 h at room temperature. After the indicated time, the reaction mixture was diluted with H_2O (5 mL). The solid was collected by filtration, washed with Et_2O (1 × 10 mL), and dried. The crude product was purified by recrystallization (methanol or toluene) to give analytically pure product. All *N*-acylsaccharins are bench-stable solids with no decomposition observed while storing on benchtop at room temperature for a period of six months.

General Procedure for Heck Cross-Coupling. An oven-dried vial equipped with a stir bar was charged with amide substrate (neat, 1.0 equiv), $PdCl_2$ (typically, 3 mol %), and olefin (typically, 2.0 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. *N*-Methyl-2-pyrrolidinone (NMP, 0.25 M) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 160 °C, and stirred for the indicated time at 160 °C. After the indicated time, the reaction mixture was cooled down to room temperature and diluted with CH_2Cl_2 (5 mL). The sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and/or GC-MS to obtain conversion, selectivity, and yield using internal standard and comparison with authentic samples. In all examples reported in the manuscript 2,1/1,2-selectivity was obtained by analysis of the crude reaction mixture. Unless indicated otherwise, in all examples reported in the manuscript single olefin isomers were observed (*E*/*Z* > 98:2). Unless indicated otherwise, only monoarylated products were observed (mono/diarylation selectivity >98:2). All yields reported in the manuscript refer to isolated yields after purification by chromatography on silica gel (hexanes/EtOAc). Unless indicated otherwise, in all examples reported in the manuscript single olefin regioisomers were obtained after the purification.

Representative Procedure for Heck Cross-Coupling. An oven-dried vial equipped with a stir bar was charged with *N*-benzoylsaccharin (neat, 57.5 mg, 0.2 mmol), $PdCl_2$ (1.1 mg, 3 mol %) and *n*-butyl acrylate (51.3 mg, 2.0 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. *N*-Methyl-2-pyrrolidinone (0.25 M) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 160 °C, and stirred for 18 h at 160 °C. After the indicated time, the reaction mixture was cooled down to room temperature and diluted with CH_2Cl_2 (5 mL). The sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, selectivity, and yield using internal standard and comparison with authentic samples. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. Purification by chromatography on silica gel (hexanes/EtOAc = 10/1) afforded the title product. Yield 82% (33.5 mg, 0.164 mmol). Colorless oil. Characterization data are included in the section below.

2.0 mmol scale coupling was performed according to the representative procedure using *N*-benzoylsaccharin (neat, 575 mg, 2.0 mmol), $PdCl_2$ (11 mg, 3 mol%) and *n*-butyl acrylate (513 mg, 2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) at 160 °C for 18 h. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. Purification by chromatography on silica gel (hexanes/EtOAc = 10/1) afforded **3a**. Yield 79% (323 mg, 1.58 mmol). Colorless oil. Characterization data are included in the section below.

2.0 mmol scale coupling using styrene was performed according to the representative procedure using *N*-benzoylsaccharin (neat, 575 mg, 2.0 mmol), $PdCl_2$ (18 mg, 5 mol%) and styrene (624 mg, 3.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) at 160 °C for 18 h. 2,1/1,2 = 92:8. *E*/*Z* > 98:2. Purification by chromatography on silica gel (hexanes/EtOAc = 10/1) afforded **3q**. Yield 87% (314 mg, 1.74 mmol). White solid. Characterization data are included in the section below.

*N-Benzoylsaccharin (**1a**).*[24] Yield 95% (0.82 g). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16−8.15 (d, *J* = 7.7 Hz, 1 H), 8.05−8.01 (m, 2 H), 7.96−7.94 (t, *J* = 7.9 Hz, 1 H), 7.80−7.78 (d, *J* = 8.3 Hz, 2 H), 7.70−7.67 (t, *J* = 7.1 Hz, 1 H), 7.55−7.52 (t, *J* = 7.7 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 157.5, 138.5, 136.4, 134.9, 133.9, 132.4, 129.6, 128.5, 126.4, 125.6, 121.3. MS = 287.0 (EI).

*N-4-Methoxylbenzoylsaccharin (**1b**).*[18c] Yield 81% (0.77 g). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16−8.15 (d, *J* = 7.7 Hz, 1 H), 8.01−8.00 (d, *J* = 4.2 Hz, 2 H), 7.95−7.92 (m, 1 H), 7.85−7.83 (d, *J* = 8.8 Hz, 2 H), 7.00−6.99 (d, *J* = 8.8 Hz, 2 H), 3.91 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 164.7, 158.0, 138.5, 136.3, 134.9, 132.8, 126.3, 125.8, 124.4, 121.2, 114.0, 55.7. MS = 317.0 (EI).

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*N-4-Trifluorobenzoylsaccharin (**1c**).*[18c] Yield 83% (0.89 g). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17−8.15 (d, J = 7.7 Hz, 1 H), 8.06−8.05 (d, J = 4.0 Hz, 2 H), 7.99−7.95 (m, 1 H), 7.87−7.85 (d, J = 8.2 Hz, 2 H), 7.80−7.78 (d, J = 8.2 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 157.2, 138.4, 136.8, 135.7, 135.1, 134.9 (q, J^2 = 32.8 Hz), 129.6, 126.6, 125.5 (q, J^3 = 3.7 Hz), 125.2, 123.4 (q, J^1 = 271.2 Hz), 121.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ −63.22. MS = 355.0 (EI).

*N-4-Fluorobenzoylsaccharin (**1d**).*[18c] Yield 79% (0.73 g). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17−8.15 (d, J = 7.7 Hz, 1 H), 8.04−8.03 (d, J = 3.9 Hz, 2 H), 7.97−7.94 (m, 1 H), 7.85−7.82 (t, J = 8.6 Hz, 2 H), 7.22−7.19 (t, J = 8.6 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2 (d, J^1 = 255.3 Hz), 165.2, 157.6, 138.4, 136.5, 135.0, 132.6 (d, J^3 = 9.6 Hz), 128.6, 126.5, 125.5, 121.3, 115.9 (d, J^2 = 22.3 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ −102.58. MS = 305.0 (EI).

*N-4-Chlorobenzoylsaccharin (**1e**).*[18c] Yield 94% (0.91 g). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17−8.16 (d, J = 7.7 Hz, 1 H), 8.04−8.03 (d, J = 4.1 Hz, 2 H), 7.98−7.94 (m, 1 H), 7.74−7.73 (d, J = 8.3 Hz, 2 H), 7.51−7.50 (d, J = 8.4 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 157.5, 140.6, 138.5, 136.6, 135.0, 131.9, 131.0, 128.9, 126.5, 125.4, 121.3. MS = 321.0 (EI).

*N-4-Bromobenzoylsaccharin (**1f**). New Compound.* Yield 85% (0.94 g). White solid. mp = 191−193 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17−8.15 (d, J = 7.7 Hz, 1 H), 8.04−8.03 (d, J = 4.1 Hz, 2 H), 8.03−8.01 (d, J = 8.5 Hz, 1 H), 7.98−7.94 (m, 1 H), 7.71−7.70 (d, J = 8.3 Hz, 1 H), 7.69−7.64 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 157.4, 138.5, 136.6, 135.0, 132.4, 131.9, 131.0, 129.2, 126.5, 125.4, 121.3. MS = 364.9 (EI). HRMS calcd for $C_{14}H_9BrO_4NS$ (M^+ + H) 365.9430, found 365.9428.

*N-4-Methoxycarbonylbenzoylsaccharin (**1g**).*[18c] Yield 91% (0.94 g). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24−8.23 (d, J = 7.7 Hz, 1 H), 8.19−8.17 (d, J = 8.3 Hz, 2 H), 8.16−8.14 (d, J = 7.8 Hz, 1 H), 8.05−8.04 (d, J = 3.4 Hz, 2 H), 7.82−7.80 (d, J = 8.3 Hz, 2 H), 3.99 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 157.2, 138.5, 136.6, 135.1, 134.4, 130.5, 130.1, 129.6, 129.2, 126.5, 125.3, 121.4, 52.6. MS = 345.0 (EI).

*N-4-Nitrobenzoylsaccharin (**1h**).*[18c] Yield 87% (0.87 g). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39−8.37 (d, J = 8.7 Hz, 2 H), 8.17−8.16 (d, J = 7.7 Hz, 1 H), 8.08−8.07 (d, J = 3.6 Hz, 2 H), 8.00−7.97 (m, 1 H), 7.91−7.89 (d, J = 8.7 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 162.6, 138.4, 137.9, 136.9, 135.2, 133.9, 130.1, 126.7, 125.0, 123.6, 121.5. MS = 332.0 (EI).

*N-2-Fluorobenzoylsaccharin (**1i**).*[18c] Yield 83% (0.76 g). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15−8.13 (d, J = 7.7 Hz, 1 H), 8.06−8.01 (m, 2 H), 7.96−7.93 (t, J = 6.7 Hz, 1 H), 7.72−7.69 (t, J = 7.5 Hz, 1 H), 7.65−7.61 (m, 1 H), 7.36−7.33 (t, J = 7.6 Hz, 1 H), 7.18−7.14 (t, J = 9.6 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 157.7 (d, J^1 = 266.4 Hz), 138.5, 136.6, 134.8, 134.8, 130.7 (d, J^3 = 1.5 Hz), 126.5, 125.2, 124.8, 124.7, 121.3, 115.9 (d, J^2 = 21.2 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ −112.53. MS = 305.0 (EI).

*N-2-Methylbenzoylsaccharin (**1j**).*[18c] Yield 95% (0.87 g). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10−8.09 (d, J = 7.7 Hz, 1 H), 8.04−8.00 (m, 2 H), 7.94−7.91 (t, J = 6.2 Hz, 1 H), 7.50−7.47 (t, J = 7.6 Hz, 1 H), 7.43−7.42 (d, J = 7.6 Hz, 1 H), 7.34−7.30 (m 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 156.8, 138.4, 136.6, 135.0, 133.1, 131.8, 130.9, 127.7, 126.4, 125.7, 125.3, 121.3, 19.39. MS = 301.0 (EI).

*(E)-Butyl Cinnamate (**3a**).*[11] According to the general procedure, the reaction of *N*-benzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol %) and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 82% yield (33.5 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt =15.46 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72−7.69 (d, J = 16.0 Hz, 1 H), 7.56−7.55 (d, J = 4.9 Hz, 2 H), 7.41−7.40 (t, J = 1.9 Hz, 3 H), 6.49−6.45 (d, J = 15.9 Hz, 1 H), 4.25−4.23 (t, J = 6.6 Hz, 2 H), 1.75−1.69 (m, 2 H), 1.51−1.43 (m, 2 H), 1.01−0.98 (t, J = 7.4 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 144.6, 134.5, 130.2, 128.9, 128.1, 118.3, 64.5, 30.8, 19.2, 13.8. MS = 204.1 (EI).

*(E)-Butyl 3-(4-methoxyphenyl)acrylate (**3b**).*[25] According to the general procedure, the reaction of *N*-4-methoxylbenzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%) and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 73% yield (34.2 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt =17.36 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68−7.65 (d, J = 16.0 Hz, 1 H), 7.51−7.49 (d, J = 8.7 Hz, 2 H), 6.94−6.92 (d, J = 8.6 Hz, 2 H), 6.35−6.32 (d, J = 16.0 Hz, 1 H), 4.24−4.21 (t, J = 6.7 Hz, 2 H), 3.86 (s, 3 H), 1.74−1.68 (m, 2 H), 1.50−1.43 (m, 2 H), 1.00−0.97 (t, J = 7.4 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 161.3, 144.2, 129.7, 127.2, 115.8, 114.3, 64.3, 55.4, 30.8, 19.2, 13.8. MS = 234.1 (EI).

*(E)-Butyl 3-(4-(Trifluoromethyl)phenyl)acrylate (**3c**).*[25] According to the general procedure, the reaction of *N*-4-trifluoromethylbenzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 78% yield (42.5 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt =13.99 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73−7.70 (d, J = 16.1 Hz, 1 H), 7.68−7.64 (t, J = 9.3 Hz, 4 H), 6.55−6.52 (d, J = 16.1 Hz, 1 H), 4.27−4.24 (t, J = 6.6 Hz, 2 H), 1.75−1.70 (m, 2 H), 1.51−1.43 (m, 2 H), 1.01−0.98 (t, J = 7.4 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 142.7, 137.9, 131.7 (q, J^2 = 32.5 Hz), 128.2, 125.9 (q, J^3 = 3.7 Hz), 123.8 (q, J^1 = 270.4 Hz), 120.9, 64.8, 30.7, 19.2, 13.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ −62.86. MS = 272.1 (EI).

*(E)-Butyl 3-(4-Fluorophenyl)acrylate (**3d**).*[25] According to the general procedure, the reaction of *N*-4-fluorobenzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 69% yield (30.7 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt =14.74 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68−7.65 (d, J = 16.0 Hz, 1 H), 7.55−7.52 (t, J = 7.5 Hz, 2 H), 7.12−7.08 (t, J = 8.3 Hz, 2 H), 6.40−6.37 (d, J = 16.0 Hz, 1 H), 4.25−4.22 (t, J = 6.6 Hz, 2 H), 1.74−1.68 (m, 2 H), 1.50−1.43 (m, 2 H), 1.00−0.97 (t, J = 7.4 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 163.9 (d, J^1 = 249.0 Hz), 143.3, 130.7, 129.9 (d, J^3 = 8.5 Hz), 118.1 (d, J^4 = 2.3 Hz), 116.0 (d, J^2 = 21.7 Hz), 64.5, 30.8, 19.2, 13.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ −109.78. MS = 222.1 (EI).

*(E)-Butyl 3-(4-Chlorophenyl)acrylate (**3e**).*[25] According to the general procedure, the reaction of *N*-4-chlorobenzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 72% yield (34.4 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt =16.51 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66−7.63 (d, J = 16.0 Hz, 1 H), 7.49−7.47 (d, J = 8.0 Hz, 2 H), 7.39−7.37 (d, J = 8.0 Hz, 2 H), 6.45−6.42 (d, J = 16.1 Hz, 1 H), 4.25−4.22 (t, J = 6.6 Hz, 2 H), 1.74−1.68 (m, 2 H), 1.50−1.42 (m, 2 H), 1.00−0.97 (t, J = 7.3 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 143.1, 136.1, 133.0, 129.2, 129.2, 118.9, 64.6, 30.8, 19.2, 13.8. MS = 238.1 (EI).

*(E)-Butyl 3-(4-Bromophenyl)acrylate (**3f**).*[25] According to the general procedure, the reaction of *N*-4-bromobenzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 63% yield (35.7 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt =17.36 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65−7.61 (d, J = 16.0 Hz, 1 H), 7.55−7.53 (d, J = 8.2 Hz, 2 H), 7.42−7.40 (d, J = 8.3 Hz, 2 H), 6.47−6.43 (d, J = 16.0 Hz, 1 H), 4.25−4.22 (t, J = 6.6 Hz, 2 H), 1.74−1.68 (m, 2 H), 1.50−1.42 (m, 2 H), 1.00−0.97 (t, J = 7.4 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 143.2, 133.4, 132.1, 129.4, 124.5, 119.0, 64.6, 30.8, 19.2, 13.8. MS = 282.0 (EI).

*(E)-Methyl 4-(3-Butoxy-3-oxoprop-1-en-1-yl)benzoate (**3g**).*[25] According to the general procedure, the reaction of *N*-4-methoxycarbonylbenzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 65% yield (34.1 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt =18.66 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08−8.06 (d, J = 7.9 Hz, 2 H), 7.73−7.69 (d, J = 16.1 Hz, 1 H), 7.61−7.60 (d, J = 7.9 Hz, 2 H), 6.56−6.52 (d, J = 16.1 Hz, 1 H), 4.26−4.23 (t, J = 6.6 Hz, 2 H), 3.95 (s, 3 H), 1.74−1.69 (m, 2 H), 1.50−1.43 (m, 2 H), 1.00−0.97 (t, J = 7.4 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6,

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166.5, 143.1, 138.7, 131.3, 130.1, 127.9, 120.7, 64.7, 52.3, 30.7, 19.2, 13.8. MS = 262.1 (EI).

*(E)-Butyl 3-(4-Nitrophenyl)acrylate (**3h**).*[25] According to the general procedure, the reaction of *N*-4-nitrobenzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 77% yield (38.4 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt =18.78 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28−8.26 (d, *J* = 8.4 Hz, 2 H), 7.74−7.71 (d, *J* = 17.4 Hz, 1 H), 7.71−7.69 (d, *J* = 8.9 Hz, 2 H), 6.60−6.57 (d, *J* = 16.0 Hz, 1 H), 4.27−4.25 (t, *J* = 6.6 Hz, 2 H), 1.75−1.70 (m, 2 H), 1.50−1.43 (m, 2 H), 1.01−0.98 (t, *J* = 7.5 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 148.5, 141.6, 140.6, 128.6, 124.2, 122.6, 64.9, 30.7, 19.2, 13.7. MS = 249.1 (EI).

*(E)-Butyl 3-(4-Fluorophenyl)acrylate (**3i**).*[25] According to the general procedure, the reaction of *N*-2-fluorobenzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 91% yield (40.5 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt =14.21 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85−7.82 (d, *J* = 16.2 Hz, 1 H), 7.58−7.55 (t, *J* = 7.6 Hz, 1 H), 7.40−7.36 (m, 1 H), 7.20−7.17 (t, *J* = 7.6 Hz, 1 H), 7.14−7.10 (t, *J* = 9.8 Hz, 1 H), 6.58−6.55 (d, *J* = 16.2 Hz, 1 H), 4.26−4.23 (t, *J* = 6.6 Hz, 2 H), 1.75−1.69 (m, 2 H), 1.50−1.43 (m, 2 H), 1.01−0.98 (t, *J* = 7.4 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 161.4 (d, J^1 = 252.3 Hz), 137.2, 131.6 (d, J^4 = 8.7 Hz), 129.1 (d, J^7 = 2.8 Hz), 124.4 (d, J^6 = 3.6 Hz), 122.6 (d, J^3 = 11.6 Hz), 120.9 (d, J^5 = 6.5 Hz), 116.2 (d, J^2 = 21.8 Hz), 64.6, 30.8, 19.2, 13.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ −114.39. MS = 222.1 (EI).

*(E)-Butyl 3-(o-Tolyl)acrylate (**3j**).*[25] According to the general procedure, the reaction of *N*-2-methylbenzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 97% yield (42.4 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt = 15.15 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02−7.98 (d, *J* = 15.9 Hz, 1 H), 7.59−7.57 (d, *J* = 7.7 Hz, 1 H), 7.31−7.28 (t, *J* = 7.2 Hz, 1 H), 7.25−7.22 (t, *J* = 6.9 Hz, 2 H), 6.40−6.37 (d, *J* = 15.9 Hz, 1 H), 4.26−4.23 (t, *J* = 6.7 Hz, 2 H), 2.47 (s, 3 H), 1.75−1.69 (m, 2 H), 1.51−1.43 (m, 2 H), 1.01−0.98 (t, *J* = 7.4 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 142.3, 137.6, 133.5, 130.8, 130.0, 126.4, 126.3, 119.3, 64.4, 30.8, 19.8, 19.2, 13.8. MS = 218.1 (EI).

*(E)-Methyl Cinnamate (**3k**).*[11] According to the general procedure, the reaction of *N*-benzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and methyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 81% yield (26.3 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt = 12.56 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74−7.71 (d, *J* = 16.0 Hz, 1 H), 7.55−7.55 (d, *J* = 2.9 Hz, 2 H), 7.42−7.41 (t, *J* = 2.5 Hz, 3 H), 6.49−6.46 (d, *J* = 16.0 Hz, 1 H), 3.84 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 144.9, 134.4, 130.3, 128.9, 128.1, 117.8, 51.7. MS = 162.1 (EI).

*(E)-N-(tert-Butyl)cinnamamide (**3l**).*[11] According to the general procedure, the reaction of *N*-benzoylsaccharin (0.20 mmol), $PdCl_2$ (5 mol%), and *N*-(*tert*-butyl)acrylate (3.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 80% yield (32.6 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt = 16.60 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61−7.58 (d, *J* = 15.6 Hz, 1 H), 7.51−7.50 (d, *J* = 7.0 Hz, 2 H), 7.40−7.37 (t, *J* = 6.6 Hz, 3 H), 6.36−6.33 (d, *J* = 15.5 Hz, 1 H), 5.45 (s, 1 H), 1.46 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 140.3, 135.0, 129.5, 128.8, 127.7, 121.9, 51.5, 28.9. MS = 203.1 (EI).

*(E)-Cinnamonitrile (**3m**).*[11] According to the general procedure, the reaction of *N*-benzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and acrylonitrile (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.80 mL) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 95% yield (24.6 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt = 12.35 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49−7.45 (t, *J* = 11.2 Hz, 5 H), 7.43−7.42 (d, *J* = 8.2 Hz, 1 H), 5.93−5.90 (d, *J* = 16.7 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.6, 133.5, 131.2, 129.1, 127.4, 118.2, 96.4. MS = 129.1 (EI).

*(E)-Methyl 2-Methyl-3-phenyl Acrylate (**3n**).*[11] According to the general procedure, the reaction of *N*-benzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and *n*-butyl methacrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 78% yield (34.1 mg). Colorless oil. Selectivity = 5.80:2.20:1.00. *E*/*Z* > 98:2. GC: rt = 15.01 min; isomers 13.74, 13.61 min. The minor isomers could not be separated by silica gel chromatography. Data for the major isomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71−7.42 (s, 1 H), 7.42−7.42 (d, *J* = 3.4 Hz, 4 H), 7.36−7.33 (m, 1 H), 4.26−4.23 (t, *J* = 6.6 Hz, 2 H), 2.14 (s, 3 H), 1.76−1.71 (m, 2 H), 1.52−1.44 (m, 2 H), 1.02−0.99 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 138.6, 136.0, 129.7, 129.0, 128.4, 128.2, 64.8, 30.8, 19.3, 14.1, 13.8. MS = 218.1 (EI).

*(E)-5-Ethyl-1-phenylnon-1-en-3-one (**3o**).*[26] According to the general procedure, the reaction of *N*-benzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and 2-ethylhexyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 75% yield (39.1 mg). Colorless oil. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt = 18.02 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72−7.69 (d, *J* = 16.0 Hz, 1 H), 7.56−7.55 (d, *J* = 4.9 Hz, 2 H), 7.41−7.41 (t, *J* = 3.2 Hz, 3 H), 6.49−6.46 (d, *J* = 16.0 Hz, 1 H), 4.16−4.14 (t, *J* = 5.1 Hz, 2 H), 1.70−1.66 (m, 1 H), 1.48−1.42 (m, 2 H), 1.38−1.34 (m, 6 H), 0.97−0.91 (m, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 144.5, 134.5, 130.2, 128.9, 128.1, 118.4, 67.0, 38.9, 30.5, 29.0, 23.9, 23.0, 14.1, 11.1. MS = 260.2 (EI).

*(E)-Dec-1-en-1-ylbenzene (**3p**).*[11] Mixture of isomers. According to the general procedure, *N*-benzoylsaccharin (0.20 mmol) was reacted with $PdCl_2$ (3 mol%), and 1-decene (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C. The compound was characterized by GC-MS analysis. The sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples. Yield =84%. Selectivity =8.44:2.72:5.99:1. GC: rt = 15.45 min; isomers 14.95, 14.51, 14.34 min. MS = 216.2 (EI). For characterization data, see ref 11.

*(E)-1,2-Diphenylethene (**3q**).*[11] According to the general procedure, the reaction of *N*-benzoylsaccharin (0.20 mmol), $PdCl_2$ (5 mol%), and styrene (3.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 85% yield (30.6 mg). White solid. 2,1/1,2 = 90.9:9.1. *E*/*Z* > 98:2. GC: rt = 15.58 min; isomer 13.81 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56−7.54 (d, *J* = 7.7 Hz, 4 H), 7.41−7.38 (t, *J* = 7.7 Hz, 4 H), 7.31−7.28 (t, *J* = 7.1 Hz, 2 H), 7.14 (s, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4, 128.7, 128.7, 127.6, 126.5. MS = 180.1 (EI).

*(E)-1-Chloro-4-styrylbenzene (**3r**).*[11] According to the general procedure, the reaction of *N*-benzoylsaccharin (0.20 mmol), $PdCl_2$ (5 mol%), and 4-chlorostyrene (3.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 89% yield (38.2 mg). White solid. 2,1/1,2 = 94.5:5.5. *E*/*Z* > 98:2. GC: rt = 16.92 min; isomer 14.72 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54−7.53 (d, *J* = 7.7 Hz, 2 H), 7.48−7.46 (d, *J* = 8.1 Hz, 2 H), 7.41−7.38 (t, *J* = 7.7 Hz, 2 H), 7.36−7.35 (d, *J* = 8.2 Hz, 2 H), 7.32−7.29 (t, *J* = 6.8 Hz, 1 H), 7.13−7.06 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.0, 135.9, 133.2, 129.3, 128.9, 128.8, 127.9, 127.7, 127.4, 126.6. MS = 214.1 (EI).

*(E)-1-Methoxy-4-styrylbenzene (**3s**).*[11] Method 1. According to the general procedure, the reaction of *N*-benzoylsaccharin (0.20 mmol), $PdCl_2$ (5 mol%), and 4-methoxystyrene (3.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 79% yield (33.2 mg). White solid. 2,1/1,2 = 81.3:18.7. *E*/*Z* > 98:2. GC: rt = 17.67 min; isomer 15.53 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53−7.51 (d, *J* = 7.8 Hz, 2 H), 7.49−7.48 (d, *J* = 8.3 Hz, 2 H), 7.39−7.36 (t, *J* = 7.6 Hz, 2 H), 7.28−7.25 (t, *J* = 8.0 Hz, 1 H), 7.11−6.99 (q, *J* = 16.3 Hz, 2 H), 6.94−6.92 (d, *J* = 8.2 Hz, 2 H), 3.86 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 137.7, 130.2, 128.7, 128.2, 127.7, 127.2, 126.6, 126.3, 114.2, 55.4. MS = 210.1 (EI). Method 2. According to the general procedure, the reaction of *N*-4-methoxylbenzoylsaccharin (0.20 mmol), $PdCl_2$ (5

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mol%), and styrene (3.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 70% yield (29.4 mg). White solid. 2,1/1,2 = 74.6:25.4. *E*/*Z* > 98:2. GC: rt = 17.74 min; isomer 15.58 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53−7.51 (d, *J* = 7.8 Hz, 2 H), 7.49−7.48 (d, *J* = 8.3 Hz, 2 H), 7.39−7.36 (t, *J* = 7.6 Hz, 2 H), 7.28−7.25 (t, *J* = 8.0 Hz, 1 H), 7.11−6.99 (q, *J* = 16.3 Hz, 2 H), 6.94−6.92 (d, *J* = 8.2 Hz, 2 H), 3.86 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 137.7, 130.2, 128.7, 128.2, 127.7, 127.2, 126.6, 126.3, 114.2, 55.4. MS = 210.1 (EI).

*(E)-1-Styryl-4-(trifluoromethyl)benzene (**3t**).*[11] According to the general procedure, the reaction of *N*-trifluoromethylbenzoylsaccharin (0.20 mmol), $PdCl_2$ (5 mol%), and styrene (3.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography the title compound in 71% yield (35.2 mg). White solid. 2,1/1,2 = 92.4:7.6. *E*/*Z* > 98:2. GC: rt = 14.66 min; isomer 12.34 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (s, 4 H), 7.57−7.56 (d, *J* = 7.6 Hz, 2 H), 7.43−7.40 (t, *J* = 7.5 Hz, 2 H), 7.34−7.32 (t, *J* = 7.3 Hz, 1 H), 7.24−7.13 (q, *J* = 16.4 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.8, 136.6, 131.2, 129.3 (q, J^2 = 32.5 Hz), 128.8, 128.3, 127.1, 126.8, 126.6, 125.7 (q, J^3 = 3.6 Hz), 124.2 (q, J^1 = 270.0 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ −62.45. MS = 248.1 (EI).

*(E)-Butyl 3-(4-((E)-Styryl)phenyl)acrylate (**3u**).*[27] Method 1. According to the published procedure,[5d] *N*-4-bromobenzoylsaccharin (0.20 mmol) was reacted with $Pd_2(dba)_3$ (1.5 mol%), $P(t\text{-}Bu)_3HBF_4$ (3 mol%), Et_3N (1.1 equiv), and styrene (2.0 equiv) in 1,4-dioxane (0.25 M) for 12 h at room temperature. The reaction mixture was filtrated, concentrated, and washed with hexanes (10 mL) to afford *E*-(4-styryl)benzoyl-saccharine (97% yield, 75.6 mg). 2,1/1,2 > 98:2. *E*/*Z* > 98:2. Without further purification, the thus obtained *E*-(4-styryl)benzoylsaccharin (0.194 mmol) was reacted with $PdCl_2$ (3 mol%) and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C to afford after workup and chromatography the title compound (83% yield, 49.4 mg). White solid. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt = 25.06 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72−7.68 (d, *J* = 16.0 Hz, 1 H), 7.55 (s, 6 H), 7.41−7.38 (t, *J* = 7.2 Hz, 2 H), 7.32−7.29 (t, *J* = 7.0 Hz, 1 H), 7.22−7.11 (q, *J* = 16.4 Hz, 2 H), 6.49−6.46 (d, *J* = 16.0 Hz, 1 H), 4.26−4.23 (t, *J* = 6.5 Hz, 2 H), 1.75−1.70 (m, 2 H), 1.51−1.44 (m, 2 H), 1.01−0.98 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 144.0, 139.3, 137.0, 133.7, 130.1, 128.8, 128.5, 128.0, 127.8, 126.9, 126.7, 117.9, 64.5, 30.8, 19.2, 13.8. MS = 306.2 (EI). Method 2. According to the general procedure, the reaction of *N*-4-bromobenzoylsaccharin (0.20 mmol), $PdCl_2$ (3 mol%), and *n*-butyl acrylate (2.0 equiv) in *N*-methyl-2-pyrrolidinone (0.25 M) for 18 h at 160 °C, afforded after workup and chromatography *n*-butyl *E*-(4-bromophenyl)acrylate (63% yield, 35.7 mg). The thus obtained *n*-butyl *E*-(4-bromophenyl)acrylate (0.126 mmol) was reacted with $Pd_2(dba)_3$ (1.5 mol%), $P(t\text{-}Bu)_3HBF_4$ (3 mol%), Et_3N (1.1 equiv), and styrene (2.0 equiv) in 1,4-dioxane (0.25 M) for 12 h at room temperature according to the previously published procedure.[5d] The reaction mixture was filtered, concentrated, and washed with hexanes (10 mL) to afforded the title compound (98% yield, 37.9 mg). White solid. 2,1/1,2 > 98:2. *E*/*Z* > 98:2. GC: rt = 25.06 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72−7.68 (d, *J* = 16.0 Hz, 1 H), 7.55 (s, 6 H), 7.41−7.38 (t, *J* = 7.2 Hz, 2 H), 7.32−7.29 (t, *J* = 7.0 Hz, 1 H), 7.22−7.11 (q, *J* = 16.4 Hz, 2 H), 6.49−6.46 (d, *J* = 16.0 Hz, 1 H), 4.26−4.23 (t, *J* = 6.5 Hz, 2 H), 1.75−1.70 (m, 2 H), 1.51−1.44 (m, 2 H), 1.01−0.98 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 144.0, 139.3, 137.0, 133.7, 130.1, 128.7, 128.5, 128.0, 127.8, 126.9, 126.7, 117.9, 64.5, 30.8, 19.2, 13.8. MS = 306.2 (EI).

General Procedure for Selectivity Studies. An oven-dried vial equipped with a stir bar was charged with two amide substrates (each 0.2 mmol, 1.0 equiv), $PdCl_2$ (0.03 equiv), olefin substrate (0.5 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. *N*-methyl-2-pyrrolidinone (0.25 M) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 160 °C, and stirred for the indicated time at 160 °C. After the indicated time, the reaction mixture was cooled down to room temperature and diluted with CH_2Cl_2 (5 mL). The sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02294.

^{1}H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Johansson-Seechurn, C. C. C.; Kitching, M. O.; Colacot, T. J.; Snieckus, V. *Angew. Chem., Int. Ed.* **2012**, *51*, 5062.

(2) (a) Heck, R. F. *Org. React.* **1982**, *27*, 345. (b) Heck, R. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon, 1991; Vol. *4*, Chapter 4.3. (c) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1995**, *33*, 2379. (d) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (e) Oestreich, M.*The Mizoroki-Heck Reaction*; Wiley, 2009. (f) Review on decarbonylative Heck reactions: Zhang, M.; Su, W. Decarbonylative Reactions of Arene Carboxylic Acid Derivatives. In *Science of Synthesis: Cross-Coupling and Heck-Type Reactions*; Molander, G. A., Wolfe, J. P., Larhed, M., Eds.; Thieme: Stuttgart, 2013; Vol. *3*, Chapter 3.1.1.1.3. (g) Ruan, J.; Xiao, J. *Acc. Chem. Res.* **2011**, *44*, 614. (h) Dounay, A. B.; Overman, L. E. *Chem. Rev.* **2003**, *103*, 2945.

(3) (a) *Metal-Catalyzed Cross-Coupling Reactions and More*; de Meijere, A., Brase, S., Oestreich, M., Eds.; Wiley: New York, 2014. (b) *Science of Synthesis: Cross-Coupling and Heck-Type Reactions*, Molander, G. A., Wolfe, J. P., Larhed, M., Eds.; Thieme: Stuttgart, 2013.

(4) (a) de Vries, J. G. *Can. J. Chem.* **2001**, *79*, 1086. (b) Beller, M.; Blaser, H. U. *Top. Organomet. Chem.* **2012**, *42*, 1. (c) Magano, J.; Dunetz, J. R. *Chem. Rev.* **2011**, *111*, 2177.

(5) (a) Herrmann, W. A.; Brossmer, C.; Öfele, K.; Reisinger, C. P.; Priermeier, T.; Beller, M.; Fischer, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1844. (b) Reetz, M. T.; Lohmer, G.; Schwickardi, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 481. (c) Shaughnessy, K. H.; Kim, P.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 2123. (d) Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 6989. (e) Cacchi, S. *Pure Appl. Chem.* **1996**, *68*, 45. (f) Ebran, J. P.; Hansen, A. L.; Gøgsig, T. M.; Skrydstrup, T. *J. Am. Chem. Soc.* **2007**, *129*, 6931. (g) Kikukawa, K.; Matsuda, T. *Chem. Lett.* **1977**, *6*, 159. (h) Taylor, J. G.; Moro, A. V.; Correia, C. R. D. *Eur. J. Org. Chem.* **2011**, *2011*, 1403.

(6) (a) Myers, A. G.; Tanaka, D.; Mannion, M. R. *J. Am. Chem. Soc.* **2002**, *124*, 11250. (b) Dams, M.; De Vos, D. E.; Celen, S.; Jacobs, P. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3512. (c) Inoue, A.; Shinokubo, H.; Oshima, K. *J. Am. Chem. Soc.* **2003**, *125*, 1484.

(7) In contrast to traditional Heck reactions, few examples of decarbonylative processes have been reported: (a) Blaser, H. U.; Spencer, A. *J. Organomet. Chem.* **1982**, *233*, 267. (b) Stephan, M. S.; Teunissen, A. J. J. M.; Verzijl, G. K. M.; de Vries, J. G. *Angew. Chem.,*

DOI: 10.1021/acs.joc.6b02294
J. Org. Chem. 2016, 81, 12023−12030

Int. Ed. **1998**, *37*, 662. (c) Gooßen, L. J.; Paetzold, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 1237. (d) Gooßen, L. J.; Paetzold, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 1095. (e) Sugihara, T.; Satoh, T.; Miura, M.; Nomura, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4672. (f) See, ref 2f.
(8) Dermenci, A.; Dong, G. *Sci. China: Chem.* **2013**, *56*, 685.
(9) (a) Ouyang, K.; Hao, W.; Zhang, W. X.; Xi, Z. *Chem. Rev.* **2015**, *115*, 12045. For a review on N−C bond cross-coupling of amides, see: (b) Meng, G.; Shi, S.; Szostak, M. *Synlett* **2016**, *27*, 2530.
(10) (a) *The Amide Linkage: Structural Significance in Chemistry, Biochemistry, and Materials Science*; Greenberg, A., Breneman, C. M., Liebman, J. F., Eds.; Wiley: New York, 2000. (b) Pattabiraman, V. R.; Bode, J. W. *Nature* **2011**, *480*, 471.
(11) Meng, G.; Szostak, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 14518.
(12) (a) Meng, G.; Szostak, M. *Org. Lett.* **2016**, *18*, 796. (b) Shi, S.; Meng, G.; Szostak, M. *Angew. Chem., Int. Ed.* **2016**, *55*, 6959.
(13) Hu, J.; Zhao, Y.; Liu, J.; Zhang, Y.; Shi, Z. *Angew. Chem., Int. Ed.* **2016**, *55*, 8718.
(14) For amide C−N coupling without decarbonylation, see: (a) Meng, G.; Szostak, M. *Org. Lett.* **2015**, *17*, 4364. (b) Meng, G.; Szostak, M. *Org. Biomol. Chem.* **2016**, *14*, 5690. (c) Shi, S.; Szostak, M. *Chem. - Eur. J.* **2016**, *22*, 10420. (d) Hie, L.; Nathel, N. F. F.; Shah, T. K.; Baker, E. L.; Hong, X.; Yang, Y. F.; Liu, P.; Houk, K. N.; Garg, N. K. *Nature* **2015**, *524*, 79. (e) Weires, N. A.; Baker, E. L.; Garg, N. K. *Nat. Chem.* **2015**, *8*, 75. (f) Li, X.; Zou, G. *Chem. Commun.* **2015**, *51*, 5089. (g) Simmons, B. J.; Weires, N. A.; Dander, J. E.; Garg, N. K. *ACS Catal.* **2016**, *6*, 3176. (h) Baker, E. L.; Yamano, M. M.; Zhou, Y.; Anthony, S. M.; Garg, N. K. *Nat. Commun.* **2016**, *7*, 11554. (i) Dander, J. E.; Weires, N. A.; Garg, N. K. *Org. Lett.* **2016**, *18*, 3934.
(15) Szostak, M.; Aubé, J. *Chem. Rev.* **2013**, *113*, 5701.
(16) (a) Szostak, R.; Shi, S.; Meng, G.; Lalancette, R.; Szostak, M. *J. Org. Chem.* **2016**, *81*, 8091. (b) Pace, V.; Holzer, W.; Meng, G.; Shi, S.; Lalancette, R.; Szostak, R.; Szostak, M. *Chem. - Eur. J.* **2016**, *22*, 14494.
(17) Dolenc, D. *Synlett* **2000**, *4*, 544 and references cited therein.
(18) (a) Ueda, T.; Konishi, H.; Manabe, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 8611. (b) Gehrtz, P. H.; Hirschbeck, V.; Fleischer, I. *Chem. Commun.* **2015**, *51*, 12574. (c) Liu, C.; Meng, G.; Liu, Y.; Liu, R.; Lalancette, R.; Szostak, R.; Szostak, M. *Org. Lett.* **2016**, *18*, 4194. Trifluoromethylthiolation: (d) Xu, C.; Ma, B.; Shen, Q. *Angew. Chem., Int. Ed.* **2014**, *53*, 9316.
(19) Jeffery, T. *Tetrahedron* **1996**, *52*, 10113.
(20) Milburn, R. R.; Snieckus, V. *Angew. Chem., Int. Ed.* **2004**, *43*, 888.
(21) (a) Qin, L.; Ren, X.; Lu, Y.; Li, Y.; Zhou, J. S. *Angew. Chem., Int. Ed.* **2012**, *51*, 5915. (b) Beller, M.; Riermeier, T. H. *Tetrahedron Lett.* **1996**, *37*, 6535.
(22) (a) Amatore, C.; Jutand, A. *Acc. Chem. Res.* **2000**, *33*, 314. (b) Knowles, J. P.; Whiting, A. *Org. Biomol. Chem.* **2007**, *5*, 31. (c) Jutand, A.; Negri, S.; de Vries, J. G. *Eur. J. Inorg. Chem.* **2002**, *2002*, 1711.
(23) Mahatthananchai, J.; Dumas, A.; Bode, J. W. *Angew. Chem., Int. Ed.* **2012**, *51*, 10954.
(24) Imai, T.; Okunoyama, T.; Ohkoshi, M. *Nippon Kagaku Kaishi* **1975**, 123.
(25) Ying, C. H.; Yan, S. B.; Duan, W. L. *Org. Lett.* **2014**, *16*, 500.
(26) Li, J.; Liu, L.; Zhou, Y. Y.; Xu, S. N. *RSC Adv.* **2012**, *2*, 3207.
(27) Zhang, X.; Liu, A.; Chen, W. *Org. Lett.* **2008**, *10*, 3849.

DOI: 10.1021/acs.joc.6b02294
J. Org. Chem. 2016, 81, 12023−12030