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Rh-Catalyzed Deformylative Coupling of Salicylaldehydes with Acrylates and Acrylamides

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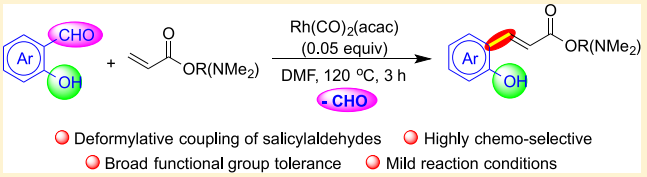
Supporting Information

ABSTRACT: An unprecedented deformylative coupling of salicylaldehydes to acrylates and acrylamides under Rh-catalyzed conditions is reported. These deformylative couplings afforded *o*-hydroxycinnamates and *o*-hydroxycinnamamides with broad functional group tolerance and high chemoselectivity under milder reaction conditions.



INTRODUCTION

Transition-metal-catalyzed bond-forming reactions allow the preparation of organic scaffolds with high functional group tolerance in organic synthesis.[1] This approach is often used in the synthesis of a variety of natural products.[2] Importantly, *o*-hydroxycinnamates are used as photolabile protecting groups with two-photon uncaging properties.[3] The *o*-hydroxycinnamate-based compounds **1A** and **1B** (Figure 1) are representative molecules serving as photolabile protecting groups.[3a,c] Further, anadanthoflavone (**1C**) isolated from aerial parts of *Anadenanthera colubrina* exhibits lipoxygenase inhibitory activity.[4]

Synthesis of multifunctional molecular skeletons often poses problems due to the presence of reactive functional groups in multistep synthesis. In the present context, Heck-coupling[5] and directed C−H activation[6] are useful tools for the synthesis of *o*-hydroxycinnamates or alkenyl phenols. However, the Heck reaction requires a halogen for the oxidative addition step, while the C−H activation demands a directing group or additional protection/deprotection as an integral part of the synthetic maneuvering. Thus, development of new synthetic methods for the direct preparation of ortho-functionalized alkenyl phenols is in high demand. Application of rhodium catalysis in organic synthesis also provides a unique opportunity for the construction of multifunctional scaffolds.[7−9] We recently reported (Scheme 1a)[10] facile reactivity of salicylaldehydes to give decarbonylative homocoupled 2,2′-dihydroxybenzophenones/xanthones under Rh-catalyzed conditions.[10a] Further, we have also disclosed the oxidative coupling reactivity of salicylaldehydes with aryl halides to furnish 2-hydroxybenzophenones.[10b] These studies led us to further investigate the reactivity of salicylaldehyde with acrylates under Rh-catalyzed conditions.

In the literature, Rh-catalyzed decarbonylative arylation of simple aryl aldehydes with acrylates was reported to give a mixture of Heck-type coupling products along with the corresponding hydrogenated products.[9b] In contrast, a similar reaction of salicylaldehyde with acrylate or amide instead leads to the formation of a hydroacylation product (Scheme 1b).[11] Further, formation of phenol as a decarbonylation product from salicylaldehyde is also known under harsh reaction conditions using rhodium catalysis.[12] With this background, we report an unprecedented Rh-catalyzed deformylative coupling of salicylaldehydes with acrylates and acrylamides under mild reaction conditions (Scheme 1c).

RESULTS AND DISCUSSION

To start with, the deformylative coupling to give *o*-hydroxycinnamate (**3a**) was first realized, albeit in trace amount (Table 1), when salicylaldehyde was reacted with excess acrylate (4 equiv) under catalytic conditions with the $RhCl_3/PPh_3$ catalyst in dimethylformamide (DMF) at 120 °C and for 3 h (entry 1, Table 1). This interesting observation led us to explore this reaction further using different catalytic conditions (entries 2−4, Table 1). For example, this reaction with $RhCl(PPh_3)_3$ and $RhCl(CO)(PPh_3)_2$ catalysts provided **3a** in 62 and 25% yields, respectively (entries 2 and 3, Table 1). However, with catalytic $Rh(CO)_2(acac)$ in DMF, this reaction afforded a successful deformylative coupling, whereby product **3a** was obtained in 92% yield (entry 4, Table 1). Further screening in different solvents using dimethylacetamide (DMA), *N*-methyl pyrrolidone (NMP), and dimethyl sulfoxide (DMSO) furnished **3a** in lowered yields (entries 5−7, Table 1). Furthermore, conducting the reaction with 2 equiv of ethyl acrylate gave **3a** in 48% yield (entry 8, Table 1). Additional investigations at 80 and 100 °C temperature conditions delivered **3a** in 8 and 58% yields, respectively (entries 9 and 10, Table 1). However, the reaction under 2 h reaction conditions afforded **3a** in 81% yield (entry 11, Table 1). A control experiment without the catalyst did not give product **3a** (entry 12, Table 1).

Thus, the catalytic protocol comprising the conditions with $Rh(CO)_2(acac)$ catalyst (0.05 equiv) in DMF at 120 °C and 3 h served as the optimized one to obtain the deformylative coupling product *o*-hydroxycinnamate (**3a**) in high yield (entry

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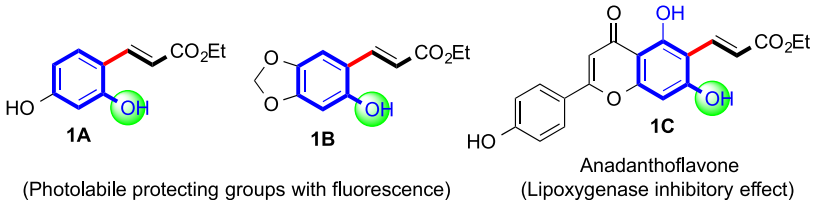


Figure 1. Some useful *o*-hydroxycinnamate compounds.

Scheme 1. Rh-Catalyzed Reactivity of Salicylaldehydes

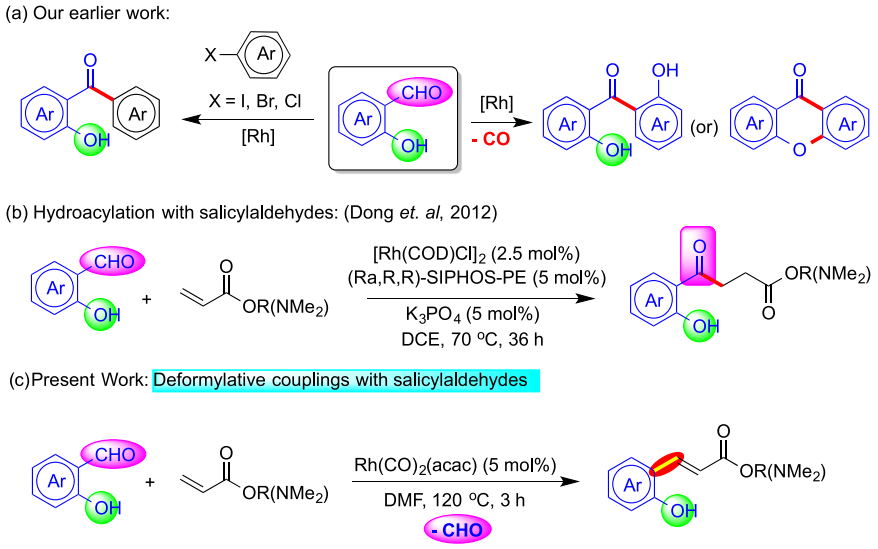
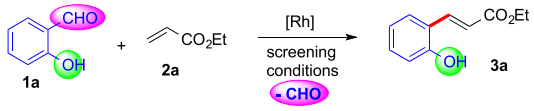


Table 1. Optimization Studies[a]



entry	catalyst	solvent	temp. (°C)	yield (%)
1	$RhCl_3/PPh_3$	DMF	120	trace
2	$RhCl(PPh_3)_3$	DMF	120	62
3	$RhCl(CO)(PPh_3)_2$	DMF	120	25
4	**$Rh(CO)_2(acac)$**	**DMF**	**120**	**92**
5	$Rh(CO)_2(acac)$	DMA	120	71
6	$Rh(CO)_2(acac)$	NMP	120	84
7	$Rh(CO)_2(acac)$	DMSO	120	16
8	$Rh(CO)_2(acac)$	DMF	120	48[b]
9	$Rh(CO)_2(acac)$	DMF	80	8
10	$Rh(CO)_2(acac)$	DMF	100	58
11	$Rh(CO)_2(acac)$	DMF	120	81[c]
12		DMF	120	

[a]Reaction conditions: **1a** (0.5 mmol, 1 equiv), **2a** (2 mmol, 4 equiv), catalyst (0.025 mmol, 0.05 equiv), solvent (2 mL), temp. (°C), 3 h. [b]**2a** (1 mmol, 2 equiv). [c]2 h.

4, Table 1). This outcome is very exciting as we could achieve the synthesis of *o*-hydroxycinnamate (**3a**) directly from salicylaldehyde and ethyl acrylate under Rh-catalyzed mild reaction conditions.

This made us further explore this reaction to establish the generality with various functionalized salicylaldehydes with an emphasis on electronic and steric effects, if any, on the deformylative coupling process under the established rhodium protocol conditions (Scheme 2).

The reaction was initially carried out with electronically different salicylaldehydes (**1a**−**1f**) functionalized with methyl, fluoro, chloro, bromo, and acetyl groups. These reactions afforded the corresponding deformylative coupling products, i.e., functionalized *o*-hydroxycinnamates (**3a**−**3f**), in 55−92% yields. Interestingly, 5-halosalicylaldehydes (**1d** and **1e**) delivered chemoselective reactivity with the nonparticipation of the reactive halo terminus during the coupling process. Further investigations using alkoxy-functionalized salicylaldehydes (**1g**−**1i**) with ethyl acrylate also gave the corresponding *o*-hydroxycinnamates (**3g**−**3i**) in 64−82% yields. Further study of 2-hydroxy-1-naphthaldehyde (**1j**) with ethyl acrylate gave the corresponding *o*-hydroxycinnamate **3j** in 31% yield along with 2-naphthol in 68% yield as a deformylative product. A scale-up experiment carried out with 3 mmol salicylaldehyde (**1a**) and ethyl acrylate (**2a**, 12 mmol) furnished deformylative coupling product **3a** in 91% yield.

Further investigation was carried out with different acrylates (Scheme 3) in combination with salicylaldehyde under the established conditions. These deformylative couplings afforded the corresponding *o*-hydroxycinnamates (**3k**−**3m**) in 81−84% yields. This vividly indicated that changing the alkoxy group in acrylates had little or no effect on cross-coupling efficacy.

Overall, the above deformylative couplings led us to investigate this reactivity with a more challenging substrate such as 4-hydroxyisophthalaldehyde (**1k**) containing two formyl groups (Scheme 4). This substrate delivered 5-formyl-*o*-hydroxycinnamate (**3n**) in 57% yield with excellent chemoselectivity.

The preferential and chemoselective deformylative coupling of the formyl group ortho to phenolic −OH in this context is noteworthy. In this case, the 5-formyl group did not participate

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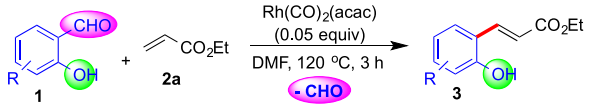
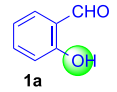
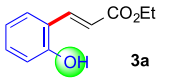
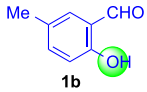
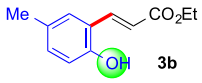
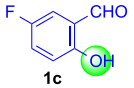
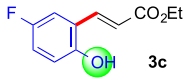
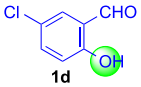
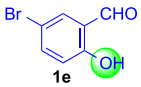
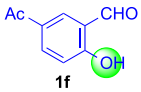
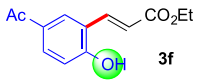
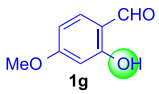
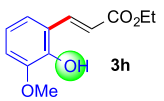
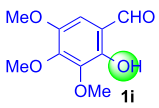
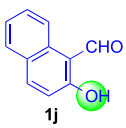
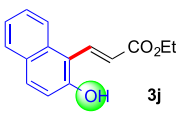
Scheme 2. Scope of Various Salicylaldehydes[a]



entry	salicylaldehyde	product	yield (%)
1	 1a	 3a	92
2	 1b	 3b	88
3	 1c	 3c	83
4	 1d	 3d	74
5	 1e	 3e	88
6	 1f	 3f	55[b]
7	 1g	 3g	64[c]
8	 1h	 3h	82
9	 1i	 3i	75[d]
10	 1j	 3j	31[e]

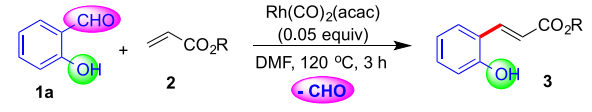
[a]Reaction conditions: **1a**−**1j** (0.5 mmol, 1 equiv), **2a** (2 mmol, 4 equiv), $Rh(CO)_2(acac)$ (0.025 mmol, 0.05 equiv), DMF (2 mL), 120 °C, 3 h. [b]Bis(2-hydroxyphenyl)methanone[10a] derived from **1f** formed in 16% yield. [c]5 h. [d]2,3,4-Trimethoxyphenol formed in 12% yield. [e]2-Naphthol formed in 68% yield.

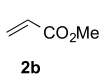
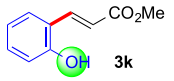
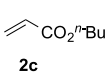
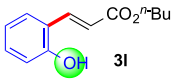
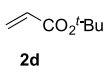
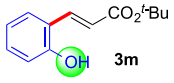
in deformylative arylation with acrylate as known under rhodium-catalyzed conditions.[9b]

Additionally, our method was further applied to the synthesis of *o*-hydroxycinnamates (**1A** and **1B**) as these compounds are important, vide supra, as two-photon-sensitive photo-removable protecting groups with uncaging properties (Figure 1).[3a] The synthetic viability of our condition in these cases was tested with salicylaldehydes (**1l** and **1m**) and ethyl acrylate under the established conditions (Scheme 5).

Encouragingly, these two reactions furnished the corresponding *o*-hydroxycinnamates **1A** and **1B** in 61 and 47% yields, respectively (eqs 1 and 2). Also, we observed the formation of the corresponding phenols as deformylative products in minor amounts. These studies thus indicated the tolerance of additional functional groups, for example, a free phenolic (**1l**) and formyl group (**1k**) delivering site-selective reactivity.

Scheme 3. Coupling with Different Acrylates[a]



entry	acrylate	product	yield (%)
1	 2b	 3k	82
2	 2c	 3l	84
3	 2d	 3m	81

[a]Reaction conditions: **1a** (0.5 mmol, 1 equiv), **2b**/**2c** or **2d** (2 mmol, 4 equiv), $Rh(CO)_2(acac)$ (0.025 mmol, 0.05 equiv), DMF (2 mL), 120 °C, 3 h.

With curiosity, our study with acrylates was extended to *N*,*N*-dimethylacrylamide (Scheme 6) and in combination with a few functionalized salicylaldehydes. It was amazing to note that acrylamides also participated well in deformylative couplings with salicylaldehydes under the above-established conditions to afford the corresponding functionalized *o*-hydroxycinnamamides (**4a**−**4d**) in 57−61% yields.

To understand the impact of phenolic −OH in deformylative coupling of salicylaldehyde, two control experiments have been performed with benzaldehyde and 2-methoxybenzaldehyde (Scheme 7). These two substrates without free phenolic −OH groups were examined with ethyl acrylate under the established conditions (eqs 3 and 4). However, these substrates did not afford the respective deformylative coupling products and starting materials were recovered in 62 and 75% yields, respectively. This in combination with the above chemoselective study (Scheme 4) clearly establishes the important role of the phenolic OH in the reactant for the reaction to proceed.[11b]

Accordingly, a probable mechanism with acrylate is proposed in Scheme 8. The initial oxidative addition of salicylaldehyde to the rhodium catalyst is expected to form rhodacycle **5a**.[11] It undergoes migratory CO deinsertion, giving aryl rhodium hydride species **5b**.[10a,13] This intermediate would in turn engage in a carbometallation with acrylate to give alkyl rhodium **5c**, and it would be followed by *β*-hydride elimination to provide *o*-hydroxycinnamate (**3**).

Thus, the liberated dihydrorhodium **5d** either is involved in catalytic transfer hydrogenation with acrylate or with the loss of H_2 regenerates the catalyst.[9b,14] The proposed intermediate **5b** is supported by the observation of the formation of phenol in gas chromatography−mass spectrometry analysis of the crude reaction mixture in some cases. Further, this mechanistic proposal as well can be extended to acrylamides for the formation of *o*-hydroxycinnamamides (**4**).

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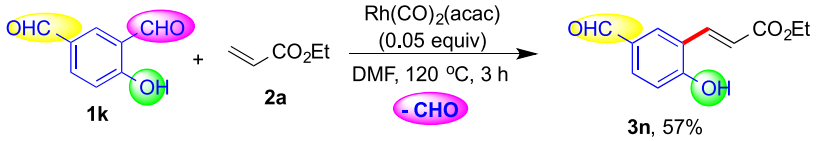
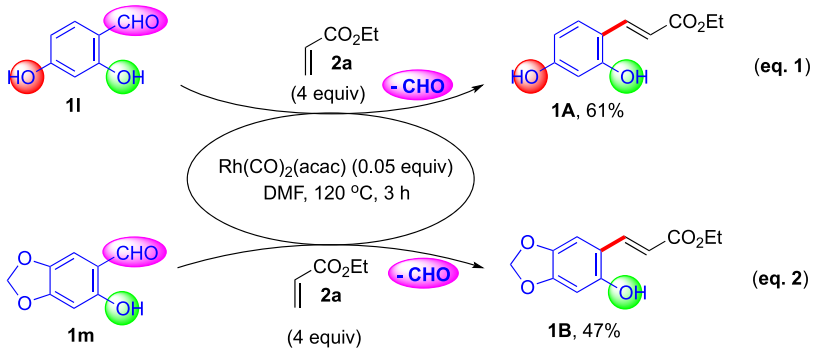
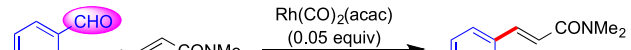
Scheme 4. Chemoselective Reactivity with 1k

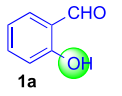
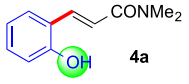
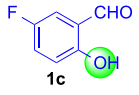
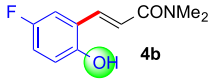
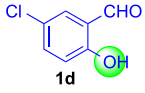
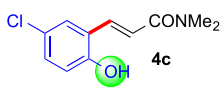
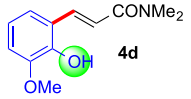


Scheme 5. Synthesis of 1A and 1B



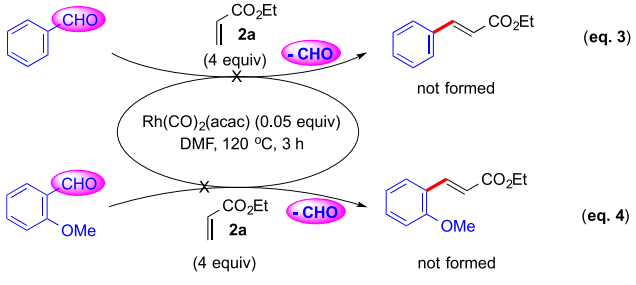
Scheme 6. Scope with *N,N*-Dimethylacrylamide[a]



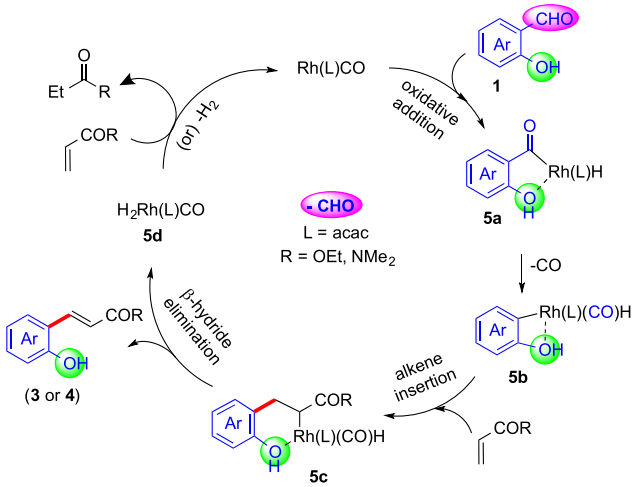
entry	salicylaldehyde	product	yield (%)
1	 1a	 4a	61[b]
2	 1c	 4b	59
3	 1d	 4c	57
4	 1h	 4d	61

[a]Reaction conditions: **1a**, **1c**, **1d**, or **1h** (0.5 mmol, 1 equiv), **2e** (2 mmol, 4 equiv), $Rh(CO)_2(acac)$ (0.025 mmol, 0.05 equiv), DMF (2 mL), 120 °C, 3 h. [b]Bis(2-hydroxyphenyl)methanone[10a] derived from **1a** formed in 15% yield.

Scheme 7. Control Experiments



Scheme 8. Proposed Mechanism



CONCLUSIONS

In conclusion, we disclosed an efficient rhodium-catalyzed protocol for the deformylative coupling of salicylaldehydes with acrylates and acrylamides. This method allowed broad and direct synthesis of the corresponding *o*-hydroxycinnamates and *o*-hydroxycinnamamides under milder reaction conditions and in high yields.

EXPERIMENTAL SECTION

General. The deformylative coupling reactions were performed in a dry Schlenk tube under nitrogen atmosphere conditions. Standard procedures were followed to dry various solvents used in coupling reactions. All of the NMR (^1H and ^{13}C) spectra were recorded on a JEOL ECS-400/ECX-500 spectrometer in $CDCl_3$ and DMSO-d_6 solvents. Infrared (IR) spectra were obtained using a PerkinElmer FT/IR spectrometer. High-resolution mass spectra (HRMS) were obtained using Waters GCT Premier-CAB155 and Waters-Q-Tof Premier-HAB213 instruments with electron ionization and electrospray ionization techniques. Melting points were determined using a Yamato melting point apparatus. Acrylates and *N,N*-dimethylacrylamide were purchased commercially and used without further purifications. Salicylaldehyde (**1a**), 3-methoxysalicylaldehyde (**1h**),

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5-bromosalicylaldehyde (**1e**), and 2-hydroxy-1-naphthaldehyde (**1j**) were purchased from commercial suppliers. The other substituted salicylaldehydes (**1b**,[15a] **1c**,[15a] **1d**,[15b] **1f**,[15c] **1g**,[16a] **1i**,[16b] **1k**,[16c] **1l**,[17a] and **1m**[17b]) were prepared by following literature-known procedures.

General Procedure for Deformylative Coupling Reactions. The deformylative coupling reaction was performed by charging a dry Schlenk tube with salicylaldehyde (**1a**) (61 mg, 0.5 mmol), ethyl acrylate (**2a**) (200 mg, 2 mmol), $Rh(CO)_2(acac)$ (6.4 mg, 0.025 mmol), and DMF (2 mL) solvent. This mixture was stirred at 120 °C in a preheated oil bath for 3 h. At the end, the contents were brought to room temperature (rt), quenched with dil. HCl, and extracted with ethyl acetate (30 mL). The organic extract was washed with water (15 mL) and brine (15 mL), dried with anhydrous $MgSO_4$, and concentrated. The crude product was purified by silica gel column chromatography using ethyl acetate/hexane as eluent. The product **3a** was obtained as a colorless solid (89 mg, 92%).

Characterization Data for the Products (3a−3n, 1A, 1B, and 4a−4d). *(E)-Ethyl 3-(2-Hydroxyphenyl)acrylate (**3a**).*[18a] Colorless solid (89 mg, 92%); mp 64−65 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 16.2 Hz, 1H), 7.47 (dd, J = 7.8, 1.6 Hz, 1H), 7.26−7.21 (m, 1H), 6.92 (td, J = 7.4, 1.0 Hz, 1H), 6.86 (dd, J = 8.1, 1.0 Hz, 1H), 6.69 (s, 1H), 6.65 (d, J = 16.2 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.6, 155.6, 140.8, 131.6, 129.3, 121.9, 120.8, 118.6, 116.6, 60.8, 14.6 ppm; IR (KBr, cm^{-1}): 3440, 3059, 2920, 1731, 1622, 1607, 1564, 1454, 1400, 1179, 1121, 929, 890, 828, 753; HRMS (EI$^+$): calcd for $C_{11}H_{12}O_3$ [M]$^+$ 192.0786, found 192.0782.

*(E)-Ethyl 3-(2-Hydroxy-5-methylphenyl)acrylate (**3b**).*[18a] Colorless solid (91 mg, 88%); mp 112−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, J = 16.2, 2.4 Hz, 1H), 7.26 (m, 1H), 7.03 (dd, J = 8.2, 2.2 Hz, 1H), 6.75 (dd, J = 8.2, 1.7 Hz, 1H), 6.61 (dd, J = 16.2, 1.9 Hz, 1H), 6.48 (s, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.27 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.6, 153.4, 140.8, 132.2, 130.0, 129.6, 121.5, 118.3, 116.4, 60.8, 20.6, 14.5 ppm; IR (KBr, cm^{-1}): 3274, 2978, 1671, 1621, 1611, 1505, 1368, 1329, 1257, 1196, 1159, 1026, 988, 822, 681; HRMS (EI$^+$): calcd for $C_{12}H_{14}O_3$ [M]$^+$ 206.0943, found 206.0941.

*(E)-Ethyl 3-(5-Fluoro-2-hydroxyphenyl)acrylate (**3c**).* Colorless solid (87 mg, 83%); mp 88−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, J = 16.2 Hz, 1H), 7.16 (dd, J = 9.2, 3.0 Hz, 1H), 7.07 (s, 1H), 6.95 (ddd, J = 8.8, 7.8, 3.0 Hz, 1H), 6.82 (dd, J = 8.9, 4.6 Hz, 1H), 6.59 (d, J = 16.2 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.5, 156.9 (d, J_{C-F} = 237.1 Hz), 151.7 (d, J_{C-F} = 1.9 Hz), 139.8 (d, J_{C-F} = 2.2 Hz), 122.8 (d, J_{C-F} = 7.5 Hz), 119.3, 118.2 (d, J_{C-F} = 23.5 Hz), 117.5 (d, J_{C-F} = 8.0 Hz), 114.5 (d, J_{C-F} = 23.11 Hz), 61.1, 14.4 ppm; IR (KBr, cm^{-1}): 3393, 3223, 2980, 1687, 1633, 1508, 1444, 1184, 1031, 861, 782, 752; HRMS (ESI$^+$): calcd for $C_{11}H_{12}FO_3$ [M + H]$^+$ 211.0770, found 211.0776.

*(E)-Ethyl 3-(5-Chloro-2-hydroxyphenyl)acrylate (**3d**).* Colorless solid (84 mg, 74%); mp 102−104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 16.2 Hz, 1H), 7.49 (s, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.18 (dd, J = 8.6, 2.6 Hz, 1H), 6.83 (d, J = 8.7 Hz, 1H), 6.64 (d, J = 16.2 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.7, 154.3, 139.7, 131.2, 128.5, 125.6, 123.2, 119.4, 117.9, 61.2, 14.4 ppm; IR (KBr, cm^{-1}): 3346, 2989, 1894, 1684, 1625, 1582, 1494, 1413, 1307, 1183, 1034, 982, 864, 820; HRMS (EI$^+$): calcd for $C_{11}H_{11}ClO_3$ [M]$^+$ 226.0397, found 226.0380.

*(E)-Ethyl 3-(5-Bromo-2-hydroxyphenyl)acrylate (**3e**).* Colorless solid (119 mg, 88%); mp 108−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 16.2 Hz, 1H), 7.57−7.54 (m, 2H), 7.31 (dd, J = 8.6, 2.4 Hz, 1H), 6.78 (d, J = 8.6 Hz, 1H), 6.64 (d, J = 16.2 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.9, 154.9, 139.8, 134.1, 131.5, 123.8, 119.3, 118.3, 112.6, 61.2, 14.4 ppm; IR (KBr, cm^{-1}): 3350, 2987, 2917, 2849, 1685, 1624, 1308, 1185, 981, 863, 822, 634; HRMS (ESI$^+$): calcd for $C_{11}H_{12}BrO_3$ [M + H]$^+$ 270.9970, found 270.9977.

*(E)-Ethyl 3-(5-Acetyl-2-hydroxyphenyl)acrylate (**3f**).* Colorless solid (65 mg, 55%); mp 152−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84 (s, 1H), 8.12−8.03 (m, 2H), 7.88 (dd, J = 8.5, 2.2 Hz, 1H), 7.00 (d, J = 8.5 Hz, 1H), 6.78 (d, J = 16.2 Hz, 1H), 4.32 (q, J = 7.1 Hz, 2H), 2.59 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 197.4, 168.9, 160.5, 140.4, 132.1, 130.7, 129.9, 121.8, 119.6, 116.7, 61.2, 26.5, 14.4 ppm; IR (KBr, cm^{-1}): 3216, 2925, 1678, 1633, 1592, 1278, 1179, 832; HRMS (ESI$^+$): calcd for $C_{13}H_{15}O_4$ [M + H]$^+$ 235.0970, found 235.0973.

*(E)-Ethyl 3-(2-Hydroxy-4-methoxyphenyl)acrylate (**3g**).*[18b] Colorless solid (71 mg, 64%); mp 118−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 16.1 Hz, 1H), 7.39 (d, J = 8.7 Hz, 1H), 7.29 (s, 1H), 6.55 (d, J = 16.1 Hz, 1H), 6.48 (dd, J = 8.6, 2.4 Hz, 1H), 6.42 (d, J = 2.4 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.3, 162.7, 157.4, 141.0, 130.6, 115.5, 115.1, 107.1, 102.0, 60.7, 55.5, 14.5 ppm; IR (KBr, cm^{-1}): 3348, 2964, 1674, 1612, 1588, 1447, 1430, 1311, 1188, 1208, 1110, 1032, 843, 810; HRMS (ESI$^+$): calcd for $C_{12}H_{15}O_4$ [M + H]$^+$ 223.0970, found 223.0970.

*(E)-Ethyl 3-(2-Hydroxy-3-methoxyphenyl)acrylate (**3h**).* Colorless solid (91 mg, 82%); mp 65−66 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 16.2 Hz, 1H), 7.09−7.06 (m, 1H), 6.86−6.83 (m, 2H), 6.60 (d, J = 16.2 Hz, 1H), 6.20 (s, 1H), 4.26 (q, J = 7.1 Hz, 2H), 3.90 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.6, 146.9, 145.4, 139.6, 121.01, 120.95, 119.7, 119.4, 111.8, 60.5, 56.3, 14.5 ppm; IR (KBr, cm^{-1}): 3384, 2984, 2936, 1702, 1630, 1588, 1482, 1366, 1261, 1178, 1073, 1034, 781; HRMS (EI$^+$): calcd for $C_{12}H_{14}O_4$ [M]$^+$ 222.0892, found 222.0882.

*(E)-Ethyl 3-(2-Hydroxy-3,4,5-trimethoxyphenyl)acrylate (**3i**).* Colorless solid (106 mg, 75%); mp 116−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 16.1 Hz, 1H), 6.72 (s, 1H), 6.50 (d, J = 16.1 Hz, 1H), 6.02 (s, 1H), 4.26 (q, J = 7.1 Hz, 2H), 3.96 (s, 3H), 3.92 (s, 3H), 3.82 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.7, 146.8, 144.0, 143.7, 140.5, 139.5, 118.0, 115.3, 106.3, 61.5, 61.2, 60.5, 56.5, 14.5 ppm; IR (KBr, cm^{-1}): 3373, 2992, 2942, 2838, 1703, 1631, 1493, 1468, 1423, 1290, 1256, 1132, 1084, 842, 621; HRMS (ESI$^+$): calcd for $C_{14}H_{19}O_6$ [M + H]$^+$ 283.1182, found 283.1183.

*(E)-Ethyl 3-(2-Hydroxynaphthalen-1-yl)acrylate (**3j**).* Colorless solid (38 mg, 31%); mp 132−134 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (d, J = 16.3 Hz, 1H), 8.04 (d, J = 9.4 Hz, 1H), 7.78−7.74 (m, 2H), 7.52 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.40−7.35 (m, 1H), 7.16 (d, J = 8.9 Hz, 1H), 6.81 (d, J = 16.3 Hz, 1H), 6.60 (s, 1H), 4.36 (q, J = 7.1 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.1, 153.3, 138.6, 132.9, 131.7, 129.0, 128.8, 127.6, 124.0, 123.4, 123.1, 118.2, 114.0, 61.0, 14.5 ppm; IR (KBr, cm^{-1}): 3067, 1728, 1565, 1279, 1177, 814, 748; HRMS (ESI$^-$): calcd for $C_{15}H_{13}O_3$ [M − H]$^-$ 241.0865, found 241.0869.

*(E)-Methyl 3-(2-Hydroxyphenyl)acrylate (**3k**).*[19a] Colorless solid (73 mg, 82%); mp 126−128 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 16.2 Hz, 1H), 7.46 (d, J = 8.8 Hz, 1H), 7.26−7.22 (m, 1H), 6.92 (t, J = 7.4 Hz, 1H), 6.87 (d, J = 8.1 Hz, 1H), 6.82 (s, 1H), 6.66 (d, J = 16.2 Hz, 1H), 3.83 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.0, 155.5, 141.0, 131.6, 129.4, 121.8, 120.9, 118.2, 116.6, 52.0 ppm; IR (KBr, cm^{-1}): 3389, 3034, 2849, 1694, 1630, 1458, 1331, 1259, 1229, 1200, 1178, 991, 761, 754; HRMS (EI$^+$): calcd for $C_{10}H_{10}O_3$ [M]$^+$ 178.0630, found 178.0637.

*(E)-n-Butyl 3-(2-Hydroxyphenyl)acrylate (**3l**).*[19b] Colorless solid (93 mg, 84%); mp 90−92 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 16.2 Hz, 1H), 7.47 (dd, J = 7.8, 1.4 Hz, 1H), 7.25−7.22 (m, 1H), 7.06 (s, 1H), 6.93−6.86 (m, 2H), 6.67 (d, J = 16.2 Hz, 1H), 4.25 (t, J = 6.7 Hz, 2H), 1.71−1.67 (m, 2H), 1.45 (h, J = 7.4 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.9, 155.7, 141.0, 131.6, 129.4, 121.9, 120.7, 118.4, 116.6, 64.8, 30.9, 19.3, 13.9 ppm; IR (KBr, cm^{-1}): 3317, 2960, 2934, 2896, 2871, 1911, 1692, 1626, 1603, 1588, 1503, 1455, 1318, 1268, 1190, 1113, 993, 905, 875, 756, 676, 601; HRMS (EI$^+$): calcd for $C_{13}H_{16}O_3$ [M]$^+$ 220.1099, found 220.1084.

*(E)-tert-Butyl 3-(2-Hydroxyphenyl)acrylate (**3m**).* Colorless solid (90 mg, 81%); mp 97−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 16.2 Hz, 1H), 7.45 (dd, J = 7.8, 1.6 Hz, 1H), 7.24−7.20 (m, 1H), 7.08 (d, J = 7.2 Hz, 1H), 6.92−6.84 (m, 2H), 6.58 (d, J = 16.2

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Hz, 1H), 1.56 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 168.3, 155.6, 139.9, 131.3, 129.1, 122.1, 120.7, 120.2, 116.5, 81.0, 28.4 ppm; IR (KBr, cm^{-1}): 3354, 2979, 2934, 1676, 1628, 1604, 1458, 1369, 1333, 1256, 1152, 989, 753; HRMS (ESI^+): calcd for $C_{13}H_{16}NaO_3$ $[M + Na]^+$ 243.0997, found 243.0998.

*(E)-Ethyl 3-(5-Formyl-2-hydroxyphenyl)acrylate (**3n**).* Colorless solid (63 mg, 57%); mp 128−130 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 9.87 (s, 1H), 8.82 (s, 1H), 8.09 (d, *J* = 16.3 Hz, 1H), 8.02 (d, *J* = 2.0 Hz, 1H), 7.80 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 16.2 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 191.0, 169.0, 161.5, 140.0, 133.0, 132.2, 129.6, 122.4, 119.8, 117.3, 61.4, 14.4 ppm; IR (KBr, cm^{-1}): 3183, 1688, 1632, 1593, 1277, 1185, 1159, 987, 866, 826, 634; HRMS (ESI^+): calcd for $C_{12}H_{13}O_4$ $[M + H]^+$ 221.0814, found 221.0819.

*(E)-Ethyl 3-(2,4-Dihydroxyphenyl)acrylate (**1A**).*[3a] Colorless solid (64 mg, 61%); mp 146−148 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 10.11 (s, 1H), 9.89 (s, 1H), 7.76 (d, *J* = 16.1 Hz, 1H), 7.40 (d, *J* = 8.6 Hz, 1H), 6.38−6.34 (m, 2H), 6.26 (dd, *J* = 8.5, 2.3 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 1.23 (t, *J* = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 167.2, 161.0, 158.5, 140.4, 130.4, 113.1, 112.6, 107.8, 102.5, 59.5, 14.3 ppm; IR (KBr, cm^{-1}): 3338, 2993, 1677, 1602, 1462, 1373, 1299, 1250, 1184, 1098, 1041, 987, 975, 834; HRMS (ESI^-): calcd for $C_{11}H_{11}O_4$ $[M - H]^-$ 207.0657, found 207.0642.

*(E)-Ethyl 3-(6-Hydroxybenzo[d][1,3]dioxol-5-yl)acrylate (**1B**).*[3a] Yellow solid (56 mg, 47%); mp 136−138 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 16.0 Hz, 1H), 6.88 (s, 1H), 6.47 (s, 1H), 6.27 (d, *J* = 16.0 Hz, 1H), 5.89 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 168.3, 153.1, 150.4, 141.4, 140.2, 114.6, 114.0, 105.9, 101.4, 98.5, 60.3, 14.5 ppm; IR (KBr, cm^{-1}): 3275, 2994, 2909, 1670, 1612, 1447, 1314, 1281, 1197, 1182, 1039, 861, 518; HRMS (ESI^+): calcd for $C_{12}H_{13}O_5$ $[M + H]^+$ 237.0763, found 237.0769.

*(E)-3-(2-Hydroxyphenyl)-N,N-dimethylacrylamide (**4a**).* Colorless solid (58 mg, 61%); mp 205−207 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 10.00 (s, 1H), 7.73 (d, *J* = 15.6 Hz, 1H), 7.64 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.20−7.15 (m, 1H), 7.13 (d, *J* = 15.6 Hz, 1H), 6.88 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.83−6.79 (m, 1H), 3.13 (s, 3H), 2.92 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 166.1, 156.2, 136.5, 130.6, 128.2, 121.9, 119.2, 117.4, 116.0, 36.8, 35.3 ppm; IR (KBr, cm^{-1}): 3418, 2255, 2128, 1643, 1049, 1026, 1003, 826, 764, 632; HRMS (ESI^+): calcd for $C_{11}H_{14}NO_2$ $[M + H]^+$ 192.1025, found 192.1026.

*(E)-3-(5-Fluoro-2-hydroxyphenyl)-N,N-dimethylacrylamide (**4b**).* Colorless solid (62 mg, 59%); mp 208−210 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 9.98 (s, 1H), 7.69 (d, *J* = 15.8 Hz, 1H), 7.57 (dd, *J* = 9.9, 2.5 Hz, 1H), 7.18 (d, *J* = 15.8 Hz, 1H), 7.04−6.99 (m, 1H), 6.86 (dd, *J* = 8.1, 5.0 Hz, 1H), 3.14 (s, 3H), 2.92 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 165.8, 155.6 (d, J_{C-F} = 232.6 Hz), 152.4 (d, J_{C-F} = 1.5 Hz), 135.2, 124.0 (d, J_{C-F} = 7.7 Hz), 118.7, 117.2, 117.0 (d, J_{C-F} = 8.1 Hz), 113.3 (d, J_{C-F} = 22.9 Hz), 36.9, 35.4 ppm; IR (KBr, cm^{-1}): 3091, 3051, 2929, 2818, 2744, 1640, 1576, 1452, 1388, 1275, 1266, 1187, 1147, 977, 853, 732; HRMS (ESI^+): calcd for $C_{11}H_{13}FNO_2$ $[M + H]^+$ 210.0930, found 210.0935.

*(E)-3-(5-Chloro-2-hydroxyphenyl)-N,N-dimethylacrylamide (**4c**).* Colorless solid (65 mg, 57%); mp 200−202 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 15.7 Hz, 1H), 7.28 (d, *J* = 2.6 Hz, 1H), 6.99 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.95 (d, *J* = 15.8 Hz, 1H), 6.78 (d, *J* = 8.8 Hz, 1H), 3.08 (s, 3H), 2.97 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.1, 155.2, 137.1, 129.8, 128.1, 123.89, 123.88, 118.6, 117.6, 37.4, 35.8 ppm; IR (KBr, cm^{-1}): 3420, 2255, 2128, 1642, 1489, 1391, 1270, 1050, 1026, 1003, 823, 764; HRMS (ESI^+): calcd for $C_{11}H_{13}ClNO_2$ $[M + H]^+$ 226.0635, found 226.0637.

*(E)-3-(2-Hydroxy-3-methoxyphenyl)-N,N-dimethylacrylamide (**4d**).* Colorless solid (68 mg, 61%); mp 144−146 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 9.16 (s, 1H), 7.77 (d, *J* = 15.6 Hz, 1H), 7.26 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.10 (d, *J* = 15.6 Hz, 1H), 6.95 (dd, *J* = 8.0, 1.4 Hz, 1H), 6.78 (t, *J* = 7.9 Hz, 1H), 3.81 (s, 3H), 3.12 (s, 3H), 2.92 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 166.0, 147.9, 145.4, 136.2, 122.2, 119.5, 118.9, 117.6, 112.4, 55.9, 36.8, 35.3 ppm; IR (KBr, cm^{-1}): 3175, 2935, 1647, 1595, 1481, 1441, 1264, 1229, 1147, 1074, 998, 863, 782, 732; HRMS (ESI^+): calcd for $C_{12}H_{16}NO_3$ $[M + H]^+$ 222.1130, found 222.1130.

*Representative Scale-Up Experiment for Deformylative Coupling Reaction (**3a**).* The scale-up deformylative coupling reaction was performed by charging a dry Schlenk tube with salicylaldehyde (**1a**) (366 mg, 3 mmol), ethyl acrylate (**2a**) (1.2 g, 12 mmol), $Rh(CO)_2(acac)$ (38.7 mg, 0.15 mmol), and DMF (10 mL) solvent. This mixture was stirred at 120 °C in a preheated oil bath for 3 h. At the end, the contents were brought to rt, quenched with dil. HCl, and extracted with ethyl acetate (100 mL). The organic extract was washed with water (60 mL) and brine (100 mL), dried with anhydrous $MgSO_4$, and concentrated. The crude product was purified by silica gel column chromatography using ethyl acetate/hexane as eluent. The product **3a** was obtained as a colorless solid in 91% yield (528 mg).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.9b00602.

Spectroscopic data (^1H, ^{13}C NMR, and HRMS) of the products including copies of ^1H and ^{13}C NMR spectra of products **3a−3n**, **1A**, **1B**, and **4a−4d** and copies of HRMS spectra of products **3a−3n**, **1A**, **1B**, and **4a−4d** (PDF)

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Notes

The authors declare no competing financial interest.

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