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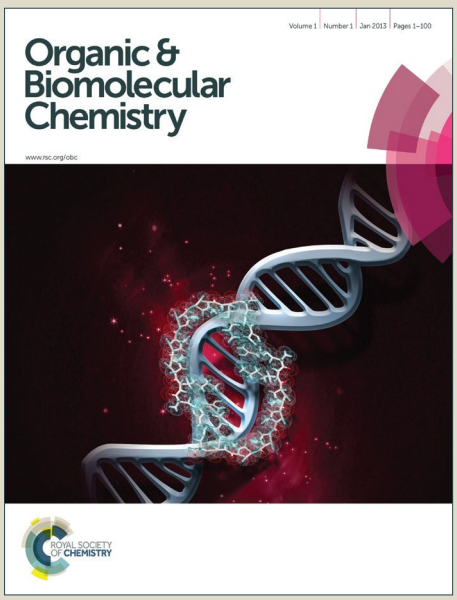

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ARTICLE TYPE

Palladium(II)–Catalyzed Direct Alkenylation of Dihydropyranones

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A Palladium(II)-catalyzed direct alkenylation reaction of dihydropyranones was developed. Various substituted dihydropyranones could afford the desired products in reasonable yields. And different acrylates were found to be good coupling partners in this coupling reaction. A Pd(0)/Pd(II) catalytic pathway was proposed to be involved in this coupling reaction.

Transition metal catalyzed dehydrogenative cross-coupling (CDC) reactions to form new carbon-carbon bonds by oxidizing two carbon-hydrogen bonds has emerged as an attractive process for their high efficiency and atom economy merits.[1] Among them, palladium-catalyzed direct C–H bond alkenylation reaction for its ease to introduce easily manipulated functionality has attracted widespread interest.[2] The pioneering work in oxidative Heck-type alkenylation was reported by Fujiwara and co-workers in the late 1960s.[3] This reaction provides a convenient method to directly synthesize various arylated olefins by using arenes and electron-deficient olefins. In 2002, de Vries and van Leeuwen et.al elegantly used amide as directing group to achieve the ortho-alkenylation of anilides.[4] In light of this result, many directing groups were designed and applied to facilitate the aryl C–H bond direct alkenylation.[5] In comparison, the direct alkene-alkene cross-coupling reaction is less common because of difficulties in activation of alkenyl C–H bond and inhibition of homo-coupling of olefin.[6] A seminal work reported by Ishii demonstrated that the acrylates could directly couple with vinyl carboxylates in the presence of palladium catalyst.[7] Following, Loh and co-workers have carried out much research work on the transition-metal catalyzed cross-coupling reactions between common olefins.[8] Recently, the research of oxidative cross-coupling between olefins has also attracted more and more attention from organic chemists.[9] Especially, Hong[10] and Lee[11] disclosed the regioselective alkenylation reaction of chromones, coumarins and phosphacoumarins respectively which well expanded the scope of palladium-catalyzed oxidative Heck coupling reaction of olefins.

It is noteworthy that the scope of functional olefins available to be directly functionalized for synthesis of useful organic building blocks still remains large space to be further explored. Functionalized pyranone skeletons are very useful building blocks as well as are common motif in many natural products with bio-, physio-, and pharmacological activities.[12] Therefore, considerable efforts have been paid on the development of efficient methods for preparation of functionalized pyranone derivatives.[13] Herein, we sought a general method of direct alkenylation of dihydropyranones at *β*-position for synthesis of multi-functionalized pyranone derivatives.

Table 1 Optimization of the coupling reaction condition of 2-phenyl-2*H*-pyran-4(3*H*)-one with *n*-butyl acrylate.[a]

1a (1 equiv) **2a** (2 equiv) **3a**

entry	oxidant (equiv)	temperature (℃)	solvent	time (h)	yield (%)[b]
1	$Cu(OAc)_2$ (2)	60	AcOH	24	28
2	$Cu(OAc)_2$ (2)	80	^{t}BuOH:AcOH:DMSO (20:5:1)	24	17
3	$Cu(OAc)_2$ (2)	115	1,4-dioxane:DMSO (7.5:1)	24	16
4	$Cu(OAc)_2$ (2)	60	DMSO	24	0
5	$Cu(OTf)_2$ (2)	60	AcOH	24	trace
6	$PhI(OAc)_2$ (2)	60	AcOH	24	trace
7	BQ (2)	60	AcOH	24	32
8	BQ (2)	60	AcOH:DMSO (10:1)	24	62
9	BQ (2)	60	AcOH:DMSO (1:1)	24	34
10	BQ (2)	40	AcOH:DMSO (10:1)	36	58
11[c]	BQ (2)	60	AcOH:DMSO (10:1)	24	30
12	BQ (1)	60	AcOH:DMSO (10:1)	24	55

[a] The general reaction procedures: The mixture of **1a** (0.3 mmol), **2a** (0.6 mmol, 2 equiv), $Pd(OAc)_2$ (0.03 mmol, 10 mol%) and oxidant in corresponding solvent was heated at the indicated temperature for 24 hours under the oxygen atmosphere (1 atm). [b] Isolated yield. [c] $Pd(OAc)_2$ (0.015 mmol, 5 mol%)

Firstly, the optimized reaction conditions were screened by using 2-phenyl-2H-pyran-4(3*H*)-one (1 equiv) and *n*-butyl arcylate (2 equiv) as substrates. The results are summarized in Table 1. Only low yields could be obtained when AcOH (Table 1, entry 1) or mixed solvents system such as 1, 4-dioxane/DMSO (v/v = 7.5/1) (Table 1, entry 3) was used, while no desired product was observed by using DMSO as solvent. Furthermore, oxidants such as $Cu(OTf)_2$, $PhI(OAc)_2$ and benzoquinone (BQ) have also been tested. The $Cu(OTf)_2$ and $PhI(OAc)_2$ were found to be inefficient to afford the desired product, while a product with 32% yield could be obtained when BQ was used. Subsequently, it was found that the product in 62% yield could be

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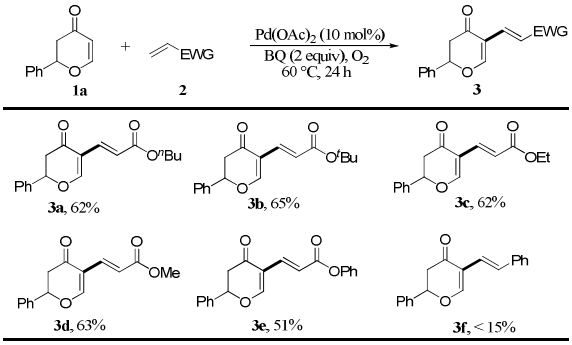
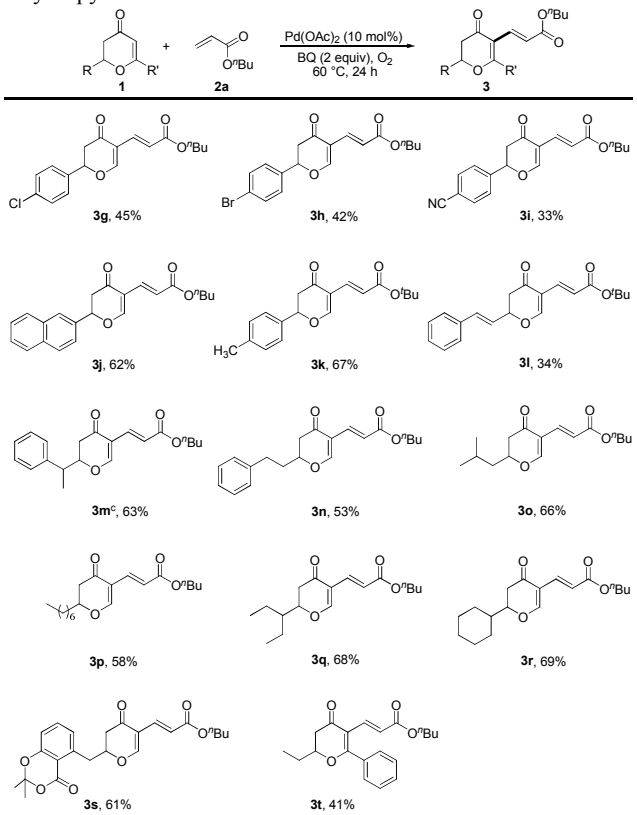
obtained when 2 equiv of BQ as oxidant was used in mixed solvents of AcOH/DMSO (v/v = 10/1) (Table 1, entry 8). Reducing the loading of the palladium catalyst or oxidant both could result a lower product's yield (Table 1, entries 11 and 12 respectively). Control experiment carried out showed that no any desired product was formed in the absence of the palladium catalyst.

Table 2 Cross-coupling reaction of **1a** with various electron-deficient alkenes.[a,b]



[a] Reaction conditions: Dihydropyranone **1a** (0.3 mmol, 1 equiv) and alkene **2** (0.6 mmol, 2 equiv), $Pd(OAc)_2$ (10 mmol%), BQ (0.6 mmol, 2 equiv) in 1 mL mixed solvents of AcOH/DMSO (v/v = 10:1) were heated for 24 h at 60 °C under the oxygen atmosphere (1 atm). [b] Isolated yield.

Table 3 Cross-coupling reaction of acrylates with various dihydropyranones.[a,b]



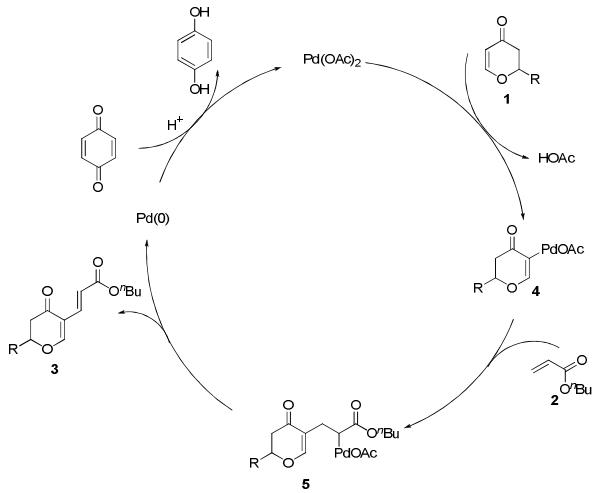
[a] Reaction conditions: Dihydropyranone **1** (0.3 mmol, 1 equiv) and acrylate **2** (0.6 mmol, 2 equiv), $Pd(OAc)_2$ (10 mmol%), BQ (0.6 mmol, 2 equiv) in 1 mL mixed solvents of AcOH/DMSO (v/v = 10:1) were heated for 24 h at 60 °C under the oxygen atmosphere (1 atm). [b] Isolated yield. [c] The dr ratio of the products is 2:1 which was determined from ^{1}H NMR spectra.

Following, different electron-deficient alkenes as coupling partners were screened (Table 2). Various acrylates (Table 2, **3a-3e**) could react well with substrate **1a**, and the desired products could be obtained in similar reasonable yields. However, only low yield of the product was detected when the styrene was applied in this coupling reaction (Table 2, **3f**).

Next, the scope of dihydropyranones was examined by using 10 mol% $Pd(OAc)_2$ as catalyst, 2 equiv of BQ as oxidant in the mixed solvents of AcOH/DMSO (v/v = 10/1) at 60 °C. Due to the higher boiling points of *tert*-butyl acrylate and *n*-butyl acrylate, both are selected as the coupling partners to react with different dihydropyranones. The results are summarized in Table 3. It was observed that the substrates with electron-withdrawing groups such as halides (Table 3, **3g** and **3h**) or cyano group (Table 3, **3i**) attached on the phenyl ring would result in a lower yields of products, while **3j** and **3k** could be obtained in 62% and 67% yields respectively. And the styryl-substituted substrate afforded the coupling product **3l** in 34% yield. Furthermore, it was noted that most of the aliphatic substituted dihydropyranones at 6-postion all could afford the corresponding coupling products in good yields (Table 3, **3m-3s**). However, when the 2-ethyl-6-phenyl-2H-pyran-4(3*H*)-one was used as a substrate, only 41% yield of the product was obtained possibly due to the steric hindrance caused by the phenyl substituent at 2-position (Table 3, **3t**).

The possible mechanism of this coupling reaction is proposed as shown in Scheme 1. A vinylpalladium species **4** could be generated *via* alkenyl C–H bond activation. Following an σ-alkylcarbopalladium intermediate **5** was formed *via* migratory addition with the *n*-butyl acrylate. Then this intermediate undergoes a *β*-H elimination to afford the product **3** and generate a Pd(0) species which could be subsequently re-oxidized back to Pd(II) by benzoquinone.

Scheme 1 Proposed possible mechanism for the palladium-catalyzed direct alkenylation of dihydropyranones.



Conclusions

In conclusion, a palladium-catalyzed direct oxidative dehydrogenation cross-coupling reaction between dihydropyranones and acrylates has been developed. Various substituted dihydropyranones were tolerated in this reaction to give very

useful coupling products in reasonable yields under mild reaction conditions.

Experimental section

General procedure for the coupling reaction of dihydropyranones with acrylates:

$Pd(OAc)_2$ (0.03 mmol, 10 mol%), BQ (0.6 mmol, 2 equiv), dihydropyranone (0.3 mmol, 1 equiv) and acrylate (0.6 mmol, 2 equiv) was added to a 10 mL round bottom flask containing AcOH/DMSO (v/v = 10/1, 1 mL). The mixture was stirred for 24 hours at 60 °C under 1 atmosphere of O_2. After cooling to room temperature, the mixture was diluted with ethyl acetate (5 mL) and was filtered through a plug of celite. The filtrate was washed with saturated $NaHCO_3$ twice (5 mL x 2), and brine (5 mL). The organic layer was dried with anhydrous $MgSO_4$ and filtered; the crude product was obtained by evaporating the organic solvent under reduced pressure. The desired product was isolated by column chromatography (ether/hexane = 3:7).

(*E*)-butyl 3-(4-oxo-2-phenyl-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3a**: yield 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.76 (s, 1H), 7.46-7.39 (m, 5H), 7.17 (d, *J* = 15.8 Hz, 1H), 6.85 (d, *J* = 15.8 Hz, 1H), 5.52-5.48 (dd, *J* = 14.1, 3.4 Hz, 1H), 4.16 (t, *J* = 6.6 Hz, 2H), 3.04-2.96 (dd, *J* = 16.7, 14.1 Hz, 1H), 2.80-2.75 (dd, *J* = 16.7, 3.4 Hz, 1H), 1.69-1.62 (m, 2H), 1.44-1.38 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.6, 167.7, 165.9, 136.9, 135.9, 129.2, 128.9, 126.1, 118.8, 114.7, 81.6, 64.2, 43.3, 30.7, 19.1, 13.7. HRMS (ESI): m/z calculated for $C_{18}H_{20}O_4Na$ $[M+Na]^+$: 323.1259, found: 323.1267.

(*E*)-*tert*-butyl 3-(4-oxo-2-phenyl-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3b**: yield 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.73 (s, 1H), 7.45-7.39 (m, 5H), 7.09 (d, *J* = 15.8 Hz, 1H), 6.75 (d, *J* = 15.8 Hz, 1H), 5.52-5.47 (dd, *J* = 14.1, 3.3 Hz, 1H), 3.03-2.95 (dd, *J* = 16.8, 14.1 Hz, 1H), 2.79-2.74 (dd, *J* = 16.8, 3.3 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.7, 166.9, 165.5, 136.9, 134.8, 129.2, 128.9, 126.1, 120.7, 114.8, 81.5, 80.1, 43.3, 28.2. HRMS (ESI): m/z calculated for $C_{18}H_{20}O_4Na$ $[M+Na]^+$: 323.1259, found: 323.1263.

(*E*)-ethyl 3-(4-oxo-2-phenyl-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3c**: Yield 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.76 (s, 1H), 7.44-7.39 (m, 5H), 7.18 (d, *J* = 15.9 Hz, 1H), 6.85 (d, *J* = 15.9 Hz, 1H), 5.53-5.49 (dd, *J* = 14.1, 3.4 Hz, 1H), 4.24-4.19 (q, *J* = 7.2 Hz, 2H), 3.04-2.96 (dd, *J* = 16.8, 14.1 Hz, 1H), 2.80-2.75 (dd, *J* = 16.8, 3.4 Hz, 1H). 1.30 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.7, 167.6, 166.0, 136.9, 135.9, 129.3, 128.9, 126.1, 118.9, 114.8, 81.7, 60.3, 43.3, 14.3. HRMS (ESI): m/z calculated for $C_{16}H_{16}O_4Na$ $[M+Na]^+$: 295.0946, found: 295.0953.

(*E*)-methyl 3-(4-oxo-2-phenyl-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3d**: yield 63%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.75 (s, 1H), 7.43-7.38 (m, 5H), 7.18 (d, *J* = 15.9 Hz, 1H), 6.86 (d, *J* = 15.9 Hz, 1H), 5.52-5.48 (dd, *J* = 14.2, 3.5 Hz, 1H), 3.75 (s, 3H), 3.03-2.95 (dd, *J* = 16.8, 14.2 Hz, 1H), 2.79-2.74 (dd, *J* = 16.8, 3.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.7, 168.1, 166.2, 136.9, 136.3, 129.3, 128.9, 126.1, 118.4, 114.7, 81.7, 51.5, 43.3. HRMS (ESI): m/z calculated for $C_{15}H_{14}O_4Na$ $[M+Na]^+$: 281.0790, found: 281.0797.

(*E*)-phenyl 3-(4-oxo-2-phenyl-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3e**: yield 51%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.81 (s, 1H), 7.47-7.36 (m, 7H), 9.32 (d, *J* = 15.8 Hz, 1H), 7.25-7.20 (dd, *J* = 11.9, 4.7 Hz, 1H), 7.14 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 15.8 Hz, 1H), 5.57-5.52 (dd, *J* = 14.0, 3.4 Hz, 1H), 3.07-2.99 (dd, *J* = 16.8, 14.1 Hz, 1H), 2.84-2.79 (dd, *J* = 16.8, 3.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.6, 166.8, 166.1, 150.9, 138.1, 136.7, 129.3, 128.9, 126.1, 125.6, 121.6, 117.8, 114.6, 81.8, 43.3. HRMS (ESI): m/z calculated for $C_{20}H_{16}O_4Na$ $[M+Na]^+$: 343.0946, found: 343.0948.

(*E*)-butyl 3-(2-(4-chlorophenyl)-4-oxo-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3g**: yield 45%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.74 (s, 1H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 15.8 Hz, 1H), 6.84 (d, *J* = 15.8 Hz, 1H), 5.50-5.46 (dd, *J* = 14.0, 3.3 Hz, 1H), 4.16 (t, *J* = 6.6 Hz, 2H), 2.98-2.90 (dd, *J* = 16.7, 14.0 Hz, 1H), 2.78-2.73 (dd, *J* = 16.7, 6.6 Hz, 1H), 1.68-1.61 (m, 2H), 1.45-1.36 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H).). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.2, 167.6, 165.7, 135.7, 135.4, 135.1, 129.2, 127.4, 119.1, 114.9, 80.8, 64.2, 43.2, 30.7, 19.1, 13.7. HRMS (ESI): m/z calculated for $C_{18}H_{19}ClO_4Na$ $[M+Na]^+$: 357.0870, found: 357.0872.

(*E*)-butyl 3-(2-94-bromophenyl)-4-oxo-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3h**: yield 42%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.73 (s, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 15.9 Hz, 1H), 6.83 (d, *J* = 15.9 Hz, 1H), 5.48-5.43 (dd, *J* = 13.9, 3.4 Hz, 1H), 4.15 (t, *J* = 6.6 Hz, 2H), 2.97-2.89 (dd, *J* = 16.8, 14.1 Hz, 1H), 2.77-2.72 (dd, *J* = 16.8, 3.5 Hz, 1H), 1.68-1.60 (m, 2H), 1.43-1.37 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.2, 167.7, 165.7, 135.9, 135.7, 132.2, 127.7, 123.3, 119.2, 114.9, 80.9, 64.3, 43.2, 30.8, 19.2, 13.7. HRMS (ESI): m/z calculated for $C_{18}H_{19}BrO_4Na$ $[M+Na]^+$: 401.0364, found: 401.0367.

(*E*)-butyl 3-(2-(4-cyanophenyl)-4-oxo-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3i**: yield 33%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.75 (s, 1H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 15.9 Hz, 1H), 6.84 (d, *J* = 15.9 Hz, 1H), 5.58-5.54 (dd, *J* = 13.7, 3.7 Hz, 1H), 4.16 (t, *J* = 6.6 Hz, 2H), 2.95-2.87 (dd, *J* = 16.8, 13.8 Hz, 1H), 2.83-2.77 (dd, *J* = 16.8, 3.7 Hz, 1H), 1.68-1.61 (m, 2H), 1.45-1.36 (qt, *J* = 15.0, 7.4 Hz, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 188.6, 167.6, 165.2, 142.0, 135.4, 132.8, 126.6, 122.5, 119.6, 118.1, 116.0, 115.2, 113.1, 80.4, 64.4, 43.3, 30.8, 19.2, 13.7. HRMS (ESI): m/z calculated for $C_{19}H_{19}NO_4Na$ $[M+Na]^+$: 348.1212, found: 348.1210.

(*E*)-butyl 3-(2-(naphthalene-2-yl)-4-oxo-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3j**: yield 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.95-7.88 (dd, *J* = 9.0, 8.0 Hz, 3H), 7.83 (s, 1H), 7.63 (d, *J* = 7.1 Hz, 1H), 7.59-7.49 (m, 3H), 7.22 (d, *J* = 15.8 Hz, 1H), 6.89 (d, *J* = 15.8 Hz, 1H), 6.27-6.23 (dd, *J* = 13.8, 3.3 Hz, 1H), 4.17 (t, *J* = 6.7 Hz, 2H), 3.19-3.11 (dd, *J* = 16.9, 13.8 Hz, 1H), 2.99-2.94 (dd, *J* = 16.9, 3.5 Hz, 1H), 1.70-1.62 (m, 2H), 1.47-1.37 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H).). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.9,

167.8, 166.2, 135.9, 133.8, 132.3, 130.0, 129.9, 129.2, 126.9, 126.2, 125.2, 123.9, 122.4, 118.9, 114.8, 78.9, 64.2, 42.7, 30.8, 19.2, 13.7. HRMS (ESI): m/z calculated for $C_{22}H_{22}O_4Na$ $[M+Na]^+$: 373.1416, found: 373.1407.

(*E*)-*tert*-butyl 3-(4-oxo-2(*p*-tolyl)-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3k**: yield 67%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.73 (s, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 15.8 Hz, 1H), 6.76 (d, *J* = 15.8 Hz, 1H), 5.49-5.45 (dd, *J* = 141. 3.3 Hz, 1H), 3.04-2.96 (dd, *J* = 16.8, 14.1 Hz, 1H), 2.78-2.73 (dd, *J* = 16.8, 3.3 Hz, 1H), 2.39 (s, 3H), 1.52 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.9, 166.9, 165.7, 139.3, 134.9, 134.0, 129.6, 126.2, 120.6, 114.8, 81.6, 80.1, 43.2, 28.2, 21.2. HRMS (ESI): m/z calculated for $C_{19}H_{22}O_4Na$ $[M+Na]^+$: 337.1416, found: 337.1411.

(*E*)-*tert*-butyl 3-(4-oxo-2-((*E*)-styryl)-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3l**: yield 34%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.66 (s, 1H), 7.41-7.29 (m, 5H), 7.05 (d, *J* = 15.9 Hz, 1H), 6.73 (d, *J* = 15.9 Hz, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 6.31-6.25 (dd, *J* = 16.0, 6.6 Hz, 1H) 5.16-5.11 (ddd, *J* = 11.3, 6.7, 4.4 Hz, 1H), 2.84-2.77 (dd, *J* = 16.7, 12.2 Hz, 1H), 2.75-2.69 (dd, *J* = 16.7, 4.3 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.5, 166.9, 165.4, 135.3, 134.9, 134.5, 128.7, 126.8, 124.1, 120.6, 114.7, 80.34, 80.14, 42.0, 28.2. HRMS (ESI): m/z calculated for $C_{20}H_{22}O_4Na$ $[M+Na]^+$: 349.1416, found: 349.1422.

(*E*)-butyl 3-(4-oxo-2-(1-phenylethyl)-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3m**: yield 63%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.69 (s, 1H), 7.63 (s, 0.5 H), 7.36-7.18 (m, 7.5 H), 7.12 (d, *J* = 15.8 Hz, 1H), 7.10 (d, *J* = 15.8 Hz, 0.5H), 6.79 (d, *J* = 15.8 Hz, 1H), 6.79 (d, *J* = 15.8 Hz, 0.5H), 4.65-4.59 (m, 0.5H), 4.55-4.49 (ddd, *J* = 11.2, 7.8, 3.4 Hz, 1H), 4.16 (t, *J* = 6.6 Hz, 3H), 2.56-2.44 (m, 2H), 2.37-2.32 (dd, *J* = 16.7, 3.4 Hz, 1H), 1.69-1.62 (m, 3H), 1.49-1.37 (m, 9H), 0.95 (t, *J* = 7.4 Hz, 4.5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 190.2, 190.1, 167.8, 166.2, 166.1, 140.9, 140.6, 136.0, 128.8, 128.6, 128.0, 127.7, 127.3, 127.2, 118.5, 118.4, 114.5, 114.3, 84.1, 83.6, 64.1, 43.7, 43.2, 40.0, 39.6, 30.7, 19.1, 17.0, 16.5, 13.7. HRMS (ESI): m/z calculated for $C_{20}H_{24}O_4Na$ $[M+Na]^+$: 351.1572, found: 351.1578.

(*E*)-butyl 3(4-oxo-2-phenethyl-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3n**: yield 53%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.66 (s, 1H), 7.29-7.17 (m, 5H), 7.11 (d, *J* = 15.8 Hz, 1H), 6.79 (d, *J* = 15.8 Hz, 1H), 4.50-4.42 (dddd, *J* = 12.4, 8.3, 8.3, 4.2 Hz, 1H), 4.14 (t, *J* = 6.6 Hz, 2H), 2.87-2.71 (m, 2H), 2.66-2.58 (dd, *J* = 16.7, 13.0 Hz, 1H), 2.56-2.51 (dd, *J* = 16.7, 4.0 Hz, 1H), 2.22-2.13 (m, 1H), 2.02-1.93 (m, 1H), 1.67-1.62 (m, 2H), 1.37-1.61 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.9, 167.8, 166.1, 140.3, 136.2, 128.7, 128.4, 126.4, 118.5, 114.5, 79.2, 64.2, 41.9, 35.8, 30.8, 30.7, 19.2, 13.7. HRMS (ESI): m/z calculated for $C_{20}H_{24}O_4Na$ $[M+Na]^+$: 351.1572, found: 351.1570.

(*E*)-butyl 3-(2-isobutyl-4-oxo-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3o**: yield 66%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.62 (s, 1H), 7.10 (d, *J* = 15.8 Hz, 1H), 6.78 (d, *J* = 15.8 Hz, 1H), 4.59-4.51 (dddd, *J* = 15.0, 10.7, 8.5, 6.1 Hz, 1H), 4.13 (t, *J* = 6.6 Hz, 2H), 2.60-2.53 (dd, *J* = 16.7, 10.7 Hz, 1H), 2.54-2.49 (dd, *J* = 16.7, 6.1 Hz, 1H), 1.87-1.77 (m, 2H), 1.69-1.59 (m, 2H), 1.47-1.34 (m, 3H), 0.95-0.90 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 190.1, 166.3, 136.3, 118.2, 114.3, 78.7, 64.1, 43.1, 42.3, 30.7, 24.1, 22.8, 22.0, 19.1, 13.7. HRMS (ESI): m/z calculated for $C_{16}H_{24}O_4Na$ $[M+Na]^+$: 303.1572, found: 303.1572.

(*E*)-butyl 3-(2-heptyl-4-oxo-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3p**: yield 58%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.63 (s, 1H), 7.10 (d, *J* = 15.8 Hz, 1H), 6.78 (d, *J* = 15.8 Hz, 1H), 4.50-4.43 (ddd, *J* = 12.0, 7.4, 5.0 Hz, 1H), 4.13 (t, *J* = 6.6 Hz, 2H), 2.62-2.55 (dd, *J* = 16.7 Hz, 12.0 Hz, 1H), 2.54-2.49 (dd, *J* = 16.7, 5.0 Hz, 1H), 1.86-1.78 (m, 1H), 1.71-1.59 (m, 3H), 1.49-1.26 (m, 12H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 190.2, 167.8, 166.4, 136.3, 118.2, 114.3, 80.4, 64.1, 41.9, 34.2, 31.7, 30.8, 29.2, 29.1, 24.7, 22.6, 19.2, 14.1, 13.7. HRMS (ESI): m/z calculated for $C_{19}H_{30}O_4Na$ $[M+Na]^+$: 345.2042, found: 345.2041.

(*E*)-butyl 3-(4-oxo-2-(pentan-3-yl)-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3q**: yield 68%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.69 (s, 1H), 7.14 (d, *J* = 15.8 Hz, 1H), 6.82 (d, *J* = 15.8 Hz, 1H), 4.52-4.46 (ddd, *J* = 14.6, 4.9, 3.3 Hz, 1H), 4.16 (t, *J* = 6.7 Hz, 2H), 2.71-2.63 (dd, *J* = 16.5, 14.8 Hz, 1H), 2.49-2.44 (dd, *J* = 16.5, 3.3 Hz, 1H), 1.69-1.34 (m, 12H), 0.95 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 190.7, 167.9, 166.8, 136.3, 118.2, 114.2, 82.1, 64.1, 44.2, 38.9, 30.7, 21.4, 21.2, 19.1, 13.7, 12.3. HRMS (ESI): m/z calculated for $C_{17}H_{26}BrO_4Na$ $[M+Na]^+$: 317.1729, found: 317.1731.

(*E*)-butyl 3-(2-cyclohexyl-4-oxo-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3r**: yield 69%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.65 (s, 1H), 7.11 (d, *J* = 15.8 Hz, 1H), 6.79 (d, *J* = 15.8 Hz, 1H), 4.27-4.21 (ddd, *J* = 13.9, 5.6, 3.6 Hz, 1H), 4.14 (t, *J* = 6.7 Hz, 2H), 2.66-2.58 (dd, *J* = 16.5, 13.9 Hz, 1H), 2.52-2.47 (dd, *J* = 16.5, 3.6 Hz, 1H), 1.88 (d, *J* = 12.6 Hz, 1H), 1.79 (d, *J* = 12.6 Hz, 2H), 1.71-1.60 (m, 6H), 1.44-1.35 (m, 2H), 1.32-1.01 (m, 5H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 190.6, 167.9, 166.6, 136.3, 118.1, 114.2, 84.3, 64.1, 41.2, 39.2, 30.7, 28.1, 27.9, 26.1, 25.7, 25.6, 19.1, 13.7. HRMS (ESI): m/z calculated for $C_{18}H_{26}O_4Na$ $[M+Na]^+$: 329.1730, found: 329.1729.

(*E*)-butyl3-(2-((2,2-dimethyl-4-oxo-4*H*-benzo[*d*][1,3]dioxin-5-yl)methyl)-4-oxo-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3s**: yield 61%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.59 (s, 1H), 7.51-7.47 (dd, *J* = 8.1, 7.7 Hz, 1H), 7.10 (d, *J* = 15.8 Hz, 1H), 6.99 (d, *J* = 7.7 Hz, 1H), 6.94 (d, *J* = 8.1 Hz, 1H), 6.79 (d, *J* = 15.8 Hz, 1H), 4.86-4.79 (m, 1H), 4.14 (t, *J* = 6.6 Hz, 2H), 3.63-3.59 (dd, *J* = 13.4, 4.6 Hz, 1H), 3.52-3.46 (dd, *J* = 13.4, 8.0 Hz, 1H), 2.74-2.63 (m, 2H), 1.73 (s, 3H), 1.71 (s, 3H), 1.68-1.61 (m, 2H), 1.45-1.36 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.8, 167.8, 165.9, 160.5, 157.3, 140.3, 136.1, 135.4, 126.8, 118.3, 116.9, 114.5, 112.2, 105.5, 80.1, 64.1, 41.6, 38.7, 30.7, 25.9, 25.3, 19.1, 13.7. HRMS (ESI): m/z calculated for $C_{23}H_{26}O_7Na$ $[M+Na]^+$: 437.1576, found: 437.1570.

(*E*)-butyl 3-(2-ethyl-4-oxo-3,4-dihydro-2*H*-pyran-5-yl)acrylate **3t**: yield 41%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.57-7.53 (m, 3H), 7.50-7.47 (m, 2H), 7.26 (d, *J* = 15.8 Hz, 1H), 7.06 (d, *J* = 15.8 Hz,

1H), 4.61-4.54 (m, 1H), 4.61-4.54 (m, 1H), 4.17-4.07 (m, 2H), 2.75-2.60 (m, 2H), ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 191.6, 175.1, 168.4, 137.5, 133.0, 131.8, 130.2, 128.5, 119.4, 110.9, 80.7, 77.3, 77.0, 76.7, 63.9, 41.8, 30.7, 27.4, 19.2, 13.7, 9.4. HRMS (ESI): m/z calculated for $C_{20}H_{24}O_4Na$ $[M+Na]^+$: 351.1572, found: 351.1570.

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