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# Palladium-Catalyzed Highly Chemo-, Regio- and Stereoselective Synthesis of Eight- to Ten-Membered Lactones from Allenyl 3-Oxoalkanoates and Organic Halides

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**Abstract:** A highly chemo-, regio-, and stereoselective synthesis of eight- to ten-membered lactones *via* the coupling cyclization of readily available allenyl 3-oxoalkanoates and organic halides through an *anti*-π-allylic palladium intermediate is reported. The yields ranged from moderate to good.

**Keywords:** allenes; π-allylic intermediates; carbopalladation; cyclization; lactones

## Introduction

Medium-sized lactones are extremely important compounds since they may be found in many natural products with biological potential,[1] including octalactin B,[2a] obtained from the surface of the Sea of Cortez gorgonian octocoral *Pacifigorgia* sp., and halicholactone,[2b] a novel fatty acid metabolite from the marine sponge, and ascidiatrienolide A[2c] (Figure 1). It is well-known that medium-sized ring compounds are difficult to synthesize not only by biosynthesis but also by artificial synthetic technology due to entropic and enthalpic factors.[3] Up to now, the most useful methodologies used to construct medium-sized lactones are lactonization[1a,4] and ring-closing metathesis (RCM),[5] usually requiring high diluted conditions, thus, the synthesis of medium-sized lactones is still a formidable challenge.

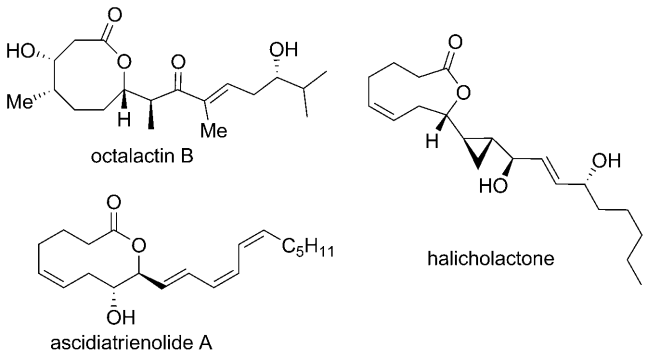
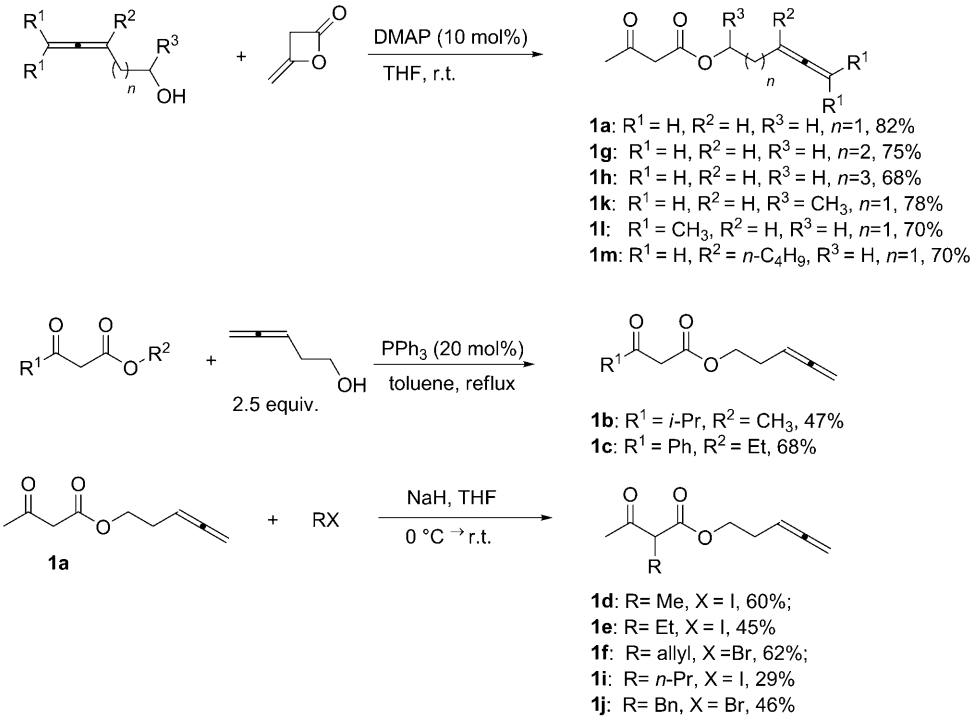


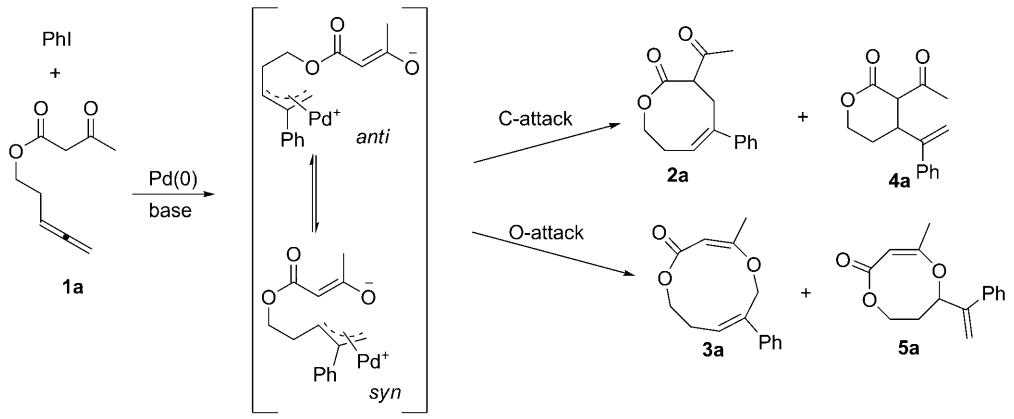

**Figure 1.** Natural eight- to ten-membered lactones.

Recently, transition metal-catalyzed cyclization reactions of functionalized allenes in the presence of organic halides have become powerful tools for the synthesis of carbo- and heterocyclic compounds.[6,7] Cyclic carbopalladation has been reported to afford 8- to 12-membered rings.[8] An intermolecular carbopalladation-allylation protocol of alkenyl halides bearing a nucleophilic moiety afforded 8-membered rings with 62:38 to 92:8 stereoselectivity.[9] In addition, Trost and co-workers reported the synthesis of 9- to 17-membered rings *via* hydropalladation of allenes under highly diluted conditions.[10] On the basis of our previous work on the carbopalladation of allenes[7] forming cyclic compounds with malonate or amine as the nucleophilic moiety,[11] we envisioned that the carbopalladation of allenyl 3-oxoalkanoate **1a** [from the reaction of readily available β-methylene-β-lactone




**Scheme 1.** Synthesis of the starting materials **1a**–**1m**.




**Scheme 2.** Possible products of the reaction of allenyl 3-oxoalkanoate **1a** with iodobenzene.

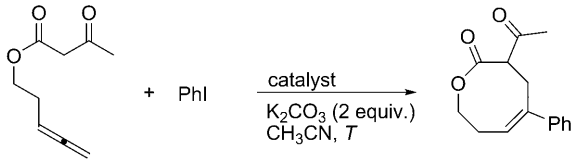
and the allenic alcohol or ester exchange reaction of 3-oxoalkanoates with 3,4-pentadienol (Scheme 1)][12] may form six-, eight-, or even ten-membered lactones **4a**, **2a**, **5a**, and **3a**, respectively with the *C*-attack[13] or *O*-attack[14] of the π-allylic palladium intermediate due to the presence of the keto ester unit (Scheme 2). It has been reported that in the absence of the substituent at the 2-position *syn*-π-allylic palladium is favored.[15] Herein, we wish to describe a highly efficient chemo-, regio-, and stereoselective protocol to construct eight- to ten-membered lactones *via* carbopalladation of readily available allenyl 3-oxoalkanoates with organic halides. The most interesting feature is the unique selectivity for the formation of the 8-membered ring over the 6-membered ring with the exclusive *C*-attack.

## Results and Discussion

When we heated allene **1a**, PhI (1.5 equiv.), and $K_2CO_3$ (2.0 equiv.) in the presence of $Pd(PPh_3)_4$ (5 mol%) in $CH_3CN$ at 85 °C for 46 h (Table 1, entry 1), interestingly, the formation of the most favored six-membered *C*-attack lactone **4a** should be $<2\%$ by NMR, if any. In addition, it should be noted that the *O*-attack products **3a** and **5a** were also not observed. Quite unexpectedly, the more difficult-to-

**Table 1.** The effects of catalyst and temperature on the Pd-catalyzed coupling-cyclization of **1a** with PhI.[a]

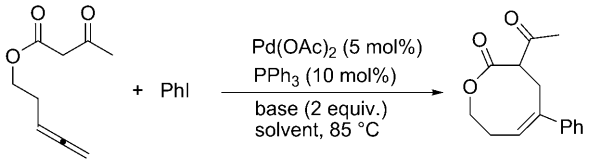



**1a** 1.5 equiv. **2a**

| Entry | Catalyst (mol%) | *T* [°C] | Time [h] | Yield of **2a** [%][b] |
|---|---|---|---|---|
| 1 | $Pd(PPh_3)_4$ (5) | 85 | 46 | 66 |
| 2 | $Pd(OAc)_2$ (5), $PPh_3$ (10) | 85 | 6 | 81 (75)[c] |
| 3 | $Pd(dba)_2$ (5), $PPh_3$ (15) | 85 | 6 | 64[d] |
| 4 | $Pd(OAc)_2$ (5), $PPh_3$ (10) | 50 | 21.7 | 69[e] |

[a] Under argon, a mixture of **1a** (0.250 mmol), PhI (0.375 mmol), $K_2CO_3$ (2 equiv.), the palladium catalyst (5 mol%), and ligand in 2 mL of $CH_3CN$ was stirred at the indicated temperature.
[b] The yield was determined by $^1H$ NMR analysis using 1,3,5-trimethylbenzene as the internal standard.
[c] The number shown in the parenthesis is the isolated yield.
[d] 5% of the starting material **1a** remained.
[e] 14% of the starting material **1a** remained.

**Table 2.** Solvent and base effects in the Pd-catalyzed coupling-cyclization of **1a** with PhI.[a]




**1a** 1.5 equiv. **2a**

| Entry | Base | Solvent | Time [h] | Recovery of **1a** [%][b] | Yield of **2a** [%][b] |
|---|---|---|---|---|---|
| 1 | $K_2CO_3$ | $CH_3CN$ | 6 | 0 | 81 |
| 2 | $K_2CO_3$ | toluene | 26 | 25 | 42 |
| 3 | $K_2CO_3$ | THF | 26 | 22 | 59 |
| 4 | $K_2CO_3$ | DCE | 30.5 | 28 | 42 |
| 5 | $K_2CO_3$ | $CH_3NO_2$ | 24 | 0 | 68 |
| 6 | $Na_2CO_3$ | $CH_3CN$ | 34 | 55 | 27 |
| 7 | $Cs_2CO_3$ | $CH_3CN$ | 11 | 0 | 8 |
| 8 | $Et_3N$ | $CH_3CN$ | 46.5 | 39 | 16 |
| 9 | KOH | $CH_3CN$ | 15.5 | 0 | 20 |
| 10 | $K_3PO_4$ | $CH_3CN$ | 15.5 | 0 | 28 |
| 11 | $CaH_2$ | $CH_3CN$ | 45.5 | 16 | trace |

[a] The reaction was carried out with **1a** (0.250 mmol), PhI (0.375 mmol), $Pd(OAc)_2$ (5 mol%), $PPh_3$ (10 mol%), and base (2 equiv.) in solvent (2 mL). THF = tetrahydrofuran, DCE = 1,2-dichloroethane.
[b] Determined by $^1H$ NMR analysis using 1,3,5-trimethylbenzene as the internal standard.

form *C*-attack eight-membered lactone **2a** was formed and isolated as the only product with a very high chemo- and regioselectivity.

A screening of palladium catalysts was then performed, and it was found that the reaction proceeded smoothly with $Pd(OAc)_2$ (5 mol%) and $PPh_3$ (10 mol%) within a short period of time affording **2a** in 75% isolated yield and the formation of **4a** should be $<2.3\%$ by NMR, if any. (Table 1, entry 2). Shortening the reaction time to 90 min, we only detected the *C*-attack product **2a** in 59% yield and 29% recovery of **1a** by NMR. The *O*-attack product was not observed. Lowering the temperature to 50 °C, the reaction became sluggish with 14% of **1a** remaining.

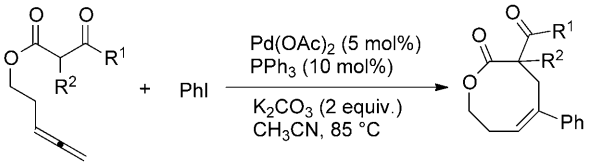
A subsequent comprehensive study of the solvent effect indicated that the reaction can afford product **2a** in all the tested solvents (Table 2, entries 1–5) with $CH_3CN$ (Table 1, entry 1) being the best. The base effect using $CH_3CN$ as solvent was then investigated: The reaction afforded the desired product **2a** in relatively lower yields with $Na_2CO_3$, $Cs_2CO_3$, $Et_3N$, KOH, $K_3PO_4$, and $CaH_2$ (Table 2, entries 6–11). Thus, the following reaction conditions [organic halide (1.5 equiv.), $Pd(OAc)_2$ (5 mol%), $PPh_3$ (10 mol%), $K_2CO_3$ (2.0 equiv.), MeCN, 85 °C] were defined as the standard for the coupling cyclization.

With the optimal conditions in hand, firstly, the scope of functionalized allenes was investigated. Changing the $R^1$ group, the reaction proceeded to afford the desired lactones in good yields (Table 3, entries 2 and 3). Notably, the reaction of more sterically hindered allenyl 2-substituted-3-oxoalkanoates also afforded the corresponding lactones in good to moderate yields, in which a quaternary carbon was constructed. It is interesting to observe that the $R^2$ substituent has a dramatic effect on the reaction time. From methyl to Bn to allyl to ethyl or propyl, the reaction requires a much longer time (Table 3, entries 4–7).

Then the standard conditions were applied to investigate the reaction of different organic halides with **1c**. The results are summarized in Table 4. Electron-rich (Table 4, entries 1–5), electron-deficient (Table 4, entry 6), Br-substituted (Table 4, entry 7) aryl iodides and 3-thienyl iodide (Table 4, entry 8) all afforded the corresponding eight-membered lactones in moderate to good yields. In addition, 1-hexenyl iodide (Table 4, entry 9) and styryl iodide (Table 4, entry 10) may also be used. The structures of all the eight-membered lactones were assigned by analogy to that of **2m**, which was determined by a single crystal X-ray diffraction study (Figure 2).[16]

**Table 3.** Substrate variation of compounds **1**.[a]

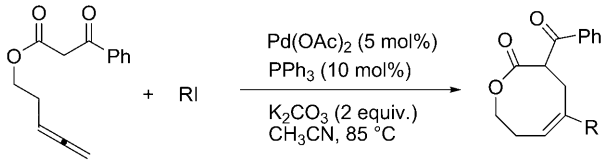



**1** **2**

| Entry | **1** $R^1$ | $R^2$ | Time [h] | Yield of **2** [%][b] |
|---|---|---|---|---|
| 1 | Me | H (**1a**) | 4.5 | 73 (**2a**) |
| 2 | *i*-Pr | H (**1b**) | 6 | 83 (**2b**) |
| 3 | Ph | H (**1c**) | 1.5 | 79 (**2c**) |
| 4 | Me | Me (**1d**) | 10.5 | 81 (**2d**)[c] |
| 4 | Me | Bn (**1j**) | 22 | 75 (**2w**)[c] |
| 5 | Me | Et (**1e**) | 81.5 | 63 (**2e**)[c,d] |
| 6 | Me | *n*-Pr (**1i**) | 82 | 67 (**2v**)[c,d] |
| 7 | Me | $CH_2$=$CHCH_2$ (**1f**) | 29 | 69 (**2f**)[c] |

[a] The reaction was carried out with **1** (0.50 mmol), PhI (0.75 mmol), $Pd(OAc)_2$ (5 mol%), $PPh_3$ (10 mol%), and $K_2CO_3$ (2 equiv.) in 4 mL of $CH_3CN$.
[b] Isolated yield.
[c] The reaction was carried out at 100 °C.
[d] 2.5 equiv. of PhI were used.

**Table 4.** Coupling cyclization of **1c** with different organic halides.[a]




**1c** **2**

| Entry | R | Time [h] | Yield of **2** [%][b] |
|---|---|---|---|
| 1 | 4-$MeC_6H_4$ | 2 | 75 (**2g**) |
| 2 | 4-$MeOC_6H_4$ | 5 | 69 (**2h**) |
| 3 | 3-$MeC_6H_4$ | 2 | 78 (**2i**) |
| 4 | 3,4-$Me_2C_6H_3$ | 1.6 | 72 (**2j**) |
| 5 | 3,4-$(OCH_2)_2C_6H_3$ | 2.5 | 66 (**2k**) |
| 6 | 4-$EtO_2CC_6H_4$ | 3 | 58 (**2l**) |
| 7 | 4-$BrC_6H_4$ | 3.5 | 63 (**2m**) |
| 8 | 3-thienyl | 2 | 70 (**2n**) |
| 9 | 1-(*E*)-hexenyl | 2.5 | 59 (**2o**) |
| 10 | (*E*)-styryl | 1.5 | 58 (**2p**) |

[a] The reaction was carried out with **1c** (0.50 mmol), RI (0.75 mmol), $Pd(OAc)_2$ (5 mol%), $PPh_3$ (10 mol%), and $K_2CO_3$ (2 equiv.) in 4 mL of $CH_3CN$.
[b] Isolated yield.

The efficiency by which eight-membered lactones formed prompted us to explore the possibility of synthesizing other lactones. To our delight, this set of standard conditions has been proven to be operative for the efficient synthesis of nine- and ten-membered lactones with highly chemo-, regio- and stereoselectivity (Scheme 3). The reaction of **1g** with 1-iodo-4-nitrobenzene gave the expected product *E*-**2s** in a satisfactory yield of 74%. The structure of *E*-**2s** was further established by single crystal X-ray diffraction study (Figure 3).[17] In addition, the ten-membered lactone *E*-**2u**[18] was obtained in 69% yield as a single stereoisomer and the configuration of C=C bond in this compound was established by single crystal X-ray dif-

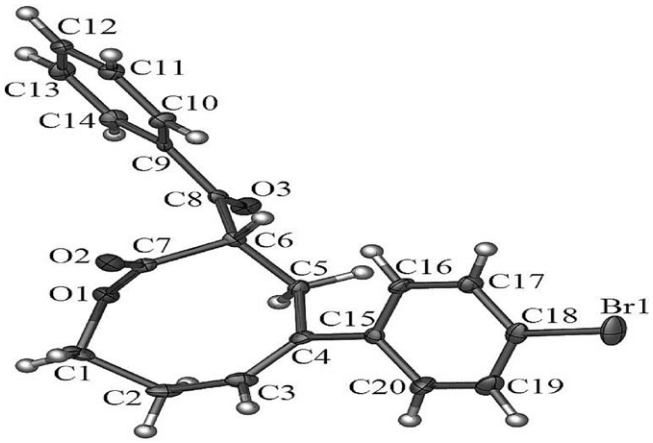
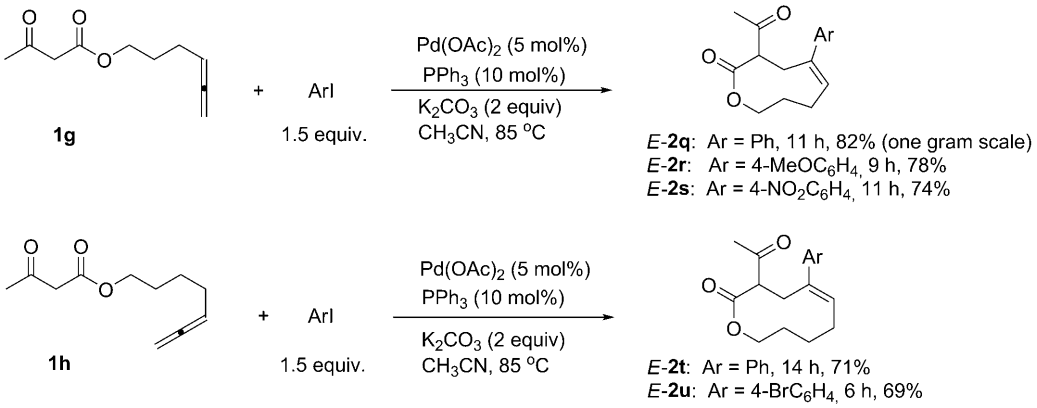



**Figure 2.** ORTEP representation of **2m**.




**Scheme 3.** Synthesis of nine- and ten-membered lactones.

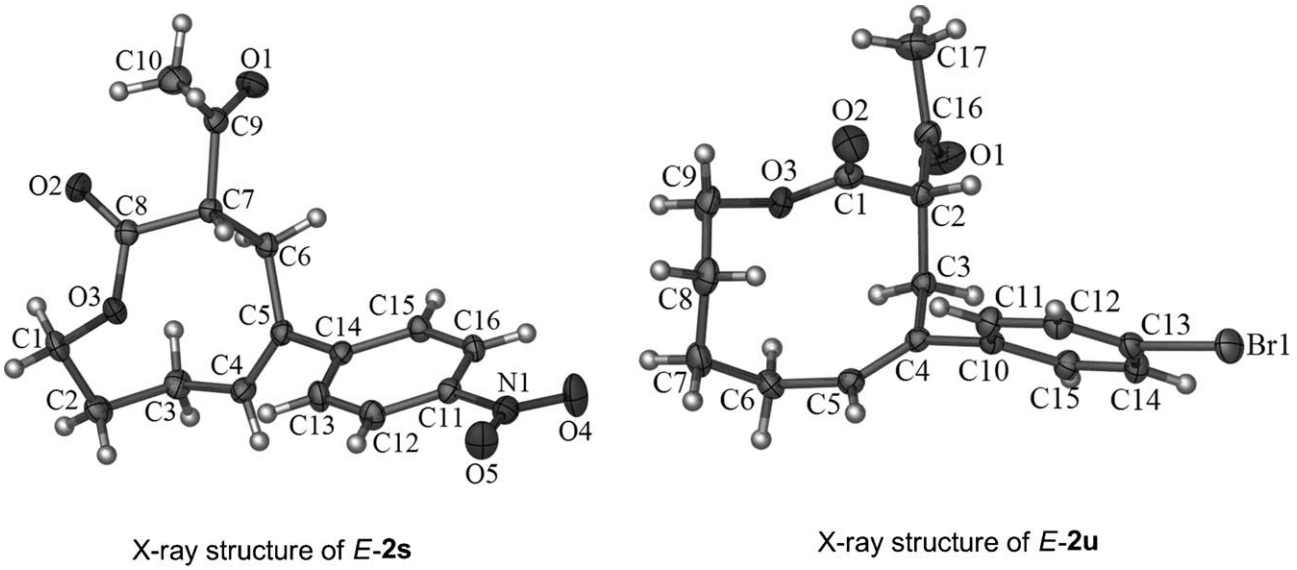



**Figure 3.** ORTEP representations of *E*-**2s** and *E*-**2u**.

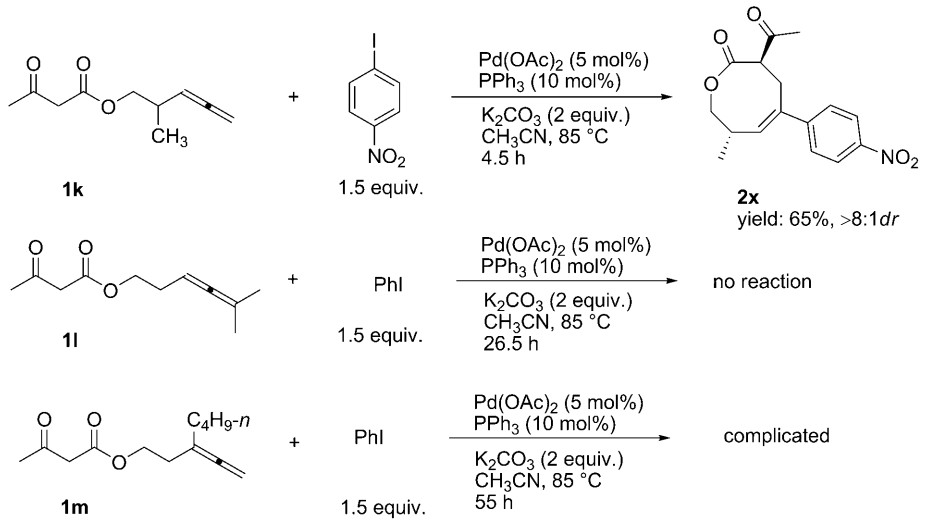
fraction study (Figure 3). The reaction of **1g** with iodobenzene afforded the product **2q** on a one-gram scale in 82% yield.

In addition, we investigated some other allenyl 3-oxoalkanoates. To our delight, the reaction of **1k** with 1-iodo-4-nitrobenzene gave lactone **2x** in 65% yield and >8:1 *dr* (Scheme 4).[19] The structure of *trans*-**2x** was further established by a single crystal X-ray diffraction study (Figure 4). However, the reactions of **1l** and **1m** bearing substitutents at the allene moiety with iodobenzene failed to afford the expected corresponding eight-membered lactones (Scheme 4).

A rationale is proposed to explain the high regio- and stereoselectivity using the reaction of **1a** and iodobenzene as the example.[11] As illustrated in Scheme 5, obviously, the existence of the phenyl group strongly favors the formation of the π-allylic palladium intermediate *anti*-**6** rather than *syn*-**6** to avoid the steric congestion between the phenyl group and the chain bearing the nucleophilic functionality.[15,20] Subsequent highly chemoselective carbon nucleophilic attack[13,14] to the π-allylic species at the less substituted terminal affords the stereodefined eight-membered lactone **2a**.

## Conclusions

In conclusion, we have developed a highly chemo-, regio-, and stereoselective methodology for the syn-




**Scheme 4.** Coupling cyclization of some other substituted allenyl 3-oxoalkanoates.

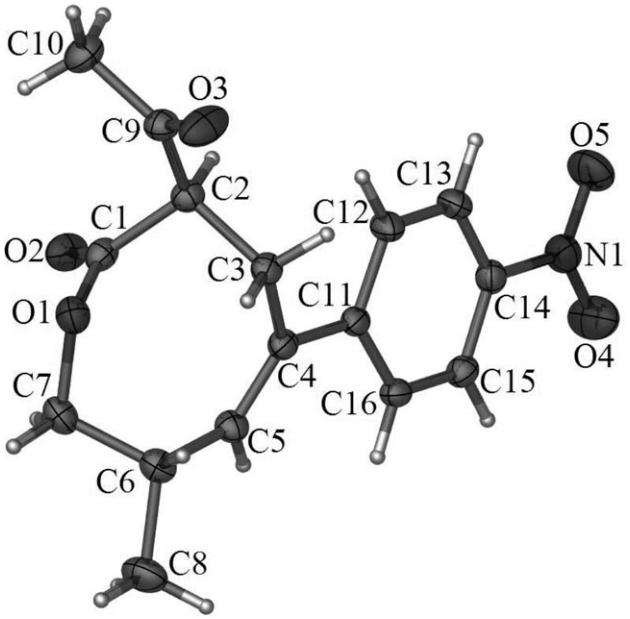



**Figure 4.** ORTEP representation of **2x**.

thesis of normally difficult-to-form eight- to ten-membered lactones by palladium-catalyzed carbon-carbon bond formation *via* the coupling cyclization of allenyl alkanoates with organic halides. Owing to the readily available nature of β-methylene-β-lactone,[12] the allenols[21] and organic halides (Scheme 1) and the importance of the lactone skeleton, the reaction will be potentially useful in organic synthesis and medicinal chemistry. In addition, the observed exclusive *C*-attack is also quite interesting. Further studies in this area are on going in our laboratory.

## Experimental Section

### General Information

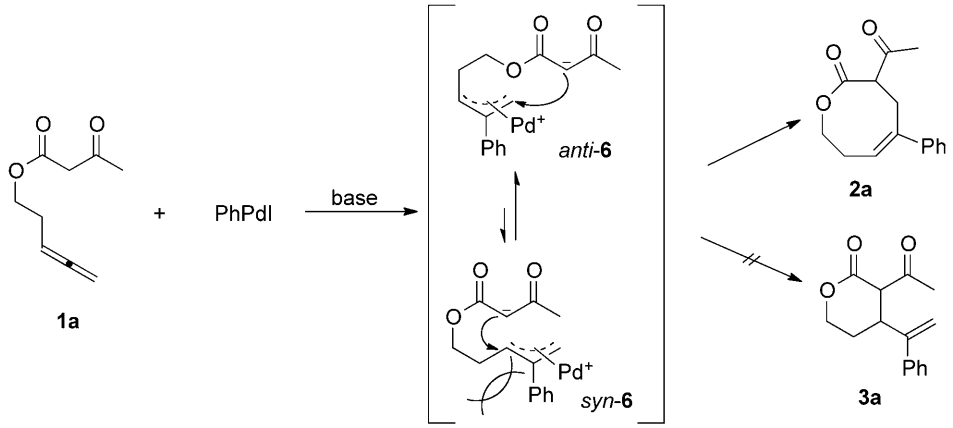
All reactions were carried out in oven-dried Schlenk tubes. $CH_3CN$ was dried over calcium hydride before distillation. All the temperatures are referred to the oil baths used. The petroleum ether was distilled before use.

### Typical Procedure for the Preparation of 2

To a flame-dried Schlenk tube were added $Pd(OAc)_2$ (5.7 mg, 0.025 mmol), $PPh_3$ (13.3 mg, 0.050 mmol), $K_2CO_3$ (138.3 mg, 1.0 mmol), $CH_3CN$ (2 mL), iodobenzene (153.6 mg, 0.75 mmol), $CH_3CN$ (1 mL), **1a** (83.2 mg, 0.50 mmol), and 1 mL of $CH_3CN$ sequentially under argon. The mixture was stirred at 85 °C in a preheated oil bath and monitored by TLC. Upon completion, the resulting mixture was filtered through a short column of silica gel and concentrated. The residue was purified by chromatography on silica gel [eluent: petroleum ether (b.p. 30–60 °C)/ethyl ether = 10/1] to afford *3-acetyl-5-phenyl-5(E)-3,4,7,8-tetrahydro-2H-oxocin-2-one* (**2a**) as an oil; yield: 88.6 mg (73%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.39–7.18 (m, 5H, Ar-H), 5.95 (t, $J$ = 8.0 Hz, 1H, =CH), 4.54 (t, $J$ = 11.3 Hz, 1H, one proton from $OCH_2$), 4.25–4.10 (m, 1H, one proton from $OCH_2$), 3.55 (dd, $J_1$ = 11.7 Hz, $J_2$ = 3.9 Hz, 1H, $O_2CCH$), 3.38 [t, $J$ = 12.3 Hz, 1H, one proton from C=C(Ph)$CH_2$], 2.91–2.68 [m, 2H, one proton from C=C(Ph)$CH_2$ and one proton from PhC=$CCH_2$], 2.34–2.12 (m, 4H, one proton from PhC=$CCH_2$ and $CH_3$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 200.7, 173.0, 142.5, 142.1, 128.3, 127.4, 126.4, 126.3, 68.7, 63.4, 30.8, 29.8, 28.7; IR (neat): $\nu$ = 2958, 1750, 1718, 1491, 1460, 1363, 1317, 1257, 1205, 1145, 1103, 1046, 1028, 1004 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 244 ($M^+$, 10.87), 43 (100); HR-MS: $m/z$ = 244.1098, calcd. for $C_{15}H_{16}O_3$ ($M^+$): 244.1099.

### Synthesis of 3-Isobutyryl-5-phenyl-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2b)

The reaction of $Pd(OAc)_2$ (5.4 mg, 0.025 mmol), $PPh_3$ (13.3 mg, 0.050 mmol), $K_2CO_3$ (138.1 mg, 1.0 mmol), iodobenzene (152.9 mg, 0.75 mmol), and **1b** (97.6 mg, 0.50 mmol)




**Scheme 5.** Rational explanation for the regio- and stereoselectivity.

in 4 mL of $CH_3CN$ afforded **2b** (eluent: petroleum ether/ethyl ether = 10/1) as a liquid; yield: 112.5 mg (83%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.37–7.21 (m, 5H, Ar-H), 5.95 (t, $J$ = 8.0 Hz, 1H, =CH), 4.57 (t, $J$ = 11.3 Hz, 1H, one proton from $OCH_2$), 4.21–4.09 (m, 1H, one proton from $OCH_2$), 3.70 (dd, $J_1$ = 11.7 Hz, $J_2$ = 4.2 Hz, 1H, $O_2CCH$), 3.45 [t, $J$ = 12.5 Hz, 1H, one proton from C=C(Ph)$CH_2$], 2.90–2.65 [m, 3H, one proton from C=C(Ph)$CH_2$, one proton from PhC=$CCH_2$, and $COCH(C)C$], 2.30–2.17 (m, 1H, one proton from PhC=$CCH_2$), 1.09 [t, $J$ = 6.5 Hz, 6H, $C(CH_3)_2$]; $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 206.8, 173.1, 142.7, 142.3, 128.4, 127.5, 126.5, 126.2, 68.7, 61.2, 40.3, 31.1, 29.9, 18.8, 17.9; IR (neat): $\nu$ = 2928, 1744, 1705, 1497, 1456, 1379, 1366, 1261, 1206, 1151, 1105, 1068, 1037, 1015 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 272 ($M^+$, 3.52), 43 (100); HR-MS: $m/z$ = 272.1413, calcd. for $C_{17}H_{20}O_3$ ($M^+$): 272.1412.

### Synthesis of 3-Benzoyl-5-phenyl-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2c)

The reaction of $Pd(OAc)_2$ (5.5 mg, 0.025 mmol), $PPh_3$ (13.4 mg, 0.050 mmol), $K_2CO_3$ (137.7 mg, 1.0 mmol), iodobenzene (152.0 mg, 0.75 mmol), and **1c** (114.9 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2c** (eluent: petroleum ether/ethyl ether = 10/1) as an oil; yield: 120.5 mg (79%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.00 (d, $J$ = 7.8 Hz, 2H, Ar-H), 7.53 (t, $J$ = 7.1 Hz, 1H, Ar-H), 7.40 (t, $J$ = 7.7 Hz, 2H, Ar-H), 7.36–7.20 (m, 5H, Ar-H), 6.01 (t, $J$ = 8.1 Hz, 1H, =CH), 4.58 (t, $J$ = 11.4 Hz, 1H, one proton from $OCH_2$), 4.36 (dd, $J_1$ = 11.6 Hz, $J_2$ = 4.1 Hz, 1H, $O_2CCH$), 4.15–4.03 (m, 1H, one proton from $OCH_2$), 3.75 [t, $J$ = 12.5 Hz, 1H, one proton from C=C(Ph)$CH_2$], 2.95–2.67 [m, 2H, one proton from C=C(Ph)$CH_2$ and one proton from PhC=$CCH_2$], 2.30–2.17 (m, 1H, one proton from PhC=$CCH_2$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 192.1, 173.1, 142.6, 142.4, 135.7, 133.7, 128.7, 128.6, 128.5, 127.5, 126.5, 126.4, 68.7, 59.1, 31.4, 28.9; IR (neat): $\nu$ = 1743, 1684, 1597, 1580, 1491, 1448, 1365, 1326, 1279, 1212, 1194, 1145, 1103, 1076, 1045, 1014 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 306 ($M^+$, 0.4), 105 (100); anal. calcd. for $C_{20}H_{18}O_3$ (%): C 78.41, H 5.92; found: C 78.41, H 5.97.

### Synthesis of 3-Acetyl-3-methyl-5-phenyl-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2d)

The reaction of $Pd(OAc)_2$ (5.7 mg, 0.025 mmol), $PPh_3$ (13.4 mg, 0.050 mmol), $K_2CO_3$ (138.5 mg, 1.0 mmol), iodobenzene (152.9 mg, 0.75 mmol), and **1d** (90.1 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2d** [eluent: petroleum ether (b.p. 30–60 °C)/ethyl ether = 10/1] as an oil; yield: 103.4 mg (81%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.36–7.19 (m, 5H, Ar-H), 5.93 (t, $J$ = 8.0 Hz, 1H, =CH), 4.62 (t, $J$ = 11.4 Hz, 1H, one proton from $OCH_2$), 4.12–3.98 (m, 1H, one proton from $OCH_2$), 3.52 [d, $J$ = 13.2 Hz, 1H, C=C(Ph)$CH_2$], 2.82–2.65 [m, 2H, one proton from C=C(Ph)$CH_2$ and one proton from PhC=$CCH_2$], 2.30–2.19 (m, 1H, one proton from PhC=$CCH_2$), 2.16 (s, 3H, $COCH_3$), 0.96 (s, 3H, $CCH_3$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 205.0, 176.0, 144.8, 143.0, 128.4, 127.5, 127.2, 126.3, 67.4, 65.5, 37.1, 30.0, 26.0, 18.5; IR (neat): $\nu$ = 1748, 1708, 1488, 1451, 1380, 1361, 1319, 1295, 1266, 1215, 1162, 1101, 1088 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 258 ($M^+$, 4.18), 43 (100); HR-MS: $m/z$ = 258.1255, calcd. for $C_{16}H_{18}O_3$ ($M^+$): 258.1256.

### Synthesis of 3-Acetyl-3-ethyl-5-phenyl-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2e)

The reaction of $Pd(OAc)_2$ (5.5 mg, 0.025 mmol), $PPh_3$ (13.2 mg, 0.050 mmol), $K_2CO_3$ (138.4 mg, 1.0 mmol), iodobenzene (255.6 mg, 1.25 mmol), and **1e** (98.5 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2e** (eluent: petroleum ether/ethyl acetate = 20/1) as a white solid; yield: 86.2 mg (63%); mp 124–125 °C (ethyl ether/petroleum ether). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.35–7.18 (m, 5H, Ar-H), 5.90 (t, $J$ = 8.0 Hz, 1H, =CH), 4.63 (t, $J$ = 11.4 Hz, 1H, one proton from $OCH_2$), 4.12–3.97 (m, 1H, one proton from $OCH_2$), 3.37 [d, $J$ = 13.2 Hz, 1H, one proton from C=C(Ph)$CH_2$], 2.88 [d, $J$ = 13.6 Hz, 1H, one proton from C=C(Ph)$CH_2$], 2.81–2.67 (m, 1H, one proton from PhC=$CCH_2$), 2.29–2.17 (m, 1H, one proton from PhC=$CCH_2$), 2.12 (s, 3H, $COCH_3$), 1.83–1.67 (m, 1H, one proton from $O_2CCCH_2C$), 1.39–1.25 (m, 1H, one proton from $O_2CCCH_2C$), 0.48 (t, $J$ = 7.6 Hz, 3H, $CCH_3$); $^{13}$C NMR (100.5 MHz, $CDCl_3$): $\delta$ = 204.4, 175.7, 144.5, 143.1, 128.3, 127.7, 127.1, 126.3, 69.9, 67.3, 32.8, 29.9, 26.7, 23.3, 7.75; IR (neat): $\nu$ = 1750, 1706, 1491, 1446, 1365, 1352, 1331, 1280, 1257, 1238, 1215, 1196, 1157, 1112, 1087, 1022 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 272 ($M^+$, 1.56), 43 (100); anal. calcd. for $C_{17}H_{20}O_3$ (%): C 74.97, H 7.40; found: C 74.91, H 7.24.

### Synthesis of 3-Acetyl-3-allyl-5-phenyl-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2f)

The reaction of $Pd(OAc)_2$ (5.7 mg, 0.025 mmol), $PPh_3$ (13.1 mg, 0.050 mmol), $K_2CO_3$ (138.7 mg, 1.0 mmol), iodobenzene (153.5 mg, 0.75 mmol), and **1f** (104.8 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2f** [eluent: petroleum ether (bp 30–60 °C)/ethyl acetate = 20/1] as a white solid; yield: 99.2 mg (69%); mp 77–78 °C (ethyl ether/petroleum ether). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.33–7.14 (m, 5H, Ar-H), 5.90 (t, $J$ = 8.0 Hz, 1H, C=CH), 5.40–5.25 (m, 1H, C=CHC), 4.87 (d, $J$ = 10.0 Hz, 1H, one proton from $CH_2$=C), 4.65 (t, $J$ = 11.4 Hz, 1H, one proton from $OCH_2$), 4.49 (d, $J$ = 17.2 Hz, 1H, one proton from $CH_2$=C), 4.10–4.00 (m, 1H, one proton from $OCH_2$), 3.40 [d, $J$ = 13.2 Hz, 1H, one proton from C=C(Ph)$CH_2$], 2.83 [d, $J$ = 13.2 Hz, 1H, one proton from C=C(Ph)$CH_2$], 2.79–2.67 (m, 1H, one proton from PhC=$CCH_2$), 2.46 (dd, $J_1$ = 14.4 Hz, $J_2$ = 6.4 Hz, 1H, one proton from $CH_2C$=C), 2.30–2.19 (m, 1H, one proton from PhC=$CCH_2$), 2.13 (s, 3H, $CH_3$), 2.46 (dd, $J_1$ = 14.8 Hz, $J_2$ = 8.2 Hz, 1H, one proton from $CH_2C$=C); $^{13}$C NMR (100.5 MHz, $CDCl_3$): $\delta$ = 203.7, 175.2, 144.6, 143.2, 131.2, 128.3, 128.0, 127.2, 126.6, 119.2, 69.4, 67.4, 35.1, 33.7, 30.0, 27.1; IR (neat): $\nu$ = 1748, 1709, 1490, 1465, 1443, 1366, 1272, 1254, 1231, 1187, 1160, 1129, 1110, 1069, 1012 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 284 ($M^+$, 1.44), 43 (100); anal. calcd. for $C_{18}H_{20}O_3$ (%): C 76.03, H 7.09; found: C 76.03, H 7.02.

### Synthesis of 3-Benzoyl-5-*p*-tolyl-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2g)

The reaction of $Pd(OAc)_2$ (5.8 mg, 0.025 mmol), $PPh_3$ (13.3 mg, 0.050 mmol), $K_2CO_3$ (138.0 mg, 1.0 mmol), *p*-meth-

ylphenyl iodide (164.1 mg, 0.75 mmol), and **1c** (115.0 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2g** (eluent: petroleum ether/ethyl ether = 10/1) as a white solid; yield: 120.1 mg (75%); mp 110–111 °C (ethyl ether/petroleum ether). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.01 (d, $J$ = 7.5 Hz, 2H, Ar-H), 7.55 (t, $J$ = 7.4 Hz, 1H, Ar-H), 7.43 (t, $J$ = 7.7 Hz, 2H, Ar-H), 7.24 (d, $J$ = 7.5 Hz, 2H, Ar-H), 7.15 (d, $J$ = 8.1 Hz, 2H, Ar-H), 6.00 (t, $J$ = 8.1 Hz, 1H, =CH), 4.59 (t, $J$ = 11.4 Hz, 1H, one proton from $OCH_2$), 4.36 (dd, $J_1$ = 11.7 Hz, $J_2$ = 4.2 Hz, 1H, $O_2CCH$), 4.15–4.05 (m, 1H, one proton from $OCH_2$), 3.73 [t, $J$ = 12.5 Hz, 1H, one proton from C=C(Ar)$CH_2$], 2.95–2.77 [m, 2H, one proton from C=C(Ar)$CH_2$ and one proton from ArC=$CCH_2$], 2.35 (s, 3H, $CH_3$), 2.30–2.17 (m, 1H, one proton from ArC=$CCH_2$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 192.1, 173.0, 142.4, 139.4, 137.3, 135.7, 133.7, 129.1, 128.7, 128.6, 126.3, 125.6, 68.8, 59.1, 31.3, 29.9, 21.0; IR (neat): $\nu$ = 1738, 1683, 1596, 1514, 1465, 1447, 1360, 1324, 1278, 1254, 1205, 1192, 1177, 1144, 1057, 1014 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 320 ($M^+$, 2.57), 105 (100); anal. calcd. for $C_{21}H_{20}O_3$ (%): C 78.73, H 6.29; found: C 78.44, H 6.29.

### Synthesis of 3-Benzoyl-5-(4-methoxyphenyl)-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2h)

The reaction of $Pd(OAc)_2$ (5.5 mg, 0.025 mmol), $PPh_3$ (13.4 mg, 0.050 mmol), $K_2CO_3$ (138.5 mg, 1.0 mmol), *p*-methoxyphenyl iodide (176.1 mg, 0.75 mmol), and **1c** (115.3 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2h** [eluent: petroleum ether (b.p. 30–60 °C)/ethyl ether = 10/1] as a white solid; yield 116.8 mg (69%); mp 132–133 °C (ethyl ether/petroleum ether). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.00 (d, $J$ = 7.8 Hz, 2H, Ar-H), 7.54 (t, $J$ = 7.4 Hz, 1H, Ar-H), 7.42 (t, $J$ = 7.5 Hz, 2H, Ar-H), 7.28 (d, $J$ = 8.7 Hz, 2H, Ar-H), 6.87 (d, $J$ = 8.7 Hz, 2H, Ar-H), 5.96 (t, $J$ = 8.0 Hz, 1H, =CH), 4.58 (t, $J$ = 11.4 Hz, 1H, one proton from $OCH_2$), 4.35 (dd, $J_1$ = 11.6 Hz, $J_2$ = 4.1 Hz, 1H, $O_2CCH$), 4.15–4.05 (m, 1H, one proton from $OCH_2$), 3.80 (s, 3H, OMe), 3.72 [t, $J$ = 12.3 Hz, 1H, one proton from C=C(Ar)$CH_2$], 2.95–2.77 [m, 2H, one proton from C=C(Ar)$CH_2$ and one proton from ArC=$CCH_2$], 2.30–2.15 (m, 1H, ArC=$CCH_2$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 192.2, 173.1, 159.2, 142.0, 135.7, 134.7, 133.7, 128.70, 128.65, 127.6, 125.0, 113.8, 69.0, 59.2, 55.2, 31.3, 29.0; IR (neat): $\nu$ = 1742, 1684, 1600, 1575, 1513, 1462, 1426, 1330, 1293, 1275, 1238, 1205, 1190, 1139, 1057, 1028, 1012 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 336 ($M^+$, 10.39), 77 (100); anal. calcd. for $C_{21}H_{20}O_4$ (%): C 74.98, H 5.99; found: C 75.02, H 6.04.

### Synthesis of 3-Benzoyl-5-(*m*-tolyl)-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2i)

The reaction of $Pd(OAc)_2$ (5.5 mg, 0.025 mmol), $PPh_3$ (13.3 mg, 0.050 mmol), $K_2CO_3$ (138.4 mg, 1.0 mmol), *m*-methylphenyl iodide (163.0 mg, 0.75 mmol), and **1c** (115.6 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2i** [eluent: petroleum ether (bp 30–60 °C)/ethyl ether = 10/1] as an oil; yield: 124.8 mg (78%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.00 (d, $J$ = 7.8 Hz, 2H, Ar-H), 7.52 (t, $J$ = 7.4 Hz, 1H, Ar-H), 7.40 (t, $J$ = 7.7 Hz, 2H, Ar-H), 7.22 (t, $J$ = 7.4 Hz, 1H, Ar-H), 7.17–7.05 (m, 3H, Ar-H), 5.99 (t, $J$ = 8.0 Hz, 1H, =CH), 4.57 (t, $J$ = 11.4 Hz, 1H, one proton from $OCH_2$), 4.35 (dd, $J_1$ = 11.7 Hz, $J_2$ = 4.2 Hz, 1H, $O_2CCH$), 4.15–4.00 (m, 1H, one proton from $OCH_2$), 3.73 [t, $J$ = 12.5 Hz, 1H, one proton from C=C(Ar)$CH_2$], 2.92–2.75 [m, 2H, one proton from C=C(Ar)$CH_2$ and one proton from ArC=$CCH_2$], 2.35 (s, 3H, $CH_3$), 2.28–2.14 (m, 1H, one proton from ArC=$CCH_2$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 192.0, 173.0, 142.6, 142.3, 137.9, 135.6, 133.6, 128.59, 128.55, 128.3, 128.2, 127.2, 126.1, 123.5, 68.6, 59.1, 31.3, 29.8, 21.3; IR (neat): $\nu$ = 1742, 1684, 1597, 1580, 1486, 1448, 1363, 1325, 1282, 1249, 1212, 1182, 1141, 1103, 1047, 1017 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 320 ($M^+$, 0.74), 105 (100); anal. calcd. for $C_{21}H_{20}O_3$ (%): C 78.73, H 6.29; found: C 78.94, H 6.64.

### Synthesis of 3-Benzoyl-5-(3,4-dimethylphenyl)-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2j)

The reaction of $Pd(OAc)_2$ (5.7 mg, 0.025 mmol), $PPh_3$ (13.3 mg, 0.050 mmol), $K_2CO_3$ (138.5 mg, 1.0 mmol), 3,4-dimethylphenyl iodide (174.5 mg, 0.75 mmol), and **1c** (113.9 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2j** [eluent: petroleum ether (b.p. 30–60 °C)/ethyl ether = 10/1] as an oil; yield: 119.2 mg (72%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.01 (d, $J$ = 7.8 Hz, 2H, Ar-H), 7.54 (t, $J$ = 7.2 Hz, 1H, Ar-H), 7.42 (t, $J$ = 7.7 Hz, 2H, Ar-H), 7.16–7.04 (m, 3H, Ar-H), 6.00 (t, $J$ = 8.0 Hz, 1H, =CH), 4.58 (t, $J$ = 11.4 Hz, 1H, one proton from $OCH_2$), 4.36 (dd, $J_1$ = 11.6 Hz, $J_2$ = 4.1 Hz, 1H, $O_2CCH$), 4.15–4.05 (m, 1H, one proton from $OCH_2$), 3.72 [t, $J$ = 12.3 Hz, 1H, one proton from C=C(Ar)$CH_2$], 2.95–2.78 [m, 2H, one proton from C=C(Ar)$CH_2$ and one proton from ArC=$CCH_2$], 2.35–2.17 (m, 7H, one proton from ArC=$CCH_2$ and 2 × Ar-$CH_3$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 192.3, 173.1, 142.5, 139.9, 136.6, 136.0, 135.8, 133.7, 129.7, 128.7, 127.8, 125.5, 123.9, 68.9, 59.2, 31.4, 29.9, 19.8, 19.3; IR (neat): $\nu$ = 1743, 1685, 1598, 1580, 1501, 1448, 1362, 1326, 1278, 1248, 1213, 1195, 1176, 1143, 1127, 1100, 1048, 1018 cm$^{-1}$; MS (70 eV, EI); $m/z$ (%) = 334 ($M^+$, 3.22), 105 (100); HR-MS: $m/z$ = 334.1567, calcd. for $C_{22}H_{22}O_3$ ($M^+$): 334.1569.

### Synthesis of 3-Benzoyl-5-(2,3 dihydrobenzo[*b*][1,4]-dioxin-6-yl)-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2k)

The reaction of $Pd(OAc)_2$ (5.5 mg, 0.025 mmol), $PPh_3$ (13.4 mg, 0.050 mmol), $K_2CO_3$ (138.9 mg, 1.0 mmol), 6-iodo-1,4-benzodioxane (196.5 mg, 0.75 mmol), and **1c** (116.0 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2k** [eluent: petroleum ether (bp 30–60 °C)/ethyl ether = 10/1] as a white solid; yield: 121.3 mg (66%); mp 142–143 °C (ethyl ether/petroleum ether). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.02 (d, $J$ = 7.8 Hz, 2H, Ar-H), 7.55 (t, $J$ = 7.4 Hz, 1H, Ar-H), 7.43 (t, $J$ = 7.4 Hz, 2H, Ar-H), 6.93–6.77 (m, 3H, Ar-H), 5.98 (t, $J$ = 8.1 Hz, 1H, =CH), 4.56 (t, $J$ = 11.6 Hz, 1H, one proton from $OCH_2$), 4.37 (dd, $J_1$ = 11.6 Hz, $J_2$ = 4.1 Hz, 1H, $O_2CCH$), 4.25 (s, 4H, $OCH_2CH_2O$), 4.15–4.02 (m, 1H, one proton from $OCH_2$), 3.70 [t, $J$ = 12.5 Hz, 1H, one proton from C=C(Ar)$CH_2$], 2.93–2.70 [m, 2H, one proton from C=C(Ar)$CH_2$ and one proton from ArC=$CCH_2$], 2.29–2.15 (m, 1H, one proton from ArC=$CCH_2$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 192.2, 173.0, 143.3, 143.2, 141.7, 135.8, 135.7, 133.7, 128.71, 128.69, 125.2, 119.5, 117.2, 115.3, 68.9, 64.4, 64.3, 59.2, 31.2, 29.9; IR (neat): $\nu$ = 1742, 1688, 1596, 1579,

1510, 1452, 1429, 1360, 1329, 1300, 1249, 1206, 1131, 1101, 1068, 1051, 1014 $cm^{-1}$; MS (70 eV, EI): *m/z* (%) = 364 ($M^+$, 8.38), 77 (100); anal. calcd. for $C_{22}H_{20}O_5$ (%): C 72.51, H 5.53; found: C 72.48, H 5.30.

### Synthesis of 3-Benzoyl-5-(4-ethoxycarbonylphenyl)-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2l)

The reaction of $Pd(OAc)_2$ (5.7 mg, 0.025 mmol), $PPh_3$ (13.3 mg, 0.050 mmol), $K_2CO_3$ (138.7 mg, 1.0 mmol), ethyl 4-iodobenzoate (206.9 mg, 0.75 mmol), and **1c** (115.9 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2l** [eluent: petroleum ether (bp 30–60 °C)/dichloromethane = 1/2] as a white solid; yield: 111.3 mg (58%); mp 123–124 °C (ethyl ether/petroleum ether). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.07–7.92 (m, 4H, Ar-H), 7.56 (t, $J$ = 7.4 Hz, 1H, Ar-H), 7.48–7.32 (m, 4H, Ar-H), 6.12 (t, $J$ = 8.0 Hz, 1H, =CH), 4.60 (t, $J$ = 11.3 Hz, 1H, one proton from $OCH_2CC$), 4.45–4.25 (m, 3H, *p*-Ar-$CO_2CH_2$ and $O_2CCH$), 4.20–4.05 (m, 1H, one proton from $OCH_2CC$), 3.78 [t, $J$ = 12.5 Hz, 1H, one proton from C=C(Ar)$CH_2$], 2.95–2.75 [m, 2H, one proton from C=C(Ar)$CH_2$ and one proton from ArC=$CCH_2$], 2.35–2.12 (m, 1H, one proton from ArC=$CCH_2$), 1.39 (t, $J$ = 7.2 Hz, 3H, $CH_3$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 191.9, 173.0, 166.3, 146.8, 142.0, 135.7, 133.8, 129.8, 129.6, 128.8, 128.7, 128.2, 126.5, 68.4, 60.9, 59.1, 31.2, 30.0, 14.3; IR (neat): $\nu$ = 1743, 1716, 1687, 1607, 1597, 1459, 1449, 1406, 1365, 1316, 1276, 1255, 1207, 1193, 1179, 1144, 1105, 1013 $cm^{-1}$; MS (70 ev, EI) *m/z* (%): 378 ($M^+$, 0.16), 105 (100); anal. calcd. for $C_{23}H_{22}O_5$ (%): C 73.00, H 5.86; found: C 72.98, H 6.08.

### Synthesis of 3-Benzoyl-5-(4-bromophenyl)-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2m)

The reaction of $Pd(OAc)_2$ (5.4 mg, 0.025 mmol), $PPh_3$ (13.5 mg, 0.050 mmol), $K_2CO_3$ (137.4 mg, 1.0 mmol), 1-bromo-4-iodobenzene (211.7 mg, 0.75 mmol), and **1c** (113.8 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2m** [eluent: petroleum ether (bp 30–60 °C)/ethyl ether = 15/1] as a solid; yield: 120.8 mg (63%); mp 136–137 °C (ethyl ether/petroleum ether). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.01 (d, $J$ = 7.5 Hz, 2H, Ar-H), 7.56 (t, $J$ = 7.4 Hz, 1H, Ar-H), 7.52–7.37 (m, 4H, Ar-H), 7.21 (d, $J$ = 8.7 Hz, 2H, Ar-H), 6.02 (t, $J$ = 8.0 Hz, 1H, =CH), 4.59 (t, $J$ = 11.4 Hz, 1H, one proton from $OCH_2$), 4.33 (dd, $J_1$ = 11.6 Hz, $J_2$ = 4.4 Hz, 1H, $O_2CCH$), 4.15–4.05 (m, 1H, one proton from $OCH_2$), 3.75 [t, $J$ = 12.5 Hz, 1H, one proton from C=C(Ar)$CH_2$], 2.95–2.75 [m, 2H, one proton from C=C(Ar)$CH_2$ and one proton from ArC=$CCH_2$], 2.32–2.13 (m, 1H, one proton from ArC=$CCH_2$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 191.9, 173.0, 141.7, 141.3, 135.6, 133.8, 131.6, 128.8, 128.6, 128.2, 127.1, 121.6, 68.5, 59.0, 31.3, 29.9; IR (neat): $\nu$ = 1748, 1681, 1596, 1580, 1487, 1446, 1424, 1394, 1364, 1324, 1310, 1275, 1253, 1208, 1194, 1177, 1145, 1108, 1074, 1057, 1010 $cm^{-1}$; MS (70 eV, EI): *m/z* (%) = 386 [$M(^{81}Br)^+$, 0.53], 384 [$M(^{79}Br)^+$, 0.56], 105 (100); anal. calcd. for $C_{20}H_{17}BrO_3$ (%): C 62.35, H 4.45; found: C 62.15, H 4.61.

### Synthesis of 3-Benzoyl-5-(3-thienyl)-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2n)

The reaction of $Pd(OAc)_2$ (5.7 mg, 0.025 mmol), $PPh_3$ (13.3 mg, 0.050 mmol), $K_2CO_3$ (138.1 mg, 1.0 mmol), 3-iodothiophene (156.5 mg, 0.75 mmol), and **1c** (114.5 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2n** [eluent: petroleum ether (bp 30–60 °C)/ethyl ether = 10/1] as a white solid; yield: 108.1 mg (70%); mp 120–122 °C (ethyl ether/petroleum ether). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.04 (d, $J$ = 7.8 Hz, 2H, Ar-H), 7.56 (t, $J$ = 7.4 Hz, 1H, Ar-H), 7.44 (t, $J$ = 7.7 Hz, 2H, Ar-H), 7.35–7.23 (m, 1H, Ar-H), 7.22–7.12 (m, 2H, Ar-H), 6.22 (t, $J$ = 8.1 Hz, 1H, =CH), 4.57 (t, $J$ = 11.4 Hz, 1H, one proton from $OCH_2$), 4.48 (dd, $J_1$ = 11.7 Hz, $J_2$ = 4.2 Hz, 1H, $O_2CCH$), 4.20–4.05 (m, 1H, one proton from $OCH_2$), 3.71 [t, $J$ = 12.5 Hz, 1H, one proton from C=C(Ar)$CH_2$], 2.95–2.75 [m, 2H, one proton from C=C(Ar)$CH_2$ and one proton from ArC=$CCH_2$], 2.30–2.15 (m, 1H, one proton from ArC=$CCH_2$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 192.2, 172.8, 142.8, 136.9, 135.7, 133.8, 128.75, 128.67, 126.1, 125.5, 124.9, 120.2, 69.1, 59.2, 30.7, 29.7; IR (neat): $\nu$ = 1742, 1685, 1598, 1579, 1461, 1448, 1424, 1358, 1324, 1286, 1268, 1249, 1204, 1174, 1133, 1102, 1040, 1013 $cm^{-1}$; MS (70 eV, EI): *m/z* (%) = 312 ($M^+$, 2.01), 77 (100); anal. calcd. for $C_{18}H_{16}O_3S$ (%): C 69.21, H 5.16, S 10.26; found: C 69.49, H 5.02, S 10.25.

### Synthesis of 3-Benzoyl-5-[(*E*)-hex-1-enyl]-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2o)

The reaction of $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $PPh_3$ (13.2 mg, 0.050 mmol), $K_2CO_3$ (138.7 mg, 1.0 mmol), (*E*)-1-iodohex-1-ene (157.3 mg, 0.75 mmol), and **1c** (114.9 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2o** [eluent: petroleum ether (b.p. 30–60 °C)/ethyl ether = 15/1] as a white solid; yield: 92.0 mg (59%); mp 70–71 °C (ethyl ether/petroleum ether). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.07 (d, $J$ = 8.1 Hz, 2H, Ar-H), 7.58 (t, $J$ = 7.4 Hz, 1H, Ar-H), 7.47 (t, $J$ = 7.5 Hz, 2H, Ar-H), 6.04 (d, $J$ = 15.9 Hz, 1H, C=CCH=C), 5.75 [t, $J$ = 8.1 Hz, 1H, CH=C(C)C=C], 5.71–5.58 (m, 1H, C=CC=CHC), 4.53 (t, $J$ = 11.4 Hz, 1H, one proton from $OCH_2$), 4.44 (dd, $J_1$ = 11.4 Hz, $J_2$ = 3.9 Hz, 1H, $O_2CCH$), 4.15–4.00 (m, 1H, one proton from $OCH_2$), 3.42 [t, $J$ = 12.6 Hz, 1H, one proton from C=C(C=C)$CH_2$], 2.87–2.63 [m, 2H, one proton from C=C(C=C)$CH_2$ and one proton from $CH_2$C=CC=C], 2.25–2.01 (m, 3H, $CH_2CC$, and one proton from $CH_2$C=CC=C), 1.47–1.20 (m, 4H, $CCH_2CH_2C$), 0.90 (t, $J$ = 6.8 Hz, 3H, $CH_3$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 192.4, 172.8, 140.2, 135.8, 133.7, 132.5, 129.5, 128.74, 128.65, 127.3, 69.8, 58.9, 32.4, 31.5, 29.6, 26.8, 22.2, 13.9; IR (neat): $\nu$ = 1744, 1686, 1597, 1581, 1453, 1422, 1380, 1353, 1325, 1284, 1264, 1248, 1206, 1188, 1173, 1140, 1120, 1056, 1010 $cm^{-1}$; MS (70 eV, EI): *m/z* (%) = 312 ($M^+$, 0.18), 105 (100); anal. calcd. for $C_{20}H_{24}O_3$ (%): C 76.89, H 7.74; found: C 77.16, H 7.99.

### Synthesis of 3-Benzoyl-5-styryl-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2p)

The reaction of $Pd(OAc)_2$ (5.7 mg, 0.025 mmol), $PPh_3$ (13.3 mg, 0.050 mmol), $K_2CO_3$ (139.0 mg, 1.0 mmol), (*E*)-(2-iodovinyl)benzene (173.3 mg, 0.75 mmol), and **1c** (115.0 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2p** [eluent: petroleum ether (b.p. 30–60 °C)/ethyl ether = 15/1] as a white solid; yield: 95.8 mg (58%); mp 116–117 °C (ethyl ether/petroleum ether); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.09 (d, $J$ = 8.1 Hz, 2H, Ar-H), 7.58 (t, $J$ = 7.1 Hz, 1H, Ar-H), 7.52–7.37 (m, 4H,

Ar-H), 7.31 (t, $J=7.4$ Hz, 2H, Ar-H), 7.22 (t, $J=7.2$ Hz, 1H, Ar-H), 6.78 [d, $J=16.2$ Hz, 1H, C=CCH=C(Ph)], 6.51 [d, $J=16.2$ Hz, 1H, C=CC=CCH(Ph)], 6.01 [t, $J=8.1$ Hz, 1H, CH=CC=C(Ph)], 4.62–4.45 (m, 2H, one proton from $OCH_2$ and $O_2CCH$), 4.20–4.05 (m, 1H, one proton from $OCH_2$), 3.54 [t, $J=12.8$ Hz, 1H, one proton from C=C(C=C)$CH_2$], 2.95–2.75 [m, 2H, one proton from C=C(C=C)$CH_2$ and one proton from (C=C)C=C$CH_2$], 2.20 [dd, $J_1=13.8$ Hz, $J_2=8.4$ Hz, 1H, one proton from (C=C)C=C$CH_2$]; $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta=192.2$, 172.7, 140.3, 137.0, 135.8, 133.8, 131.4, 130.7, 128.8, 128.7, 128.6, 127.5, 127.2, 126.4, 69.5, 58.9, 29.9, 26.7; IR (neat): $\nu=1742$, 1684, 1597, 1580, 1495, 1448, 1356, 1325, 1275, 1249, 1212, 1182, 1129, 1075, 1015 cm$^{-1}$; MS (70 eV, EI): *m/z* (%) = 332 ($M^+$, 6.13), 105 (100); anal. calcd. for $C_{22}H_{20}O_3$ (%): C 79.50, H 6.06; found: C 79.56, H 6.27.

### Synthesis of 3-Acetyl-5-phenyl-5(*E*)-3,4,8,9-tetrahydrooxonin-2(3*H*)-one (2q)

To a three-necked flask were added $Pd(OAc)_2$ (67.3 mg, 0.3 mmol), $PPh_3$ (158.0 mg, 0.6 mmol), $K_2CO_3$ (1.6581 g, 12.0 mmol), $CH_3CN$ (28 mL), iodobenzene (1.8366 g, 9.0 mmol), $CH_3CN$ (1 mL), **1g** (1.0947 g, 6.0 mmol), and $CH_3CN$ (1 mL) sequentially under argon. The mixture was stirred at 85 °C with a preheated oil bath and monitored by TLC. Upon completion, the resulting mixture was filtered to remove the solid and the filtrate was concentrated. The residue was purified by chromatography on silica gel to afford **2q** (eluent: petroleum ether/ethyl acetate = 10/1) as a liquid; yield: 1.2690 g (82%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta=$ 7.39–7.17 (m, 5H, Ar-H), 5.77 (dd, $J_1=11.1$ Hz, $J_2=6.6$ Hz, 1H, =CH), 4.60–4.46 (m, 1H, one proton from $OCH_2$), 4.25–4.12 (m, 1H, one proton from $OCH_2$), 3.33–3.17 [m, 2H, $O_2CCH$, and one proton from C=C(Ph)$CH_2$], 2.86 [dd, $J_1=19.7$ Hz, $J_2=11.1$ Hz, 1H, one proton from C=C(Ph)$CH_2$], 2.47–2.27 [m, 1H, one proton from (Ph)C=$CCH_2$], 2.27–2.12 [m, 4H, one proton from (Ph)C=$CCH_2$ and $CH_3$], 2.06–1.85 (m, 2H, $CCH_2C$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta=201.6$, 170.7, 142.4, 136.6, 131.9, 128.3, 127.1, 126.7, 63.3, 58.2, 30.0, 28.8, 26.9, 23.3; IR (neat): $\nu=1714$, 1598, 1492, 1462, 1445, 1377, 1358, 1275, 1218, 1150, 1064, 1042, 1028 cm$^{-1}$; MS (70 eV, EI): *m/z* (%) = 258 ($M^+$, 16.80), 43 (100); HR-MS: *m/z* = 258.1258, calcd. for $C_{16}H_{18}O_3$ ($M^+$): 258.1256.

### Synthesis of 3-Acetyl-5-(4-methoxyphenyl)-5(*E*)-3,4,8,9-tetrahydrooxonin-2(3*H*)-one (2r)

The reaction of $Pd(OAc)_2$ (5.8 mg, 0.025 mmol), $PPh_3$ (13.3 mg, 0.05 mmol), $K_2CO_3$ (138.5 mg, 1.0 mmol), *p*-methoxyphenyl iodide (174.6 mg, 0.75 mmol), and **1g** (92.1 mg, 0.5 mmol) in 4 mL of $CH_3CN$ afforded **2r** (eluent: petroleum ether/ethyl acetate = 10/1) as a liquid; yield: 114.4 mg (78%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta=7.21$ (d, $J=8.7$ Hz, 2H, Ar-H), 6.84 (d, $J=8.7$ Hz, 2H, Ar-H), 5.71 (dd, $J_1=$ 11.1 Hz, $J_2=6.3$ Hz, 1H, =CH), 4.58–4.46 (m, 1H, one proton from $OCH_2$), 4.25–4.12 (m, 1H, one proton from $OCH_2$), 3.79 (s, 3H, $OCH_3$), 3.30–3.16 [m, 2H, $O_2CCH$ and one proton from C=C(Ar)$CH_2$], 2.88–2.75 [m, 1H, one proton from C=C(Ar)$CH_2$], 2.46–2.27 [m, 1H, one proton from (Ar)C=$CCH_2$], 2.27–2.12 [m, 4H, one proton from (Ar)C=$CCH_2$ and $COCH_3$], 2.06–1.85 (m, 2H, $CCH_2C$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta=201.7$, 170.7, 158.8, 136.0, 134.7, 130.5, 127.7, 113.7, 63.3, 58.3, 55.2, 30.0, 28.8, 26.9, 23.2; IR (neat): $\nu=1714$, 1607, 1573, 1510, 1462, 1358, 1291, 1244, 1218, 1178, 1150, 1064, 1030 cm$^{-1}$; MS (70 eV, EI): *m/z* (%) = 288 ($M^+$, 27.16), 43 (100); HR-MS: *m/z* = 288.1361, calcd. for $C_{17}H_{20}O_4$ ($M^+$): 288.1362.

### Synthesis of 3-Acetyl-5-(4-nitrophenyl)-5(*E*)-3,4,8,9-tetrahydrooxonin-2(3*H*)-one (2s)

The reaction of $Pd(OAc)_2$ (5.4 mg, 0.025 mmol), $PPh_3$ (13.1 mg, 0.05 mmol), $K_2CO_3$ (138.0 mg, 1.0 mmol), 1-iodo-4-nitrobenzene (186.6 mg, 0.75 mmol), and **1g** (91.5 mg, 0.5 mmol) in 4 mL of $CH_3CN$ afforded **2s** (eluent: petroleum ether/ethyl ether = 5/1) as a yellow solid; yield: 112.8 mg (74%); mp 115–116 °C (ethyl ether/petroleum ether). $^1$H NMR (300 MHz, $CDCl_3$): $\delta=8.15$ (d, $J=8.7$ Hz, 2H, Ar-H), 7.43 (d, $J=8.7$ Hz, 2H, Ar-H), 5.92 (dd, $J_1=11.1$ Hz, $J_2=6.6$ Hz, 1H, =CH), 4.57–4.46 (m, 1H, one proton from $OCH_2$), 4.31–4.17 (m, 1H, one proton from $OCH_2$), 3.37–3.15 [m, 2H, $O_2CCH$ and one proton from C=C(Ar)$CH_2$], 2.86 [dd, $J_1=13.2$ Hz, $J_2=3.3$ Hz, 1H, one proton from C=C(Ar)$CH_2$], 2.48–2.33 [m, 1H, one proton from (Ar)C=$CCH_2$], 2.33–2.17 [m, 4H, one proton from (Ar)C=$CCH_2$ and $CH_3$], 2.11–1.88 (m, 2H, $CCH_2C$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta=201.0$, 170.4, 149.0, 146.8, 135.3, 135.2, 127.4, 123.7, 63.3, 57.9, 29.5, 28.8, 26.8, 23.5; IR (neat): $\nu=1710$, 1592, 1511, 1460, 1441, 1343, 1317, 1284, 1263, 1209, 1159, 1149, 1100, 1060, 1025 cm$^{-1}$; MS (70 eV, EI): *m/z* (%) = 303 ($M^+$, 3.07), 43 (100); anal. calcd. for $C_{16}H_{17}NO_5$ (%): C 63.36, H 5.65, N 4.62; found: C 63.33, H 5.64, N 4.61.

### Synthesis of 3-Acetyl-5-phenyl-5(*E*)-3,4,7,8,9,10-hexahydro-2*H*-oxecin-2-one (2t)

The reaction of $Pd(OAc)_2$ (5.7 mg, 0.025 mmol), $PPh_3$ (13.1 mg, 0.05 mmol), $K_2CO_3$ (137.4 mg, 1.0 mmol), iodobenzene (152.2 mg, 0.75 mmol), and **1h** (97.8 mg, 0.5 mmol) in 4 mL of $CH_3CN$ afforded **2t** [eluent: petroleum ether (b.p. 30–60 °C)/ethyl acetate = 15/1] as a solid; yield: 96.4 mg (71%); m.p.: 100–101 °C (ethyl ether/petroleum ether). $^1$H NMR (300 MHz, $CDCl_3$): $\delta=7.40$–7.17 (m, 5H, Ar-H), 5.56 (dd, $J_1=12.3$ Hz, $J_2=3.9$ Hz, 1H, =CH), 4.93–4.81 (m, 1H, one proton from $OCH_2$), 3.79 (t, $J=11.4$ Hz, 1H, one proton from $OCH_2$), 3.40–3.25 [m, 2H, $O_2CCH$ and one proton from C=C(Ph)$CH_2$], 2.93–2.64 (m, 2H), 2.28–2.12 (m, 4H), 2.12–1.85 (m, 1H), 1.85–1.72 (m, 2H), 1.59–1.45 (m, 1H); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta=202.0$, 168.1, 142.1, 136.9, 131.6, 128.4, 127.2, 126.7, 67.2, 59.4, 28.5, 27.8, 27.4, 27.2, 25.0; IR (neat): $\nu=1712$, 1573, 1489, 1456, 1442, 1384, 1354, 1315, 1292, 1257, 1220, 1206, 1178, 1149, 1049, 1028 cm$^{-1}$; MS (70 eV, EI): *m/z* (%) = 272 ($M^+$, 4.88), 43 (100); anal. calcd. for $C_{17}H_{20}O_3$ (%): C 74.97, H 7.40; found: C 74.65, H 7.29.

### Synthesis of 3-Acetyl-5-(4-bromophenyl)-5(*E*)-3,4,7,8,9,10-hexahydro-2*H*-oxecin-2-one (2u)

The reaction of $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $PPh_3$ (13.1 mg, 0.05 mmol), $K_2CO_3$ (138.1 mg, 1.0 mmol), 1-bromo-4-iodobenzene (212.6 mg, 0.75 mmol), and **1h** (98.9 mg, 0.5 mmol) in 4 mL of $CH_3CN$ afforded **2u** (eluent:

petroleum ether/dichloromethane = 1/1→2/3) as a yellow solid; yield: 122.4 mg (69%); mp 95–96 °C (ethyl ether/petroleum ether); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.40 (d, $J$ = 8.4 Hz , 2H, Ar-H), 7.12 (d, $J$ = 8.4 Hz, 2H, Ar-H), 5.54 (dd, $J_1$ = 12.3 Hz, $J_2$ = 3.9 Hz, 1H, =CH), 4.90–4.76 (m, 1H, one proton from $OCH_2$), 3.77 (t, $J$ = 11.1 Hz, 1H, one proton from $OCH_2$), 3.35–3.20 [m, 2H, $O_2CCH$ and one proton from C=C(Ar)$CH_2$], 2.87–2.55 (m, 2H), 2.26–2.10 (m, 4H), 1.99–1.68 (m, 3H), 1.57–1.43 (m, 1H); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 201.5, 167.9, 140.9, 135.8, 132.2, 131.5, 128.3, 121.0, 67.2, 59.2, 28.5, 27.5, 27.4, 27.1, 24.9; IR (neat): $\nu$ = 1736, 1705, 1482, 1455, 1432, 1392, 1362, 1315, 1291, 1264, 1223, 1204, 1182, 1154, 1100, 1071, 1046, 1020, 1009 cm$^{-1}$; MS (70 eV, EI): $m/z$ = (%): 353 [M($^{81}$Br)$^+$, 0.87], 351 [M($^{79}$Br)$^+$, 0.79], 43 (100); anal. calcd. for $C_{17}H_{19}BrO_3$ (%): C 58.13, H 5.45; found: C 58.13, H 5.17.

### Synthesis of 3-Acetyl-3-propyl-5-phenyl-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2v)

The reaction of $Pd(OAc)_2$ (5.5 mg, 0.025 mmol), $PPh_3$ (13.2 mg, 0.050 mmol), $K_2CO_3$ (138.5 mg, 1.0 mmol), iodobenzene (255.1 mg, 1.25 mmol), and **1i** (106.0 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2v** [eluent: petroleum ether/ethyl ether = 10/1] as a white solid; yield: 96.1 mg (67%); mp 111–112 °C (ethyl ether/petroleum ether). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.33–7.19 (m, 5H, Ar-H), 5.91 (t, $J$ = 7.8 Hz, 1H, C=CH), 4.62 (t, $J$ = 11.1 Hz, 1H, one proton from $OCH_2$), 4.11–4.00 (m, 1H, one proton from $OCH_2$), 3.37 [d, $J$ = 13.2 Hz, 1H, one proton from C=C(Ph)$CH_2$], 2.90 [d, $J$ = 13.2 Hz, 1H, one proton from C=C(Ph)$CH_2$], 2.81–2.65 (m, 1H, one proton from PhC=$CCH_2$), 2.29–2.17 (m, 1H, one proton from PhC=$CCH_2$), 2.11 (s, 3H, $COCH_3$), 1.73–1.59 (m, 1H, one proton from $O_2CCCH_2C$), 1.28–1.15 (m, 2H), 1.00–0.69 (m, 2H, one proton from $O_2CCCCH_2$), 0.44 (t, $J$ = 7.2 Hz, 3H, $CCH_3$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 204.3, 175.7, 144.5, 143.2, 128.3, 127.4, 127.1, 126.3, 69.5, 67.4, 33.0, 32.3, 29.9, 26.6, 16.7, 13.8; IR (neat): $\nu$ = 1749, 1709, 1598, 1490, 1462, 1442, 1360, 1320, 1301, 1268, 1248, 1193, 1159, 1106, 1078, 1051, 1032, 1008 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 286 (M$^+$, 1.57), 43 (100); anal. calcd. for $C_{18}H_{22}O_3$ (%): C 75.50, H 7.74; found: C 75.44, H 7.82.

### Synthesis of 3-Acetyl-3-benzyl-5-phenyl-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2w)

The reaction of $Pd(OAc)_2$ (5.4 mg, 0.025 mmol), $PPh_3$ (13.0 mg, 0.050 mmol), $K_2CO_3$ (138.0 mg, 1.0 mmol), iodobenzene (155.0 mg, 0.75 mmol), and **1j** (128.8 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2w** [eluent: petroleum ether/ethyl ether = 10/1] as a white solid; yield: 124.9 mg (75%); m.p.114–115 °C (ethyl ether/petroleum ether). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.37–7.22 (m, 5H, Ar-H), 7.15–7.05 (m, 3H, Ar-H), 6.70–6.65 (m, 2H, Ar-H), 5.90 (t, $J$ = 8.0 Hz, 1H, C=CH), 4.69 (t, $J$ = 11.0 Hz, 1H, one proton from $OCH_2$), 4.15–4.05 (m, 1H, one proton from $OCH_2$), 3.41 (d, $J$ = 12.9 Hz, 1H), 3.17 (d, $J$ = 14.1 Hz, 1H), 2.89 (d, $J$ = 13.2 Hz, 1H), 2.78–2.62 (m, 1H, one proton from PhC=$CCH_2$), 2.57 (d, $J$ = 14.4 Hz, 1H), 2.35–2.22 (m, 1H, one proton from PhC=$CCH_2$), 1.93 (s, 3H, $COCH_3$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 205.6, 175.4, 144.9, 143.3, 135.7, 129.8, 128.4, 128.3, 128.1, 127.3, 127.0, 126.7, 70.6, 67.0, 38.5, 36.5, 29.9, 28.8; IR (neat): $\nu$ = 1746, 1709, 1600, 1491, 1459, 1437, 1360, 1321, 1298, 1262, 1227, 1210, 1172, 1154, 1111, 1067, 1050, 1006 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 334 (M$^+$, 1.34), 43 (100); anal. calcd. for $C_{22}H_{22}O_3$ (%): C 79.02, H 6.63; found: C 79.09, H 6.64.

### Synthesis of 3-acetyl-5-(4-nitrophenyl)-5(*E*)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (2x)

The reaction of $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $PPh_3$ (13.0 mg, 0.050 mmol), $K_2CO_3$ (138.7 mg, 1.0 mmol), 1-iodo-4-nitrobenzene (186.5 mg, 0.75 mmol), and **1k** (92.1 mg, 0.50 mmol) in 4 mL of $CH_3CN$ afforded **2x** [eluent: petroleum ether/ethyl acetate = 9/1] as a solid; yield: 99.6 mg (65%); mp 144–145 °C ($CH_2Cl_2$/petroleum ether). The major isomer: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.15 (d, $J$ = 8.7 Hz, 2H, Ar-H), 7.41 (d, $J$ = 8.7 Hz, 2H, Ar-H), 5.72 (d, $J$ = 7.2 Hz, 1H, C=CH), 4.29 (t, $J$ = 11.0 Hz, 1H, one proton from $OCH_2$), 4.02 (dd, $J_1$ = 10.7 Hz, $J_2$ = 4.4 Hz, 1H), 3.51 (dd, $J_1$ = 11.9 Hz, $J_2$ = 4.1 Hz, 1H), 3.38 (t, $J$ = 12.5 Hz, 1H), 3.07–2.91 (m, 1H, $CHCH_3$), 2.79 (dd, $J_1$ = 13.2 Hz, $J_2$ = 3.9 Hz, 1H), 2.22 (s, 3H, $COCH_3$), 1.06 (d, $J$ = 6.9 Hz, 3H, $CCH_3$); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$ = 200.1, 172.5, 148.7, 147.1, 139.6, 137.5, 127.3, 123.7, 72.9, 63.8, 35.2, 31.3, 28.9, 15.8; IR (neat) $\nu$ = 2962, 2926, 1754, 1705, 1592, 1511, 1456, 1342, 1259, 1207, 1175, 1143, 1112, 1072, 1038, 1000 cm$^{-1}$; MS (70 eV, EI): $m/z$ (%) = 303 (M$^+$, 1.63), 43 (100); anal. calcd. for $C_{16}H_{17}NO_5$ (%): C 63.36, H 5.65, N 4.62; found: C 63.36, H 5.62, N 4.41.

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[17] Crystal data for compound **2s**: $C_{16}H_{17}NO_5$; $MW=$ 303.31, triclinic, space group P-1, final $R$ indices [$I>2\sigma(I)$], $R1=0.0372$, $wR2=0.0972$, $R$ indices (all data) $R1=0.0468$, $wR2=0.1035$, $a=8.1581(6)$ Å, $b=9.5889(7)$ Å, $c=10.4998(8)$ Å, $\alpha=109°$, $\beta=106°$, $\gamma=95°$, $V=733.42(9)$ Å$^3$, $T=296(2)$ K, $Z=2$, reflections collected/unique 7843/2585 ($R_{int}=0.0396$), number of observations [$>2\sigma(I)$] 2135, parameters: 199. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Centre under CCDC 801335. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.
[18] Crystal data for compound **2u**: $C_{17}H_{19}BrO_3$; $MW=$ 351.23, monoclinic, space group *C*2/*c*, final $R$ indices [$I>2\sigma(I)$], $R1=0.0295$, $wR2=0.0717$, $R$ indices (all data) $R1=0.0386$, $wR2=0.0769$, $a=27.5708(9)$ Å, $b=6.0338(2)$ Å, $c=19.6616(7)$ Å, $\alpha=90°$, $\beta=102°$, $\gamma=90°$, $V=3200.57(19)$ Å$^3$, $T=296(2)$ K, $Z=8$, reflections collected/unique 17661/2809 ($R_{int}=0.0285$), number of observations [$>2\sigma(I)$] 2354, parameters: 190. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Centre under CCDC 801334. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.
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