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SYNTHESIS OF 4-ARYL-SUBSTITUTED BUTENOLIDES AND PENTENOLIDES BY COPPER-CATALYZED HYDROARYLATION[‡]

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Abstract – We have investigated the effect of the type of protecting group used and the tether length of 4- and 5-hydroxy-substituted 2-alkynoates on the yields and selectivity of the product of hydroarylation. The use of methyl, methoxymethyl, and *tert*-butyldimethylsilyl (TBS) as protecting groups increased the total yield of the products. While the protected 4-hydroxy-2-butynoates afforded products formed from two or more alkyne substrates, 5-hydroxy-2-pentynoate derivatives exclusively yielded 1:1 adducts. These facts suggest that the product selectivity depends on the distance of the alkoxy group from the alkyne moiety rather than the type of the protecting group. Among the protecting groups used in this study, the TBS group was found to produce butenolides and pentenolides in good total yields via the one-pot hydroarylation/lactonization.

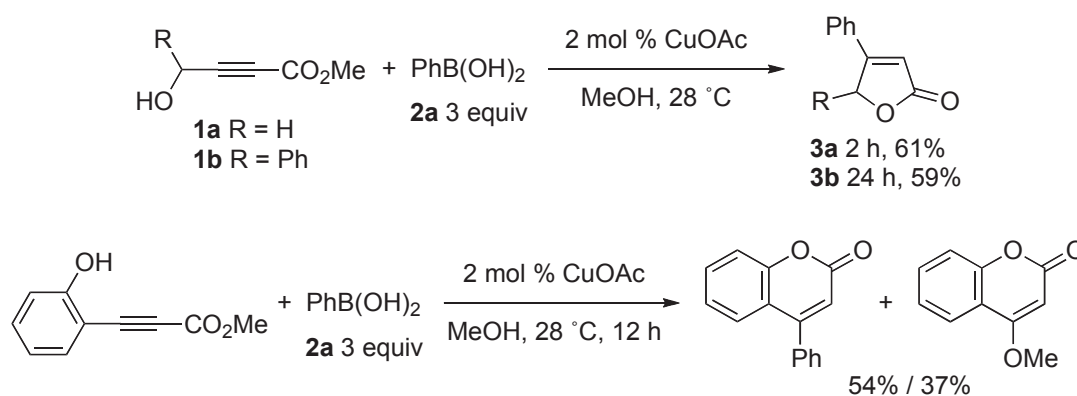
INTRODUCTION

Furan-2(5*H*)-one (butenolide) is a privileged oxygen heterocycle, which is widely distributed in nature, and its naturally occurring derivatives exhibit interesting biological activities. Therefore, a considerable number of studies have been devoted to the development of an efficient and versatile method to synthesize butenolides.¹ In contrast, 5,6-dihydro-2*H*-pyran-2-one (pentenolide), which is homologous to butenolide, has not received significant attention, even though this structural motif found in natural products is also exhibit bioactivity.²

[‡] This paper is dedicated to Prof. Akira Suzuki on the occasion of his 80th birthday.

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Recently, we have reported that the Cu-catalyzed hydroarylation of alkynoates with arylboronic acids stereoselectively produced trisubstituted cinnamate derivatives in good yields.³ On the basis of the success of the above study, we envisaged that by applying this method to alkynoate substrates with a hydroxy terminal, we can obtain unsaturated lactones via concomitant cyclization between the hydroxy and ester carbonyl groups. In fact, we obtained 4-phenylbutenolide (**3a**), albeit in a moderate yield of 61%, when methyl 4-hydroxy-2-butynoate (**1a**) reacted with phenylboronic acid (**2a**) under our optimal conditions (Scheme 1). As an extension of this sequential hydroarylation/lactonization process, we also developed the synthetic method for 4-arylcoumarins, which constitute a subgroup of flavonoids (neoflavones), using phenol-derived propiolates as substrates.⁴ During this study, we found that the undesired 4-methoxycoumarin is produced in a significant yield along with the formation of 4-phenylcoumarin, by carrying out the reaction between **2a** and methyl 3-(2-hydroxyphenyl)propiolate (Scheme 1). In contrast, when substrates protected with an easily removable methoxymethyl (MOM) group were used, the desired 4-arylcoumarins were selectively produced in high yields after the acidic deprotection of the MOM group in one pot. This result indicated the importance of the protection of the hydroxy moiety in the substrates. In this paper, we report the results of the synthesis of 4-aryl-substituted butenolides and pentenolides by Cu-catalyzed hydroarylation, with the emphasis on the effect of protecting groups on the yields and selectivity of the products.^{5,6}

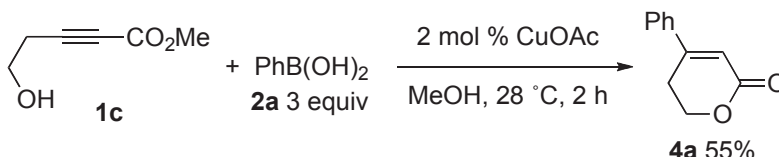


Scheme 1. Hydroarylation/lactonization of 4-hydroxy-2-butynoates **1** and methyl 3-(2-hydroxyphenyl)-2-propiolate

RESULTS AND DISCUSSION

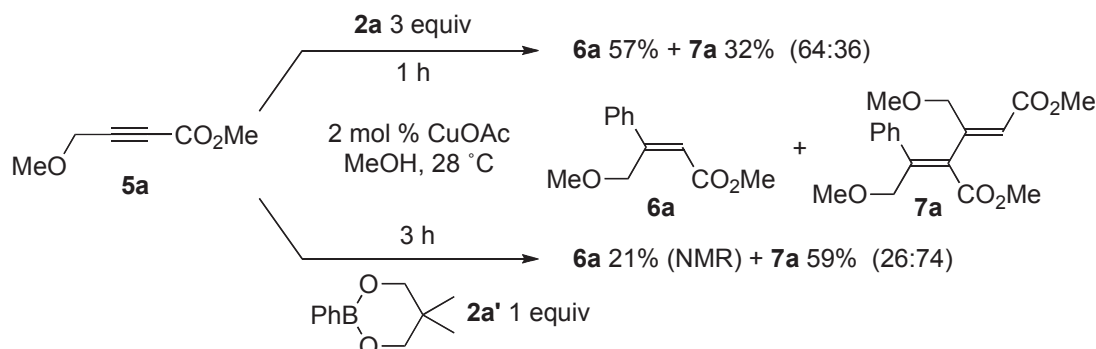
At the outset of this study, we revisited the Cu-catalyzed hydroarylation of alkynoates with a terminal hydroxy group. As mentioned above, the hydroarylation of the alkyne triple bond in **1a** and the subsequent lactonization of the resultant adduct resulted in the formation of **3a** in 61% yield. We then carried out this reaction using phenyl-substituted butynoate **1b** as the substrate to obtain the corresponding 4,5-diphenylbutenolide **3b** in a yield of 59%, which is comparable to the above reaction

(Scheme 1). In order to examine the effect of the tether length between the alkyne and hydroxy moieties on the reaction, we carried out the Cu-catalyzed hydroarylation of 5-hydroxy-2-pentynoate **1c** and obtained 4-phenylpentenolide **4a** in 55% yield as the sole product (Scheme 2). In contrast to the result obtained from 3-(2-hydroxyphenyl)propiolate with the same tether length (Scheme 1), the corresponding 4-methoxypentenolide was not formed from **1c**.

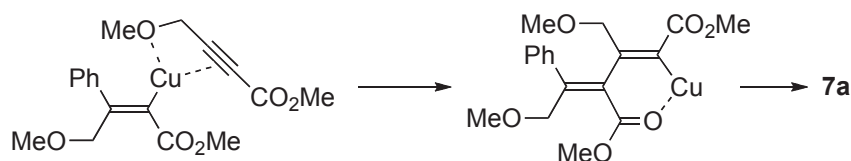


Scheme 2. Hydroarylation/lactonization of 5-hydroxy-2-butynoate **1c**

We then studied the hydroarylation of substrates with protected hydroxy groups with the aim of improving the product yields. First, we carried out the hydroarylation of 4-methoxy-2-butynoate **5a** with 3 equivalents of phenylboronic acid **2a** (Scheme 3). After stirring the reaction mixture for 1 h, the products were purified by column chromatography on silica gel to afford the desired 1:1 adduct **6a** along with an unexpected 2:1 adduct **7a** in yields of 57% and 32%, respectively.⁷ The total yield of 89% obtained by this method is much higher than that of **3a** (61%) obtained by using the unprotected substrate **1a** (Scheme 1). Therefore, the protection of the terminal hydroxy moiety enhances the product yield. The unexpected formation of **7a** is ascribed to the strong bidentate coordination of **5a** to a presumed vinyl copper intermediate (Scheme 4). As a result, the second molecule of **5a** was incorporated into the C–Cu bond prior to methanolysis of the vinyl copper species. We believed that if this were the case, then by using cyclic boronate **2a'**, the rate of methanolysis must be lowered, resulting in an increase in the yield of **7a**. Therefore, to verify the above speculation, we repeated the reaction with 1 equivalent of **2a'** with stirring for 3 h and obtained **7a** as a major product in 59% yield along with **6a** in ca. 20% yield. Moreover, it is worth noting that the geometries of both the alkene moieties in **7a** have been demonstrated to be controlled perfectly via *syn* carbocupration.

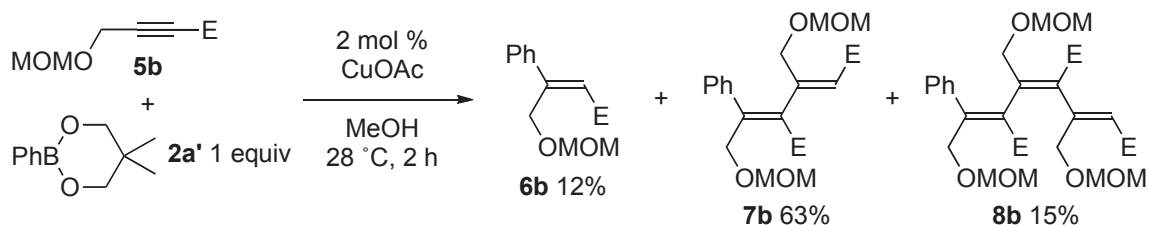


Scheme 3. Hydroarylation of 4-methoxy-2-butynoate **5a**



Scheme 4. Proposed pathway to 2:1 adduct **7a**

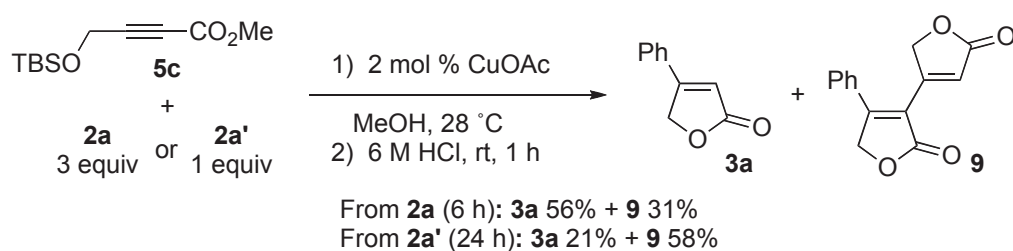
With the aim of obtaining the corresponding butenolides, we examined the use of different easily removable protecting groups. First, MOM-protected **5b** was allowed to react with 1 equivalent of phenylboronate **2a'** for 2 h by following the same procedure as above to obtain a 2:1 adduct **7b** as the major product along with a 1:1 adduct **6b** in yields of 63% and 12%, respectively (Scheme 5). In this case, a 3:1 adduct **8b** was also obtained in 15% yield, suggesting that the two oxygen atoms of the MOM protecting group enhance the coordination ability of **5b** and hence facilitate its incorporation into the C–Cu bond. We then attempted to carry out lactonization of the obtained products by the removal of MOM groups under acidic conditions (6 M HCl in MeOH). However, the reaction was sluggish at ambient temperature and led to a low total yield of less than 25%. The deprotection reaction at elevated temperature, on the other hand, resulted in the decomposition of products.



Scheme 5. Hydroarylation of 4-(methoxymethoxy)-2-butynoate **5b** (E = CO₂Me)

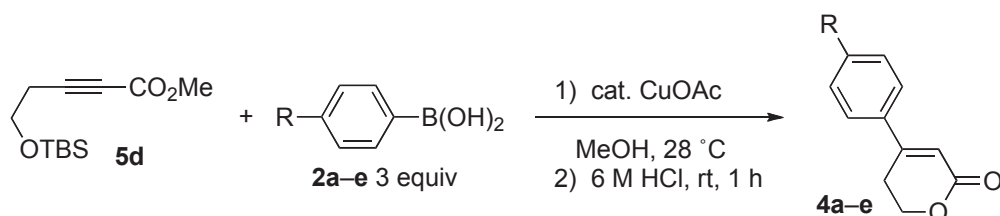
The use of *tert*-butyldimethylsilyl (TBS) instead of MOM as the protecting group proved to be advantageous (Scheme 6). The hydroarylation of 4-siloxy-2-butynoate **5c** with 3 equivalents of **2a** was carried out by stirring for 6 h under optimal conditions to produce 1:1 and 2:1 adducts, which were detected by TLC analysis. When the reaction mixture was treated with 6 M HCl in the same reaction vessel, the deprotection effectively took place even at ambient temperature for 1 h, and butenolide **3a** was obtained as the major product in 56% yield along with bis(butenolide) **9** in 31% yield.⁸ In contrast, when this reaction was carried out using 1 equivalent of phenylboronate **2a'** instead of **2a** with stirring for 24 h, **9** was obtained as the major product in 58% yield along with **3a** in 21% yield (Scheme 6).

Finally, we investigated the use of this one-pot Cu-catalyzed hydroarylation/lactonization method for the synthesis of 4-arylpentenolides **4** from 5-silyloxy-2-pentynoate **5d** (Scheme 7 and Table 1). In the presence of 2 mol % CuOAc, **5d** was treated with 3 equivalents of phenylboronic acid **2a** in MeOH at 28

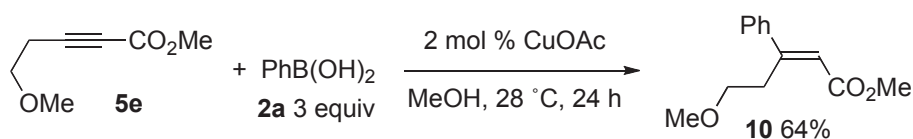


Scheme 6. Hydroarylation/lactonization of 4-(*tert*-butyldimethylsilyloxy)-2-butyne-1-carboxylate methyl ester **5c**

°C for 3 h and subsequent acidic removal of the TBS group at room temperature for 1 h afforded the desired product 4-phenylpentenolide **4a** in a high yield of 86% (Table 1, entry 1). In the case of the homopropargyl system **5d**, it was found that only 1:1 coupling of the alkyne and arylboronic acid occurred, indicating that the ease of the insertion of the second alkyne molecule is influenced by the tether length between the alkyne and silyloxy moieties rather than the protecting groups used. In fact, when the methoxy analogue of **5d**, i.e., **5e**, was subjected to hydroarylation with **2a**, it afforded a 1:1 adduct **10** in a moderate yield (Scheme 8); this result supports the above inference. We have previously reported that a bishomo congener such as methyl 6-methoxy-2-hexynoate also exclusively yields a 1:1 adduct on hydroarylation.³



Scheme 7. Hydroarylation/lactonization of 5-(*tert*-butyldimethylsilyloxy)-2-pentyne-1-carboxylate methyl ester **5d**



Scheme 8. Hydroarylation of 5-(methoxy)-2-pentyne-1-carboxylate methyl ester **5e**

In order to demonstrate the feasibility of this method, the performance of different substituted arylboronic acids was also examined, and the results are summarized in Table 1. *p*-Tolylboronic acid **2b** underwent hydroarylation to afford **4b** in a high yield comparable to that obtained in the case of **2a**; however, a longer reaction time of 6 h was required (Table 1, entry 2). The hydroarylation using sterically demanding *o*-tolylboronic acid did not proceed to completion for 24 h, even though an increased amount of catalyst was employed (6 mol %). It was found that this one-pot hydroarylation/lactonization method gave good

results with arylboronic acids that possess both electron-donating and electron-withdrawing substituents such as **2c–e** (entries 3–5); although in the cases of electron-deficient arylboronic acids **2d** and **2e**, an increased amount of copper catalyst was required.

Table 1. Synthesis of 4-arylpentenolides **4a–e** from **5d**

Entry	R	ArB(OH) ₂	Cat. [mol %]	Hydroarylation [h]	Products, yield [%]
1	H	2a	2	3	4a , 86
2	Me	2b	2	6	4b , 88
3	OMe	2c	2	2	4c , 86
4	Cl	2d	4	4	4d , 78
5	CHO	2e	4	4	4e , 61

In conclusion, we have demonstrated that the use of protecting groups such as methyl, MOM, and TBS increased the yields of hydroarylation, and the product selectivity mainly depends on the distance between the alkoxy group and the alkyne moiety rather than the type of protecting group. Among the protecting groups used in this study, the TBS group was found to produce butenolides and pentenolides in high total yields by the proposed one-pot hydroarylation/lactonization method.

EXPERIMENTAL

Column chromatography was performed on silica gel (Cica silica gel 60N) with mixed solvents [hexane / AcOEt]. ¹H and ¹³C NMR spectra were obtained on a Varian Gemini 2000 NMR spectrometer for samples in CDCl₃ solutions at 25 °C. ¹H NMR chemical shifts are reported in terms of chemical shift (δ, ppm) relative to the singlet at 7.26 ppm for chloroform. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; sept, septet; m, multiplet. Coupling constants are reported in Hz. ¹³C NMR spectra were fully decoupled and are reported in terms of chemical shift (δ, ppm) relative to the triplet at 77.0 ppm for CDCl₃. EI mass measurements were performed with a Shimadzu GCMS-QP2010 plus mass spectrometer. ESI mass spectra were recorded on a JEOL JMS-T100CS mass spectrometer as a MeOH solution. Elemental analyses were performed at Center for Advanced Materials Analysis of Tokyo Institute of Technology. Melting points were obtained in capillary tubes. All solvents and CuOAc were purchased and used as received. Alkynoates **1b**,^{9a} **1c**,^{9b} **5a**,^{9c} **5b**,^{9c} **5c**,^{9b} **5d**,^{9d} and **5e**^{9e} were prepared according to the procedures reported in the literatures. Products **3a**,^{10a} **3b**,^{10b} and **4a**^{10c} are known compounds.

Representative Procedure for Cu-catalyzed Hydroarylation of Alkynoates with Phenylboronic Acid:
Synthesis of Butenolide 3b from Alkynoate 1b and Phenylboronic acid 2a. To a solution of **1b** (95

mg, 0.5 mmol) and **2a** (183 mg, 1.5 mmol) in MeOH (1.0 mL) was added CuOAc (1.23 mg, 0.01 mmol). The reaction mixture was degassed at $-78\text{ }^{\circ}\text{C}$, and then stirred at $28\text{ }^{\circ}\text{C}$ under Ar atmosphere for 24 h. After filtration through a pad of celite to remove insoluble materials, the filtrate was concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane/AcOEt 10:1–5:1) to give 4,5-diphenyl-2(5*H*)-furanone (**3b**) (70 mg, 59%) as colorless solids (mp $154\text{--}157\text{ }^{\circ}\text{C}$, lit.,^{10b} mp $147.5\text{--}150\text{ }^{\circ}\text{C}$): ^1H NMR (300 MHz, CDCl_3): δ 6.33 (d, $J = 1.6\text{ Hz}$, 1 H), 6.55 (d, $J = 1.6\text{ Hz}$, 1 H), 7.30–7.43 (m, 10 H); ^{13}C NMR (75 MHz, CDCl_3): δ 84.1, 114.4, 127.4, 127.7, 128.8, 129.0, 129.4, 129.5, 131.1, 134.8, 165.7, 172.4.

4-Phenyl-5,6-dihydro-2*H*-pyran-2-one (**4a**): colorless solid (mp $55\text{--}57\text{ }^{\circ}\text{C}$, lit.,^{10c} mp $56\text{--}58\text{ }^{\circ}\text{C}$); ^1H NMR (300 MHz, CDCl_3): δ 2.87 (dt, $J = 6.0, 0.9\text{ Hz}$, 2 H), 4.54 (t, $J = 6.0\text{ Hz}$, 2 H), 6.38 (t, $J = 0.9\text{ Hz}$, 1 H), 7.44–7.48 (m, 3 H), 7.53–7.57 (m, 2 H); ^{13}C NMR (75 MHz, CDCl_3): δ 26.2, 65.9, 114.9, 125.9, 128.9, 130.6, 135.9, 155.2, 164.8.

Methyl 4-methoxy-3-phenylbut-2-enoate (**6a**): colorless oil; ^1H NMR (300 MHz, CDCl_3): δ 3.33 (s, 3 H), 3.77 (s, 3 H), 4.94 (d, $J = 0.9\text{ Hz}$, 2 H), 6.21 (d, $J = 0.9\text{ Hz}$, 1 H), 7.35–7.41 (m, 3 H), 7.49–7.53 (m, 2 H); ^{13}C NMR (75 MHz, CDCl_3): δ 51.2, 58.0, 67.9, 119.4, 127.0, 128.3, 129.0, 138.7, 154.9, 166.2; MS (EI): m/z (%): 206 (87) [M^+], 191 (23) [$\text{M}^+ - \text{CH}_3$], 174 (36) [$\text{M}^+ - \text{CH}_3\text{OH}$], 159 (100) [$\text{M}^+ - \text{CH}_3\text{OH} - \text{CH}_3$]; Anal. Calcd (%) for $\text{C}_{12}\text{H}_{14}\text{O}_3$ (206.09): C 69.88; H 6.84. Found: C 69.83; H 6.83.

Dimethyl 4-(2-methoxy-1-phenylethylidene)-3-(methoxymethyl)pent-2-enedioate (**7a**): colorless oil; ^1H NMR (300 MHz, CDCl_3): δ 3.31 (s, 3 H), 3.33 (s, 3 H), 3.57 (s, 3 H), 3.79 (s, 3 H), 4.41 (d, $J = 2.1\text{ Hz}$, 2 H), 4.55 (s, 2 H), 5.50 (t, $J = 2.1\text{ Hz}$, 1 H), 7.21–7.34 (m, 5 H); ^{13}C NMR (75 MHz, CDCl_3): δ 51.0, 51.9, 58.1, 58.8, 71.3, 72.5, 120.8, 127.9, 128.0, 128.2, 132.5, 138.8, 148.0, 155.4, 165.7, 167.0; MS (ESI): calcd for $\text{C}_{18}\text{H}_{22}\text{O}_6$ (334.14): found m/z 357.05 [$\text{M} + \text{Na}$] $^+$; Anal. Calcd (%) for $\text{C}_{18}\text{H}_{22}\text{O}_6$ (334.36): C 64.66; H 6.63. Found: C 64.66; H 6.71.

Methyl 5-methoxy-3-phenylpent-2-enoate (**10**): colorless oil; ^1H NMR (300 MHz, CDCl_3): δ 3.30 (s, 3 H), 3.37–3.42 (m, 2 H), 3.48–3.53 (m, 2 H), 3.76 (s, 3 H), 6.12 (s, 1 H), 7.36–7.40 (m, 3 H), 7.45–7.50 (m, 2 H); ^{13}C NMR (75 MHz, CDCl_3): δ 31.6, 51.2, 58.4, 71.3, 118.3, 126.7, 128.5, 129.0, 141.1, 157.3, 166.6; MS (EI): m/z (%): 220 (10) [M^+], 188 (100) [$\text{M}^+ - \text{CH}_3\text{OH}$], 175 (62) [$\text{M}^+ - \text{CH}_2\text{OCH}_3$], 157 (28) [$\text{M}^+ - \text{CH}_3\text{OH} - \text{OCH}_3$]; Anal. Calcd (%) for $\text{C}_{13}\text{H}_{16}\text{O}_3$ (220.26): C 70.89; H 7.32. Found: C 70.69; H 7.52.

Representative Procedure for Cu-catalyzed Hydroarylation of Protected Hydroxyalkynoates with Phenylboronate: Reaction of Alkynoate 5b and Phenylboronate 2a'. To a solution of **5b** (633 mg, 4.0 mmol) and **2a'** (760 mg, 4.0 mmol) in MeOH (8.0 mL) was added CuOAc (9.81 mg, 0.08 mmol). The

reaction mixture was degassed at $-78\text{ }^{\circ}\text{C}$, and then stirred at $28\text{ }^{\circ}\text{C}$ under Ar atmosphere for 2 h. After filtration through a pad of celite to remove insoluble materials, the filtrate was concentrated in vacuo. The residue was purified by alumina short column chromatography (hexane/AcOEt 1:2) to remove residual **2a'**. The crude products were purified by silica gel flash column chromatography (hexane/AcOEt 20:1) to give methyl 4-(methoxymethoxy)-3-phenylbut-2-enoate (**6b**) (113 mg, 12%) as colorless oil: ^1H NMR (300 MHz, CDCl_3): δ 3.30 (s, 3 H), 3.77 (s, 3 H), 4.65 (s, 2 H), 5.08 (d, $J = 0.3$ Hz, 2 H), 6.20 (d, $J = 0.3$ Hz, 1 H), 7.36–7.42 (m, 3 H), 7.49–7.54 (m, 2 H); ^{13}C NMR (75 MHz, CDCl_3): δ 51.3, 55.4, 63.5, 96.4, 119.4, 127.0, 128.3, 129.0, 138.9, 154.5, 166.1; MS (EI): m/z (%): (no molecular ion peak) 204 (23) [$\text{M}^+ - \text{CH}_3\text{OH}$], 191 (56) [$\text{M}^+ - \text{CH}_2\text{OCH}_3$], 175 (33) [$\text{M}^+ - \text{OCH}_2\text{OCH}_3$], 159 (100) [$\text{M}^+ - \text{C}_6\text{H}_5$]; MS (ESI): calcd for $\text{C}_{13}\text{H}_{16}\text{O}_4$ (236.10): found m/z 259.06 [$\text{M} + \text{Na}$] $^+$; Anal. Calcd (%) for $\text{C}_{13}\text{H}_{16}\text{O}_4$ (236.26): C 66.09; H 6.83. Found: C 66.05; H 6.87.

Further elution (hexane/AcOEt 3:1) gave dimethyl 4-(2-(methoxymethoxy)-1-phenylethylidene)-3-((methoxymethoxy)methyl)pent-2-enedioate (**7b**) (497 mg, 63%) as colorless oil: ^1H NMR (300 MHz, CDCl_3): δ 3.25 (s, 3 H), 3.36 (s, 3 H), 3.57 (s, 3 H), 3.79 (s, 3 H), 4.60–4.62 (m, 6 H), 4.71 (s, 2 H), 5.49 (t, $J = 2.0$ Hz, 1 H), 7.25–7.30 (m, 5 H); ^{13}C NMR (75 MHz, CDCl_3): δ 51.2, 52.0, 55.3, 55.4, 66.9, 67.6, 96.1, 96.5, 121.5, 128.0, 128.2, 128.3, 132.8, 139.0, 148.3, 154.8, 165.7, 166.8; MS (ESI): calcd for $\text{C}_{20}\text{H}_{26}\text{O}_8$ (394.16): found m/z 417.07 [$\text{M} + \text{Na}$] $^+$; Anal. Calcd (%) for $\text{C}_{20}\text{H}_{26}\text{O}_8$ (394.42): C 60.90; H 6.64. Found: C 60.71; H 6.83.

Further elution (hexane/AcOEt 1:1) gave trimethyl 7-(methoxymethoxy)-2,4-bis((methoxymethoxy)methyl)-6-phenylhepta-1,3,5-triene-1,3,5-trioate (**8b**) (113 mg, 15%) as colorless gummy oil: ^1H NMR (300 MHz, CDCl_3): δ 3.18 (s, 3 H), 3.25 (s, 3 H), 3.37 (s, 3 H), 3.62 (s, 3 H), 3.70 (s, 3 H), 3.81 (s, 3 H), 4.16 (s, 2 H), 4.51 (s, 2 H), 4.55 (s, 2 H), 4.63 (s, 6 H), 5.80 (br s, 1 H), 7.29–7.31 (m, 5 H); ^{13}C NMR (75 MHz, CDCl_3): δ 51.2, 51.7, 52.0, 55.2, 55.4, 65.9, 67.3, 68.1, 95.8, 96.1, 96.3, 120.8, 128.0, 128.4, 128.5, 130.3, 132.2, 138.3, 144.6, 147.4, 151.7, 165.8, 166.3, 167.3; MS (ESI): calcd for $\text{C}_{27}\text{H}_{36}\text{O}_{12}$ (552.22): found m/z 575.11 [$\text{M} + \text{Na}$] $^+$; Anal. Calcd (%) for $\text{C}_{27}\text{H}_{36}\text{O}_{12}$ (552.57): C 58.69; H 6.57. Found: C 58.73; H 6.52.

Representative Procedure for Cu-catalyzed One-pot Hydroarylation/lactonization of Silyloxyalkynoates: Reaction of 5c with Phenylboronic Acid 2a. To a solution of **5c** (114 mg, 0.5 mmol) and **2a** (183 mg, 1.5 mmol) in MeOH (1.0 mL) was added CuOAc (1.23 mg, 0.01 mmol). The reaction mixture was degassed at $-78\text{ }^{\circ}\text{C}$, and then stirred at $28\text{ }^{\circ}\text{C}$ under Ar atmosphere for 6 h. To this solution was added MeOH (2 mL) and 6 M HCl (1 mL) in this order, and the reaction mixture was stirred for 1 h at room temperature. The resultant mixture was extracted with AcOEt (10 mL $\times$ 3). The combined organic layer was washed with H_2O (15 mL) and brine (15 mL), dried over Na_2SO_4 , and concentrated in

vacuo. The residue was purified by silica gel flash column chromatography (hexane/AcOEt 5:1) to give 4-phenylfuran-2(5*H*)-one (**3a**) (45 mg, 56%) as colorless solids (mp 92–93 °C, lit.,^{10a} mp 91–93 °C); ¹H NMR (300 MHz, CDCl₃): δ 5.24 (d, *J* = 1.8 Hz, 2 H), 6.39 (t, *J* = 1.8 Hz, 1 H), 7.46–7.52 (m, 5 H); ¹³C NMR (75 MHz, CDCl₃): δ 71.0, 113.0, 126.4, 129.3, 129.6, 131.7, 163.9, 173.8.

Further elution (hexane/AcOEt 3:1) gave 4-phenyl-3,3'-bifuran-2,5'(2'*H*,5*H*)-dione (**9**) (19 mg, 31%) as pale-yellow solids (mp 115–118 °C): ¹H NMR (300 MHz, CDCl₃): δ 5.01 (d, *J* = 2.0 Hz, 2 H), 5.13 (s, 2 H), 6.55 (t, *J* = 2.0 Hz, 1 H), 7.36–7.40 (m, 2 H), 7.50–7.60 (m, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 71.6, 72.4, 118.3, 119.1, 126.9, 129.7, 130.0, 131.6, 153.1, 164.8, 170.6, 172.8; MS (ESI): calcd for C₁₄H₁₀O₄ (242.06): found *m/z* 265.00 [M + Na]⁺; Anal. Calcd (%) for C₁₄H₁₀O₄ (242.23): C 69.42; H 4.16. Found: C 69.32; H 4.26.

4-*p*-Tolyl-5,6-dihydro-2*H*-pyran-2-one (**4b**): colorless solid (mp 90–91 °C); ¹H NMR (300 MHz, CDCl₃): δ 2.40 (s, 3 H), 2.85 (dt, *J* = 6.0, 1.2 Hz, 2 H), 4.52 (t, *J* = 6.0 Hz, 2 H), 6.35 (t, *J* = 1.2 Hz, 1 H), 7.25 (d, *J* = 8.4 Hz, 2 H), 7.45 (d, *J* = 8.4 Hz, 2 H); ¹³C NMR (75 MHz, CDCl₃): δ 21.2, 26.1, 65.9, 113.9, 125.8, 129.6, 132.9, 141.1, 155.1, 165.1; MS (EI): *m/z* (%): 188 (100) [M⁺], 158 (67) [M⁺ – CH₂O], 130 (60) [M⁺ – CH₂O – CO]; Anal. Calcd (%) for C₁₂H₁₂O₂ (188.22): C 76.57; H 6.43. Found: C 76.45; H 6.36.

4-(4-Methoxyphenyl)-5,6-dihydro-2*H*-pyran-2-one (**4c**): colorless solid (mp 97–98 °C); ¹H NMR (300 MHz, CDCl₃): δ 2.84 (t, *J* = 6.0 Hz, 2 H), 3.86 (s, 3 H), 4.51 (t, *J* = 6.0 Hz, 2 H), 6.31 (s, 1 H), 6.95 (d, *J* = 8.7 Hz, 2 H), 7.52 (d, *J* = 8.7 Hz, 2 H); ¹³C NMR (75 MHz, CDCl₃): δ 26.0, 55.3, 65.8, 112.6, 114.3, 127.5, 128.0, 154.6, 161.6, 165.3; MS (EI): *m/z* (%): 204 (100) [M⁺], 174 (39) [M⁺ – CH₂O], 146 (41) [M⁺ – CH₂O – CO]; Anal. Calcd (%) for C₁₂H₁₂O₃ (204.22): C 70.57; H 5.92. Found: C 70.60; H 5.89.

4-(4-Chlorophenyl)-5,6-dihydro-2*H*-pyran-2-one (**4d**): colorless solid (mp 96–98 °C); ¹H NMR (300 MHz, CDCl₃): δ 2.84 (dt, *J* = 6.0, 1.2 Hz, 2 H), 4.53 (t, *J* = 6.0 Hz, 2 H), 6.36 (t, *J* = 1.2 Hz, 1 H), 7.42 (d, *J* = 8.7 Hz, 2 H), 7.48 (d, *J* = 8.7 Hz, 2 H); ¹³C NMR (75 MHz, CDCl₃): δ 26.1, 65.8, 115.3, 127.2, 129.2, 134.3, 136.7, 153.8, 164.6; MS (EI): *m/z* (%): 208 (100) [M⁺], 178 (77) [M⁺ – CH₂O], 150 (35) [M⁺ – CH₂O – CO]; Anal. Calcd (%) for C₁₁H₉ClO₂ (208.64): C 63.32; H 4.35. Found: C 63.09; H 4.34.

4-(4-Formylphenyl)-5,6-dihydro-2*H*-pyran-2-one (**4e**): colorless solid (mp 137–139 °C); ¹H NMR (300 MHz, CDCl₃): δ 2.91 (dt, *J* = 6.0, 1.2 Hz, 2 H), 4.57 (t, *J* = 6.0 Hz, 2 H), 6.46 (t, *J* = 1.2 Hz, 1 H), 7.70 (d, *J* = 8.7 Hz, 2 H), 7.96 (d, *J* = 8.7 Hz, 2 H), 10.07 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ 26.2, 65.9, 117.4, 126.5, 130.02, 137.3, 141.6, 153.7, 164.2, 191.2; MS (EI): *m/z* (%): 202 (100) [M⁺], 172 (9) [M⁺ – CH₂O], 144 (50) [M⁺ – CH₂O – CO]; Anal. Calcd (%) for C₁₂H₁₀O₃ (202.21): C 71.28; H 4.98. Found: C 71.09; H 5.10.

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