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# Keto furanylidene building blocks from silyl ethers of monoalkynylated β-keto carbonyls with iron(III) chloride hexahydrate-iodine

**Abstract:** Keto furanylidene building blocks are synthesized from the unique silyl ethers of monoalkynylated β-keto carbonyls. The procedure consists of a desilylation, cyclization, and alkyne hydration facilitated by either a one-pot reaction with iron(III) chloride hexahydrate-iodine or a two-step procedure with tosylic acid and gold(I) chloride. Notably, the hydration of the terminal alkyne with iron(III) chloride hexahydrate-iodine reagent is a safer and new alternative to the use of mercury(II) salts.

**Keywords:** deiodination; (*E*)-diastereoselectivity; furanylidene; iodohydration.

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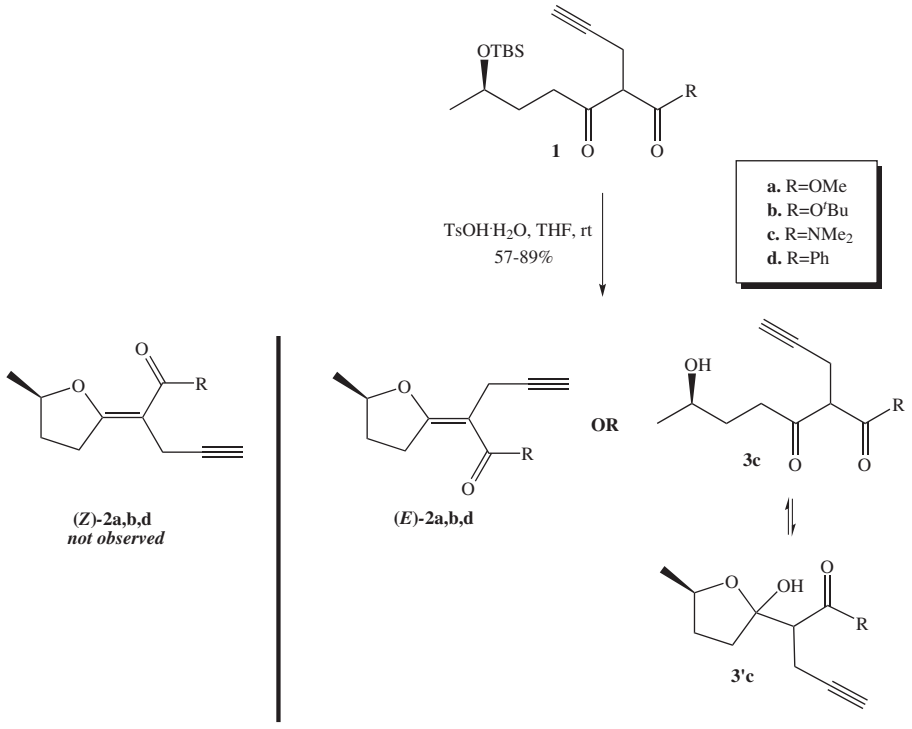
## Introduction

Furans are present in a variety of important molecules such as natural products (Boto et al., 2011), pharmaceuticals (Sperry et al., 2005), and materials (for example, Moreau et al., 2004). As such, the development of many synthetic methods has targeted these ring systems. However, as stated by Brichacek et al. (2009), "One method does not fit all." Each method has its limitations with regards to the type of furan system that it can provide and the tolerance of the chemistry for different functional groups. In the case of furanylidene systems, previous reports have detailed acid-mediated syntheses from 6-hydroxy-1,3-dicarbonyls and their alcohol-protected derivatives (Bryson, 1973; Lygo, 1988; Sato et al., 1991; Kim et al., 2000; Solladié et al., 2000; Oxford et al., 2011). However, most of these syntheses are limited to furanylidene esters with hydrogen or methyl substituents at the α-position (Bryson, 1973; Lygo, 1988; Sato et al., 1991; Solladié et al., 2000). Our group has reported a tosylic acid-mediated synthesis of the α-alkynylated furanylidene building blocks **(*E*)-2** from unique silyl ethers of monoalkynylated β-keto carbonyls **1** (Oxford et al., 2011), a desilylation-cyclization reaction (Scheme 1). Here in, we report the synthesis of keto furanylidene building blocks using the same substrates and additional analogues of **1** (Schemes 1 and 2). The current study demonstrates the ability to design one-pot procedures that couple the desilylation-cyclization chemistry of **1** with an acid-mediated reaction that will also derivatize the alkyne moiety *in situ*. Hence, beyond the generation of building blocks with the potential for further diversification at the enol-ether and carbonyl moieties, the results described herein suggest promise for the generation of a variety of functionally diverse furanylidene building blocks directly from alkynylated substrates **1** using Brønsted or Lewis acid-mediated reactions that have been traditionally devoted to reactions of alkynes.

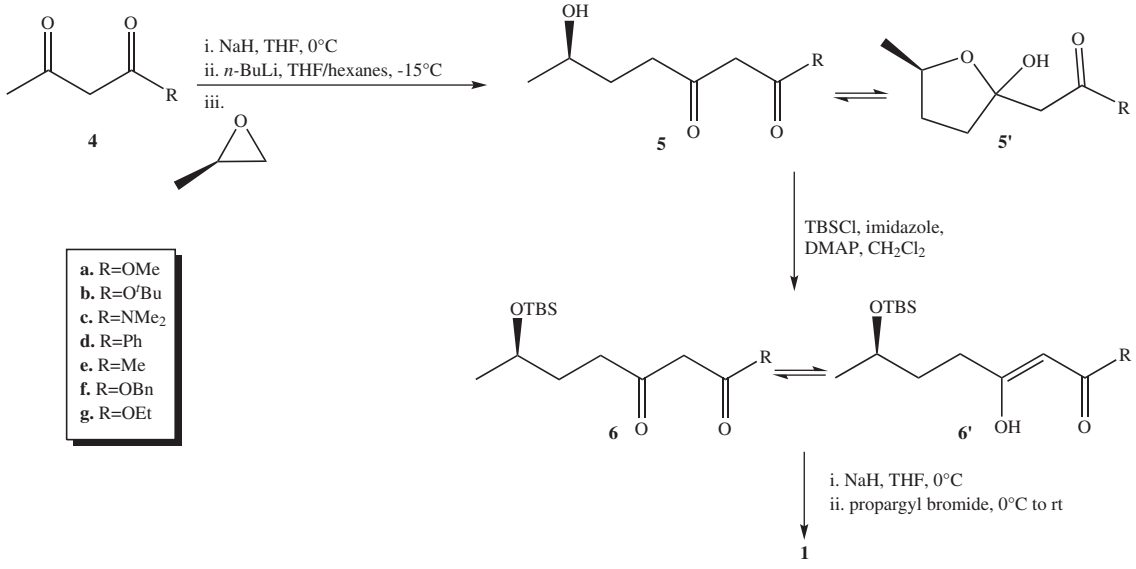
As in our previous study, with the exception of substrate **1e**, our reactions generate one isomer of the keto furanylidene building blocks, exclusively.

A featured chemistry in this study is a one-pot, 30-min procedure that consists of desilylation, cyclization, and alkyne hydration using iron(III) chloride hexahydrate-iodine at room temperature. Notably, the room temperature hydration of the terminal alkyne with iron(III) chloride hexahydrate-iodine is a safer and, to the best of our knowledge, new alternative to mercury(II) salts (Hintermann et al., 2007). Other groups have reported the hydration of terminal alkynes using




**Scheme 1** Tosylic acid-mediated desilylation of silyl ethers **1a–d** (Oxford et al., 2011).

anhydrous iron(III) chloride with longer reaction times of 2–72 h (Damiano et al., 1996; Miranda et al., 2005; Wu et al., 2009; Li et al., 2011). All of these reports deem the iron(III) chloride hexahydrate to be unsuitable or inactive under their reaction conditions. In most cases, the authors report that the iron(III) hydrations of alkynes require elevated temperatures, 75–260°C (Wu et al., 2009; Li et al., 2011) or the presence of a Brønsted acid at room temperature (Miranda et al., 2005). One group has reported the formation of α-iodoketones from alkynes in the presence of iodine, water, and 2-iodoxybenzoic acid (Yadav et al., 2008), but none has reported a direct formation of the non-substituted ketone from alkynes with iodine reagent.



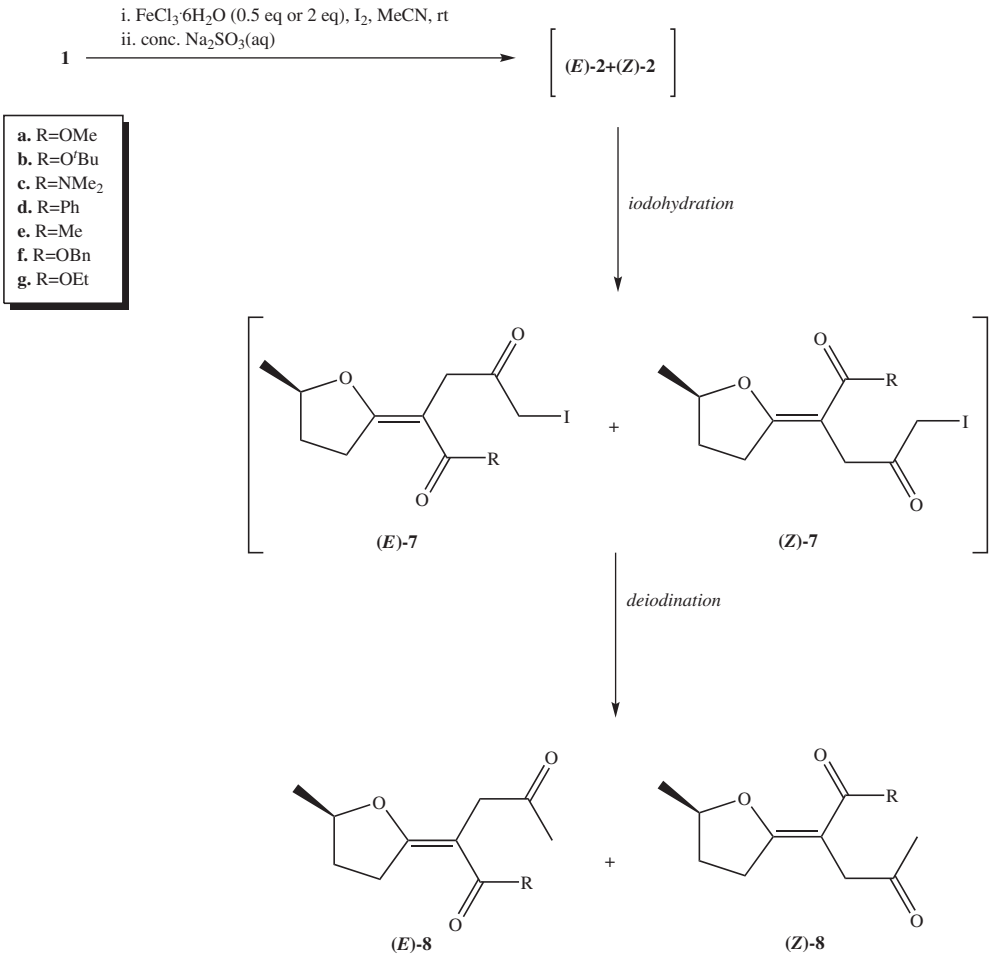

**Scheme 2** Synthesis of **1a–g** (Oxford et al., 2011).

## Results and discussion

The iron(III) chloride hexahydrate-iodine system was developed by Su et al. (2011) for the intramolecular cyclization of alkynols to make furans and pyrans. Instead of an intramolecular cyclization, treatment of our substrate **1a** with iron(III) chloride hexahydrate-iodine resulted in the formation of keto furanylidene **8a** after a reaction time of 30 min (Scheme 3; Table 1). An analysis of the reaction progress with sequential additions of the iron(III) chloride hexahydrate and iodine provided some mechanistic insight (Scheme 3). Using isolated samples of alkynylated furanylidene **(*E*)-2a** as a reference, our observations suggest that iron(III) chloride hexahydrate facilitates a desilylation-cyclization of **1a** that produces alkynylated furanylidene **(*E*)-2a** as an intermediate in the reaction. Compound **(*E*)-2a** is stable in the presence of hexahydrate salt for an extended period and does not undergo hydration in the presence of Lewis acid. Subsequent addition of iodine results in the generation of a second intermediate, which we hypothesize is the α-iodoketone **7a** from an iodohydration reaction. In turn, intermediate **7a** undergoes deiodination to keto furanylidene **8a** upon quenching of the reaction mixture with concentrated aqueous sodium sulfite. The deiodination of the α-iodoketone intermediate **8a** most likely results from a combination of iron(III) and a buildup of the iodide [$I^-$] in the reaction mixture (Townsend et al., 1971; Gemal et al., 1980; Olah et al., 1980; Ono et al., 1986, 1987). Direct treatment of **1a** with molecular iodine results in a complex mixture of products.

An investigation of the tolerance of other groups for the iron(III) chloride hexahydrate-iodine chemistry was made with esters **1b**, **1f**, and **1g**; amide **1c**; and ketones **1d** and **1e**. These substrates were synthesized in three steps using procedures described previously (Oxford et al., 2011) (Scheme 2).

Treatment of ketones **1d** and **1e** with the iron(III) chloride hexahydrate-iodine system smoothly provided keto furanylidenes **8d** and **8e** in yields of 50% and 56%, respectively (Table 1). Keto furanylidene **8d** was produced




**Scheme 3** $FeCl_3 \cdot 6H_2O$-$I_2$-mediated synthesis of **8**.

| Entry | Silyl ether | R | 8 | |
|---|---|---|---|---|
| | | | Isolated yield, % | *dr*[a] |
| 1 | **1a** | OMe | 41[b] | 1:0 |
| 2 | **1b** | O$^t$Bu | 35[c] | 1:0 |
| 3 | **1c** | $NMe_2$ | 0 | – |
| 4 | **1d** | Ph | 50[b] | 1:0 |
| 5 | **1e** | Me | 56[b] | 2:1 |
| 6 | **1f** | OBn | –[c,d] | 1:0 |
| 7 | **1g** | OEt | 40[b] | 1:0 |

**Table 1** Synthesis of keto furanylidenes **8** from silyl ether **1**.
[a]*dr* was based on the analysis of $^1$H NMR spectra of the crude products.
[b]Reagent: iron(III) chloride hexahydrate-iodine.
[c]Reagent: tosylic acid-gold(I) chloride.
[d]Isolation from byproducts proved difficult.

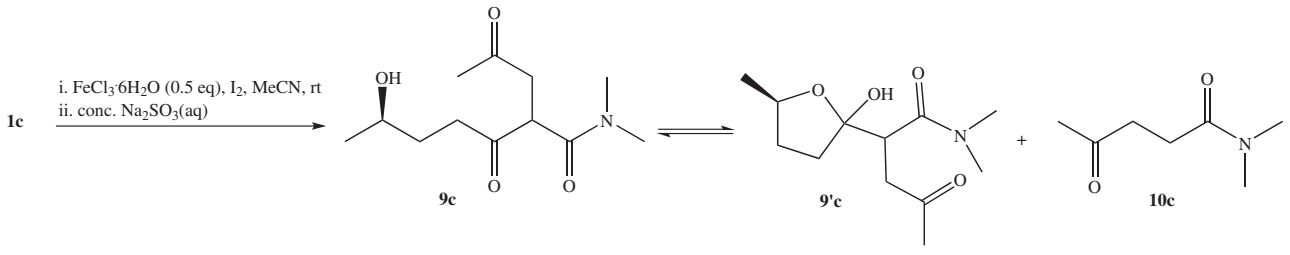
as a single isomer, which we assume is the (*E*) product. Unlike other substrates that were successfully reacted with iron(III) chloride hexahydrate-iodine, the use of the methyl ketone **1e** produced isomers of **8e** in a diastereomeric ratio (*dr*) of 2:1. Treatment of **1e** with only iron(III) chloride hexahydrate revealed that the 2:1 *dr* for **8e** originated in the desilylation-cyclization step, i.e., the $^1$H NMR spectrum for crude product **2e** from this reaction showed a 2:1 *dr* as well.

The *t*-butyl ester **1b**, benzyl ester **1f**, and amide **1c**, upon exposure to iron(III) chloride hexahydrate-iodine, failed to convert to the keto furanylidene products **8b**, **8f**, and **8c**, respectively. The reaction of amide **1c** provided a complicated mixture of products, which included 4-oxopentanamide **10c** (Hilgenkamp et al., 2001) and what appears to be hemiacetal **9′c** (Scheme 4). In previous studies, the treatment of amide **1c** with tosylic acid resulted in hemiketal **3/3′c** as the only product under both room temperature and reflux conditions (Scheme 1). Cyclization to the furanylidene did not occur (Oxford et al., 2011). However, this is the first instance in which the authors have observed the apparent cleavage of the resulting hemiketal. γ-Ketoamide **10c** was most likely formed from **9′c**. Separation of **9′c** from **10c** proved difficult.

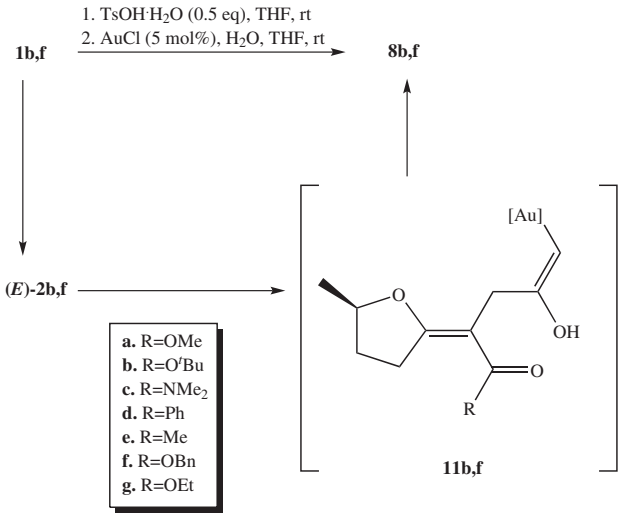
Under the iron(III) chloride hexahydrate-iodine reaction conditions, degradation occurred with both the *t*-butyl ester **1b** and the benzyl ester **1f**. Treatment of each ester **1b** and **1f** with iron(III) chloride hexahydrate resulted in clean formation of the respective products **(*E*)-2b** and **(*E*)-2f**. However, **(*E*)-2b** and **(*E*)-2f** deteriorated with the subsequent addition of iodine. As a solution, the authors explored an alternative route to keto furanylidenes **8b** and **8f**, which involved the treatment of **1b** and **1f** with tosylic acid monohydrate and gold(I) chloride in the presence of water. A one-pot treatment of **1b** with the tosylic acid monohydrate, gold(I) chloride and water provided **5b** in 16% yield. However, a stepwise procedure in which the isolated, crude product from the tosylic acid reaction was treated with the gold(I) salt and water brought about a significant improvement in the yield, 35% (Scheme 5). The same stepwise procedure with benzyl ester **1f** produced a complex mixture that appeared to contain a single isomer of **8f** in addition to a number of byproducts. Isolation of **8f** from byproducts in the reaction mixture proved difficult.

As with the methyl ester **1a**, ethyl ester **1g** was smoothly converted to a single isomer of **8g** in 40% yield upon the treatment with iron(III) chloride hexahydrate-iodine reagent (Table 1). The smooth conversion of **1a** and **1g** was in stark contrast to the complex outcome of the reaction with the *t*-butyl ester **1b** and the benzyl ester **1f**. The authors noted that the *t*-butyl ester **1b** and the benzyl ester **1f**, unlike methyl ester **1a** and ethyl ester **1g**, can undergo cleavage of their alkoxy moieties to form stable carbocations – this feature appears to be a limitation in the iron(III) chloride hexahydrate-iodine reaction. Hence, only esters **1a** and **1g** cleanly hydrated with iron(III) chloride hexahydrate-iodine.

In conclusion, we report the use of iron(III) chloride hexahydrate-iodine in a one-pot procedure for the desilylation, cyclization, and alkyne hydration of unique silyl ethers of monoalkynylated β-keto carbonyls **1** to form keto furanylidene building blocks **8**. The hydration of the terminal alkyne with iron(III) chloride hexahydrate-iodine is a safer and, to the best of our knowledge, new alternative to the use of mercury(II) salts (Hintermann et al., 2007).




**Scheme 4** $FeCl_3 \cdot 6H_2O$-$I_2$ treatment of **1c**.




**Scheme 5** TsOH·$H_2O$/AuCl synthesis of **5b,f**.

Our results suggest that amides, *t*-butyl esters and benzyl esters present limitations to this chemistry. However, the reaction of the iron(III) chloride hexahydrate-iodine proceeds smoothly with the methyl ester, ethyl ester and, ketone carbonyls.

# Experimental section

## General

Unless noted, all reactions were performed under an atmosphere of argon in oven-dried glassware. Solvents for air-sensitive reactions were obtained from commercial sources and purified with MBraun Manual Solvent Purification System before use. Solvents for the iron(III) chloride hexahydrate-iodine and tosylic acid reactions and all chemicals were obtained from commercial sources and used without further purification. Chromatography was performed with Selecto Scientific Si-gel (particle size 100–200 μm), and the chromatography solvents were purchased from commercial sources and used without further purification. NMR spectra were recorded on a Bruker 250 Multi-Nuclear NMR instrument at 250 MHz for $^1$H NMR and 63 MHz for $^{13}$C NMR in deuterated chloroform ($CDCl_3$). High-resolution mass spectrometry was performed using Waters Micromass Q-Tof micro Mass Spectrometer with ESI in positive ion mode.

Compounds **1a–f** were synthesized using the procedure outlined by Oxford et al. (2011), and the characterization of compounds **1a–d** was in full agreement with previous reports.

## Synthesis of 5e–g

Compounds **5e–g** were synthesized according to a known procedure with one modification (Lygo and O'Connor, 1992). Modification: The final reaction mixture was cooled in an ice-water bath (0°C) and quenched with an aqueous solution of saturated ammonium chloride. After isolation from the reaction mixture, compounds **5e**, **5f**, and **5g** were subjected to a flash silica-gel chromatography (50% ethyl acetate in hexanes) and, upon concentration under reduced pressure, were used in the synthesis of **6e**, **6f**, and **6g**.

## Synthesis of 6e–g

**7-(*t*-Butyldimethylsilyloxy)octane-2,4-dione (6e) and 7-(*t*-butyldimethylsilyloxy)-4-hydroxyoct-3-en-2-one (6′e)** An oven-dried round-bottom flask equipped with a stir bar and argon inlet was charged with dichloromethane (15 mL), imidazole (882 mg, 12.9 mmol) and 4-(N,N-dimethylamino)pyridine (50 mg, 0.4 mmol). After the solids dissolved completely, the solution was treated with *t*-butyldimethylchlorosilane (977 mg, 6.7 mmol) followed by **5e** (1.025 g, assume 6.5 mmol) in a solution of dichloromethane (10 mL). The resulting white suspension was stirred vigorously for 18 h, then quenched with deionized water (10 mL), and the product was extracted twice with diethyl ether (40 mL). The combined diethyl ether extract was washed with brine (10 mL) and then dried with sodium sulfate. The dried organic extract was concentrated under reduced pressure, and the crude yellow product was purified by flash silica-gel chromatography (3% ethyl acetate in hexanes, $R_f$=0.1, followed by 5% ethyl acetate in hexanes) to provide **6e/6′e** as a pale yellow oil (1.04 g, 25% over two steps). Products **6f** and **6g** were obtained in a similar manner.

**Product 6′e** $^1$H NMR: δ 5.52 (s, 1H), 3.86 (m, 1H), 2.35 (m, 2H), 2.07 (s, 3H), 1.73 (m, 2H), 1.15 (d, 3H, J=6.1 Hz), 0.91 (s, 9H), 0.07 (s, 6H) Mixture **6e** and **6′e**: $^{13}$C NMR: δ 204.0, 203.0, 194.8, 190.6, 99.7, 67.6, 67.1, 57.0, 40.0, 34.9, 34.5, 33.0, 31.0, 25.8, 24.7, 23.6, 17.9, -4.4, -4.9. HRMS. Calcd for $[M+Na]^+$: m/z 295.1705. Found: m/z 295.1701.

**Benzyl 6-(*t*-butyldimethylsilyloxy)-3-oxoheptanoate (6f)** Flash column chromatography was conducted with 2% ethyl acetate in hexanes, $R_f$=0.09; pale yellow oil, yield 19% over two steps; $^1$H NMR: δ 7.38 (s, 5H), 5.20 (s, 2H), 3.85 (m, 1H), 3.53 (s, 2H), 2.74–2.53 (m, 2H), 1.86–1.57 (m, 2H), 1.13 (d, *J*=6.2 Hz, 3H), 0.91 (s, 9H), 0.06 (s, 3H) 0.05 (s, 3H); $^{13}$C NMR: δ 202.6, 166.9, 135.2, 128.5, 128.4, 128.3, 67.2, 67.0, 49.2, 39., 32.7, 25.8, 23.6, 17.9, -4.5, -4.9. HRMS. Calcd for $[M+Na]^+$: m/z 387.1968. Found: m/z 387.1963.

**Ethyl 6-(*t*-butyldimethylsilyloxy)-3-oxoheptanoate (6g)** Flash column chromatography was conducted using 3% ethyl acetate in hexanes, $R_f$=0.09, followed by 10% ethyl acetate in hexanes; pale yellow oil yield 46% over two steps; $^1$H NMR: δ 4.20 (q, *J*=7.1 Hz, 2H), 3.85 (m, 1H), 3.46 (s, 2H), 2.56–2.63 (m, 2H), 1.67–1.76 (m, 2H),1.28 (t, *J*=7.1 Hz, 3H), 1.13 (d, *J*=6.2 Hz, 3H), 0.91 (s, 9H), 0.05 (s, 3H) 0.04 (s, 3H); $^{13}$C NMR: δ 202.9, 167.2, 67.2, 61.2, 49.3, 38.9, 32.7, 25.7, 23.6, 17.9, 14.0, -4.5, -4.9. HRMS. Calcd for $[M+Na]^+$: m/z 325.1811. Found: m/z 325.1802.

## Synthesis of 1e–g

Sodium hydride (60% oil dispersion, 115 mg, 2.87 mmol) was added to tetrahydrofuran (THF) (10 mL) in an oven-dried round-bottom flask equipped with a stir bar and an argon inlet. The resulting white

suspension was cooled in an ice-water bath (0°C) and a solution of **6e** (703 mg, 2.57 mmol) in THF (5 mL) was added dropwise. After 30 min, the mixture was treated dropwise with propargyl bromide (80% toluene solution, 0.42 mL, 2.84 mmol). The mixture was stirred overnight at 0°C and then allowed to warm to room temperature. The resulting orange-brown suspension was quenched with distilled water (10 mL), and the crude product as extracted twice with ethyl acetate (30 mL). The combined ethyl acetate extract was washed with brine (10 mL) and then dried with sodium sulfate. The dried organic extract was concentrated under reduced pressure, and the crude product was purified by flash column chromatography eluting with 3% ethyl acetate in hexanes, $R_f$=0.1, followed by 6% ethyl acetate in hexanes to yield 300 mg (38%) of **1e** as a pale yellow oil.

**7-(*t*-Butyldimethylsilyloxy)-3-(prop-2-yn-1-yl)octane-2,4-dione (1e)** Flash column chromatography was conducted eluting with 3% ethyl acetate in hexanes, $R_f$=0.1, followed by 6% ethyl acetate in hexanes to yield 300 mg (38%) of **1e** as a pale yellow oil; $^1$H NMR: δ 3.75–3.93 (m, 2H), 2.78–2.56 (m, 4H), 2.30–2.20 (two s, 3H), 2.04–2.07 (two s, 2H), 1.63–1.70 (m, 2H), 1.09–1.23 (m, 3H), 0.91 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).

**7-(*t*-butyldimethylsilyloxy)-4-hydroxy-3-(prop-2-yn-1-yl)oct-3-en-2-one/8-(*t*-butyldimethylsilyloxy)-4-(l-hydroxyethylidene)non-1-yn-5-one (1′e)** $^{13}$C NMR: δ 204.4, 202.1, 194.7, 189.7, 105.9, 99.6, 81.7, 80.3, 72.1, 70.7, 68.6, 67.6, 67.2, 65.9, 65.8, 38.7, 38.6, 34.4, 32.5, 32.0, 29.2, 25.7, 23.6, 22.7, 17.9, 17.4, 16.8, -4.4, -4.8. HRMS. Calcd for [M+Na]$^+$: m/z 333.1862. Found: m/z 333.1851.

**Benzyl 6-(*t*-butyldimethylsilyloxy)-3-oxo-2-(prop-2-yn-1-yl)heptanoate (1f)** Flash column chromatography was conducted using 3% ethyl acetate in hexanes, $R_f$=0.1; pale yellow oil; yield 75%; $^1$H NMR: δ 7.43–7.25 (m, 5H), 5.25–5.16 (s, 2H), 3.71–3.90 (m, 2H), 2.39–2.85 (m, 4H), 2.00 (s, 1H), 1.56–1.86 (m, 2H), 1.04–1.67 (m, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); $^{13}$C NMR: δ 203.3, 167.9, 134.9, 128.5, 128.4, 128.2, 80.3, 70.2, 67.4, 67.3, 57.4, 38.9, 38.7, 32.6, 25.8, 23.5, 17.9, 17.5, -4.48, -4.87. HRMS. Calcd for [M+Na]$^+$: m/z 425.2124. Found: m/z 425.2118.

**Ethyl 6-(*t*-butyldimethylsilyloxy)-3-oxo-2-(prop-2-yn-1-yl)heptanoate (1g)** Flash column chromatography was conducted using 10% ethyl acetate in hexanes, $R_f$=0.5; pale yellow oil; yield 60%; $^1$H NMR: δ 4.22 (q, *J*=7.0 Hz, 2H), 3.85 (m, 1H), 3.73 (t, *J*=7.5 Hz, 1H), 2.40–2.98 (m, 4H), 2.70 (broad s, 1H), 1.59–1.88 (m, 2H), 1.29 (t, *J*=7.0 Hz, 3H), 1.14 (d, *J*=6.0 Hz, 3H), 0.90 (s, 9H), 0.06 (broad s, 6H); $^{13}$C NMR: δ 203.5, 168.1, 80.4, 70.1, 67.3, 61.70, 57.4, 38.8, 32.6, 25.8, 23.5, 17.9, 17.5, 13.9, -4.5, -4.9. HRMS. Calcd for [M+Na]$^+$: m/z 363.1968. Found: m/z 363.1971.

## Procedure for the $FeCl_3$-$I_2$-mediated syntheses of 8a, 8d, 8e, and 8g

A vial equipped with a stir bar was charged with a solution of **1a** (0.5 mmol) in acetonitrile (10 mL), iron(III) chloride hexahydrate (279 mg, 1.0 mmol), and iodine (254 mg, 1.0 mmol). The progress of the reaction was monitored by TLC. Upon completion, after approximately 30 min, the reaction was quenched with concentrated aqueous sodium sulfite (3 mL). The resulting orange suspension was extracted twice with ethyl acetate (10 mL). The combined extracts were washed with deionized water (10 mL) followed by brine (10 mL) and dried with sodium sulfate. The dried organic extract was concentrated under reduced pressure, and the crude product was purified by flash column chromatography eluting with 10% ethyl acetate in hexanes followed by 20% ethyl acetate in hexanes.

**Methyl (2*E*)-2-(5-methyldihydrofuran-2(3*H*)-ylidene)-4-oxopentanoate (8a)** Pale yellow oil; yield 34.7 mg (41%); $^1$H NMR: δ 4.56 (m, 1H), 3.69 (s, 3H), 3.42 (s, 2H), 3.31 (m, 1H), 3.05 (m, 1H), 2.26 (m, 1H), 2.16 (s, 3H), 1.69 (m, 1H), 1.35 (d, 3H, *J*=6.2 Hz); $^{13}$C NMR: δ 207.2, 172.8, 168.6, 95.7, 80.3, 50.9, 41.1, 31.4, 31.1, 28.9, 20.4. HRMS. Calcd for [M+Na]$^+$: m/z 235.0946. Found: m/z 235.0942.

**(2*E*)-2-(5-Methyldihydrofuran-2(3*H*)-ylidene)-1-phenylpentane-1,4-dione (8d)** A 0.5 equivalent of iron(III) chloride hexahydrate was used; pale yellow oil; yield 50%; $^1$H NMR: δ 7.59 (d, 2H, *J*=9.6 Hz), 7.48–7.41 (m, 3H), 4.53 (m, 1H), 3.64 (d, 1H, *J*=17.4 Hz), 3.55 (d, 1H, *J*=17.4 Hz), 2.56 (m, 2H), 2.18 (s, 3H), 2.12 (m, 1H), 1.62 (m, 1H), 1.00 (d, 3H, *J*=6.8 Hz); $^{13}$C NMR: δ 206.8, 197.0, 172.6, 141.5, 130.6, 128.3, 127.6, 106.5, 80.2, 42.4, 32.1, 31.9, 29.4, 20.4. HRMS. Calcd for [M+Na]$^+$: m/z 281.1154. Found: m/z 281.1160.

**(3*Z*)- and (3*E*)-3-(5-methyldihydrofuran-2(3*H*)-ylidene)hexane-2,5-dione (8e)** A 0.5 equivalent of iron(III) chloride hexahydrate was used; pale yellow oil; yield 56%; $^1$H NMR: δ 4.69 (m, 1H, $CH_2OC\underline{H}CH_3$), 4.55 (m, 1H, $CH_2OC\underline{H}CH_3$), 3.49 (s, 2H, $CH_3C(O)C\underline{H}_2C{=}C$), 3.20–3.40 (m, 4H, $CH_3C(O)C\underline{H}_2C{=}C$, $CH_2C\underline{H}_2C{=}C$), 3.04 (m, 2H, $CH_2C\underline{H}_2C{=}C$), 2.76 (m, 2H, $CH_2C\underline{H}_2C{=}C$), 2.44 (s, 3H, $C\underline{H}_3C(O)CH_2$ or $C\underline{H}_3C(O)C{=}C$), 2.07–2.38 (m, 8H, $C\underline{H}_3C(O)CH_2$, $C\underline{H}_2CH_2C{=}C$, $C\underline{H}_3C(O)C{=}C$), 1.72 (m, 2H, $C\underline{H}_2CH_2C{=}C$), 1.46 (d, *J*=6.1 Hz, 3H, $CH_2OCHC\underline{H}_3$), 1.34 (d, *J*=6.1 Hz, 3H, $CH_2OCHC\underline{H}_3$); $^{13}$C NMR: δ 207.5 ($CH_3\underline{C}(O)CH_2$), 207.3 ($CH_3\underline{C}(O)CH_2$), 197.4 ($CH_3\underline{C}(O)C{=}C$), 196.6 ($CH_3\underline{C}(O)C{=}C$), 172.7 ($C{=}\underline{C}{-}O$), 171.5 ($C{=}\underline{C}{-}O$), 106.2 ($\underline{C}{=}C{-}O$), 106.1 ($\underline{C}{=}C{-}O$), 82.6 ($CH_2O\underline{C}HCH_3$), 80.0 ($CH_2O\underline{C}HCH_3$), 42.5 ($CH_3C(O)\underline{C}H_2C{=}C$), 42.1 ($CH_3C(O)\underline{C}H_2C{=}C$), 32.2 ($CH_2\underline{C}H_2C{=}C$), 31.7 ($CH_2\underline{C}H_2C{=}C$), 31.6 ($\underline{C}H_2CH_2C{=}C$), 31.5 ($\underline{C}H_2CH_2C{=}C$), 30.24 ($\underline{C}H_3C(O)CH_2$ or $\underline{C}H_3C(O)C{=}C$), 29.43 ($\underline{C}H_3C(O)CH_2$ or $\underline{C}H_3C(O)C{=}C$), 29.21($\underline{C}H_3C(O)CH_2$ or $\underline{C}H_3C(O)C{=}C$), 29.17 ($\underline{C}H_3C(O)CH_2$ or $\underline{C}H_3C(O)C{=}C$), 20.6 ($CH_2OCH\underline{C}H_3$), 20.4 ($CH_2OCH\underline{C}H_3$). HRMS. Calcd for [M+Na]$^+$: m/z 219.0997. Found: m/z 219.0998.

**Intermediate (3*Z*)- and (3*E*)-3-(5-methyldihydrofuran-2(3*H*)-ylidene)hex-5-yn-2-one[(*E*)/(Z)-2e]** $^1$H NMR: δ 4.71 (m, 1H, $CH_2OC\underline{H}CH_3$ ), 4.59 (m, 1H, $CH_2OC\underline{H}CH_3$), 3.44–2.81 (m, 4H, $HC{\equiv}CC\underline{H}_2C{=}C$, $CH_2C\underline{H}_2C{=}C$), 2.47–2.16 (m, 4H, $C\underline{H}_2CH_2C{=}C$, $C\underline{H}_3C(O)C{=}C$), 1.98 (t, *J*=2.7 Hz, 1H, $\underline{H}C{\equiv}CCH_2C{=}C$), 1.93 (t, *J*=2.7 Hz, 1H, $\underline{H}C{\equiv}CCH_2C{=}C$) 1.71 (m, 1H, $C\underline{H}_2CH_2C{=}C$), 1.46 (d, *J*=6.2 Hz, 3H, $CH_2OCHC\underline{H}_3$), 1.40 (d, *J*=6.2 Hz, 3H, $CH_2OCHC\underline{H}_3$); $^{13}$C NMR: δ 197.9 ($CH_3\underline{C}(O)C{=}C$), 195.8 ($CH_3\underline{C}(O)C{=}C$), 172.1 ($C{=}\underline{C}{-}O$), 170.9 ($C{=}\underline{C}{-}O$), 107.2 ($\underline{C}{=}C{-}O$), 106.2 ($\underline{C}{=}C{-}O$), 83.2 ($HC{\equiv}\underline{C}CH_2C{=}C$), 83.0 ($HC{\equiv}\underline{C}CH_2C{=}C$), 82.5 ($CH_2O\underline{C}HCH_3$), 80.2 ($CH_2O\underline{C}HCH_3$), 67.2 ($H\underline{C}{\equiv}CCH_2C{=}C$), 66.9 ($H\underline{C}{\equiv}CCH_2C{=}C$), 32.3 ($CH_2\underline{C}H_2C{=}C$), 31.7 ($CH_2\underline{C}H_2C{=}C$), 31.4 ($\underline{C}H_2CH_2C{=}C$), 30.3 ($\underline{C}H_2CH_2C{=}C$), 29.6 ($\underline{C}H_3C(O)C{=}C$), 28.9 ($\underline{C}H_3C(O)C{=}C$), 20.6 ($CH_2OCH\underline{C}H_3$), 20.5 ($CH_2OCH\underline{C}H_3$), 16.8 ($HC{\equiv}C\underline{C}H_2C{=}C$), 16.6 ($HC{\equiv}C\underline{C}H_2C{=}C$).

**Ethyl (2*E*)-2-(5-methyldihydrofuran-2(3*H*)-ylidene)-4-oxopentanoate (8g)** A 2.0 equivalent of iron(III) chloride hexahydrate was used; pale yellow oil; yield 40%; $^1$H NMR: δ 4.54 (m, 1H), 4.15 (q, *J*=7.1 Hz, 2H), 3.46–3.26 (m, 3H), 3.05 (dt, *J*=18.3, 9.1 Hz, 1H), 2.06–2.46 (m, 4H), 1.69 (m, 1H), 1.35 (d, *J*=6.0 Hz, 3H), 1.26 (t, *J*=7.1 Hz, 3H); $^{13}$C NMR:

δ 207.6, 172.8, 168.4, 96.2, 80.5, 59.9, 41.3, 31.7, 31.6, 29.3, 20.7, 14.5. HRMS. Calcd for $[M+Na]^+$: m/z 249.1103. Found: m/z 249.1100.

**TsOH·$H_2O$/AuCl-mediated synthesis of *t*-butyl (2*E*)-2-(5-methyldihydrofuran-2(3*H*)-ylidene)-4-oxopentanoate (8b)** A vial equipped with a stir bar was charged with **1b** (138 mg, 0.37 mmol), THF (1.12 mL), and *p*-toluenesulfonic acid monohydrate (36.0 mg, 0.19 mmol). The mixture was stirred overnight, quenched with concentrated aqueous sodium bicarbonate, and extracted three times with ethyl acetate (15 mL). The combined extracts were washed sequentially with deionized water and brine, dried with sodium sulfate, and concentrated under reduced pressure to provide the crude product as a yellow oil.

The crude product was dissolved in THF (1.1 mL) and treated with gold(I) chloride (2.60 mg, 11 μmol) and deionized water (18 μL). After 13 min, additional gold(I) chloride (1.50 mg, 7.5 μmol) and water (20 μL) were added. The reaction progress was monitored by TLC. After 30 min, the mixture was diluted with water and extracted three times with ethyl acetate. The combined organic extract was washed with brine, dried with sodium sulfate, and concentrated under reduced pressure. The crude product was purified by flash column chromatography eluting with 3% ethyl acetate in hexanes followed by 5% ethyl acetate in hexanes and then 10% ethyl acetate in hexanes to provide **8b** as a colorless oil; yield 33.3 mg (35%); $^1$H NMR: δ 4.52 (m, 1H), 3.37 (s, 2H), 3.29 (m, 1H), 3.02 (m, 1H), 2.20 (m, 1H), 2.15 (s, 3H), 1.67 (m, 1H), 1.44 (s, 9H), 1.37 (d, 3H, $J$=6.2 Hz); $^{13}$C NMR: δ 207.5, 171.5, 167.6, 97.5, 79.9, 79.5, 41.5, 31.5, 31.4, 28.9, 28.4, 20.5. HRMS. Calcd for $[M+Na]^+$: m/z 277.1416. Found: 277.1420.

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