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Iodoaromatization Reactions of Enyne−Dioxinones: Syntheses of 4*H*-1,3-Benzodioxin-4-ones, Masked Pentasubstituted Arenes

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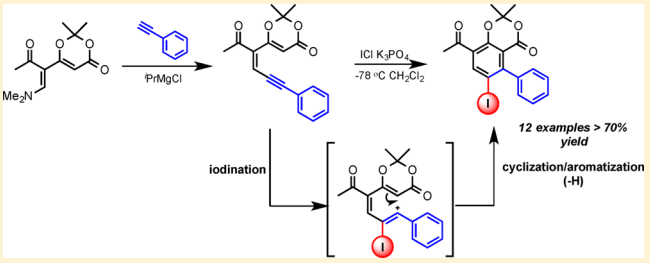
Supporting Information

ABSTRACT: Sequential reaction of a keto-dioxinone with dimethylformamide dimethyl acetal and a range of magnesium acetylides gave the corresponding enyne−dioxinones as mixtures of *E* and *Z* isomers (*E* > *Z*). Subsequent reaction with iodine monochloride resulted in cycloaromatization, presumably via an iodovinyl cation, giving a range of 4*H*-1,3-benzodioxin-4-ones.



INTRODUCTION

Substituted arenes and biaryls are important compounds and are the core of many pharmaceutical, agrochemical, and electronically useful substances, to name but a few applications.[1] Over the last 150 years, very significant progress has been made in the modular assembly of highly functionalized aromatic systems. Electrophilic and nucleophilic aromatic substitution reactions have been central to the development of this chemistry.[2] Friedel−Crafts alkylations and acylations were among the earliest examples of this type of reaction[3] and are still in common use today. Although useful, these methodologies may encounter problems as the degree of substitution of the aromatic ring increases. For example, regioselectivity issues can arise depending upon the substituent's electronic nature, location, and steric bulk, and multiple substitutions may occur at highly reactive centers. In consequence, several methods have been invented to combat these problems, including functional-group-directed metalation/functionalization processes, transition-metal-catalyzed coupling reactions, and the use of blocking and directing groups.[4,4b] These approaches may be less than ideal in that they require lengthy sequences of transformations, which are not necessarily straightforward. Furthermore, there are general limitations to the type of functional groups that can be incorporated by these methods alone. To this end, several methods have been developed to construct predefined polysubstituted benzene derivatives from acyclic starting materials.[5−8] Herein we report a method for the conversion of a simple keto-dioxinone derivative into a range of 4*H*-1,3-benzodioxin-4-ones, which are masked pentasubstituted arenes. The approach complements biomimetic aromatization reactions of diketo-dioxinones to provide resorcylate derivatives,[9−11] which are illustrated in Figure 1, and utilizes known intramolecular electrophilic cyclizations of alkynes onto arenes.[9−16]

RESULTS AND DISCUSSION

Enamino ketone **5** was synthesized in 91% yield via the rapid (15 min) condensation reaction[17] of dimethylformamide dimethyl acetal with diketo-dioxinone **2** (Scheme 1).[11] Once formed, the product was found to be unstable under the reaction conditions, and prolonged reaction times resulted in diminished yields as a result of product decomposition.

Subsequent reaction of enamino ketone **5** with the magnesium acetylide derived from 4-methoxyphenylacetylene and *i*PrMgCl at −20 °C, as reported by Mellor for related enamines,[18] gave enyne **7** in 85% yield. The product was obtained as a mixture of geometric isomers in a ratio favoring the required *E* isomer (*E*/*Z* = 4:1). Although the (*Z*)-alkene was formed, this was easily removed via chromatography. At this stage, a range of electrophile-mediated cyclization reactions of enyne **7** were examined (Table 1).

The reaction of *N*-iodosuccinimide (NIS) with (*E*)-enyne **7** under Larock's conditions[20,21] in the presence of tripotassium phosphate in dichloromethane gave aromatic iodide **8** in 85% yield. When the cyclization reaction was carried out using (*E*)-enyne **7** containing its *Z* isomer, the latter was recovered unchanged in the NIS-mediated cyclization. Thus, the presence of the minor *Z* isomer was inconsequential, and crude enyne **7** as a mixture of geometric isomers could be submitted directly to the cyclization step, thereby minimizing the number of purification steps. Having achieved cyclization with NIS, a range of known iodinating, brominating, and chlorinating reagents were examined in an attempt to increase the yield and to incorporate other halogens into the newly formed aromatic ring. These experiments showed that iodine monochloride was superior, providing arene **8** in the highest yield (96%), and therefore, no further reaction conditions were explored for iodoaromatizations. *N*-Bromosuccinimide (NBS) and tripotas-

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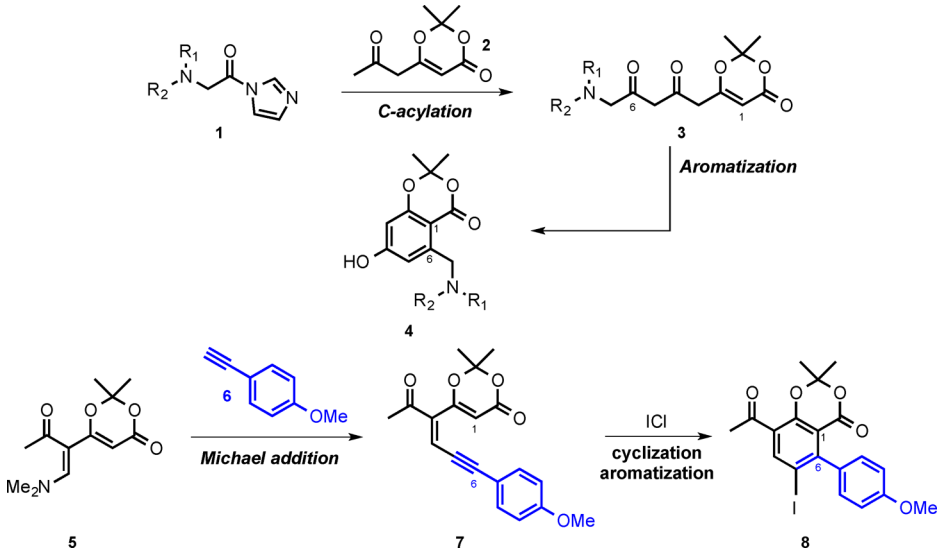


Figure 1. Overview of biomimetic aromatization reactions to provide resorcylates and the enyne−dioxinone iodination/electrocyclizations reported herein.

Scheme 1. Preparation of Enamino Ketone 5 and Its Conversion to Enyne−Dioxinone 7

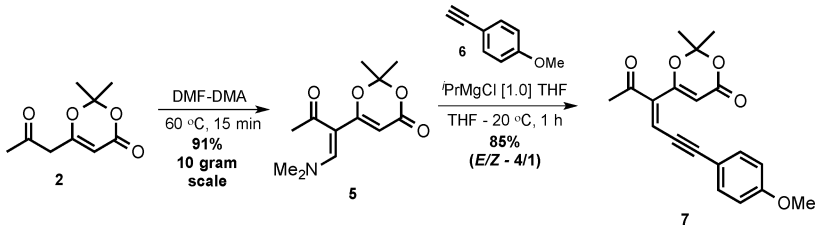
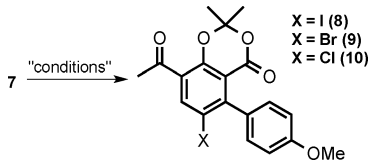


Table 1. Evaluation of the Halogenation/Cyclization/Aromatization Reaction[a]



entry	halogen source	time (h)	temp (°C)	product	yield (%)
1	NIS	3	−78	**8**	85
2	ICl [1.0 M in CH_2Cl_2]	3	−78	**8**	96
3[b]	NBS	3	−50	**9**	88
4	NBS + cat. H_2SO_4	3	−50	**9**	81
5	$Et_2SBr{\cdot}SbCl_5Br$[19]	3	0	**9**	23[c]
6	NCS	24	25	–	0[d]
7	NCS + cat. H_2SO_4	24	25 or 72	–	0[d]

[a]Unless otherwise stated, reactions were conducted at 0.3 M concentration in dichloromethane using 2 equiv of K_3PO_4. [b]The reaction was conducted in DMF. [c]A largely intractable mixture of products was formed (the same observation was also noted at low temperature). [d]Starting material was recovered unchanged.

sium phosphate gave the corresponding aromatic bromide in 88% yield. However, attempts to improve this yield through catalytic activation of NBS with sulfuric acid or through the use of diethylbromosulfonium bromopentachloroantimonate ($Et_2SBr{\cdot}SbCl_5Br$)[19] were not preparatively useful. Attempts at chloraromatization using NCS alone or in the presence of sulfuric acid were unsuccessful.

It is reasonable to speculate that the mechanism of the iodo(bromo)aromatization reactions involved the transformations shown in Scheme 2, with the intermediacy of the iodotrienyl cation **12a**, which would be stabilized by the *p*-anisyl residue as shown by resonance form **12b**, and a 6-*endo*-*dig* cyclization followed by proton loss. A similar mechanism was suggested by Larock with related transformations.[21] It is also possible that the conversion of trienyl cation **12a** into dienyl cation **13** involved an electrocyclization pathway. In consequence of the potential of the *p*-anisyl group to lower the energy of intermediate **12**, we anticipated that enyne precursors with electron-donating groups replacing the *p*-anisyl group should undergo iodoaromatization but enyne precursors with electron-withdrawing groups would be more difficult to cyclize.

The substitution reaction of enamino ketone **5** with magnesium acetylide reagents was extended to a range of aromatic, heteroaromatic, and aliphatic terminal acetylenes as well as trimethyl- and triisopropylsilylacetylenes, and the results are shown in Table 2. Enynes **15a−s** were all obtained in >70% yield, and in each case the ratio of *E* and *Z* geometric isomers was always biased in favor of the desired *E* isomer required for the subsequent step. These Grignard Michael addition and retro-Michael elimination reactions were applicable to a diverse range of substrates, and only the 2-pyridyl-substituted derivative **15t** failed to provide any product.

The scope of the iodocyclization/aromatization reaction was assessed, and the results are presented in Table 3; the structures of the products are shown in Scheme 3. Phenyl-substituted enyne **15a** smoothly underwent iodoaromatization to provide the corresponding aromatic iodide **16** in 72% yield (entry 2). In

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Scheme 2. Proposed Mechanism for the ICl-Induced Electrophilic Cyclization/Aromatization of Enyne 7

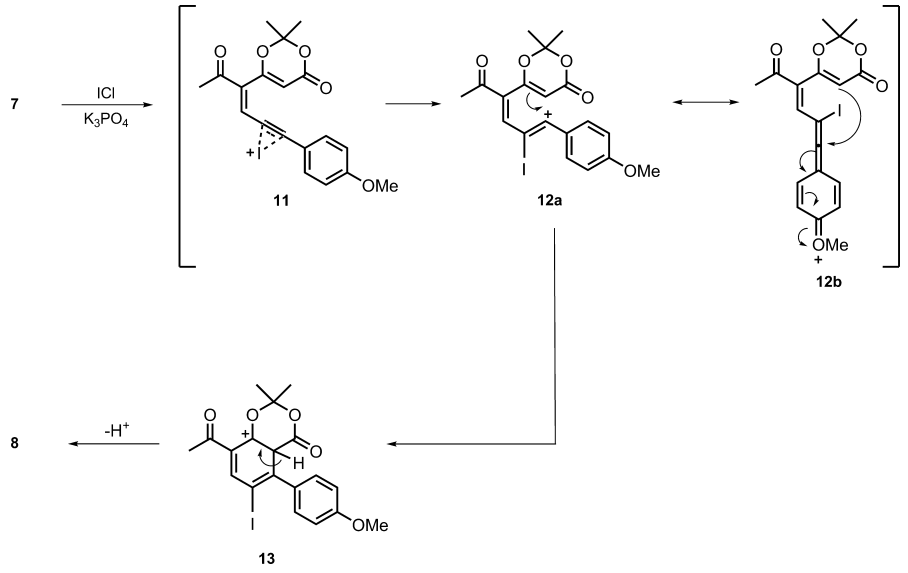
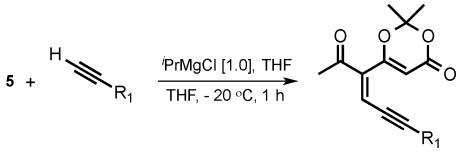


Table 2. Synthesis of a Diverse Library of Enyne Halocyclization/Aromatization Substrates[a]

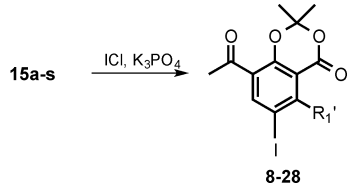


14a-14t 15a-15t

entry	alkyne[b] (R_1)	product	yield (%)	E/Z[d]
1	**6** (4-MeO-C_6H_4)	**7**	85	4/1
2	**14a** (Ph)	**15a**	81	2.5/1
3	**14b** (4-Me-C_6H_4)	**15b**	90	3/1
4	**14c** (1-naphthyl)	**15c**	79	5/1
5	**14d** (9-phenanthrenyl)	**15d**	71	2/1
6	**14e** (4-Ph-C_6H_4)	**15e**	79	3/1
7	**14f** (4-Me_2N-C_6H_4)	**15f**	85	2.5/1
8	**14g** (4-^{t}Bu-C_6H_4)	**15g**	82	2/1
9	**14h** (*n*Bu)	**15h**	91	4/1
10	**14i** (cyclopropyl)	**15i**	83	6/1
11	**14j** (4-CF_3-C_6H_4)	**15j**	86	5/1
12	**14k** (3-Cl-C_6H_4)	**15k**	88	3/1
13	**14l** (2-thienyl)	**15l**	77	2.5/1
14	**14m** (3,5-$F_2C_6H_3$)	**15m**	89	5/1
15	**14n** (3,5-$(MeO)_2C_6H_3$)	**15n**	83	3/1
16	**14o** (3,6-$Me_2C_6H_3$)	**15o**	75	5/1
17[c]	**14p** (2-$(HOCH_2)$-C_6H_4)	**15p**	81	5/1
18	**14q** ($SiMe_3$)	**15q**	80	3/1
19	**14r** (Si(*i*Pr)$_3$)	**15r**	88	3/1
20	**14s** (4-MeO-2-Me-C_6H_3)	**15s**	83	3/1
21	**14t** (2-pyridyl)	**15t**	0[e]	–

[a]Reaction conditions, unless otherwise stated: alkyne (1.5 equiv), ^{i}PrMgCl (1.5 equiv), and enamino ketone **5** (1.0 equiv) in THF at −20 to 0 °C over 1 h. [b]All of the alkynes were used as received from commercial suppliers. [c]2.0 equiv of ^{i}PrMgCl was used. [d]Determined by integration of the ^{1}H NMR spectra of the initial crude products. [e]Attempted substitution by the lithiated alkyne was also unsuccessful.

Table 3. Assessment of the Scope of the Halocyclization/Aromatization Reaction with Respect to R_1[a]



8-28

entry	enyne (R_1)	product	yield (%)
1	**7** (4-MeO-C_6H_4)	**8**	96
2	**15a** (Ph)	**16**	72
3	**15b** (4-Me-C_6H_4)	**17**	82
4	**15c** (1-naphthyl)	**18**	71
5	**15d** (9-phenanthrenyl)	**19**	93
6	**15e** (4-Ph-C_6H_4)	**20**	93
7	**15f** (4-Me_2N-C_6H_4)	**21**	92
8	**15g** (4-^{t}Bu-C_6H_4)	**22**	87
9[b]	**15h** (*n*Bu)	**23**	trace
10	**15i** (cyclopropyl)	**24**	79
11[b]	**15j** (4-CF_3-C_6H_4)	**25**	trace
12	**15k** (3-Cl-C_6H_4)	**26**	61
13	**15l** (2-thienyl)	**27**	49
14	**15m** (3,5-$F_2C_6H_3$)	–	–
15	**15n** (3,5-$(MeO)_2C_6H_3$)	–	–
16	**15o** (3,6-$Me_2C_6H_3$)	–	–
17	**15p** (2-$(HOCH_2)$-C_6H_4)	–	–
18	**15q** ($SiMe_3$)	–	–
19	**15r** (Si(*i*Pr)$_3$)	–	–
20	**15s** (4-MeO-2-Me-C_6H_3)	**28**	75

[a]Reaction conditions: enyne (1.0 equiv), ICl (1.0 M in CH_2Cl_2), and K_3PO_4 (2.0 equiv) in CH_2Cl_2 at −78 °C to −50 °C over 3 h. [b]Traces of the product were tentatively identified via analysis of the ^{1}H NMR spectra of the crude reaction mixtures with an aromatic singlet, which was consistent with the presence of the iodoarene.

addition, enynes with electron-rich aromatic groups (entries 1, 3−8, 12, 13, and 20) also gave rise to the corresponding arenes upon reaction with iodine monochloride. It is also noteworthy that the cyclopropyl-substituted enyne **15i** gave the corresponding iodoarene without cyclopropane ring scission (entry 10). In contrast, attempted iodoaromatization reactions with an *n*-butyl substituent (entry 9), phenyl groups with electron-withdrawing substituents (entries 11 and 14), or silyl groups

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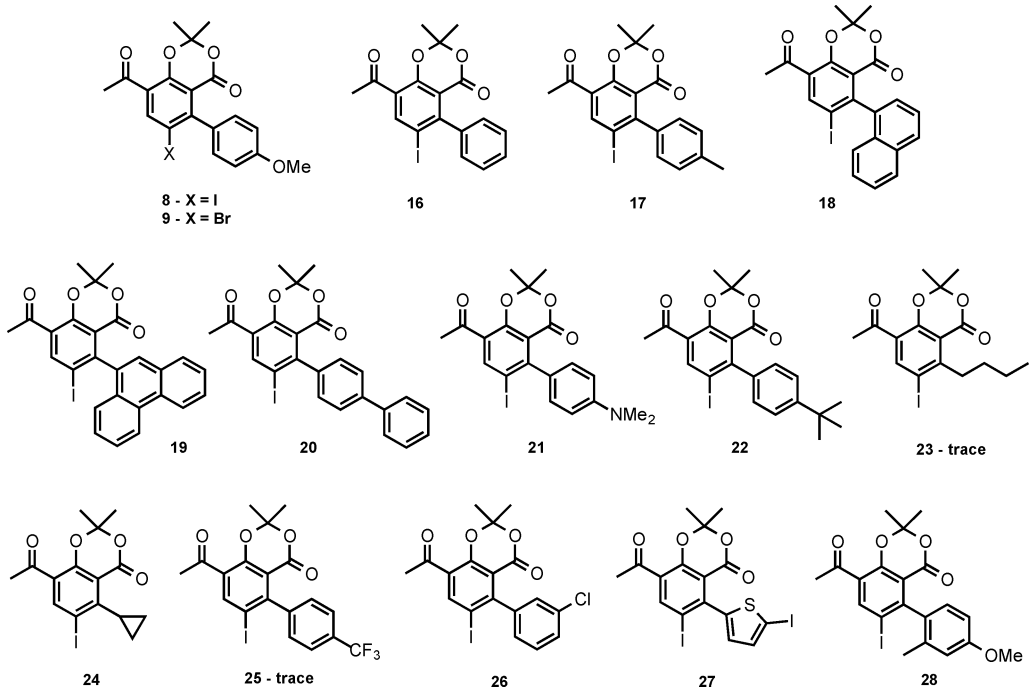
Scheme 3. Structures of the Product Iodoarenes



(entries 18 and 19) failed to provide the corresponding iodoarenes. The failure of the iodoaromatization reaction of the *n*-butyl-substituted enyne **15h** has been encountered by other groups in related reactions. Zeni and co-workers described a method of halo-induced electrophilic cyclization of 3-alkynyl-substituted thiophenes.[22] In assessing the reaction scope, they found that primary alkyl substitution provided insufficient electronic stabilization to the transient cationic species formed during the reaction, and therefore, no 5-*endo*-*dig* ring closure occurred. Conversely, in Larock's synthesis of naphthalenes and 2-naphthols via electrophilic cyclization,[21] these systems were more amenable to reaction with an *n*-butyl-substituted alkyne. Enynes with *ortho* substituents failed to provide the corresponding iodoarenes (entries 16 and 17), presumably because of steric congestion. It is less clear why the 3,5-dimethoxyphenyl-substituted system (entry 15) did not undergo cyclization, but the expected iodo-4*H*-1,3-benzodioxin-4-one was not detected. The reaction of 2-thienyl-substituted enyne **15l** (entry 13) with iodine monochloride resulted in both iodoaromatization and thiophene ring iodination, giving rise to diiodide **27**.

■ CONCLUSIONS

We have developed a simple two-step synthesis of 4*H*-1,3-benzodioxin-4-one derivatives from the enamino keto-dioxinone **5**. The compounds possess three different oxygen-containing functionalities (ketone, ester, and alcohol) as well as a ring iodine, which should allow for further transformations.

■ EXPERIMENTAL SECTION

General Information. The reactions were carried out in oven-dried glassware under N_2 using commercially supplied solvents and reagents, unless otherwise stated. THF and CH_2Cl_2 were distilled from Na/Ph_2CO and CaH_2, respectively. The term "hexanes" refers to petroleum spirit (bp 40−60 °C). Column chromatography was carried out on silica gel using flash techniques (eluents are given in parentheses). Melting points were recorded on a melting point apparatus and are uncorrected. Infrared spectra were recorded on an FTIR spectrometer with automated background subtraction. Reported absorptions are given in wavenumbers (cm^{-1}). ^1H NMR spectra were recorded at room temperature (unless stated otherwise) on 400 or 500 MHz spectrometers. Chemical shifts are reported in parts per million, and coupling constants (*J*), which refer to apparent peak multiplications, are reported in hertz. ^{13}C NMR spectra were recorded at 100 MHz and chemical shifts are reported in parts per million. A time-of-flight mass analyzer used to obtain the HRMS data.

*2,2-Dimethyl-6-(2-oxopropyl)-4H-1,3-dioxin-4-one (**2**).*[11] The procedure reported by Patel and Barrett[11] was followed. Dioxinone (20.0 g, 141 mmol) in THF (150 mL) was added dropwise with stirring to lithium hexamethyldisilazide in THF (1.0 M; 183 mL, 183 mmol) and THF (100 mL) at −20 °C. After 45 min, Et_2Zn in hexanes (1.0 M; 183 mL, 183 mmol) was added dropwise over 30 min. After a further 30 min, *N*-acetylimidazole (20.1 g, 183 mmol) was added portionwise over 15 min. After 3 h, the reaction was quenched by the addition of saturated aqueous NH_4Cl (100 mL) and 1 M aqueous HCl until the solution was at pH 2, and EtOAc (200 mL) was added. The layers were separated, and the aqueous layer was further extracted with EtOAc (2 × 80 mL). The combined organic extracts were dried ($MgSO_4$), rotary-evaporated, and chromatographed (hexanes/EtOAc 3:1 to 1:1) to give keto-dioxinone **2** (14.53 g, 56%) as a light-yellow crystalline solid, which was identical by ^1H NMR and TLC with authentic material.[11] R_f 0.40 (hexanes/EtOAc 1:1); ^1H NMR ($CDCl_3$, 400 MHz) δ 5.36 (s, 1H), 3.37 (s, 2H), 2.26 (s, 3H), 1.73 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.8, 164.3, 160.5, 107.0, 96.5, 47.7, 30.0, 24.8.

*(E)-6-(1-(Dimethylamino)-3-oxobut-1-en-2-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**5**).* Ketodioxinone **2** (10.0 g, 54 mmol) in $Me_2NCH(OMe)_2$ (15 mL, 113 mmol) was heated at 60 °C for 20 min. The solution was cooled to room temperature and diluted with EtOAc (50 mL) and H_2O (100 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (5 × 30 mL). The combined organic phases were washed with H_2O (3 × 20 mL) and brine (2 × 15 mL), dried ($MgSO_4$), rotary-evaporated, and chromatographed (CH_2Cl_2/MeOH 40:1 to 20:1) to give enamino ketone **5** (11.75 g, 91%) as an orange solid. Mp (EtOAc) 41−43 °C; R_f 0.35 (CH_2Cl_2/MeOH 20:1); IR 1701, 1602, 1569, 1376, 1278, 1251, 1220, 1121, 1021, 960, 816 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.56 (br s, 1H), 5.19 (s, 1H), 3.06 (br s, 6H), 2.19 (s, 3H), 1.79 (s,

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6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.6, 165.5, 161.9, 153.8, 106.0, 102.8, 97.3, 47.2, 40.2, 27.4, 25.1; *m/z* [TOF MS ES$^+$] found 240.1235 [M + H]$^+$, $C_{12}H_{18}NO_4$ [M + H]$^+$ calcd 240.1236.

General Procedure A: Substitution of Enamino Ketone 5 with Acetylenic Grignard Reagents. The alkyne (1.5 equiv) in THF (actual volume quoted per compound in mL) was cooled to −20 °C under an atmosphere of nitrogen. ^{i}PrMgCl in THF (2.0 M; 1.5 equiv) was added dropwise with stirring, and the mixture was allowed to warm to 0 °C over 1 h. The mixture was recooled to −50 °C, at which point enamino ketone **5** (1.0 equiv) in THF (3 mL in all examples) was added dropwise over 2 min. The mixture was allowed to warm to room temperature over 60 min, by which point **5** had been consumed (as determined by TLC). The reaction was quenched with the addition of aqueous 1 M HCl (3 mL), and the mixture was diluted with EtOAc (15 mL). The product was extracted with EtOAc (3 × 20 mL), and the combined organic extracts were washed with brine, dried ($MgSO_4$), rotary-evaporated, and chromatographed (hexanes/EtOAc 6:1 to 2:1) (unless stated otherwise) to give the desired enyne. The *E*/*Z* ratios were calculated via integration of NMR spectra of the crude products before chromatography. Samples of the desired *E* isomer **7** or **15a**−**s** (~90% purity) were obtained by chromatography. Yields correspond to the overall material obtained and therefore incorporate masses of both *E* and *Z* geometric isomers. In all cases, the *Z* isomer displayed a greater R_f value than the *E* isomer upon normal-phase TLC analysis.

*(E)-6-(6-(4-Methoxyphenyl)-2-oxohex-3-en-5-yn-3-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**7**).* General procedure A was used. 4-Methoxyphenylacetylene (663 mg, 5.02 mmol) in THF (12 mL) and ^{i}PrMgCl (2.51 mL, 5.02 mmol) were allowed to react to form the desired alkynyl Grignard, when enamino ketone **5** (800 mg, 3.34 mmol) in THF was added. Enyne **7** (926 mg, 85%) was obtained as a yellow crystalline solid (*E*/*Z* = 4:1). Mp (EtOAc) 68−70 °C; R_f 0.50 (hexanes/EtOAc 1:1); IR 2179, 1721, 1685, 1557, 1363, 1253, 1175, 1157, 840, 820 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44 (d, *J* = 8.9, 2H), 7.06 (s, 1H), 6.91 (d, *J* = 8.9, 2H), 5.89 (s, 1H), 3.86 (s, 3H), 2.40 (s, 3H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.5, 162.6, 161.4, 161.1, 138.9, 134.3, 125.9, 114.5, 113.4, 109.5, 107.4, 98.8, 85.3, 55.5, 27.8, 25.1; *m/z* [TOF MS ES$^+$] found 327.1244 [M + H]$^+$, $C_{19}H_{19}O_5$ [M + H]$^+$ calcd 327.1232.

*(E)-2,2-Dimethyl-6-(2-oxo-6-phenylhex-3-en-5-yn-3-yl)-4H-1,3-dioxin-4-one (**15a**).* General procedure A was used. Ethynylbenzene (444 mg, 4.40 mmol) in THF (10 mL) and ^{i}PrMgCl (2.20 mL, 4.40 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (700 mg, 2.93 mmol) in THF was added. Enyne **15a** (702 mg, 81%) was obtained as a light-yellow crystalline solid (*E*/*Z* = 2.5:1). Mp (EtOAc) 38−40 °C; R_f 0.36 (hexanes/EtOAc 10:1); IR 2194, 1717, 1692, 1364, 1319, 1267, 1198, 1158, 900, 819, 762 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51−7.35 (m, 5H), 7.05 (s, 1H), 5.88 (s, 1H), 2.42 (s, 3H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.4, 162.3, 160.9, 140.1, 132.3, 130.4, 128.8, 125.3, 121.4, 108.1, 107.4, 98.9, 85.3, 27.7, 25.1; *m/z* [TOF MS ES$^+$] found 297.1130 [M + H]$^+$, $C_{18}H_{17}O_4$ [M + H]$^+$ calcd 297.1127.

*(E)-2,2-Dimethyl-6-(2-oxo-6-p-tolylhex-3-en-5-yn-3-yl)-4H-1,3-dioxin-4-one (**15b**).* General procedure A was used. 1-Ethynyl-4-methylbenzene (218 mg, 1.88 mmol) in THF (4 mL) and ^{i}PrMgCl (941 μL, 1.88 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (300 mg, 1.25 mmol) in THF was added. Enyne **15b** (348 mg, 90%) was obtained as a light-yellow crystalline solid (*E*/*Z* = 3:1). Mp (EtOAc) 65−67 °C; R_f 0.59 (hexanes/EtOAc 1:1); IR 2183, 1718, 1691, 1565, 1374, 1268, 1226, 1197, 819 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38 (d, *J* = 8.1, 2H), 7.19 (d, *J* = 8.1, 2H), 7.04 (s, 1H), 5.87 (s, 1H), 2.40 (s, 3H), 2.39 (s, 3H), 1.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.4, 162.4, 161.0, 141.1, 139.6, 132.3, 129.6, 125.6, 118.4, 108.8, 107.4, 98.8, 85.2, 27.7, 25.0, 21.2; *m/z* [TOF MS ES$^+$] found 311.1286 [M + H]$^+$, $C_{19}H_{19}O_4$ [M + H]$^+$ calcd 311.1283.

*(E)-2,2-Dimethyl-6-(6-(naphthalen-1-yl)-2-oxohex-3-en-5-yn-3-yl)-4H-1,3-dioxin-4-one (**15c**).* General procedure A was used. 1-Ethynylnapthalene (286 mg, 1.88 mmol) in THF (4 mL) and ^{i}PrMgCl (941 μL, 1.88 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (300 mg, 1.25 mmol) was added. Enyne **15c** (341 mg, 79%) was obtained as a light-yellow oil (*E*/*Z* = 5:1). R_f 0.56 (hexanes/EtOAc 1:1); IR 2181, 1720, 1691, 1562, 1358, 1319, 1247, 1226, 1197, 801, 772 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.23 (d, *J* = 8.3, 1H), 7.94 (d, *J* = 8.3, 1H), 7.88 (d, *J* = 7.7, 1H), 7.77−7.74 (m, 1H), 7.68−7.64 (m, 1H), 7.60−7.55 (m, 1H), 7.51−7.47 (m, 1H), 7.20 (s, 1H), 5.95 (s, 1H), 2.45 (s, 3H), 1.84 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.4, 162.9, 160.9, 139.8, 133.1, 132.4, 131.2, 128.5, 127.9, 127.0, 125.7, 125.5, 125.3, 119.1, 117.6, 107.6, 98.9, 96.1, 89.9, 27.6, 25.1; *m/z* [TOF MS ES$^+$] found 347.1279 [M + H]$^+$, $C_{22}H_{19}O_4$ [M + H]$^+$ calcd 347.1283.

*(E)-2,2-Dimethyl-6-(2-oxo-6-(phenanthren-9-yl)hex-3-en-5-yn-3-yl)-4H-1,3-dioxin-4-one (**15d**).* General procedure A was used. 7-Ethynylanthracene (613 mg, 3.12 mmol) in THF (7 mL) and ^{i}PrMgCl (1.56 mL, 3.12 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (500 mg, 2.09 mmol) was added. Enyne **15d** (585 mg, 71%) was obtained as a yellow crystalline solid (*E*/*Z* = 2:1). Mp (EtOAc) 83−85 °C; R_f 0.63 (hexanes/EtOAc 1:1); IR 2185, 1721, 1671, 1391, 1327, 1244, 1195, 994, 901, 753, 724 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.70−8.65 (m, 2H), 8.33−8.30 (m, 1H), 8.09 (s, 1H), 7.91 (dd, *J* = 8.0, 1.0, 1H), 7.77−7.70 (m, 3H), 7.66−7.62 (m, 1H), 7.21 (s, 1H), 5.99 (s, 1H), 2.46 (s, 3H), 1.86 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.3, 162.8, 160.9, 139.9, 134.7, 131.2, 130.8, 130.5, 130.0, 129.3, 128.7, 127.8, 127.6, 127.2, 126.5, 125.4, 122.9, 122.7, 118.1, 107.6, 106.7, 98.9, 89.5, 27.6, 25.2; *m/z* [TOF MS ES$^+$] found 397.1447 [M + H]$^+$, $C_{26}H_{21}O_4$ [M + H]$^+$ calcd 397.1440.

*(E)-6-(6-(Biphenyl-4-yl)-2-oxohex-3-en-5-yn-3-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**15e**).* General procedure A was used. 1-Ethynyl-4-phenylbenzene (556 mg, 3.12 mmol) in THF (7 mL) and ^{i}PrMgCl (1.56 mL, 3.12 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (500 mg, 2.09 mmol) was added. Enyne **15e** (615 mg, 79%) was obtained as a yellow crystalline solid (*E*/*Z* = 3:1). Mp (EtOAc) 94−96 °C; R_f 0.61 (hexanes/EtOAc 1:1); IR 2192, 1718, 1666, 1583, 1389, 1327, 1245, 1197, 825, 762, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65−7.61 (m, 4H), 7.58−7.55 (m, 2H), 7.51−7.47 (m, 2H), 7.43−7.40 (m, 1H), 7.08 (s, 1H), 5.92 (s, 1H), 2.43 (s, 3H), 1.85 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.3, 162.4, 160.9, 143.2, 139.9, 139.8, 132.8, 128.9, 128.1, 127.4, 127.1, 125.3, 120.2, 108.2, 107.4, 98.9, 86.1, 27.7, 25.1; *m/z* [TOF MS ES$^+$] found 373.1435 [M + H]$^+$, $C_{24}H_{21}O_4$ [M + H]$^+$ calcd 373.1440.

*(E)-6-(6-(4-(Dimethylamino)phenyl)-2-oxohex-3-en-5-yn-3-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**15f**).* General procedure A was used. 1-Ethynyl-4-dimethylaminobenzene (452 mg, 3.12 mmol) in THF (7 mL) and ^{i}PrMgCl (1.56 mL, 3.12 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (500 mg, 2.09 mmol) was added. Enyne **15f** (602 mg, 85%) was obtained as a bright-red crystalline solid (*E*/*Z* = 2.5:1). Mp (EtOAc) 118−120 °C; R_f 0.45 (pentanes/EtOAc 1:1); IR 2156, 1708, 1682, 1547, 1367, 1320, 1227, 1193, 818 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37 (d, *J* = 9.0, 2H), 7.10 (s, 1H), 6.65 (d, *J* = 9.0, 2H), 5.91 (s, 1H), 3.05 (s, 6H), 2.38 (s, 3H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.5, 162.9, 161.3, 151.5, 136.9, 134.3, 126.7, 113.1, 111.7, 107.1, 106.6, 98.5, 86.4, 40.0, 27.7, 25.1; *m/z* [TOF MS ES$^+$] found 340.1556 [M + H]$^+$, $C_{20}H_{22}NO_4$ [M + H]$^+$ calcd 340.1549.

*(E)-6-(6-(4-tert-Butylphenyl)-2-oxohex-3-en-5-yn-3-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**15g**).* General procedure A was used. 1-Ethynyl-4-*tert*-butylbenzene (507 mg, 3.12 mmol) in THF (7 mL) and ^{i}PrMgCl (1.56 mL, 3.12 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (500 mg, 2.09 mmol) was added. Enyne **15g** (603 mg, 82%) was obtained as a yellow crystalline solid (*E*/*Z* = 2:1). Mp (EtOAc) 76−79 °C; R_f 0.72 (hexanes/EtOAc 1:1); IR 2695, 2188, 1716, 1690, 1562, 1362, 1270, 1227, 1197, 838, 822 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44−7.40 (m, 4H), 7.05 (s, 1H), 5.88 (s, 1H), 2.41 (s, 3H), 1.83 (s, 6H), 1.33 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.4, 162.4, 160.9, 154.1, 139.7, 132.2, 125.8, 125.6, 118.4, 1088, 107.4, 98.9, 85.2, 35.1, 31.0, 27.7, 25.1; *m/z* [TOF MS ES$^+$] found 353.1756 [M + H]$^+$, $C_{22}H_{25}O_4$ [M + H]$^+$ calcd 353.1753.

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*(E)-2,2-Dimethyl-6-(2-oxodec-3-en-5-yn-3-yl)-4H-1,3-dioxin-4-one (**15h**).* General procedure A was used. 1-Hexyne (154 mg, 1.88 mmol) in THF (4 mL) and ^{i}PrMgCl (941 μL, 1.88 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (300 mg, 1.25 mmol) in THF was added. Enyne **15h** (314 mg, 91%) was obtained as a light-yellow oil (*E*/*Z* = 4:1). R_f 0.71 (hexanes/EtOAc 1:1); IR 2211, 1728, 1677, 1377, 1322, 1245, 1198, 1018, 900, 815 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.82 (t, *J* = 2.3, 1H), 5.72 (s, 1H), 2.47 (td, *J* = 6.9, 2.2, 2H), 2.41 (s, 3H), 1.79 (s, 6H), 1.59−1.53 (m, 2H), 1.47−1.41 (m, 2H), 0.94 (t, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.6, 162.6, 160.9, 140.2, 126.4, 111.4, 107.3, 98.5, 30.1, 27.5, 25.0, 21.9, 19.9, 13.5; *m*/*z* [TOF MS ES$^+$] found 277.1451 [M + H]$^+$, $C_{16}H_{21}O_4$ [M + H]$^+$ calcd 277.1440.

*(E)-6-(6-Cyclopropyl-2-oxohex-3-en-5-yn-3-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**15i**).* General procedure A was used. Cyclopropylacetylene (159 μL, 1.88 mmol) in THF (4 mL) and ^{i}PrMgCl (941 μL, 1.88 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (300 mg, 1.25 mmol) was added. Enyne **15i** (369 mg, 83%) was obtained as a light-yellow crystalline solid (*E*/*Z* = 6:1). Mp (EtOAc) 39−41 °C; R_f 0.43 (hexanes/EtOAc 1:1); IR 2194, 1721, 1683, 1560, 1350, 1319, 1198, 1153, 1012, 849, 815, 615 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.79 (d, *J* = 2.5, 1H), 5.70 (s, 1H), 2.35 (s, 3H), 1.79 (s, 6H), 1.53−1.46 (m, 1H), 1.05−1.00 (m, 1H), 0.89−0.85 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.5, 162.6, 161.0, 139.5, 126.6, 115.8, 107.2, 98.4, 72.8, 27.5, 25.0, 10.2, 1.3; *m*/*z* [TOF MS ES$^+$] found 261.1123 [M + H]$^+$, $C_{15}H_{17}O_4$ [M + H]$^+$ calcd 261.1127.

*(E)-2,2-Dimethyl-6-(2-oxo-6-(4-(trifluoromethyl)phenyl)hex-3-en-5-yn-3-yl)-4H-1,3-dioxin-4-one (**15j**).* General procedure A was used. 4-Trifluoromethyl-1-ethynylbenzene (530 mg, 3.12 mmol) in THF (5 mL) and ^{i}PrMgCl (1.56 mL, 3.12 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (500 mg, 2.09 mmol) in THF was added. Enyne **15j** (663 mg, 86%) was obtained as a light-yellow crystalline solid (*E*/*Z* = 5:1). Mp (EtOAc) 58−60 °C; R_f 0.66 (hexanes/EtOAc 1:1); IR 2197, 1721, 1692, 1621, 1316, 1171, 1158, 1130, 1067, 1011, 838, 817 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.63 (d, *J* = 8.3, 2H), 7.57 (d, *J* = 8.3, 2H), 7.02 (s, 1H), 5.85 (s, 1H), 2.41 (s, 3H), 1.81 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.2, 162.0, 160.8, 141.2, 132.7, 131.8, 125.6, 125.0, 124.3, 107.6, 105.2, 99.1, 86.8, 27.7, 24.9; *m*/*z* [TOF MS ES$^+$] found 365.1018 [M + H]$^+$, $C_{19}H_{16}F_3O_4$ [M + H]$^+$ calcd 365.1001.

*(E)-6-(6-(3-Chlorophenyl)-2-oxohex-3-en-5-yn-3-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**15k**).* General procedure A was used. 3-Chloro-1-ethynylbenzene (231 μL, 1.88 mmol) in THF (4 mL) and ^{i}PrMgCl (941 μL, 1.88 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (300 mg, 1.25 mmol) was added. Enyne **15k** (363 mg, 88%) was obtained as a light-yellow crystalline solid (*E*/*Z* = 3:1). Mp (EtOAc) 55−57 °C; R_f 0.57 (hexanes/EtOAc 1:1); IR 2194, 1717, 1688, 1554, 1380, 1317, 1221, 1197, 1013, 903, 790 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43−7.42 (m, 1H), 7.39−7.28 (m, 3H), 7.00 (s, 1H), 5.83 (s, 1H), 2.40 (s, 3H), 1.80 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.3, 162.1, 160.8, 140.7, 134.6, 131.8, 130.5, 130.2, 130.0, 124.6, 123.1, 107.5, 105.7, 98.9, 85.9, 27.7, 25.0; *m*/*z* [TOF MS ES$^+$] found 331.0742 [M + H]$^+$, $C_{18}H_{16}ClO_4$ [M + H]$^+$ calcd 331.0737.

*(E)-2,2-Dimethyl-6-(2-oxo-6-(thiophen-2-yl)hex-3-en-5-yn-3-yl)-4H-1,3-dioxin-4-one (**15l**).* General procedure A was used. 2-Ethynylthiophene (250 mg, 2.30 mmol) in THF (5 mL) and ^{i}PrMgCl (1.15 mL, 2.30 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (366 mg, 1.25 mmol) in THF was added. Enyne **15l** (355 mg, 77%) was obtained as an impure light-orange crystalline solid (*E*/*Z* = 2.5:1) that was not fully purified but was used directly in the next step. Mp (EtOAc) 32−34 °C; R_f 0.59 (hexanes/EtOAc 1:1); IR 2173, 1722, 1676, 1390, 1324, 1269, 1247, 1198, 1017, 899, 852 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45 (d, *J* = 4.9, 1H), 7.33 (d, *J* = 3.5, 1H), 7.04 (dd, *J* = 5.0, 3.8, 1H), 7.02 (s, 1H), 5.79 (s, 1H), 2.42 (s, 3H), 1.81 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.8, 160.8, 156.0, 139.0, 135.1, 131.1, 127.9, 124.8, 107.5, 98.8, 97.8, 90.2, 26.6, 25.1; *m*/*z* [TOF MS ES$^+$] found 303.0709 [M + H]$^+$, $C_{16}H_{15}O_4S$ [M + H]$^+$ calcd 303.0691.

*(E)-6-(6-(3,5-Difluorophenyl)-2-oxohex-3-en-5-yn-3-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**15m**).* General procedure A was used. 3,5-Difluoro-1-ethynylbenzene (259 mg, 1.88 mmol) in THF (4 mL) and ^{i}PrMgCl (941 μL, 1.88 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (300 mg, 1.25 mmol) was added. Enyne **15m** (369 mg, 89%) was obtained as a light-yellow crystalline solid (*E*/*Z* = 5:1). Mp (EtOAc) 70−72 °C; R_f 0.64 (hexanes/EtOAc 1:1); IR 2197, 1729, 1692, 1616, 1581, 1368, 1234, 1193, 1124, 992, 858 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.98−6.95 (m, 2H), 6.97 (s, 1H), 6.88 (tt, *J* = 8.8, 2.3, 1H), 5.81 (s, 1H), 2.41 (s, 3H), 1.80 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.1, 164.0, 161.8, 161.3, 160.6, 141.4, 123.9, 115.0, 107.5, 106.3, 103.9, 99.0, 86.2, 27.7, 24.9; *m*/*z* [TOF MS ES$^+$] found 333.0941 [M + H]$^+$, $C_{18}H_{15}F_2O_4$ [M + H]$^+$ calcd 333.0938.

*(E)-6-(6-(3,5-Dimethoxyphenyl)-2-oxohex-3-en-5-yn-3-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**15n**).* General procedure A was used. 3,5-Dimethoxy-1-ethynylbenzene (304 mg, 1.88 mmol) in THF (4 mL) and ^{i}PrMgCl (941 μL, 1.88 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (300 mg, 1.25 mmol) was added. Enyne **15n** (369 mg, 83%) was obtained as a yellow crystalline solid (*E*/*Z* = 3:1). Mp (EtOAc) 78−80 °C; R_f 0.51 (hexanes/EtOAc 1:1); IR 2190, 1723, 1695, 1595, 1583, 1335, 1201, 1150, 1014, 837, 620 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.03 (s, 1H), 6.64 (d, *J* = 2.3, 2H), 6.55 (t, *J* = 2.2, 1H), 5.90 (s, 1H), 3.82 (s, 6H), 2.42 (s, 3H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.3, 162.3, 160.9, 160.7, 140.4, 125.3, 122.6, 109.8, 109.5, 108.1, 107.4, 104.0, 99.1, 96.2, 84.9, 55.6, 27.7, 25.0; *m*/*z* [TOF MS ES$^+$] found 357.1342 [M + H]$^+$, $C_{20}H_{21}O_6$ [M + H]$^+$ calcd 357.1338.

*(E)-6-(6-(2,5-Dimethylphenyl)-2-oxohex-3-en-5-yn-3-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**15o**).* General procedure A was used. 1-Ethynyl-2,5-dimethylbenzene (268 μL, 1.88 mmol) in THF (4 mL) and ^{i}PrMgCl (941 μL, 1.88 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (300 mg, 1.25 mmol) was added. Enyne **15o** (304 mg, 75%) was obtained as a yellow crystalline solid (*E*/*Z* = 5:1). Mp (EtOAc) 52−54 °C; R_f 0.67 (hexanes/EtOAc 1:1); IR 2187, 1719, 1678, 1621, 1377, 1325, 1245, 1196, 1134, 901, 888 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.27 (s, 1H), 7.14 (br s, 2H), 7.11 (s, 1H), 5.85 (s, 1H), 2.42 (s, 3H), 2.40 (s, 3H), 2.33 (s, 3H), 1.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.5, 162.7, 160.9, 139.5, 138.3, 135.5, 133.3, 131.5, 129.7, 125.7, 121.1, 107.8, 107.5, 98.8, 88.5, 27.6, 25.1, 20.7, 20.2; *m*/*z* [TOF MS ES$^+$] found 325.1442 [M + H]$^+$, $C_{20}H_{21}O_4$ [M + H]$^+$ calcd 325.1440.

*(E)-6-(6-(2-(Hydroxymethyl)phenyl)-2-oxohex-3-en-5-yn-3-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**15p**).* General procedure A was used. 2-Ethynylbenzyl alcohol (248 mg, 1.88 mmol) in THF (4 mL) and ^{i}PrMgCl (941 μL, 1.88 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (300 mg, 1.25 mmol) was added. Enyne **15p** (329 mg, 81%) was obtained as a light-yellow crystalline solid (*E*/*Z* = 5:1). Mp (EtOAc) 63−65 °C; R_f 0.35 (hexanes/EtOAc 1:1); IR 2169, 1716, 1572, 1602, 1269, 1248, 1196, 1036, 1018, 763 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.55−7.49 (m, 2H), 7.46−7.42 (m, 1H), 7.30−7.28 (m, 1H), 7.10 (s, 1H), 5.97 (s, 1H), 4.77 (d, *J* = 3.4, 2H), 3.08 (br s, 1H, OH), 2.36 (s, 3H), 1.81 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.7, 162.8, 161.9, 143.3, 139.6, 133.4, 130.9, 128.0, 127.7, 125.6, 119.8, 107.7, 106, 5, 98.6, 89.1, 63.2, 27.8, 24.9; *m*/*z* [TOF MS ES$^-$] found 325.1081 [M + H]$^+$, $C_{19}H_{17}O_5$ [M + H]$^+$ calcd 325.1076.

*(E)-2,2-Dimethyl-6-(2-oxo-6-(trimethylsilyl)hex-3-en-5-yn-3-yl)-4H-1,3-dioxin-4-one (**15q**).* General procedure A was used. Ethynyltrimethysilane (400 mg, 4.07 mmol) in THF (10 mL) and ^{i}PrMgCl (2.04 mL, 4.07 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (650 mg, 2.71 mmol) in THF was added. Enyne **15q** (633 mg, 80%) was obtained as a light-yellow oil (*E*/*Z* = 3:1). R_f 0.69 (hexanes/EtOAc 10:1); IR 1729, 1700, 1618, 1576, 1360, 1248, 1063, 839, 814 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.77 (s, 1H), 5.75 (s, 1H), 2.37 (s, 3H), 179 (s, 6H), 0.24 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.4, 161.9, 160.7, 141.4, 124.5, 115.8, 107.3, 99.4, 98.9, 27.6, 25.0, −0.61; *m*/*z* [TOF MS ES$^+$] found 293.1225 [M + H]$^+$, $C_{15}H_{21}O_4Si$ [M + H]$^+$ calcd 293.1209.

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*(E)-2,2-Dimethyl-6-(2-oxo-6-(triisopropylsilyl)hex-3-en-5-yn-3-yl)-4H-1,3-dioxin-4-one (**15r**).* General procedure A was used. (Triisopropylsilyl)acetylene (1.01 g, 5.58 mmol) in THF (15 mL) and ^{i}PrMgCl (2.79 mL, 5.58 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (890 mg, 3.72 mmol) in THF was added. Enyne **15r** (1.23 g, 88%) was obtained as a colorless oil (E/Z = 3:1). R_f 0.37 (hexanes/Et_2O 5:1); IR 1728, 1389, 1271, 1246, 1200, 1015, 881, 731 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.82 (s, 1H), 5.73 (s, 1H), 2.37 (s, 3H), 1.78 (s, 6H), 1.11 (sept, J = 7.1, 3H), 1.09 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.4, 160.8, 159.1, 144.2, 117.0, 111.1, 106.9, 101.8, 96.1, 31.1, 25.0, 18.5, 11.2; m/z [TOF MS ES$^+$] found 377.2154 [M + H]$^+$, $C_{21}H_{33}O_4Si$ [M + H]$^+$ calcd 377.2148.

*(E)-6-(6-(4-Methoxy-2-methylphenyl)-2-oxohex-3-en-5-yn-3-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (**15s**).* General procedure A was used. 1-Ethynyl-4-methoxy-2-methylbenzene (456 mg, 3.12 mmol) in THF (7 mL) and ^{i}PrMgCl (1.56 mL, 3.12 mmol) were allowed to react to form the desired alkynyl Grignard, and enamino ketone **5** (500 mg, 2.09 mmol) was added. Enyne **15s** (590 mg, 83%) was obtained as a light-yellow crystalline solid (E/Z = 3:1). Mp (EtOAc) 56−59 °C; R_f 0.57 (pentanes/EtOAc 1:1); IR 2166, 1720, 1688, 1558, 1377, 1365, 1240, 1200, 1159, 809 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (d, J = 8.4, 1H), 6.76 (d, J = 2.4, 1H), 6.73 (dd, J = 8.5, 2.6, 1H), 5.83 (s, 1H), 3.82 (s, 3H), 2.41 (s, 3H), 2.39 (s, 3H), 1.80 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.4, 162.8, 161.4, 160.9, 143.7, 138.5, 134.8, 126.0, 115.4, 113.4, 111.9, 108.7, 106.8, 98.7, 88.6, 55.4, 27.6, 25.1, 20.9; m/z [TOF MS ES$^+$] found 341.1404 [M + H]$^+$, $C_{20}H_{21}O_5$ [M + H]$^+$ calcd 341.1389.

General Procedure B: Iodine Monochloride-Mediated Aromatization Reaction. The enyne (1.0 equiv) and K_3PO_4 (2.0 equiv) were suspended in CH_2Cl_2 (actual volume quoted per compound in mL), and the suspension was cooled to −78 °C under an atmosphere of nitrogen. ICl in CH_2Cl_2 (1.0 M; 1.5 equiv) was added dropwise with stirring, and the mixture was allowed to warm to −50 °C over 3 h. Upon further warming to 0 °C, the reaction was quenched with the addition of saturated aqueous $Na_2S_2O_3$ (5 mL) and H_2O (5 mL). The product was extracted with EtOAc (3 × 10 mL), and the combined organic extracts were washed with brine, dried ($MgSO_4$), rotary-evaporated, and chromatographed (hexanes/EtOAc 6:1 to 3:1) or (where stated) recrystallized from EtOH to give the desired aromatic product **8**, **9**, or **16**−**28**.

*8-Acetyl-6-iodo-5-(4-methoxyphenyl)-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (**8**).* General procedure B was used. Enyne **7** (48 mg, 0.15 mmol) and K_3PO_4 (64 mg, 0.30 mmol) were suspended in CH_2Cl_2 (1 mL). ICl (220 μL, 0.22 mmol) was added in one portion. Following workup and purification, aryl iodide **8** (64 mg, 96%) was obtained as a light-yellow crystalline solid. Mp (EtOAc) 137−139 °C; R_f 0.71 (hexanes/EtOAc 1:1); IR 1739, 1674, 1607, 1514, 1380, 1306, 1243, 1197, 1174, 1067, 1030, 825 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.57 (s, 1H), 7.05 (d, J = 8.8, 2H), 7.01 (d, J = 8.8, 2H), 3.90 (s, 3H), 2.66 (s, 3H), 1.85 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.1, 159.5, 157.4, 155.7, 153.1, 145.6, 135.1, 129.2, 128.3, 115.1, 113.7, 105.9, 95.7, 55.2, 31.7, 25.9; m/z [CI$^+$] found 470.0465 [M + NH_4]$^+$, $C_{19}H_{21}INO_5$ [M + NH_4]$^+$ calcd 470.0464.

*8-Acetyl-6-bromo-5-(4-methoxyphenyl)-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (**9**).* Enyne **7** (30 mg, 0.08 mmol) was suspended in DMF (500 μL), and the suspension was cooled to −50 °C under an atmosphere of argon. NBS (16 mg, 0.087 mmol) was added in one portion, and the mixture was allowed to warm to ambient temperature over 12 h. The mixture was diluted with EtOAc (5 mL), and the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (2 mL). The product was extracted with EtOAc (3 × 5 mL), and the combined organic extracts were washed with brine, dried ($MgSO_4$), rotary-evaporated, and chromatographed (hexanes/EtOAc 4:1) to give aryl iodide **9** (28 mg, 88%) as a light-yellow crystalline solid. Mp (EtOAc) 119−121 °C; R_f 0.69 (hexanes/EtOAc 1:1); IR 1746, 1683, 1515, 1380, 1302, 1291, 1245, 1199, 1177, 1058, 768 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.33 (s, 1H), 7.12 (d, J = 8.7, 2H), 7.01 (d, J = 8.7, 2H), 3.89 (s, 3H), 2.67 (s, 3H), 1.86 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.1, 159.5, 157.6, 154.9, 149.4, 139.6, 131.1, 129.4, 127.9, 119.8, 115.6, 113.6, 105.9, 55.2, 31.7, 25.8; m/z [TOF MS ES$^+$] found 405.0333 [M + H]$^+$, $C_{19}H_{18}BrO_5$ [M + H]$^+$ calcd 405.0338.

*8-Acetyl-6-iodo-2,2-dimethyl-5-phenyl-4H-benzo[d][1,3]dioxin-4-one (**16**).* General procedure B was used. Enyne **15a** (53 mg, 0.18 mmol) and K_3PO_4 (76 mg, 0.36 mmol) were suspended in CH_2Cl_2 (1 mL). ICl (270 μL, 0.27 mmol) was added in one portion. Following workup and purification, aryl iodide **16** (55 mg, 72%) was obtained as a light-yellow crystalline solid. Mp (EtOAc) 115−117 °C; R_f 0.69 (hexanes/EtOAc 1:1); IR 1745, 1682, 1578, 1436, 1378, 1299, 1254, 1198, 1056, 738, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.58 (s, 1H), 7.53−7.47 (m, 3H), 7.13−7.11 (m, 2H), 2.67 (s, 3H), 1.85 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.2, 157.2, 155.7, 153.2, 145.7, 142.8, 132.3, 128.5, 127.7, 125.3, 114.9, 105.9, 95.0, 31.7, 25.9; m/z [TOF MS ES$^+$] found 423.0103 [M + H]$^+$, $C_{18}H_{16}IO_4$ [M + H]$^+$ calcd 423.0093.

*8-Acetyl-6-iodo-2,2-dimethyl-5-p-tolyl-4H-benzo[d][1,3]dioxin-4-one (**17**).* General procedure B was used. Enyne **15b** (85 mg, 0.27 mmol) and K_3PO_4 (116 mg, 0.54 mmol) were suspended in CH_2Cl_2 (1.5 mL). ICl (411 μL, 0.41 mmol) was added in one portion. Following workup and purification, aryl iodide **17** (96 mg, 82%) was obtained as a light-orange crystalline solid. Mp (EtOAc) 118−120 °C; R_f 0.45 (hexanes/EtOAc 3:1); IR 1747, 1681, 1554, 1390, 1379, 1302, 1284, 1256, 1193, 1055, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.57 (s, 1H), 7.30 (d, J = 7.7, 2H), 7.01 (d, J = 8.0, 2H), 2.66 (s, 3H), 2.46 (s, 3H), 1.85 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.1, 157.3, 155.7, 153.4, 145.6, 139.9, 138.1, 129.0, 128.4, 127.7, 115.0, 105.9, 95.3, 31.7, 25.9, 21.6; m/z [TOF MS ES$^+$] found 437.0261 [M + H]$^+$, $C_{19}H_{18}IO_4$ [M + H]$^+$ calcd 437.0250.

*8-Acetyl-6-iodo-2,2-dimethyl-5-(naphthalen-1-yl)-4H-benzo[d][1,3]dioxin-4-one (**18**).* General procedure B was used. Enyne **15c** (155 mg, 0.45 mmol) and K_3PO_4 (190 mg, 0.90 mmol) were suspended in CH_2Cl_2 (2 mL). ICl (671 μL, 0.67 mmol) was added in one portion. Following workup and purification (recrystallization from EtOH), aryl iodide **18** (151 mg, 71%) was obtained as a light-brown crystalline solid. Mp (EtOH) 150−152 °C; R_f 0.61 (hexanes/EtOAc 1:1); IR 1748, 1684, 1550, 1396, 1378, 1302, 1257, 1200, 1058, 778 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.64 (s, 1H), 7.97 (t, J = 8.7, 2H), 7.59 (dd, J = 8.1, 7.2, 1H), 7.51 (ddd, J = 8.2, 6.9, 1.0, 1H), 7.41 (ddd, J = 8.2, 6.9, 1.2, 1H), 7.23 (d, J = 8.4, 1H), 7.20 (dd, J = 7.2, 1.2, 1H), 2.72 (s, 3H), 1.85 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.2, 156.7, 155.7, 152.1, 145.8, 140.7, 133.5, 130.7, 128.9, 128.7, 128.6, 126.5, 126.0, 125.3, 124.3, 116.0, 105.9, 95.9, 31.7, 26.2, 25.7; m/z [TOF MS ES$^+$] found 473.0248 [M + H]$^+$, $C_{22}H_{18}IO_4$ [M + H]$^+$ calcd 473.0250.

*8-Acetyl-6-iodo-2,2-dimethyl-5-(phenanthren-9-yl)-4H-benzo[d][1,3]dioxin-4-one (**19**).* General procedure B was used. Enyne **15d** (100 mg, 0.25 mmol) and K_3PO_4 (106 mg, 0.50 mmol) were suspended in CH_2Cl_2 (2 mL). ICl (378 μL, 0.38 mmol) was added in one portion. Following workup and purification (recrystallization from EtOH), aryl iodide **19** (122 mg, 93%) was obtained as a pale-yellow crystalline solid. Mp (EtOAc) 100−104 °C; R_f 0.75 (hexanes/EtOAc 1:1); IR 1751, 1736, 1680, 1554, 1377, 1292, 1255, 1195, 1060, 769, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.82−8.76 (m, 2H), 8.65 (s, 1H), 7.91−7.89 (m, 1H), 7.73−7.61 (m, 3H), 7.52−7.48 (m, 1H), 7.45 (s, 1H), 7.30−7.28 (m, 1H), 2.72 (s, 3H), 1.85 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.2, 156.7, 155.7, 151.9, 145.9, 143.1, 139.6, 131.4, 130.5, 130.4, 129.9, 128.9, 127.1, 126.8, 126.7, 125.1, 123.4, 122.8, 116.2, 106.1, 99.4, 96.0, 31.7, 26.4, 25.5; m/z [TOF MS ES$^+$] found 523.0388 [M + H]$^+$, $C_{26}H_{20}IO_4$ [M + H]$^+$ calcd 523.0406.

*8-Acetyl-5-(biphenyl-4-yl)-6-iodo-2,2-dimethyl-4H-benzo[d][1,3]-dioxin-4-one (**20**).* General procedure B was used. Enyne **15e** (100 mg, 0.27 mmol) and K_3PO_4 (114 mg, 0.54 mmol) were suspended in CH_2Cl_2 (2 mL). ICl (400 μL, 0.40 mmol) was added in one portion. Following workup and purification (recrystallization from EtOH), aryl iodide **20** (125 mg, 93%) was obtained as a pale-yellow crystalline solid. Mp (EtOAc) 154−155 °C; R_f 0.74 (hexanes/EtOAc 1:1); IR 1738, 1681, 1546, 1376, 1301, 1279, 1198, 1053, 774, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.59 (s, 1H), 7.73−7.70 (m, 4H), 7.49−7.44 (m, 2H), 7.39−7.36 (m, 1H), 7.20−7.18 (d, J = 8.2, 2H), 2.67 (s, 3H), 1.85 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.1, 157.3,

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155.7, 152.9, 145.8, 141.7, 140.9, 140.6, 128.8, 128.3, 127.5, 127.2, 126.9, 115.0, 105.9, 99.4, 95.1, 31.7, 25.9; *m/z* [TOF MS ES$^+$] found 499.0419 [M + H]$^+$, $C_{24}H_{20}IO_4$ [M + H]$^+$ calcd 499.0406.

*8-Acetyl-5-(4-(dimethylamino)phenyl)-6-iodo-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (**21**).* General procedure B was used. Enyne **15f** (100 mg, 0.29 mmol) and K_3PO_4 (125 mg, 0.59 mmol) were suspended in CH_2Cl_2 (2 mL). ICl (442 μL, 0.44 mmol) was added in one portion. Following workup and purification, aryl iodide **21** (124 mg, 92%) was obtained as a brick-red crystalline solid. Mp (EtOH) 163−167 °C; R_f 0.64 (hexanes/EtOAc 1:1); IR 1736, 1681, 1605, 1526, 1359, 1286, 1233, 1191, 1170, 1050, 799 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.56 (s, 1H), 7.01 (d, *J* = 8.8, 2H), 6.79 (d, *J* = 8.8, 2H), 3.05 (s, 6H), 2.64 (s, 3H), 1.84 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.1, 157.5, 155.9, 153.8, 150.0, 145.5, 130.6, 129.2, 127.7, 115.2, 111.5, 105.7, 96.3, 40.3, 31.6, 25.8; *m/z* [TOF MS ES$^+$] found 466.0536 [M + H]$^+$, $C_{20}H_{21}INO_4$ [M + H]$^+$ calcd 466.0515.

*8-Acetyl-5-(4-tert-butylphenyl)-6-iodo-2,2-dimethyl-4H-benzo-[d][1,3]dioxin-4-one (**22**).* General procedure B was used. Enyne **15g** (100 mg, 0.28 mmol) and K_3PO_4 (121 mg, 0.57 mmol) were suspended in CH_2Cl_2 (2 mL). ICl (426 μL, 0.43 mmol) was added in one portion. Following workup and purification (recrystallization from EtOH), aryl iodide **22** (117 mg, 87%) was obtained as a pale-yellow crystalline solid. Mp (EtOAc) 90−93 °C; R_f 0.86 (hexanes/EtOAc 1:1); IR 1744, 1688, 1554, 1390, 1378, 1301, 1256, 1194, 1060, 833 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.55 (s, 1H), 7.47 (d, *J* = 8.4, 2H), 7.03 (d, *J* = 8.3, 2H), 2.65 (s, 3H), 1.83 (s, 6H), 1.39 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.1, 157.3, 155.7, 153.5, 151.2, 145.6, 139.8, 127.4, 125.1, 115.0, 105.9, 99.3, 95.5, 34.7, 31.6, 31.4, 25.9; *m/z* [TOF MS ES$^+$] found 479.0724 [M + H]$^+$, $C_{22}H_{24}IO_4$ [M + H]$^+$ calcd 479.0719.

*8-Acetyl-5-cyclopropyl-6-iodo-2,2-dimethyl-4H-benzo[d][1,3]-dioxin-4-one (**24**).* General procedure B was used. Enyne **15i** (100 mg, 0.38 mmol) and K_3PO_4 (161 mg, 0.76 mmol) were suspended in CH_2Cl_2 (2 mL). ICl (570 μL, 0.57 mmol) was added in one portion. Following workup and purification (recrystallization from EtOH), aryl iodide **24** (147 mg, 79%) was obtained as a white crystalline solid. Mp (EtOH) 115−117 °C; R_f 0.72 (hexanes/EtOAc 1:1); IR 1730, 1677, 1555, 1384, 1301, 1253, 1199, 1059, 974, 915 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.44 (s, 1H), 2.64 (s, 3H), 2.14 (tt, *J* = 8.5, 6.0, 1H), 1.77 (s, 6H), 1.40−1.35 (m, 2H), 0.50−0.46 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.9, 157.3, 155.4, 154.7, 145.5, 126.9, 118.2, 105.6, 97.0, 31.6, 25.6, 21.7, 12.3; *m/z* [TOF MS ES$^+$] found 387.0087 [M + H]$^+$, $C_{15}H_{16}IO_4$ [M + H]$^+$ calcd 387.0093.

*8-Acetyl-5-(3-chlorophenyl)-6-iodo-2,2-dimethyl-4H-benzo[d]-[1,3]dioxin-4-one (**26**).* General procedure B was used. Enyne **15k** (46 mg, 0.14 mmol) and K_3PO_4 (57 mg, 0.27 mmol) were suspended in CH_2Cl_2 (1 mL). ICl (208 μL, 0.21 mmol) was added in one portion. Following workup and purification, aryl iodide **26** (38 mg, 61%) was obtained as a light-yellow crystalline solid. Mp (EtOH) 133−135 °C; R_f 0.75 (hexanes/EtOAc 1:1); IR 1741, 1683, 1555, 1378, 1297, 1255, 1197, 1056, 979, 743 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.57 (s, 1H), 7.46−7.40 (m, 2H), 7.10−7.08 (m, 1H), 7.03−7.01 (m, 1H), 2.67 (s, 3H), 1.85 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.9, 157.1, 155.6, 151.4, 145.9, 144.3, 134.1, 129.6, 128.9, 128.5, 127.9, 126.2, 114.8, 106.1, 94.5, 31.6, 26.0, 25.8; *m/z* [TOF MS ES$^+$] found 456.9700 [M + H]$^+$, $C_{18}H_{15}ClIO_4$ [M + H]$^+$ calcd 456.9704.

*8-Acetyl-6-iodo-5-(5-iodothiophen-2-yl)-2,2-dimethyl-4H-benzo-[d][1,3]dioxin-4-one (**27**).* General procedure B was used. Enyne **15l** (40 mg, 0.13 mmol) and K_3PO_4 (56 mg, 0.26 mmol) were suspended in CH_2Cl_2 (1 mL). ICl (195 μL, 0.20 mmol) was added in one portion. Following workup and purification (recrystallization from EtOH), aryl iodide **27** (35 mg, 49%) was obtained as a light-yellow crystalline solid. Mp (EtOH) 142−145 °C; R_f 0.39 (hexanes/EtOAc 2:1); IR 1735, 1669, 1377, 1292, 1255, 1200, 1059, 987, 930, 794 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz) δ 8.50 (s, 1H), 7.26 (d, *J* = 3.7, 1H), 6.60 (d, *J* = 3.7, 1H), 2.62 (s, 3H), 1.81 (s, 6H); ^{13}C NMR (CD_3OD, 100 MHz) δ 196.6, 158.6, 157.9, 156.9, 150.5, 146.6, 145.8, 138.1, 130.9, 130.5, 107.9, 97.2, 75.6, 31.7, 25.7; *m/z* [TOF MS ES$^+$] found 554.8619 [M + H]$^+$, $C_{16}H_{13}I_2O_4S$ [M + H]$^+$ calcd 554.8624.

*8-Acetyl-6-iodo-5-(4-methoxy-2-methylphenyl)-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (**28**).* General procedure B was used. Enyne **15s** (100 mg, 0.29 mmol) and K_3PO_4 (125 mg, 0.59 mmol) were suspended in CH_2Cl_2 (2 mL). ICl (442 μL, 0.44 mmol) was added in one portion. Following workup and purification, aryl iodide **28** (101 mg, 75%) was obtained as a white crystalline solid. Mp (EtOH) 107−109 °C; R_f 0.62 (hexanes/EtOAc 1:1); IR 1745, 1681, 1574, 1377, 1299, 1223, 1198, 1165, 1040, 756 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz, 323 K) δ 8.40 (s, 1H), 6.84−6.83 (m, 1H), 6.81−6.75 (m, 2H), 3.79 (s, 3H), 2.60 (s, 3H), 1.90 (s, 3H), 1.76 (s, 6H); ^{13}C NMR (DMSO-d_6, 400 MHz, 323 K) δ 194.9, 158.7, 156.5, 154.8, 151.7, 144.1, 136.9, 135.4, 135.2, 128.2, 114.8, 110.9, 106.1, 105.9, 96.5, 54.8, 25.4, 24.5, 19.4; *m/z* [TOF MS ES$^+$] found 467.0371 [M + H]$^+$, $C_{20}H_{20}IO_5$ [M + H]$^+$ calcd 467.0355.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all new synthetic compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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