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Note

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Regioselective Synthesis of 5-Metalated 2-Pyrones by Intramolecular Oxymetalation of Carbonyl-Ene-Yne Compounds Using Indium Trihalide

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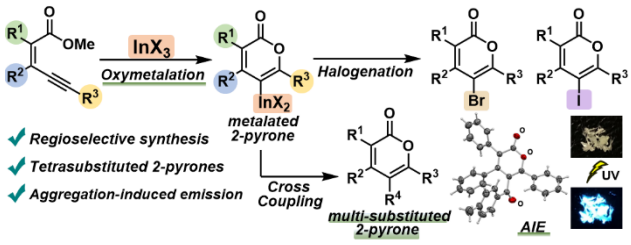
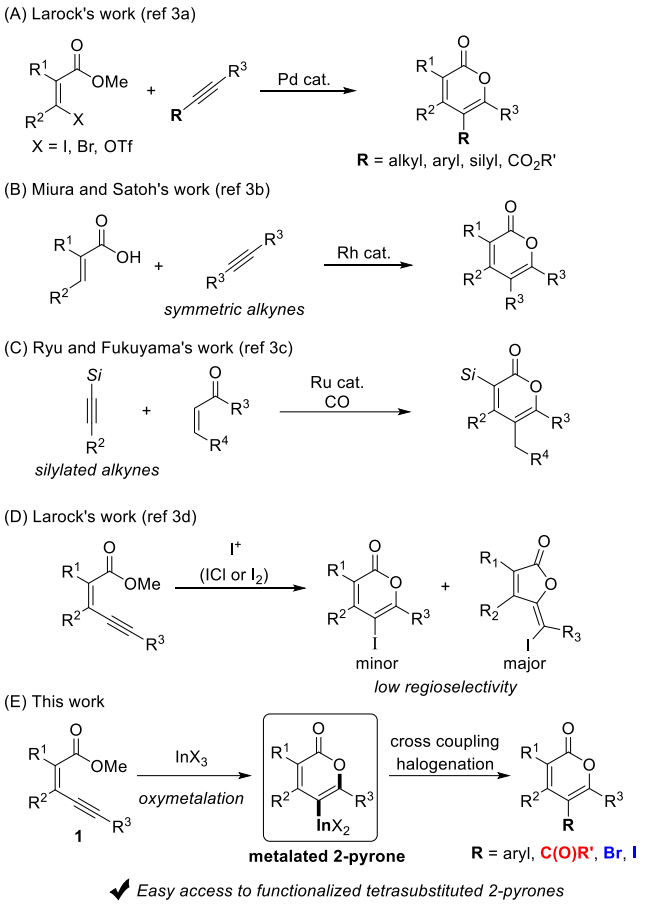
Supporting Information Placeholder



ABSTRACT: The oxyindation of carbonyl-ene-yne compounds with indium trihalides proceeded efficiently to give di-, tri-, and tetrasubstituted 2-pyrones bearing a carbon-indium bond. The metalated 2-pyrone and a zwitterion intermediate were identified by X-ray crystallographic analysis. The application of organoindium compounds to oxidation or cross-coupling provided easy access to various multi-functionalized 2-pyrones. Some 2-pyrone derivatives show intensefluorescence only in the solid state (aggregation-induced emission).

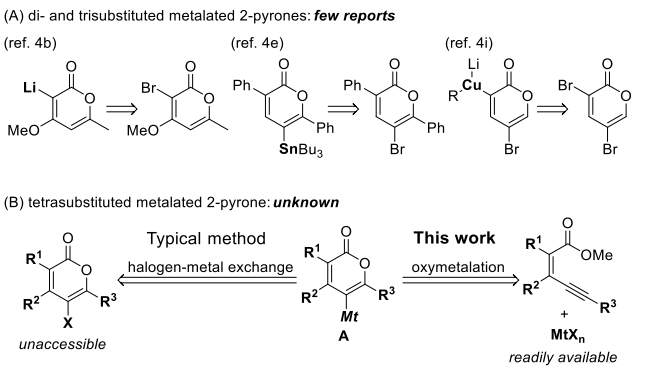
2-Pyrones are an important class of oxygen-containing heterocycles with a broad range of biological activities and are versatile building blocks in organic synthesis.[1] Therefore, the development of general and selective synthetic methods for highly substituted 2-pyrones, particularly tetra-substituted versions, holds great significance. Intramolecular or intermolecular ring-forming reactions catalyzed by transition metals have been recognized as typical methods for the construction of 2-pyrone frameworks. Established general procedures are sufficient for the synthesis of di- and trisubstiututed 2-pyrones.[2] In contrast, only a few studies have focused on the synthesis of tetrasubstituted 2-pyrones.[3] Larock reported a palladium-catalyzed intermolecular [2+4] cyclization between internal alkynes and α,β-unsaturated esters. [3a] This reaction system is an efficient methodology to achieve regioselective synthesis of di-, tri-, and tetrasubstituted 2-pyrones containing aryl, alkyl, silyl, and ester groups (Scheme 1A). Miura and Satoh reported a rhodium-catalyzed oxidative coupling of substituted acrylic acids with alkynes, in which only symmetric alkynes were used for tetrasubstituted 2-pyrones (Scheme 1B).[3b] Ryu and Fukuyama accomplished a Ru-catalyzed [3+2+1] cycloaddition of α,β-unsaturated ketones with silylated alkynes and CO toward the synthesis of tetrasubstituted 2-pyrones. Alkynes other than silylacetylenes were not applicable to this three-compornet reaction (Scheme 1C).[3c] The Larock group established a transition-metal-catalyst-free iodolactonization of carbonyl-ene-ynes with I_2. In this case, tetrasubstituted 2-pyrones were synthesized, but the regioselectivity in the cyclization was low (Scheme 1D).[3d] In this context, we envisioned a strategy employing 2-pyrones with a carbon-metal bond (metalated 2-pyrones) after receiving a hint from our developed oxyindation to afford metalated isocoumarins.[6,7] Transformations of the metal-carbon bond selectively gives multi-substituted pyrones.[4] Herein, we describe a novel selective synthetic method for highly substituted 2-pyrones, including tetrasubstituted versions, by using metalated 2-pyrones synthesized via the intramolecular oxyindation carbonyl-ene-yne compounds **1** with InI_3 (Scheme 1E). With this method, it is possible to obtain tetrasubstituted 2-pyrones containing bromine, iodine, and ketone moieties, which have not been prepared by previous methods.

Scheme 1. (A) Reported Work: The Synthesis of Tetrasubstituted 2-Pyrones; (B) This Work: Oxyindation of Carbonyl-ene-yne Compound 1 with InI_3 to Access Di-, Tri- and Tetrasubstituted Metalated 2-Pyrones



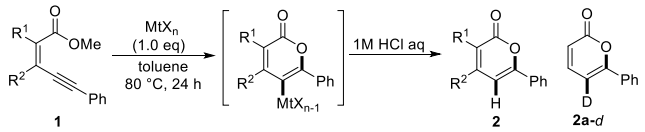
A metalated 2-pyrone is the key compound in our stratey. Almost all reported syntheses of metalated 2-pyrones depend on a halogen-metal exchange of halogenated 2-pyrones. Therefore, the lack of a facile synthetic procedure for di- or trisubstituted halogenated 2-pyrones[5] has led to an underdevelopment in the synthesis of highly substituted metalated 2-pyrones (Scheme 2A).[4] In addition, a synthesis of tetrasubstituted 2-pyrones has not been achieved (Scheme 2B). With the present synthetic method, the establishment of an oxymetalation of fully substituted carbonyl-ene-ynes **1**, which are easily synthesized from iodoacrylate derivatives and acetylene derivatives, achieves the preparation of 5-metalated 2-pyrones **A**, which includes di-, tri-, and tetrasubstituted versions. This is the first report of the synthesis of tetrasubstituted metalated 2-pyrones.

Scheme 2. Retrosynthesis of Metalated 2-Pyrones: (A) Di- and Trisubstituted Metalated 2-Pyrones, (B) Tetrasubstituted Metalated 2-Pyrones



First, various metal salts were surveyed in an intramolecular oxymetalation of carbonyl-ene-yne **1a** (Table 1). Recently, we reported an indium salt-mediated oxymetalation of 2-alkynylbenzoates to synthesize metalated isocoumarins.[6] Therefore, oxyindations of **1a** were conducted using indium halides. A solution of **1a** and InX_3 (X = Cl, Br, and I) in toluene was heated at 80 °C, and then the reaction mixture was

Table 1. Effect of Lewis Acids on the Oxymetalation of 1a, 1b, and 1c[a].



entry	**1** (R^1, R^2)	MtX_n	yield of **2** /%
1	**1a** (H, H)	$InCl_3$	**2a**:0
2	**1a** (H, H)	$InBr_3$	**2a**:88
3[c]	**1a** (H, H)	InI_3	**2a**:100 (**2a**-*d*:82% D)
4	**1a** (H, H)	BBr_3	**2a**:0
5	**1a** (H, H)	$ZnBr_2$	**2a**:14
6	**1a** (H, H)	$AlBr_3$	**2a**:0
7	**1a** (H, H)	$GaBr_3$	**2a**:45
8	**1a** (H, H)	$PdCl_2$	**2a**:0
9	**1a** (H, H)	AuCl	**2a**:6
10	**1a** (H, H)	AgOTf	**2a**:0
11	**1b** (H, Ph)	InI_3	**2b**:92
12[d]	**1b** (H, Ph)	ClBcat	**2b**:0
13	**1c** (Et, Ph)	InI_3	**2c**:95

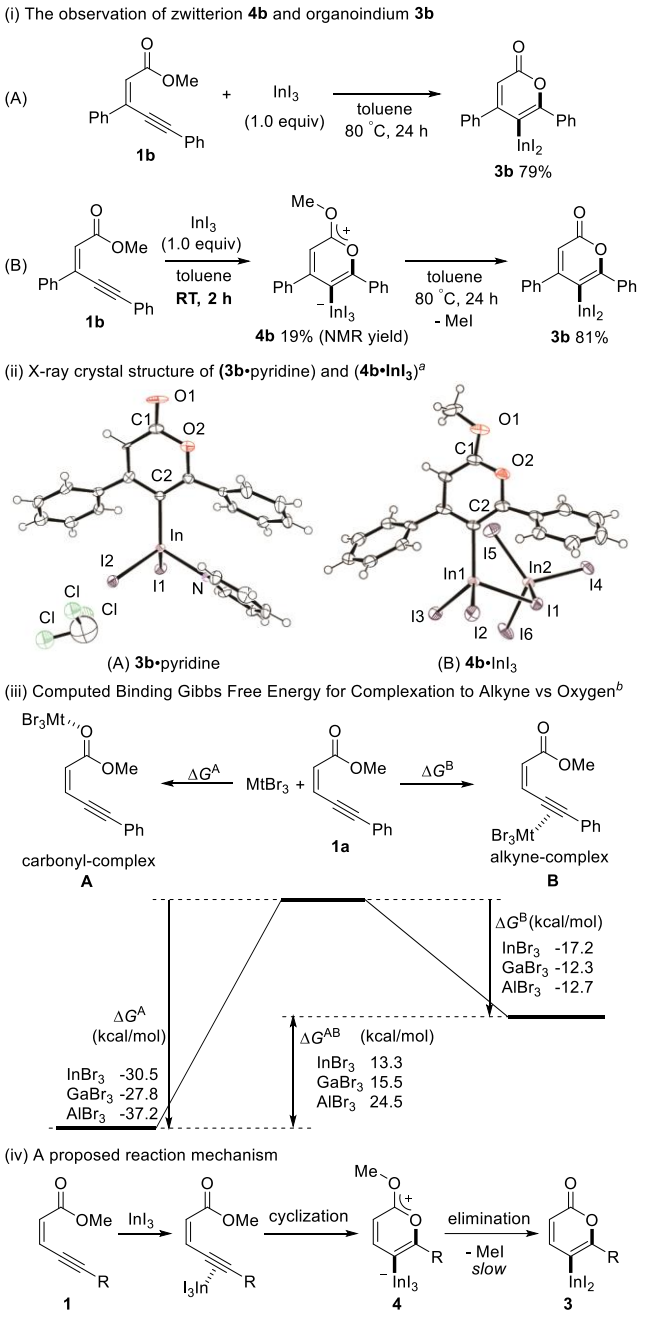
[a]**1** (0.5 mmol), MX_n (0.5 mmol), toluene (1 mL) [b]The yield of **2** was determined by ^1H NMR. [c]The reaction mixture was quenched by 1 M DCl in D_2O (1 mL) and a subsequent addition of H_2O (10 mL).[d]**1b** (0.5 mmol), ClBcat (1.4 eq.), toluene (1 mL) 24 h, 100 °C, and then quenched by pinacol (3 eq.) and NEt_3 (1 mL).

quenched using 1 M HCl aq. The use of $InCl_3$ resulted in no reaction (Table 1, entry 1). On the other hand, $InBr_3$ and InI_3 gave the desired product **2a** in 88 and 100% yields, respectively (Table 1, entries 2 and 3). When the reaction using InI_3 was quenched by DCl in D_2O, product **2a**-*d* deuterated at the 5-position was obtained. Typical Lewis acids such as BBr_3, $ZnBr_2$, $AlBr_3$ and $GaBr_3$ were unsuitable (Table 1, entries 4-7). Subjecting the other alkynophilic Lewis acids such as $PdCl_2$, AuCl, and AgOTf to the present oxymetalation resulted in decomposition or recovery of the starting material **1a** (Table 1, entries 8-10). To our delight, a more substituted carbonyl-ene-yne **1b** or **1c** afforded the highly substituted 2-pyrones **2b** or **2c**, respectively (Table 1, entries 11 and 13). Blum and co-workers reported an oxyboration of carbonyl-ene-yne **1a** using *B*-chlorocatecholborane (ClBcat) to afford borylated 2-pyrone,[8] but the oxyboration system was not applicable to multi-substituted substrates such as **1b** (Table 1, entry 12).

When the reaction of **1b** with InI_3 was performed under the optimal conditions (Table 1, entry 11) without acid-quenching, metalated 2-pyrone **3b** bearing an InI_2 group at the 5-position was obtained as a white solid (Scheme 3(i), (A)) and protonated product **2b** was hardly observed. This result suggested the oxyindation proceeded. The structure of a **3b**·pyridine complex was identified by X-ray crystallographic analysis (Scheme 3(ii),

(A)). (See Supporting Information (SI) for details of the experiments). Oxyindation at room temperature also afforded a white solid (Scheme 3(i), (B)), and, interestingly, it was not **3b.** ^{1}H NMR spectroscopic and X-ray crystallographic analysis clarified the formation as that of zwitterion **4b** (Scheme 3(ii), (B)). An indium atom (In1) of **4b** in the solid state was bound to three iodine atoms (I1, I2, and I3) and a carbon atom (C2), and displayed a

Scheme 3. Mechanistic Studies and Proposed Mechanism



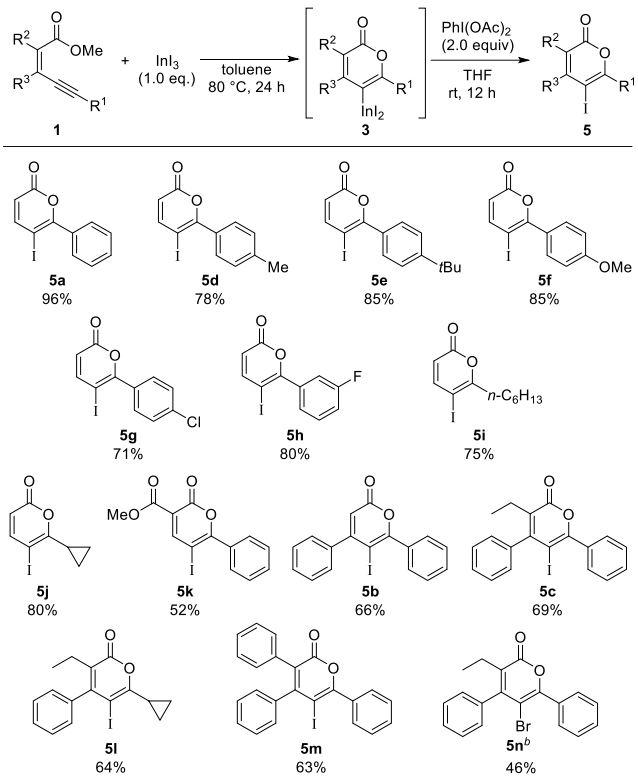
[a]The thermal ellipsoids shown at 50% probability. [b]B3LYP/6-31+G(d,p) for H, C, DGDZVP for Al, Ga, In and Br.

distorted tetrahedral geometry. One of the iodine atoms on In1 coordinated to InI_3 in a crystal structure. The bond lengths of the two carbon-oxygen bonds (C1-O1 = 1.300(10) Å, C1-O2 = 1.327(11) Å) in **4b** showed values that fell between that of a typical C-O double bond (1.233 Å) and a single bond (1.401 Å) of the **3b**·pyridine complex. Thus, the positive charge was delocalized in the ester moiety.[9] Subjecting zwitterion **4b** to heating conditions gave metalated 2-pyrone **3b** via the elimination of MeI.

To gain insight into the reaction mechanism, the coordination mode of carbonyl-ene-yne **1a** to a Lewis acid was investigated by DFT calculation (Scheme 3(iii)). In the coordination of either the alkyne moiety (**B**) or the carbonyl oxygen (**A**) in **1a** to $InBr_3$, the Gibbs energy changes were -17.2 kcal mol^{-1} and -30.5 kcal mol^{-1}, respectively. Therefore, both complexations were thermodynamically stable, but carbonyl coordination was more favorable. The energy gap between carbonyl complex **A** and alkyne complex **B** of $AlBr_3$ was very large ($\Delta G^{A\ to\ B}$ = 24.5 kcal mol^{-1}), but $InBr_3$ showed a relatively small value ($\Delta G^{A\ to\ B}$ = 13.3 kcal mol^{-1}). Consequently, $InBr_3$ was more susceptible to the subsequent alkyne coordination compared with $AlBr_3$ after dissociation of the carbonyl coordination (See SI).

A possible reaction mechanism is depicted in Scheme 3(iv). First, InI_3 acts as an efficient π-electrophilic Lewis acid for the activation of the alkyne moiety of carbonyl-ene-yne **1**[7], and then the intramolecular nucleophilic attack of a carbonyl oxygen atom occurs to generate zwitterion **4**. Then, the elimination of MeI gives metalated 2-pyrone **3**. The elimination is a rate-determinig step.

Scheme 4. Sequential Oxymetalation/halogenation of Various Types of Carbonyl-ene-yne[a]

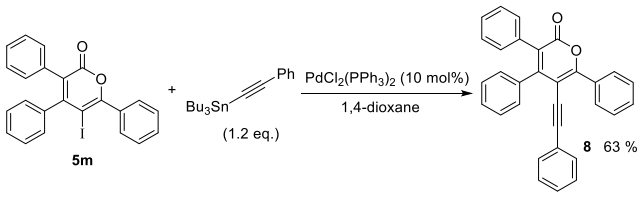


[a]First step: **1** (0.5 mmol), InI_3 (0.5 mmol), toluene (1 mL), 80 °C, 24 h. Second step: $PhI(OAc)_2$ (1.0 mmol), THF (2 mL), rt, 12 h. The isolated yields are shown. [b]$InBr_3$ was used instead of InI_3.

Various types of carbonyl-ene-ynes **1** were applied to the synthesis of 2-pyrone derivatives via the present oxyindation (Scheme 4). Oxyindation of **1a** using InI_3 followed by oxidation of **3a** with $PhI(OAc)_2$ was carried out in a one-pot procedure to

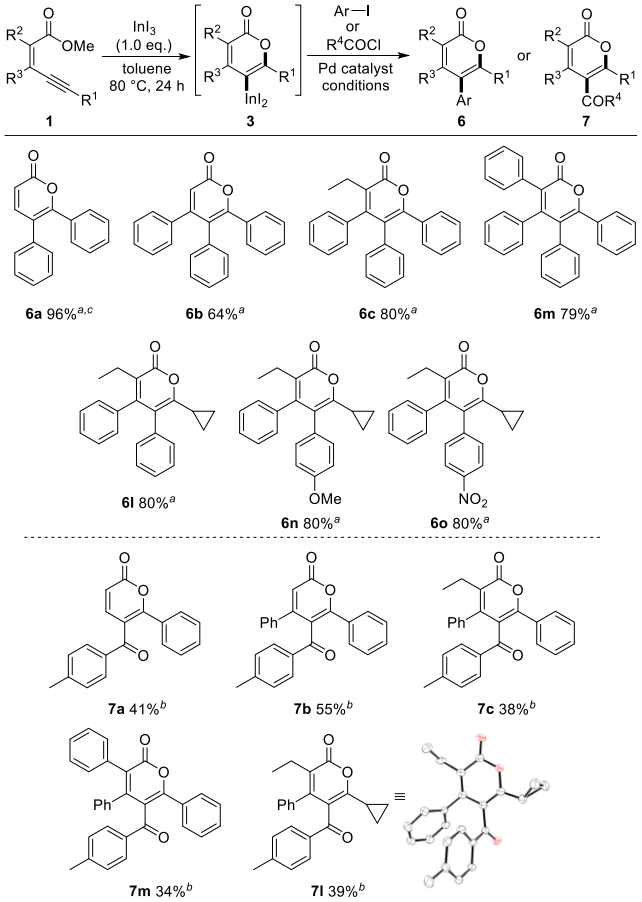
afford 5-iodo-2-pyrone **5a** in a 96% yield.[6] Substrates **1** with substituents such as Me, *tert*-Bu, MeO, Cl, and F groups on the aromatic ring bindng to an alkyne moiety gave the target products **5d**, **5e**, **5f**, **5g**, and **5h**, respectively. The substrates bearing aliphatic alkyne moieties **1i** and **1j** also worked well. Dicarbonyl-ene-yne compound **1k** provided the desired trisubstituted 2-pyrone **5k** in a moderate yield. Subjecting **1b** to halogenation yielded 5-iodo-4,6-diphenyl-2-pyrone **5b**. α,β-Disubstituted substrate **1c** was surveyed in the sequential oxyindation/halogenation process to afford tetrasubstituted 2-pyrone **5c**. Gratifyingly, 2-pyrone **5l** bearing four different substituents on the ring was produced by the reaction using **1l**. The oxyindation of **1m** proceeded in 6-*endo* cyclization to exclusively give 2-pyrone **5m** in contrast to Larock's iodocyclization of **1m** with ICl giving a 5-membered oxacycle as a major product.[3d] Therefore, this result shows our developed method is more effective for the synthesis of multisubstituted 2-pyrones. To our delight, subjecting $InBr_3$ instead of InI_3 to the oxyindation reaction provided fully substituted brominated 2-pyrones **5n** in a moderate yield. Therefore, our approach accomplished the synthesis of tetrasubstituted brominated 2-pyrones as well as iodinated ones. Iodinated 2-pyrone **5m** was used for further transformations with Migita-Kosugi-Stille coupling to give tetra-carbon-substitued 2-pyrones (Scheme 5).[10]

Scheme 5. Synthesis of Tetrasubstituted 2-Pyrones Using Stille Coupling



Palladium-catalyzed, cross-coupling syntheses of metalated 2-pyrones **3** with aryl iodides or acid chlorides were performed (Scheme 6).[11] After the oxyindation of **1a** with InI_3, iodobenzene, $Pd_2(dba)_3$ catalyst, NaOMe, and DMF were added to the reaction mixture involving InI_2-substituted 2-pyrone **3a**. The Pd-catalyzed coupling reaction between **3a** and iodobenzene smoothly proceeded to produce 5,6-diphenyl-2-pyrone **6a** in a 96% yield. The trisubstituted metalated 2-pyrone derived from **1b** also underwent coupling to afford 4,5,6-triphenyl-2*H*-pyran-2-one **6b**. Various types of tetrasubstituted metalated 2-pyrones derived from **1c**, and **1l-1o** were employed to produce tetra-carbon-substitued 2-pyrones **6c** and **6l-6o**, respectively.

Scheme 6. One-pot Formation of Highly Substituted 2-Pyrones by Palladium-catalyzed Cross Coupling



[a]Oxyindation conditions: **1** (0.5 mmol), InI_3 (0.5 mmol), toluene (1 mL), 80 °C, 24 h. Second step conditions: Pd_2dba_3 (0.025 mmol), NaOMe (1.0 mmol), ArI (Ar = 0.35 mmol), DMF (2.5 mL), 110 °C, 24 h. [b]Oxyindation conditions: **1** (0.5 mmol), InI_3 (0.5 mmol), toluene (1 mL), 80 °C, 24 h. Second step conditions: Pd_2dba_3 (0.025 mmol), R^4COCl (1.0 mmol), 1,3-dimethyl-2-imidazolidinone (2.5 mL), 80 °C, 24 h. The isolated yields are shown. [c]The cross coupling was run at 80 °C and KCl was used instead of NaOMe.

Both electron-rich and -poor aryl iodides worked as feasible coupling partners to afford 2-pyrones **6n** and **6o** bearing four different carbon substitutents. Furthermore, the Pd-catalyzed cross coupling of InI_2-substituted 2-pyrones **3** with an acid chloride also proceeded under condition B to give multi-functionalized 2-pyrones **7a**-**7c**, **7l**, and **7m**. The structure of 2-pyrone **7l** was confirmed by X-ray crystallographic analysis. The present oxyindation/cross-coupling sequential process established a modular synthesis of multi-functionalized 2-pyrones.

Tetrasubstituted 2-pyrones **6m** and **7m** had no fluorescence properties in the solution, but an aggregation-induced emission (AIE) was observed in the solid state. Triphenylated 2-pyrone **2c** is known to possess AIE properties and exhibit a higher quantum yield than Alq_3, which is generally used in electroluminescence devices.[12] However, tetrasubstituted 2-pyrones have not been investigated in detail because relatively little is known about a facile synthetic method. We expected to improve the light emission properties by installing a substituent at the 5-position, and thus **6m** and **7m** exhibited greater quantum yields than **2c** (Figure 1A). This result can be ascribed to the fact that the installation of either a phenyl- or an aloyl group changed the intermolecular interactions in the solid state. Figure 1B shows the molecular packing diagrams of compound

6m, **7m** and **2c**[12]. In the crystal structure of these compounds, there are C-H···π interactions and/or hydrogen bonds among molecules. These interactions limited the molecular motions, giving rise to the emission enhancement in the solid state. A quenching effect is caused by the stacking interactions between 2-pyrone structures in **6m** and **2c**, but not in **7m**. Inhibition of the stacking by the steric hindrance of benzoyl group at the 5-position achieved the strongest light emission of **7m**. The distance between the 2-pyrone skeleton of **6m** is longer than that of **2c** due to the Ph group at the 5-position, so **6m** shows stronger light emission than **2c**.

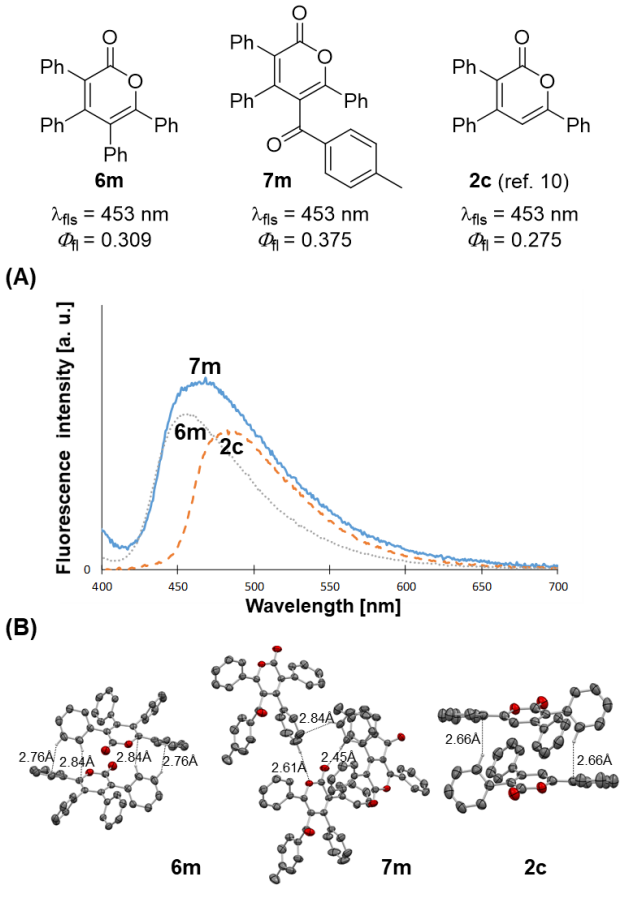


Figure 1. (A) Fluorescence spectra of **6m** and **7m** and **2c** in the solid state upon excitation at 365 nm. The fluorescence intensities of their compounds were calculated based on quantum yield. (B) Packing mode and multiple interactions of compound **6m** and **7m** and **2c**.

In conclusion, we developed a process fo the oxyindation of carbonyl-ene-yne compounds to give 2-pyrones bearing a carbon-indium bond at the 5-position. Metalated 2-pyrones **3** and zwitterion intermediate **4** were fully characterized by X-ray crystallographic analysis and NMR spectroscopy. These results supported a reaction mechanism that is composed of two steps: an indium trihalide-mediated cyclic oxymetalation and the sequential elimination of MeI from **4**. The bromination or iodination of **3** provided 5-halo-2-pyrones **5** which are quite useful as synthetic precursors to multi-substituted 2-pyrones. We developed a general synthesis method for highly substituted 2-pyrones via a cross-coupling reaction using **3**. The synthesized tetrasubstituted 2-pyrones showed aggregation-induced emission (AIE). The oxyindation chemistry described herein could contribute to a modular synthesis of multi-functionalized 2-pyrones.

EXPERIMENTAL SECTION

General Information.

NMR spectra were recorded on a JEOL JNM-400 (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR) spectrometer. Chemical shifts were reported in ppm on the δ scale relative to tetramethylsilane (δ = 0 for ^{1}H NMR) and residual $CHCl_3$ (δ = 77.0 for ^{13}C NMR) as an internal reference. New compounds were characterized by ^{1}H, ^{13}C, ^{13}C off-resonance techniques, COSY, HMQC, and HMBC. Infrared (IR) spectra were recorded on a JASCO FT/IR-6200 Fourier transform infrared spectrophotometer. Column chromatographies were performed with silica gel. Purification by recycle HPLC was performed using the SHIMADZU recycle HPLC system (SPD-20A, RID-10A, DGU-20A, LC-6AD, and FCV-20H2) from the Japan Analytical Industry Co. (NEXT recycling preparative HPLC). High-resolution mass spectra were obtained using a magnetic sector type mass spectrometer. Reactions were carried out in dry solvents under a nitrogen atmosphere, unless otherwise stated. Reagents were purchased from Aldrich or Tokyo Chemical Industry Co., Ltd. (TCI), FUJIFILM Wako Pure Chemical Corporation and used either after purification by distillation or without purification for solid substrates. X-ray diffraction analysis was carried out via Rigaku XtaLAB Synergy with a Hypix-6000HE. Steady-state emission spectra were recorded on a HAMAMATSU C11347-01 spectrometer with an integrating sphere.

Materials

Dehydrated solvents, such as toluene, THF, 1,4-dioxane, DMF, and DMI were purchased from FUJIFILM Wako Pure Chemical Corporation and used as obtained. $PhI(OAc)_2$ was purchased from Tokyo Chemical Industry Co., Ltd., and used without further purification. Carbonyl-ene-yne compounds, **1a**, **1b**, **1d-1k**, and **1m** were synthesized by reported procedures, and the spectral data for these compounds are provided in the Supporting Information. Carbonyl-ene-ynes **1c** and **1l** are new compounds, and the synthetic methods and spectral data for these compounds are shown below. InI_3 (Indium Triiodide 99.99%) was purchased from Kojundo Chemical Laboratory. All other reagents were commercially available.

General Procedure for the synthesis of carbonyl-ene-yne 1a[3d], 1b[13], 1d[14], 1e[14], 1f[14], 1g[14], 1h[14], 1i[15], 1j[8], 1k[16], and 1m.[3d]

To a solution of methyl (*Z*)-3-iodoacrylate (5 mmol, 1 equiv) in Et_3N (20 mL) were added $PdCl_2(PPh_3)_2$ (0.1 mmol, 0.02 equiv), CuI (0.1 mmol, 0.02 equiv) and acetylene (6.5 mmol, 1.3 equiv). The resulting mixture was heated under nitrogen atmosphere at 55 °C by oil bath. The reaction was monitored by TLC to establish completion. When the reaction was complete, the mixture was quenched by NH_4Cl aq (30 mL). The solution was extracted by Et_2O (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography. Product-containing fractions were combined and concentrated in vacuo to afford **1**.

methyl (Z)-2-ethyl-3,5-diphenylpent-2-en-4-ynoate (1c)

The 3-Phenyl-2-propyn-1-ol (20.2 mmol, 2.67 g), dry Et_2O (30 mL), and CuI (2.35 mmol, 0.448 g) were added to a three-necked flask. To the cooled, stirred mixture at 0 °C was added a 3.0M EtMgBr in diethyl ether (17 mL). Upon complete addition of the Grignard reagent, the mixture was allowed to warm up to room temperature and stirred for 20 h. The dark green mixture was then cooled to 0 °C and I_2 (22.2 mmol, 5.63 g) was added. After warming up to room temperature and stirring at room temperature for 1 h, the reaction mixture was cooled to 0 °C and quenched with sat. NH_4Cl aq (20 mL). The organic layer was separated and the aqueous layer was extracted with ether (3 x 50 mL). The combined ether layers were dried over $MgSO_4$, filtered, and concen-

trated in vacuo and then the crude (*Z*)-2-{iodo(phenyl)methylene}butan-1-ol (12.3 mmol, 3.56 g) was obtained. The crude (*Z*)-2-{iodo(phenyl)methylene}butan-1-ol was used without further purification.

To a solution of (*Z*)-2-{iodo(phenyl)methylene}butan-1-ol (12.3 mmol, 3.56 g), CH_2Cl_2 (123 mL), and MnO_2 (247 mmol, 21.8 g) were added to a three-necked flask. The reaction mixture was stirred at room temperature for 2 h. The black precipitate was filtered off and the filtrate was concentrated in vacuo and then the crude (*Z*)-2-{iodo(phenyl)methylene}butanal (11.7 mmol, 3.34 g) was obtained. The crude (*Z*)-2-{iodo(phenyl)methylene}butanal was used without further purification.

The (*Z*)-2-{iodo(phenyl)methylene}butanal (11.7 mmol, 3.34 g), MeOH (150 mL), NaCN (47.7 mmol, 2.34 g), AcOH (17.5 mmol, 1.05 g), and MnO_2 (238 mmol, 20.7 g) were added to a three-necked flask. The mixture was stirred at room temperature for 12 h under N_2 atm. The black precipitate was filtered off and the filtrate was concentrated under vacuo. The resulting residue was partitioned between 80 mL of H_2O and 80 mL of Et_2O. The organic layer was separated and the aqueous layer was extracted with ether (3 x 50 mL). The combined ether layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 5:95, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the methyl (*Z*)-2-{iodo(phenyl)methylene}butanoate (**9**) as a yellow oil (3.45 g, 54%).

IR: (neat) 1733 (C=O) cm^{-1}, ^1H NMR: (400 MHz, $CDCl_3$) 7.38-7.32 (m, 2H), 7.30-7.24 (m, 3H), 3.88 (s, 3H), 2.25 (q, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 169.6 (s), 144.7 (s), 142.5 (s), 128.3 (d), 127.7 (d), 96.8 (s), 52.3 (q), 26.2 (t), 13.1 (q), HRMS: (EI, 70 eV) Calculated ($C_{12}H_{13}O_2I$) 315.9960 (M^+) Found 315.9962

To a solution of methyl (*Z*)-2-{iodo(phenyl)methylene}butanoate (5.43 mmol, 1.72 g) in Et_3N (20 mL) were added $PdCl_2(PPh_3)_2$ (0.114 mmol, 0.0800 g), CuI (0.105 mmol, 0.0200 g) and phenylacetylene (6.51 mmol, 0.665 g). The resulting mixture was heated under nitrogen atmosphere at 55 °C. The reaction was monitored by TLC to establish completion. When the reaction was complete, the mixture was quenched by NH_4Cl aq (30 mL). The solution was extracted by Et_2O (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 nm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a yellow oil (1.24 g, 78%). IR: (neat) 2196 (C≡C), 1721 (C=O) cm^{-1}, ^1H NMR: (400 MHz, $CDCl_3$) 7.43-7.26 (m, 10H), 3.90 (s, 3H), 2.40 (q, *J* = 7.4 Hz, 2H), 1.04 (t, *J* = 7.4 Hz, 3H), ^{13}C NMR: (100 MHz, $CDCl_3$) 168.8 (s), 141.4 (s), 138.2 (s), 131.6 (d), 128.5 (d), 128.4 (d), 128.3 (d), 128.2 (d), 128.0 (s), 128.0 (s), 123.1 (s), 96.8 (s), 89.1 (s), 51.9 (q), 24.0 (t), 13.4 (q), HRMS: (EI, 70 eV) Calculated ($C_{20}H_{18}O_2$) 290.1307 (M^+) Found 290.1306

methyl (Z)-5-cyclopropyl-2-ethyl-3-phenylpent-2-en-4-ynoate (1l)

To a solution of methyl (*Z*)-2-{iodo(phenyl)methylene}butanoate (**9**) (2.91 mmol, 0.921 g) (The experimental procedure and characterization of this compound (**9**) were described in experimental procedure of methyl (*Z*)-2-ethyl-3,5-diphenylpent-2-en-4-ynoate (**1c**)) in Et_3N (12 mL) were added $PdCl_2(PPh_3)_2$ (0.0329 mmol, 0.0231 g), CuI (0.0735 mmol, 0.0140 g) and phenylacetylene (3.49 mmol, 0.230 g). The resulting mixture was heated under an N_2 atmosphere at 55 °C. The reaction was monitored by TLC to establish completion. When the reaction was complete, the mixture was quenched by NH_4Cl aq (10 mL). The solution was extracted by Et_2O (3 x 10 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 nm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a yellow oil (0.443 g, 60%). IR: (KBr) 2212 (C≡C), 1722 (C=O) cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) 7.38-7.27 (m, 5H), 3.84 (s, 3H), 2.30 (q, *J* = 7.5 Hz, 2H), 1.43-1.36 (m, 1H), 0.97 (t, *J* = 7.5 Hz, 3H), 0.86-0.82 (m, 2H), 0.76-0.72 (m, 2H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 169.0 (s), 139.9 (s), 138.8 (s), 128.7 (s), 128.2 (d), 128.1 (d), 127.8 (d), 102.5 (s), 75.8 (s), 51.7 (q), 23.7 (t), 13.5 (q), 9.1 (t), 0.7 (d), HRMS: (CI, 70 eV) Calculated ($C_{17}H_{19}O_2$): 255.1385 $[M+H]^+$Found 255.1387

General Procedure for oxymetalation of methyl (Z)-5-phenylpent-2-en-4-ynoate followed by protonolysis (Table 1)

In a glove box filled for nitrogen, to a sealed vial, InI_3 (0.5 mmol, 1 equiv), toluene (1 mL) and methyl (*Z*)-5-phenylpent-2-en-4-ynoate **1a** (0.5 mmol, 1 equiv) were added. The solution was stirred at 80 °C for 24 h in a heated aluminum block and the reaction mixture was quenched by 1 M HCl aq (1 mL). After addition of water (10 mL), the solution was extracted with CH_2Cl_2 (5 mL x 3). The collected organic layer was dried over $MgSO_4$. The solvent was evaporated and the yield of 6-phenyl-2*H*-pyran-2-one **2** was determined by ^1H NMR using internal standards (1,1,2,2-tetrachloroethane)

Oxymetalation of a carbonyl-ene-yne using InI_3 (1.0 mmol Scale)

To a 10 mL vial filled with InI_3 (0.999 mmol, 0.495 g) in toluene (2 mL) was added methyl (*Z*)-5-phenylpent-2-en-4-ynoate **1a** (1.01mmol, 0.187 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h in a heated aluminum block and the reaction mixture was quenched by water (10 mL) and 1 M HCl aq (2 mL). The solution was extracted by dichloromethane (3 x 10 mL) and the combined organic solution was dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel). Fractions containing the desired product were combines and concentrated in vacuo to give the product **2a** as a pale yellow solid (0.115 g, 67%). (The experimental procedure at 0.5 mmol scale and characterization of **2a** were shown below)

Observation of Zwitterion Intermediate 4b by ^1H NMR spectroscopy and X-ray Crystallographic Analysis (Scheme 3)

Oxyindation of methyl (*Z*)-3,5-diphenylpent-2-en-4-ynoate **1b** (0.501 mmol, 0.131 g) with InI_3 (0.505 mmol, 0.250 g) was carried out in toluene (1 mL) at room temperature for 2 h to give a white solid, and then the toluene was evaporated and the residual solid was dissolved in $CDCl_3$. ^1H NMR spectroscopy measurements showed that the solid was mixture of two compounds, which were neither the metalated pyrone **3b** nor the starting material **1b**. Recrystallization of the mixture from $CHCl_3$ and heptane provided a crystal and X-ray crystallographic analysis revealed that the one of the two components was the zwitterion intermediate **4b** (CCDC 1910563).

Isolation of Organoindium Compounds 3b and 3b·pyridine (Scheme 3-i-A and Scheme 3-ii-A)

All operations were carried out in a nitrogen-filled glove box. To a 10 mL vial filled with InI_3 (0.502 mmol, 0.249 g) in toluene (1 mL) was added methyl (*Z*)-3,5-diphenylpent-2-en-4-ynoate (0.493 mmol, 0.129 g). The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, the solvent was removed by decantation to obtain a white solid and the solid was washed by $CHCl_3$ (3 mL x 6). The residue was dried under vacuum to give the product **3b** as a white solid (0.297 g, 81%). **3b** was added to pyridine (0.399 mmol, 0.0316 g) and recrystallized from $CHCl_3$ and heptane to give a single crystal of **3b·pyridine**. The structure was determined by X-ray crystallographic analysis (CCDC 1910738). Characterization by NMR study was also carried out. ^1H NMR: (400 MHz, $CDCl_3$) 8.27 (d, J = 4.8 Hz, 2H, 15-H x 2), 7.77-7.72 (m, 3H), 7.54-7.48 (m, 2H, 8-H x 2), 7.36-7.34 (m, 6H), 7.28-7.26 (m, 2H, 16-H x 2), 6.35 (s, 1H, 3-H), ^{13}C NMR: (100 MHz, $CDCl_3$) 167.2 (s, C-6), 162.7 (s), 162.6 (s), 148.0 (d, C-15), 141.1 (s, C-7), 139.1 (d, C-17), 136.0 (s, C-11), 131.2 (d), 130.1 (d), 129.6 (d), 129.09 (d), 129.06 (d), 127.7 (d, C-8), 124.9 (d, C-16), 118.9 (s, C-5), 111.8 (d, C-3).

General Procedure for oxymetalation of carbonyl-ene-yne compounds followed by halogenation (Scheme 4)

In a glove box filled with nitrogen, to a sealed vial, InI_3 (0.5 mmol, 1 equiv), toluene (1 mL) and carbonyl-ene-yne compound **1** (0.5 mmol, 1 equiv) were added. After stirring at 80 °C for 24 h in a heated aluminum block, the suspension was diluted by THF (2.5 mL) and $PhI(OAc)_2$ (1.0 mmol, 1 equiv) was added to the solution in the glove box. The reaction mixture was stirred at rt for 24 h and then quenched by water (5 mL) and 1 M HCl aq (1 mL). The solution was extracted with CH_2Cl_2 (30 mL x 2) and the collected organic layer was dried over $MgSO_4$. The solvent was evaporated and the residue was purified by column chromatography.

General Procedure for oxymetalation of carbonyl-ene-yne compounds followed by palladium catalyzed cross coupling with iodoarenes (Scheme 6, Conditions A)

In a glove box filled with nitrogen, to a sealed vial, InI_3 (0.5 mmol, 1.4 equiv), toluene (1 mL) and carbonyl-ene-yne compound **1** (0.5 mmol, 1.4 equiv) were added, and the solution was stirred at 80 °C for 24 h in a heated aluminum block. $Pd_2(dba)_3$ (0.025 mmol, 0.071 equiv), a base such as KCl and NaOMe (2.9 equiv or none), ArI (0.35 mmol, 1 equiv) and DMF (2.5 mL) was added to the reaction mixture in the glove box and the mixture was stirred at 110 °C for 24 h. The reaction mixture was quenched by water (5 mL) and 1 M HCl aq (1 mL). The solution was extracted with dichloromethane (3 x 30 mL) and the collected organic layer was dried over $MgSO_4$. The solvent was evaporated and the residue was purified by column chromatography.

General Procedure for oxymetalation of carbonyl-ene-yne compounds followed by palladium catalyzed cross coupling with acid chlorides (Scheme 6, Conditions B)

In a glove box filled with nitrogen, to a sealed vial, InI_3 (0.5 mmol, 1 equiv), toluene (1 mL) and carbonyl-ene-yne compound **1** (0.5 mmol, 1 equiv) were added, and the solution was stirred at 80 °C for 24 h in a heated aluminum block. $Pd_2(dba)_3$ (0.025 mmol, 0.05 equiv), 4-methylbenzoyl chloride (1.0 mmol, 2 equiv) and 1,3-dimethyl-2-imidazolidinone (2.5 mL) was added to the reaction mixture in the glove box and the mixture was stirred at 80 °C for 24 h in a heated aluminum block. The reaction mixture was quenched by water (5 mL) and 1 M HCl aq (1 mL). The solution was extracted with dichloromethane (3 x 30 mL) and the collected organic layer was dried over $MgSO_4$. The solvent was evaporated and the residue was purified by column chromatography.

6-phenyl-2H-pyran-2-one (2a)

To a 10 mL vial filled with InI_3 (0.503 mmol, 0.249 g) in toluene (1 mL) was added methyl (*Z*)-5-phenylpent-2-en-4-ynoate (0.500mmol, 0.0931 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h and the reaction mixture was quenched by water (5 mL), 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and the combined organic solution was dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel) Product-containing fractions were combines and concentrated in vacuo to give the product as a yellow solid (0.0797 g, 93%). The NMR date was agreement with the literature[17].

4,6-diphenyl-2H-pyran-2-one (2b)

To a 10 mL vial filled with InI_3 (0.503 mmol, 0.249 g) in toluene (1 mL) was added methyl (*Z*)-3,5-diphenylpent-2-en-4-ynoate (0.500mmol, 0.131 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h and the reaction mixture was quenched by water (5 mL), 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and the combined organic solution was dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel) Product-containing fractions were combines and concentrated in vacuo to give the product as a white solid (0.100 g, 81%). The NMR date was agreement with the literature[2a].

3-ethyl-4,6-diphenyl-2H-pyran-2-one (2c)

To a 10 mL vial filled with InI_3 (0.504 mmol, 0.248 g) in toluene (1 mL) was added methyl (*Z*)-2-ethyl-3,5-diphenylpent-2-en-4-ynoate (0.502 mmol, 0.146 g) in a nitrogen-filled glove box. The vial was sealed and the mixture was stirred at 80 °C for 24 h and the mixture was quenched by water (3 mL) and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and combined organic solution was dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a white solid (0.126 g, 90%). IR: (KBr) 1716 (C=O) cm^{-1}, mp: 59-61 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.82 (d, *J* = 5.1 Hz, 2H), 7.51-7.41 (m, 6H), 7.35 (d, *J* = 7.4 Hz, 2H), 6.62 (s, 1H), 2.50 (q, *J* = 7.4 Hz, 2H), 1.16 (t, *J* = 7.4 Hz, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 163.2 (s), 156.3 (s), 152.2 (s), 137.9 (s), 131.4 (s), 130.2 (d), 128.7 (d), 128.6 (d), 127.4 (d), 125.5 (s), 125.2 (d), 104.6 (d), 21.2 (t), 13.3 (q), HRMS:(EI, 70 eV) Calculated ($C_{19}H_{16}O_2$) 276.1150 (M^+) Found 276.1151.

5-iodo-6-phenyl-2H-pyran-2-one (5a)

To a 10 mL vial filled with InI_3 (0.503 mmol, 0.249 g) in toluene (1 mL) was added methyl (*Z*)-5-phenylpent-2-en-4-ynoate (0.500 mmol, 0.931 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.331 g, 1.03 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (5 mL), 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and the combined organic solution was washed by sat. $Na_2S_2O_3$ aq. (1 x 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel) Product-containing fractions were combines and concentrated in vacuo to give the product as a yellow solid (0.143 g, 96%). The NMR date was agreement with the literature[3d].

5-iodo-4,6-diphenyl-2H-pyran-2-one (5b)

To a 10 mL vial filled with InI_3 (0.500 mmol, 0.248 g) in toluene (1 mL) was added methyl (*Z*)-5-phenylpent-2-en-4-ynoate (0.500 mmol, 0.931 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.331 g, 1.03 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (5 mL), 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and the combined organic solution was washed by sat. $Na_2S_2O_3$ aq. (1 x 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel) Product-containing fractions were combines and concentrated in vacuo to give the product as a yellow solid (0.123 g, 66%). The NMR date was agreement with the literature[16].

3-ethyl-5-iodo-4,6-diphenyl-2H-pyran-2-one (5c)

To a 10 mL vial filled with InI_3 (0.518 mmol, 0.257 g) in toluene (1 mL) was added methyl (*Z*)-2-ethyl-3,5-diphenylpent-2-en-4-ynoate (0.502 mmol, 0.146 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.195 g, 0.604 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (3 mL) and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and combined organic solution was washed by sat. $Na_2S_2O_3$ aq (1 x 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a yellow solid (0.139 g, 69%). IR: (KBr) 1714 (C=O) cm^{-1}, mp: 143-144 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.71-7.69 (m, 2H), 7.50-7.46 (m,

6H), 7.16 (d, *J* = 6.8 Hz, 2H), 2.35 (q, *J* = 7.4 Hz, 2H), 1.04 (t, *J* = 7.4 Hz, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 162.1 (s), 157.9 (s), 155.7 (s), 140.8 (s), 134.9 (s), 130.3 (d), 129.6 (d), 128.6 (d), 128.5 (d), 128.0 (d), 127.5 (d), 127.3 (s), 77.5 (s), 23.4 (t), 13.1 (q), HRMS: (EI, 70 eV) Calculated ($C_{19}H_{15}O_2I$) 402.0122 (M^+) Found 402.0117.

5-iodo-6-(p-tolyl)-2H-pyran-2-one (5d)

To a 10 mL vial filled with InI_3 (0.503 mmol, 0.249 g) in toluene (1 mL) was added methyl (*Z*)-5-(*p*-tolyl)pent-2-en-4-ynoate (0.510 mmol, 0.102 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.324 g, 1.01 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (5 mL), 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and the combined organic solution was washed by sat. $Na_2S_2O_3$ aq. (1 x 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel) Product-containing fractions were combines and concentrated in vacuo to give the product as a yellow solid (0.131 g, 84%). IR: (KBr) 1715 (C=O) cm^{-1}, mp: 83-84 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.68-7.61 (m, 3H), 7.27 (d, *J* = 7.7 Hz, 2H), 6.09 (d, *J* = 9.7 Hz, 1H), 2.42 (s, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 161.05 (s), 160.98 (s), 153.2 (d), 141.4 (s), 130.5 (s), 129.2 (d), 128.9 (d), 115.2 (d), 66.2 (s), 21.6 (q), HRMS : (EI, 70 eV) Calculated ($C_{12}H_9O_2I$) 311.9647 (M^+) Found 311.9649.

6-{4-(tert-butyl)phenyl}-5-iodo-2H-pyran-2-one (5e)

To a 10 mL vial filled with InI_3 (0.503 mmol, 0.249 g) in toluene (1 mL) was added methyl (*Z*)-5-{4-(*tert*-butyl)phenyl}pent-2-en-4-ynoate (0.499 mmol, 0.121 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.331 g, 1.03 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (5 mL), 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and the combined organic solution was washed by sat. $Na_2S_2O_3$ aq (1 x 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethel acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel) Product-containing fractions were combines and concentrated in vacuo to give the product as a yellow solid (0.150 g, 84%). IR: (KBr) 1731 (C=O) cm^{-1},mp: 107-109 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.71 (d, *J* = 8.7 Hz, 2H), 7.63 (d, *J* = 9.2 Hz, 1H), 7.47 (d, *J* = 8.7 Hz, 2H), 6.08 (d, *J* = 9.2 Hz, 1H), 1.35 (s, 9H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 160.92 (s), 160.88 (s), 154.3 (s), 153.2 (d), 130.4 (s), 129.0 (d), 125.1 (d), 115.1 (d), 66.0 (s), 35.0 (s), 31.1 (q), HRMS : (EI, 70 eV) Calculated ($C_{15}H_{15}O_2I$) 354.0117 (M^+) Found 354.0111.

5-iodo-6-(4-methoxyphenyl)-2H-pyran-2-one (5f)

To a 10 mL vial filled with InI_3 (0.500 mmol, 0.248 g) in toluene (1 mL) was added methyl (*Z*)-5-(4-methoxyphenyl)pent-2-en-4-ynoate (0.513 mmol, 0.111 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.330 g, 1.02 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (5 mL) and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and the combined organic solution was washed by sat. $Na_2S_2O_3$ aq (25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a yellow solid (0.139 g, 85%). IR: (KBr) 1748 (C=O) cm^{-1}, mp: 117-118 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.74 (d, *J* = 8.7 Hz, 2H), 7.62 (d, *J* = 9.7 Hz, 1H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.05 (d, *J* = 9.7 Hz, 1H), 3.85 (s, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 161.3 (s), 160.9 (s), 160.5 (s), 153.3 (d), 130.9 (d), 125.4 (s), 114.5 (d), 113.4 (d), 65.5 (s), 55.3 (q), HRMS : (EI, 70 eV) Calculated ($C_{12}H_9O_3I$) 327.9596 (M^+) Found 327.9601.

6-(4-chlorophenyl)-5-iodo-2H-pyran-2-one (5g)

To a 10 mL vial filled with InI_3 (0.500 mmol, 0.248 g) in toluene (1 mL) was added methyl (*Z*)-5-(4-chlorophenyl)pent-2-en-4-ynoate (0.499 mmol, 0.110 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.324 g, 1.01 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (5 mL) and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and the combined organic solution was washed by sat. $Na_2S_2O_3$ aq (25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel) Product-containing fractions were combined and concentrated in vacuo to give the product as a yellow solid (0.115 g, 71%). IR: (KBr) 1715 (C=O) cm^{-1}, mp: 129-130 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.70 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 9.7 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 2H), 6.12 (d, *J* = 9.7 Hz, 1H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 160.3 (s), 159.4 (s), 152.8 (d), 136.8 (s), 131.6 (s), 130.5 (d), 128.4 (d), 115.6 (d), 66.8 (s), HRMS: (EI, 70 eV) Calculated ($C_{11}H_6ClO_2I$) 331.9101 (M^+) Found 331.9098.

6-(3-fluorophenyl)-5-iodo-2H-pyran-2-one (5h)

To a 10 mL vial filled with InI_3 (0.507 mmol, 0.251 g) in toluene (1 mL) was added methyl (*Z*)-5-(3-fluorophenyl)pent-2-en-4-ynoate (0.509 mmol, 0.104 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.195 g, 0.604 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (3 mL) and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and combined organic solution was washed by sat. $Na_2S_2O_3$ aq (25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a yellow solid (0.126 g, 80%). IR: (KBr) 1724 (C=O) cm^{-1}, mp: 82-83 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.64 (d, *J* = 9.7 Hz, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.46-7.43 (m, 2H), 7.20 (m, 1H), 6.14 (d, *J* = 9.7 Hz, 1H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 162.1 (d, $^1J_{CF}$ = 247.4 Hz), 160.3 (s), 159.2 (s), 152.9 (d), 135.1 (d, $^3J_{CF}$ = 8.2 Hz), 130.0 (dd, $^3J_{CF}$ = 8.2 Hz), 125.1 (dd, $^4J_{CF}$ = 3.3 Hz), 117.9 (dd, $^2J_{CF}$ = 21.3 Hz), 116.5 (dd, $^2J_{CF}$ = 23.8 Hz), 116.0 (d), 67.0 (s), HRMS : (EI, 70 eV) Calculated ($C_{11}H_6FO_2I$) 315.9397 (M^+) Found 315.9397.

6-hexyl-5-iodo-2H-pyran-2-one (5i)

To a 10 mL vial filled with InI_3 (0.500 mmol, 0.248 g) in toluene (1 mL) was added methyl (*Z*)-undec-2-en-4-ynoate (0.500 mmol, 0.0971 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.331 g, 1.03 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (5 mL), 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and the combined organic solution was washed by sat. $Na_2S_2O_3$ aq. (1 x 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combines and concentrated in vacuo to give the product as a yellow oil (0.115 g, 75%). The NMR date was agreement with the literature[15].

6-cyclopropyl-5-iodo-2H-pyran-2-one (5j)

To a 10 mL vial filled with InI_3 (0.501 mmol, 0.248 g) in toluene (1 mL) was added methyl (*Z*)-5-cyclopropylpent-2-en-4-ynoate (0.507 mmol, 0.0762 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.334 g, 1.04 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (3 mL) and 1 M HCl aq (1 mL). The solution was

extracted by dichloromethane (2 x 30 mL) and combined organic solution was washed by sat. $Na_2S_2O_3$ aq (1 x 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combines and concentrated in vacuo to give the product as a yellow solid (0.105 g, 64%). IR: (KBr) 1714 (C=O) cm^{-1}, mp: 87-88 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.44 (d, *J* = 9.2 Hz, 1H), 5.92 (d, *J* = 9.2 Hz, 1H), 2.24-2.17 (m, 1H), 1.21-1.20 (m, 2H), 1.07-1.05 (m, 2H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 165.3 (s), 160.7 (s), 151.9 (d), 113.1 (d), 66.2 (s), 17.5 (d), 9.8 (t), HRMS: (EI, 70 eV) Calculated ($C_8H_7O_2I$) 261.9491 (M^+) Found 261.9490.

methyl 5-iodo-2-oxo-6-phenyl-2H-pyran-3-carboxylate (5k)

To a 10 mL vial filled with InI_3 (0.500 mmol, 0.248 g) in toluene (1 mL) was added dimethyl 2-(3-phenylprop-2-yn-1-ylidene)malonate (0.501 mmol, 0.122 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.318 g, 0.987 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (5 mL), 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and combined organic solution was washed by sat. $Na_2S_2O_3$ aq (1 x 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel) Product-containing fractions were combines and concentrated in vacuo to give the product as a yellow solid (0.0920 g, 52%). IR: (KBr) 1757 (C=O) cm^{-1}, mp: 144-146 °C, ^1H NMR: (400 MHz, $CDCl_3$) 8.53 (s, 1H), 7.82 (d, *J* = 7.2 Hz, 2H), 7.58-7.47 (m, 3H), 3.94 (s, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 165.5 (s), 162.7 (s), 158.9 (d), 156.6 (s), 132.5 (s), 131.8 (d), 129.4 (d), 128.3 (d), 115.7 (s), 64.8 (s), 53.0 (q), HRMS: (EI, 70 eV) Calculated ($C_{13}H_9O_4I$) 355.9546 (M^+) Found 355.9550.

6-cyclopropyl-3-ethyl-5-iodo-4-phenyl-2H-pyran-2-one (5l)

To a 10 mL vial filled with InI_3 (0.301 mmol, 0.149 g) in toluene (1 mL) was added methyl (*Z*)-5-cyclopropyl-2-ethyl-3-phenylpent-2-en-4-ynoate (0.30 mmol, 0.0765 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.195 g, 0.604 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (3 mL), 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and combined organic solution was washed by sat. $Na_2S_2O_3$ aq (1 x 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combines and concentrated in vacuo to give the product as a yellow solid (0.0701 g, 64%). IR: (KBr) 1714 (C=O) cm^{-1}, mp: 83-84 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.49-7.40 (m, 3H), 7.08-7.05 (m, 2H), 2.40-2.38 (m, 1H), 2.24 (q, *J* = 7.5 Hz, 2H), 1.28-1.16 (m, 2H), 1.05-1.00 (m, 2H), 0.95 (t, *J* = 7.5 Hz, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 161.9 (s), 161.1 (s), 155.6 (s), 140.7 (s), 128.40 (d), 128.36 (d), 127.3 (s), 125.0 (s), 76.5 (s), 23.1 (t), 18.3 (d, C-13), 13.1 (q, C-8), 9.4 (t, C-14), HRMS: (EI, 70 eV) Calculated ($C_{16}H_{15}O_2I$) 366.0117 (M^+) Found 366.0113.

5-iodo-3,4,6-triphenyl-2H-pyran-2-one (5m)

To a 10 mL vial filled with InI_3 (0.503 mmol, 0.249 g) in toluene (1 mL) was added methyl (*Z*)-2,3,5-triphenylpent-2-en-4-ynoate (0.499 mmol, 0.1691 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.331 g, 1.03 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (5 mL), 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (2 x 30 mL) and the combined organic solution was washed by sat. $Na_2S_2O_3$ aq (1 x 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel) Product-containing fractions were combines and concentrated in vacuo to give the product as a yellow solid (0.1424 g, 63%). The NMR date was agreement with the literature[3d].

5-bromo-3-ethyl-4,6-diphenyl-2H-pyran-2-one (5n)

To a 10 mL vial filled with $InBr_3$ (0.499 mmol, 0.177 g) in toluene (1 mL) was added methyl (*Z*)-2-ethyl-3,5-diphenylpent-2-en-4-ynoate (0.496 mmol, 0.144 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, iodobenzene diacetate (0.324 g, 1.01 mmol) in THF (2.5 mL) was added to the reaction mixture at room temperature. After stirring for 24 h, the mixture was quenched by water (3 mL) and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 20 mL) and combined organic solution was washed by sat. $Na_2S_2O_3$ aq (1 x 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 95:5, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a yellow solid (0.0812 g, 46%). IR: (KBr) 1714 (C=O) cm^{-1}, mp: 114-116 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.79-7.78 (m, 2H), 7.50-7.46 (m, 6H), 7.20 (d, *J* = 6.8 Hz, 2H), 2.33 (q, *J* = 7.2 Hz, 2H), 1.05 (t, *J* = 7.2 Hz, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 161.7 (s), 155.0 (s), 153.6 (s), 137.3 (s), 132.6 (s), 130.3 (d), 129.3 (d), 128.5 (d), 128.4 (d), 128.2 (s), 128.1 (d), 127.6 (d), 102.7 (s), 22.9 (t), 13.0 (q), HRMS: (EI, 70 eV) Calculated ($C_{19}H_{15}O_2Br$) 354.0255 (M^+) Found 354.0253

5,6-diphenyl-2H-pyran-2-one (6a)

To a 10 mL vial filled with InI_3 (0.507 mmol, 0.251 g) in toluene (1 mL) was added methyl (*Z*)-5-phenylpent-2-en-4-ynoate (0.499 mmol, 0.0930 g) in a nitrogen-filled glove box. The vial was sealed and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0317 mmol, 0.0290 g), NaOMe (1.02 mmol, 0.0551 g), iodobenzene (0. 350 mmol, 0.0715 g), DMF (2.5 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL), and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80:20, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a pale yellow solid (0.0834 g, 96%). The NMR date was agreement with the literature[3b].

4,5,6-triphenyl-2H-pyran-2-one (6b)

To a 10 mL vial filled with InI_3 (0.505 mmol, 0.250 g) in toluene (1 mL) was added methyl (*Z*)-3,5-diphenylpent-2-en-4-ynoate (0.499 mmol, 0.131 g) in a nitrogen-filled glove box. The vial was sealed and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0317 mmol, 0.0290 g), NaOMe (1.02 mmol, 0.0551 g), iodobenzene (0. 350 mmol, 0.0715 g), DMF (2.5 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL), and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80:20, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a pale yellow solid (0.0727 g, 64%). The NMR date was agreement with the literature[18].

3-ethyl-4,5,6-triphenyl-2H-pyran-2-one (6c)

To a 10 mL vial filled with InI_3 (0.507 mmol, 0.251 g) in toluene (1 mL) was added methyl (*Z*)-2-ethyl-3,5-diphenylpent-2-en-4-ynoate (0.503 mmol, 0.146 g) in a nitrogen-filled glove box. The vial was sealed and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0317 mmol, 0.0290 g), NaOMe (1.02 mmol, 0.0551 g), iodobenzene (0. 350 mmol, 0.0715 g), DMF (2.5 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL), and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80 :

20, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a pale yellow solid (0.0987 g, 80%). IR: (KBr) 1706 (C=O) cm^{-1}, mp: 159-161 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.28 (d, *J* = 8.7 Hz, 2H), 7.22-7.14 (m, 6H), 7.04-6.99 (m, 3H), 6.95-6.92 (m, 2H), 6.86-6.82 (m, 2H), 2.37 (q, *J* = 7.4 Hz, 2H), 1.09 (t, *J* = 7.4 Hz, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 162.8 (s), 154.7 (s), 154.5 (s), 136.3 (s), 135.1 (s), 132.7 (s), 131.1 (d), 129.1 (d), 128.1 (d), 127.9 (d), 127.81 (d), 127.78 (d), 127.4 (d), 127.0 (d), 126.7 (s), 119.4 (s), 22.0 (t), 13.3 (q), HRMS: (EI, 70 eV) Calculated ($C_{25}H_{20}O_2$) 352.1463 (M^+) Found 352.1465.

6-cyclopropyl-3-ethyl-4,5-diphenyl-2H-pyran-2-one (6l)

To a 10 mL vial filled with InI_3 (0.300 mmol, 0.148 g) in toluene (0.6 mL) was added methyl (*Z*)-5-cyclopropyl-2-ethyl-3-phenylpent-2-en-4-ynoate (0.300 mmol, 0.0763 g) in a nitrogen-filled glove box. The vial was sealed and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0165mmol, 0.0151 g), NaOMe (0.583 mmol, 0.0315 g), iodobenzene (0.225 mmol, 0.046 g), DMF (1.5 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL), and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80:20, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a pale yellow solid (0.0605 g, 85%). IR: (KBr) 1699 (C=O) cm^{-1}, mp: 138-140 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.18-7.10 (m, 6H), 7.00 (d, *J* = 7.7 Hz, 2H), 6.90 (d, *J* = 7.2 Hz, 2H), 2.28 (q, *J* = 7.4 Hz, 2H), 1.62-1.57 (m, 1H), 1.23-1.19 (m, 2H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.83-0.78 (m, 2H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 162.9 (s), 159.2 (s), 154.1 (s), 136.6 (s), 135.1 (s), 131.0 (d), 128.0 (d), 127.9 (d), 127.7 (d), 127.3 (d), 126.9 (d), 123.7 (s), 118.3 (s), 21.7 (t), 13.4 (q), 12.4 (d), 8.5 (t), HRMS: (EI, 70 eV) Calculated ($C_{22}H_{20}O_2$) 316.1463 (M^+) Found 316.1460.

3,4,5,6-tetraphenyl-2H-pyran-2-one (6m)

To a 10 mL vial filled with InI_3 (0.300 mmol, 0.148 g) in toluene (0.6 mL) was added methyl (*Z*)-2,3,5-triphenylpent-2-en-4-ynoate (0.300 mmol, 0.0763 g) in a nitrogen-filled glove box. The vial was sealed and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0165mmol, 0.0151 g), NaOMe (0.583 mmol, 0.0315 g), iodobenzene (0.225 mmol, 0.046 g), DMF (1.5 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL), and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80:20, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a white solid (0.0712 g, 79%). The NMR date was agreement with the literature[3b]. This compound was identified by X-ray crystallographic analysis (CCDC 1910558).

6-cyclopropyl-3-ethyl-5-(4-methoxyphenyl)-4-phenyl-2H-pyran-2-one (6n)

To a 10 mL vial filled with InI_3 (0.520 mmol, 0.258 g) in toluene (1 mL) was added methyl (*Z*)-5-cyclopropyl-2-ethyl-3-phenylpent-2-en-4-ynoate (0.500 mmol, 0.127 g) in a nitrogen-filled glove box. The vial was sealed and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0285 mmol, 0.0261 g), NaOMe (0.102 mmol, 0.0551 g), 4-iodoanisole (0.0351 mmol, 0.0821 g), and DMF (2.5 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL), and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80:20, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a yellow solid (0.101 g, 80%). IR: (KBr) 1698 (C=O) cm^{-1}, mp: 109-111 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.16-7.06 (m, 6H), 6.80-6.78 (m, 2H), 6.60 (d, *J* = 8.2 Hz, 1H), 3.58 (s, 3H), 2.32-2.22 (m, 2H), 1.56-1.51 (m, 1H), 1.20-1.18 (m, 2H), 1.02 (t, *J* = 7.5 Hz, 3H), 0.81-0.76 (m, 2H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 163.3 (s), 159.1 (s), 157.0 (s), 154.8 (s), 136.7 (s), 132.5 (d), 129.2 (d), 127.8 (d), 127.6 (d), 127.2, 127.15, 127.10, 124.0 (s), 123.5 (d), 120.0 (d), 114.7 (s), 110.2 (d), 54.9 (q), 21.7 (t), 13.4 (q), 12.2 (d), 8.13 (t), 8.06 (t), HRMS: (EI, 70 eV) Calculated ($C_{23}H_{22}O_3$) 346.1569 (M^+) Found 346.1570.

6-cyclopropyl-3-ethyl-5-(4-nitrophenyl)-4-phenyl-2H-pyran-2-one (6o)

To a 10 mL vial filled with InI_3 (0.520 mmol, 0.258 g) in toluene (1 mL) was added methyl (*Z*)-5-cyclopropyl-2-ethyl-3-phenylpent-2-en-4-ynoate (0.500 mmol, 0.127 g) in a nitrogen-filled glove box. The vial was sealed and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0263 mmol, 0.0241 g), NaOMe (0.990 mmol, 0.0540 g), 1-iodo-4-nitrobenzene (0.354 mmol, 0.0881 g), and DMF (2.5 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL) and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80:20, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a yellow solid (0.102 g, 80%). IR: (KBr) 1714 (C=O) cm^{-1}, mp: 167-169 °C, ^1H NMR: (400 MHz, $CDCl_3$) 8.01 (d, *J* = 8.2 Hz, 2H), 7.24-7.15 (m, 5H), 6.93-6.86 (m, 2H), 2.29 (q, *J* = 7.4 Hz, 2H), 1.52-1.46 (m, 1H), 1.30-1.24 (m, 2H), 1.03 (t, *J* = 7.4 Hz, 3H), 0.90-0.83 (m, 2H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 162.2 (s), 159.6 (s), 152.8 (s), 146.7 (s), 142.6 (s), 135.8 (d), 132.1 (d), 128.2 (s), 128.0 (s), 127.8 (s), 124.5 (s), 123.1 (d), 116.6 (s), 21.7 (t), 13.3 (q), 12.6 (d), 8.9 (t), HRMS: (EI, 70 eV) Calculated ($C_{22}H_{19}NO_4$) 361.1314 (M^+) Found 361.1312.

5-(4-methylbenzoyl)-6-phenyl-2H-pyran-2-one (7a)

To a 10 mL vial filled with InI_3 (0.502 mmol, 0.249 g) in toluene (1 mL) was added methyl (*Z*)-5-phenylpent-2-en-4-ynoate (0.499 mmol, 0.0930 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0262 mmol, 0.0240 g), *p*-toluoyl chloride (0.990 mmol, 0.153 g), DMI (2.5 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL), and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80:20, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a yellow oil (0.0595 g, 41%). IR: (neat) 1743 (C=O), 1651 (C=O) cm^{-1}, ^1H NMR: (400 MHz, $CDCl_3$) 7.60 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 9.4 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.32-7.27 (m, 1H), 7.23 (t, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 6.39 (d, *J* = 9.4 Hz, 1H), 2.31 (s, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 193.3 (s), 163.0 (s), 160.7 (s), 144.7 (s), 144.5 (d), 133.5 (s), 131.22 (d), 131.16 (s), 129.8 (d), 129.2 (d), 128.9 (d), 128.4 (d), 116.6 (s), 113.6 (d), 21.6 (q), HRMS: (EI, 70 eV) Calculated ($C_{19}H_{14}O_3$) 290.0943 (M^+) Found 290.0941.

5-(4-methylbenzoyl)-4,6-diphenyl-2H-pyran-2-one (7b)

To a 10 mL vial filled with InI_3 (0.507 mmol, 0.251 g) in toluene (1 mL) was added methyl (*Z*)-3,5-diphenylpent-2-en-4-ynoate (0.511 mmol, 0.134 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0247 mmol, 0.0226 g), *p*-toluoyl chloride (0.100 mmol, 0.155 g), DMI (2.5 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL), and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80:20, column length 11 cm, diameter 26 mm,

spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a white solid (0.101 g, 55%). IR: (KBr) 1724 (C=O), 1662 (C=O) cm^{-1}, mp: 199-201 °C, d^1H NMR: (400 MHz, $CDCl_3$) 7.58-7.53 (m, 4H), 7.32-7.19 (m, 8H), 7.05 (d, *J* = 8.2 Hz, 2H), 6.36 (s, 1H), 2.29 (s, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 193.4 (s), 161.0 (s), 159.9 (s), 157.2 (s), 144.8 (s), 135.9 (s), 134.7 (s), 131.5 (s), 130.9 (d), 129.4 (d), 129.3 (d), 128.6 (d), 128.52 (d), 128.45 (d), 127.5 (d), 118.0 (s), 113.2 (d), 21.7 (q), HRMS : (EI, 70 eV) Calculated ($C_{25}H_{18}O_3$) 366.1256 (M^+) Found 366.1259.

3-ethyl-5-(4-methylbenzoyl)-4,6-diphenyl-2H-pyran-2-one (7c)

To a 10 mL vial filled with InI_3 (0.502 mmol, 0.249 g) in toluene (1 mL) was added methyl (*Z*)-2-ethyl-3,5-diphenylpent-2-en-4-ynoate (0.506 mmol, 0.147 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0263 mmol, 0.0229 g), *p*-toluoyl chloride (0.996 mmol, 0.154 g), DMI (2.5 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL), and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80:20, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a white solid (0.0749 g, 38%). IR: (KBr) 1715 (C=O), 1661 (C=O) cm^{-1}, mp: 192-194 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.55 (d, *J* = 7.2 Hz, 2H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.28-7.20 (m, 6H), 7.03 (d, *J* = 8.2 Hz, 4H), 2.36 (q, *J* = 7.2 Hz, 2H), 2.29 (s, 3H), 1.08 (t, *J* = 7.2 Hz, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 193.7 (s), 162.2 (s), 155.5 (s), 151.6 (s), 144.6 (s), 134.8 (s), 131.5 (s), 130.4 (d), 129.4 (d), 129.1 (d), 128.4 (d), 128.25 (d), 128.22 (d), 128.1 (d), 127.8 (d), 127.3 (s), 119.0 (s), 21.6 (s), 21.5 (s), 13.2 (s), HRMS: (EI, 70 eV) Calculated ($C_{27}H_{22}O_3$) 394.1569 (M^+) Found 394.1574.

5-(4-methylbenzoyl)-3,4,6-triphenyl-2H-pyran-2-one (7m)

To a 10 mL vial filled with InI_3 (0.500 mmol, 0.248 g) in toluene (1 mL) was added methyl (*Z*)-2,3,5-triphenylpent-2-en-4-ynoate (0.501 mmol, 0.169 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0263 mmol, 0.0229 g), *p*-toluoyl chloride (1.01 mmol, 0.157 g), DMI (2.5 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL), and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80:20, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a white solid (0.0750 g, 34%). IR: (KBr) 1722 (C=O), 1663 (C=O) cm^{-1}, mp: 158-159 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.62 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.35-7.26 (m, 3H), 7.21-6.89 (m, 12H), 2.29 (s, 3H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 193.5 (s), 161.5 (s), 157.5 (s), 152.7 (s), 144.7 (s), 134.9 (s), 134.8 (s), 133.0 (s), 131.5 (s), 130.8 (d), 130.6 (d), 129.4 (d), 129.2 (d), 128.9 (d), 128.51 (d), 128.50 (d), 128.1 (d), 127.8 (d), 127.7 (d), 125.2 (s), 119.3 (s), 21.7 (q), HRMS : (EI, 70 eV) Calculated ($C_{31}H_{22}O_3$) 442.1569 (M^+) Found 442.1571. This compound was identified by X-ray crystallographic analysis (CCDC 1910562).

6-cyclopropyl-3-ethyl-5-(4-methylbenzoyl)-4-phenyl-2H-pyran-2-one (7l)

To a 10 mL vial filled with InI_3 (0.301 mmol, 0.149 g) in toluene (0.6 mL) was added methyl (*Z*)-5-cyclopropyl-2-ethyl-3-phenylpent-2-en-4-ynoate (0.300 mmol, 0.0763 g) in a nitrogen-filled glove box. The vial was sealed, and the mixture was stirred at 80 °C for 24 h. Then, Pd_2dba_3 (0.0154 mmol, 0.0141 g), *p*-toluoyl chloride (0.598 mmol, 0.0924 g), DMI (1.6 mL) were added to the reaction mixture at room temperature. After stirring at 110 °C for 24 h, the mixture was quenched by water (5 mL), and 1 M HCl aq (1 mL). The solution was extracted by dichloromethane (3 x 30 mL) and dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (hexane/ethyl acetate = 80 : 20, column length 11 cm, diameter 26 mm, spherical silica gel). Product-containing fractions were combined and concentrated in vacuo to give the product as a white solid (0.0419 g, 39%). IR: (KBr) 1715 (C=O), 1659 (C=O) cm^{-1}, mp: 120-121 °C, ^1H NMR: (400 MHz, $CDCl_3$) 7.60 (d, *J* = 8.2 Hz, 2H), 7.17-7.15 (m, 5H), 6.99-6.98 (m, 2H), 2.37 (s, 3H), 2.29 (q, *J* = 7.4 Hz, 2H), 1.62-1.58 (m, 1H), 1.26-1.25 (m, 2H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.88-0.86 (m, 2H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 194.0 (s), 162.1 (s), 160.5 (s), 151.3 (s), 144.6 (s), 135.2 (s), 135.1 (s), 129.5 (d), 129.2 (d), 128.1 (d), 128.0 (d), 127.7 (d), 124.5 (s), 118.2 (s), 21.7 (q), 21.1 (t), 13.2 (q), 12.9 (d), 8.9 (t), HRMS: (EI, 70 eV) Calculated ($C_{24}H_{22}O_3$) 358.1569 (M^+) Found 358.1567. This compound was identified by X-ray crystallographic analysis (CCDC 1910561).

3,4,6-triphenyl-5-(phenylethynyl)-2H-pyran-2-one (8)

To a solution of 5-iodo-3,4,6-triphenyl-2*H*-pyran-2-one (0.206 mmol, 0.0928 g) and $PdCl_2(PPh_3)_2$ (0.0245 mmol, 0.0172 g) in 1,4-dioxane (1 mL) was added tributyl(phenylethynyl)stannane (0.249 mmol, 0.0977 g). The mixture was stirred at 90 °C for 14 h. The mixture was quenched by H_2O (1 mL) and was extracted with dichloromethane (3 x 10 mL). The collected organic layer was dried over $MgSO_4$. The solvent was evaporated and the residue was purified by column chromatography (hexane/ethyl acetate = 99:1, column length 10 cm, diameter 26 mm silica gel) to give the product (0.0555 g, 63%) IR: (KBr) 1722 (C=O) cm^{-1}, mp : 208-210 °C, ^1H NMR: (400 MHz, $CDCl_3$) 8.30-8.26 (m, 2H), 7.52-7.50 (m, 3H), 7.28-7.16 (m, 13H), 6.95 (dd, *J* = 8.0, 1.7 Hz, 2H), $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) 161.0 (s), 154.9 (s), 136.1 (s), 133.3 (s), 131.8 (s), 131.0 (s), 130.7 (d), 130.5 (d), 129.3 (d), 128.7 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.7 (d), 127.61 (d), 127.57 (d), 125.5 (d), 124.4 (s), 122.5 (s), 104.9 (d), 102.7 (s), 97.6 (s), 84.4 (s), HRMS: (EI, 70 eV) Calculated ($C_{31}H_{20}O_2$) 424.1463 (M^+) Found 424.1466 This compound was identified by X-ray crystallographic analysis (CCDC 1915263).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on theACS Publications websiteat DOI:.

Electronic Supplementary Information of NMR Spectra (PDF)

Electronic Supplementary Information of Computational Section (PDF)

Electronic Supplementary Information of Observation of Zwitterion 4b and Metalated 2-Pyrone 3b (PDF)

Electronic Supplementary Information of X-Ray Diffraction Data of 6m, 7m, 7l, 8, 3b·pyridine, 4b (PDF)

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Notes

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