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Regio- and Stereoselective Iodoacyloxylations of Alkynes

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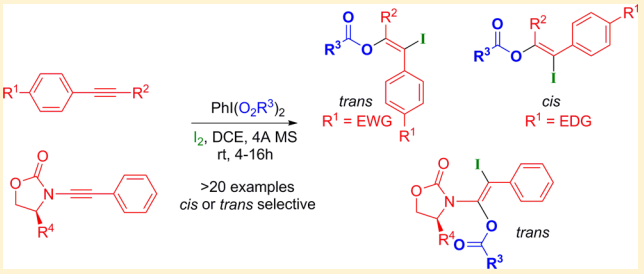
Supporting Information

ABSTRACT: A new method for the regioselective and stereoselective iodoacyloxylation of alkynes has been developed. This protocol utilizes a combination of an iodobenzene dicarboxylate and iodine to functionalize a series of activated and unactivated alkynes in an entirely selective and predictable fashion. The resultant iodo-enol esters were subsequently coupled with boronic acids to afford tetrasubstituted alkene derivatives, which could be further converted to the corresponding 1,1-disubstituted acetophenone.



INTRODUCTION

Multisubstituted alkenes (of which enol esters are an important subclass) have been utilized as key intermediates in the synthesis of natural products and applied as reagents in numerous synthetic transformations including cycloadditions, heterocycle formation and aldol-type reaction processes.[1] The synthesis, however, of multisubstituted alkenes (including enol esters), in an efficient and predictable manner still presents a significant challenge to the modern organic chemist.[2] One recent example that elegantly addressed this issue was the Rh/Cu catalyzed multicomponent synthesis of enol esters from dialkyl alkynes reported by Pham and Cramer involving the CH-activation of heterocycles.[3]

Alkenes and enol esters that contain a halide substituent are particularly valuable substrates in organic synthesis, applicable to subsequent cross-coupling reactions to provide access to various tri- and tetra-substituted alkene derivatives.[4] Okamoto and Yanada recently demonstrated that iodo-enol esters could undergo a Sonogashira cross-coupling to afford alkynylated enol esters that subsequently cyclized to yield tetra-substituted furans.[1g] Geary and Hultin described the preparation of dienes, trienes and enynes from chloro-substituted enol esters,[4g] and Shimizu and co-workers showed that tetra-substituted alkenes containing a trifluoromethyl substituent could be accessed from bromo-substituted enol sulfonates.[4h] As such, the synthesis of halo-substituted enol esters using methodology that allows control over both the regio- and stereochemistry is highly desirable. In 1971, Ogata and Urasaki reported the conversion of diphenylacetylene (**1a**) to (*E*)-2-iodo-1,2-diphenylvinyl acetate (**2a**) following the in situ generation of iodine monoacetate (IOAc) from a combination of per-acetic acid and iodine in acetic acid.[5,6] Subsequently, the Barluenga research group reported a similar cohalogenation of alkynes using $I(Py)_2{\cdot}BF_4$ and an appropriate nucleophile in the presence of tetrafluoroboric acid.[7] In 1999, Togo and co-workers described the iodo-tosyloxylation of various internal and terminal alkynes using a combination of Koser's reagent and iodine.[8]

More recently, Yanada and co-workers reported the cohalogenation of alkynes to afford vinylic iodo esters **2** using a combination of acetic acid and *N*-iodosuccinimide (NIS).[9] Although a range of vinyl iodides were accessible using these conditions, the reaction conditions were only applicable to polarized alkynes possessing an electron donating group on one end of the triple bond. To enhance the utility of the cohalogenation reactions and expand the scope to include unactivated alkynes, a new method was required to facilitate the rapid preparation of a range of vinylic iodo enol esters using common reagents and mild conditions that provides predictable control over both regio- and stereochemistry.

RESULTS AND DISCUSSION

Initially, the conditions reported by Yanada using acetic acid and NIS in 1,2-dichloroethane (DCE) at 40 °C were trialed for the functionalization of diphenylacetylene (**1a**) but failed to afford the desired product **2a** (Table 1, entry 1).[9] Inspired by a recent publication from the Yu group whereby iodine monoacetate was generated in situ from the reaction of silver acetate or iodobenzene diacetate with molecular iodine,[10] the iodoacetoxylation of diphenylacetylene was further explored. The reaction using silver acetate and iodine in DCE provided **2a** in modest yield (58%, entry 2) with a significant amount of benzil (**3**) also identified from over oxidation. The use of iodobenzene diacetate and iodine to generate the reactive iodine monoacetate led to the formation of **2a** in excellent yield of 82% with the *trans*-isomer formed as the major product (Table 1, entry 3).[11]

By lowering the reaction temperature to ambient temperatures, formation of the *trans*-isomer was favored (entry 4) and

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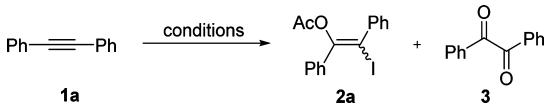
Table 1. Optimization of the Iodoacetyloxylation of Diphenylacetylene



1a 2a 3

entry	conditions[a]	*cis*:*trans* (%)	yield (%)
1	AcOH, NIS, DCE, 40 °C, 16 h	–	0
2	Ag(OAc), I_2, DCE, 40 °C, 16 h	22:78	58 (36)[b]
3	$PhI(OAc)_2$, I_2, DCE, 40 °C, 16 h	29:71	82 (16)[b]
4	$PhI(OAc)_2$, I_2, DCE, 25 °C, 4 h	12:88	85 (10)[b]
5	$PhI(OAc)_2$, I_2, DCE, 4Å MS, 25 °C, 4 h	0:100	91 (trace)[b]
6	$PhI(OAc)_2$, I_2, CH_2Cl_2, 4Å MS, 25 °C, 16 h	8:92	95
7	$PhI(OAc)_2$, I_2, $CHCl_3$, 4Å MS, 25 °C, 16 h	–	0
8	$PhI(OAc)_2$, I_2, THF, 4Å MS, 25 °C, 16 h	–	0
9	$PhI(OAc)_2$, I_2, DMF, 4Å MS, 25 °C, 16 h	–	0
10	$PhI(OAc)_2$, I_2, MeCN, 4Å MS, 25 °C, 16 h	–	0
11	$PhI(OAc)_2$, I_2, 1,4-dioxane, 4Å MS, 25 °C, 16 h	–	0
12	$PhI(OAc)_2$, I_2, PhMe, 4Å MS, 25 °C, 16 h	10:90	85 (10)[b]
13	$PhI(OAc)_2$, TBAI, DCE, 4Å MS, 25 °C, 16 h	–	0
14	$PhI(OAc)_2$, NIS, DCE, 4Å MS, 25 °C, 16 h	–	0
15	$PhI(OAc)_2$, ICl, DCE, 4Å MS, 25 °C, 16 h	–	0
16	$PhI(OAc)_2$, NaI, DCE, 4Å MS, 25 °C, 16 h	–	0

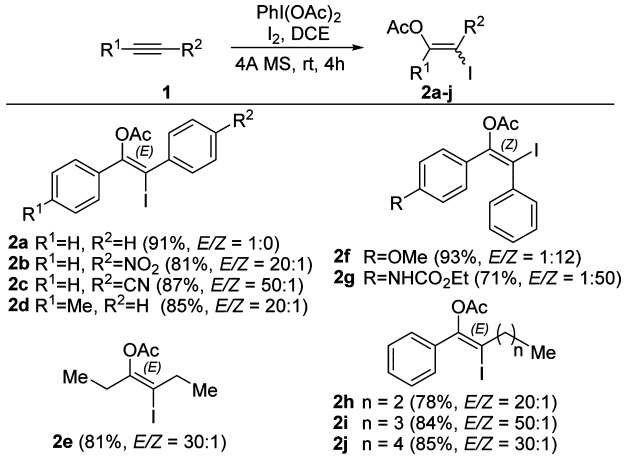
[a]To suppress formation of di-iodostilbene, all reactions were conducted in the dark by wrapping the reaction flask in aluminum foil. [b]Yield of benzil (**3**) in brackets.

the inclusion of 4Å molecular sieves suppressed the side reaction, the oxidation of diphenylacetylene to **3** (entry 5). Following a very simple workup procedure, the product **2a** was readily obtained after recrystallization from ethanol to afford exclusively the *trans*-isomer in excellent yield of 91%. The use of alternative solvents was then investigated. When performed in dichloromethane, vinyl iodide **2a** was obtained in excellent yield; however, a slight loss in stereoselectivity was observed (Table 1, entry 6). The reaction failed to proceed when conducted in other solvents including chloroform, acetonitrile, THF, 1,4-dioxane and DMF (Table 1, entries 7−11). Good yields and selectivities were obtained when toluene was applied as the solvent (entry 12). Other iodine sources including sodium iodide, iodine monochloride, tetrabutylammonium iodide and NIS did not react to form the desired product **2a** (entries 13−16), and the use of molecular bromine instead of iodine afforded only α,α'-dibromostilbene.

With a new protocol in-hand employing a combination of iodine and iodobenzene diacetate for the high-yielding stereoselective iodoacetoxylation of alkynes, a range of diaryl, dialkyl and aryl-alkyl substituted internal alkynes were subjected to the previously optimized reaction conditions (Scheme 1). It was observed that for the diaryl alkynes, electronically neutral and electron deficient alkynes reacted well to afford almost exclusively the *trans*-isomer of the corresponding vinylic iodides **2a**−**2d** where the acetate group added to the most electron deficient end of the alkyne (Scheme 1). Both the regiochemistry and the *trans*-stereochemistry were confirmed by X-ray crystallography of cyano-derivative **2c** (Figure S1).[12] Reactions performed with terminal alkynes failed to afford synthetically useful yields of the corresponding vinyl acetate.

When a strongly electron-donating group was present on one of the aryl groups, the *cis*-isomer was the major stereoisomer formed with the acetate group adding to the end of the alkyne closest to the EDG (Scheme 1, **2f**,**g**). Aryl-alkyl substituted alkynes and dialkyl substituted alkynes also performed well in this reaction process to afford predominantly the *trans*-isomer

Scheme 1. Exploration of the Scope of Alkynes Tolerated in This Reaction Process



of the corresponding vinyl iodides in excellent yield (Scheme 1, **2e**,**h**−**j**). For unsymmetrically substituted diaryl acetylenes containing only moderately electron-withdrawing or electron-donating groups such as chloro- and fluoro-substituted diphenylacetylene, the reaction proceeded well; however, a mixture of regioisomers was obtained with the *trans*-stereoisomer still favored in each case (**2k**−**m**, Figure 1).[12]

To further explore the scope of this reaction process, a range of substituted iodobenzene dicarboxylate derivatives were investigated. The iodobenzene dicarboxylate reagents were prepared by azeotroping off the acetic acid from iodobenzene diacetate in the presence of the desired carboxylic acid in chlorobenzene.[13] In a one-pot process, the iodobenzene dicarboxylates were synthesized and subsequently reacted with iodine and diphenylacetylene to afford a series of iodo-enol ester stilbenes (Scheme 2). Using this approach, both aryl (**2n**−**p**) and alkyl (**2q**−**t**) substituted carboxylic acids could be added across diphenylacetylene to afford a range of previously

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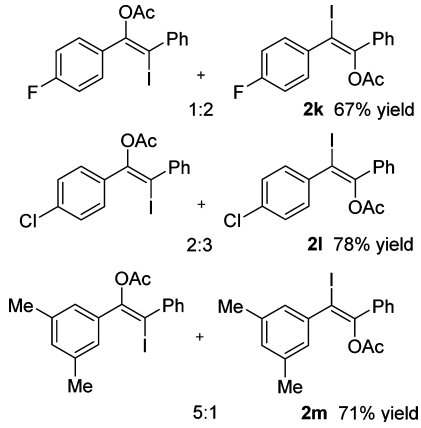
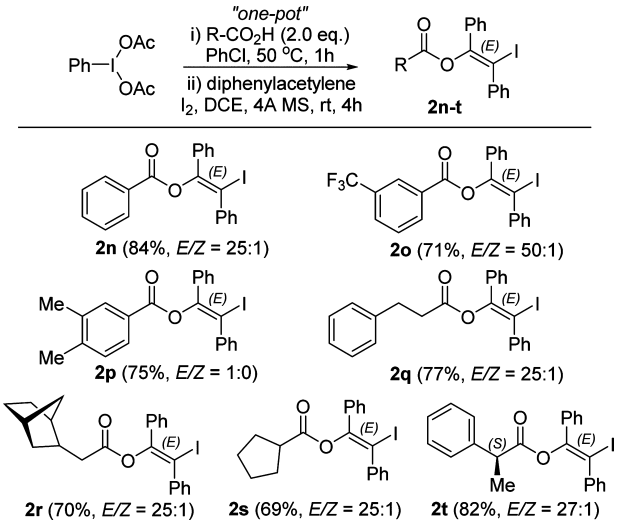


Figure 1. An inseparable mixture of regio-isomers was obtained from some reaction attempts.

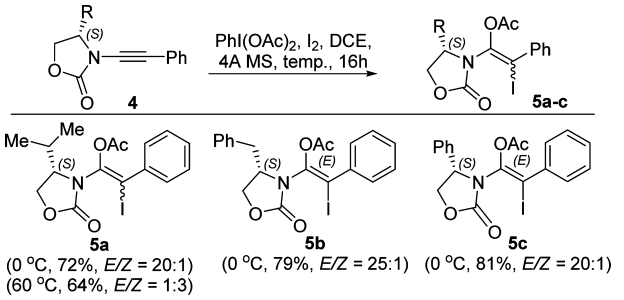
Scheme 2. Extending the Scope of the Iodoacyloxylation of Diphenylacetylene Using Various Iodobenzene Dicarboxylates



inaccessible *trans*-substituted iodo enol esters in high-yield and with very high stereoselectivity (Scheme 2). The structure and stereochemistry of the products obtained from this investigation were confirmed through X-ray crystal analysis of benzoyl derivative **2n**, which again clearly shows the *trans*-orientation of the iodine and benzoyloxy groups (Figure S2).[12]

Ynamides are key molecular building blocks that have found application in numerous synthetic transformations.[14] To enhance the utility of the methodology described herein, the iodo-acetoxylation of ynamides was then pursued. Using the previously optimized reaction conditions, chiral ynamides **4a–c** were readily converted in good yield to the corresponding iodo-enolamides **5a–c**, a previously unreported class of tetrasubstituted alkenes (Scheme 3). It was observed that at elevated temperatures a mixture of stereoisomers was obtained with formation of the *cis*-isomer favored; however, when the reaction was performed at 0 °C, the *trans*-stereoisomer was almost exclusively formed. The regio- and stereochemistry of the products obtained were further confirmed by X-ray crystallography of enolamide derivative **5b** (Figure S3),[12] which shows the acetoxy group added to the side of the alkyne closest to the oxazolidinone moiety and oriented *trans* to the iodine atom. Additional reaction attempts using *N*-phenylethynyl-*S*-methyl-

Scheme 3. Iodine Monoacetate Addition to Ynamides



S-phenylsulfoximine and oxazolidinone-based ynamides derived from 1-hexyne and 3,5-dimethoxyphenylacetylene failed to afford to the corresponding iodo-substituted enolamides.

To further understand this reaction process, a mechanism based on the results presented herein and of others is proposed.[5,7,15] When an electronically neutral or electron-deficient alkyne is applied to the standard reaction conditions, following activation of the alkyne by iodine monoacetate, pathway **A** ensues (R = CN, Scheme 4), where the kinetic process involving an S_N2-type attack of a secondary acetate anion affords vinyl iodide **2c** as a single regioisomer with very high selectivity for the *trans*-stereoisomer. In the case of electron-rich alkynes (R = OMe, Scheme 4), pathway **B** prevails, whereby following alkyne activation, fragmentation of the iodine monoacetate takes place to afford an iodo-allenic cation which is resonance stabilized by the electron-rich aryl group. It is proposed that pathway **B** proceeds via a six-membered transition state in what could be considered a near-concerted fashion in which the acetate anion released from the iodine monoacetate during the fragmentation process forms an ion pair with the allenic cation facilitating rapid *syn*-addition of the acetoxy group to afford tetrasubstituted alkene **2f** as the *cis*-stereoisomer with the opposite regiochemistry to that observed in pathway **A** (Scheme 4).

For the iodoacetoxylation of the ynamide derivative **4a**, at elevated temperatures the thermodynamic pathway was favored leading to formation of a higher portion of the *cis*-isomer **5a′**; however, at 0 °C the kinetic pathway predominates to afford almost exclusively the *trans*-isomer **5a**. To further probe the effect of temperature on this reaction process, the iodoacetoxylation of **1c** was performed at elevated temperature (60 °C) in an attempt to generate the *cis*-adduct; however, once again the *trans*-isomer of **2c** was formed as the major product (83% yield, *E*/*Z* = 40:1). The iodoacetoxylation of **1f** was then conducted at −20 °C to observe if the kinetic pathway to form the *trans*-isomer could be favored; however, the *cis*-isomer of **2f** was again isolated as the major product (86% yield, *E*/*Z* = 1:12). Thus, the electronic characteristics of the diaryl alkynes predetermine the regio- and stereoselectivity of the product formed, whereas in the case of the ynamides, formation of either the *cis*- or *trans*-stereoisomer can be favored by controlling the reaction temperature. This proposed mechanism (Scheme 4) involving electronic factors to determine the regio- and stereochemistry differs to those previously described where only steric interactions were proposed to be the cause of the observed stereo- and regioselectivity.[5,15]

To further highlight the value of the products obtained using the method described herein, vinyl iodide **2a** was subjected to Suzuki cross-coupling with 3,5-dimethylphenyl boronic acid to afford tetrasubstituted alkene **6** which was subsequently

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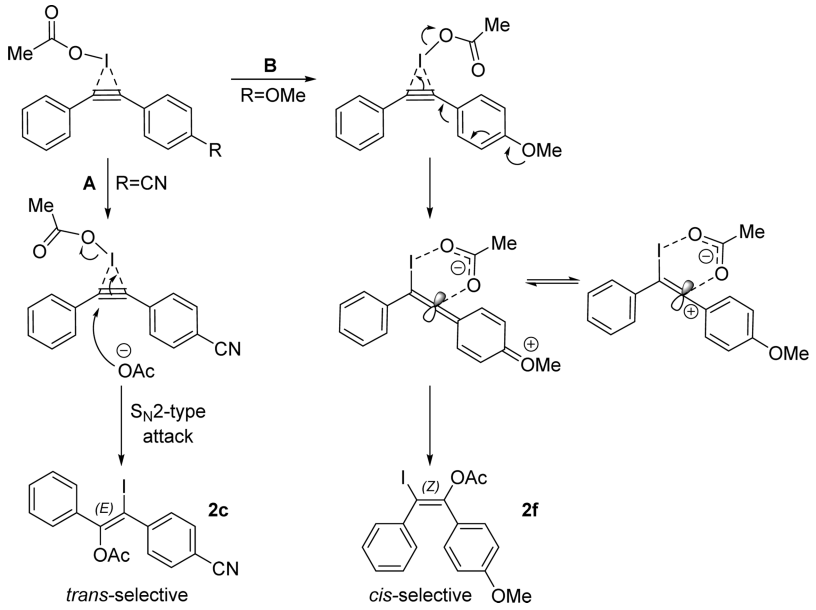
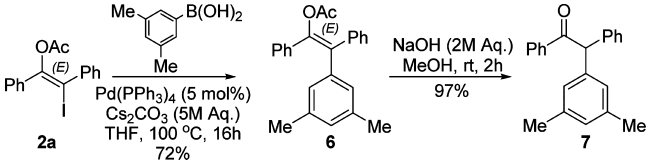
Scheme 4. Proposed Mechanism to Account for the Observed Regio- And Stereo-Selectivity of This Process



hydrolyzed to afford the 1,1-disubstituted acetophenone derivative 7 (Scheme 5). This synthetic strategy utilizing aryl-

Scheme 5. Additional Functionalization of the Vinyl Iodides



boronic acids to incorporate the second aryl moiety provides a complementary approach to that recently reported by Taillefer and co-workers for the synthesis of 1,1-disubstituted acetophenone derivatives where aryl halides were applied.[16]

In summary, a highly regio- and stereoselective method for the functionalization of activated and unactivated alkynes has been developed under mild conditions. This reaction process provides access to a series of useful iodo-enol ester derivatives with predictable control over both the regio- and stereochemistry. In addition, this method has facilitated the synthesis of halo-substituted enolamides from ynamides, a previously unreported class of tetrasubstituted alkenes. To further understand this transformation, additional synthetic and theoretical studies are ongoing in our laboratory.

EXPERIMENTAL SECTION

General Experimental. Iodobenzene diacetate, iodine and the solvents used in reaction extractions and chromatography were supplied by commercial vendors without further purification or drying. Diphenylacetylene and 3-hexyne were supplied by commercial vendors, all other alkynes were prepared by palladium-catalyzed Sonogashira cross-coupling reaction following a literature procedure.[17] Chiral ynamides **4a–c** were also prepared using a literature method.[18] All reactions were performed under an inert atmosphere of anhydrous N_2. 1,2-Dichloroethane (DCE) was purchased in anhydrous form and stored under nitrogen. Petroleum spirits with a boiling point range of 40–60 °C were used in chromatography. Column (flash) chromatography was performed on 40–60 μm silica gel. ^{1}H and ^{13}C NMR spectra were recorded at 400.13 and 100.62 MHz, respectively. Chemical shifts (d, ppm) are reported relative to the solvent peak ($CDCl_3$: 7.26 [^{1}H] or 77.16 [^{13}C]). Proton resonances are annotated as chemical shift (d), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), coupling constant (*J*, Hz), and number of protons. High resolution MS was performed on a TOF LC–MS. All data were acquired and reference mass corrected via a dual-spray electrospray ionization (ESI) source. Each scan or data point on the total ion chromatogram (TIC) is an average of 13 700 transients, producing a spectrum every second. Mass spectra were created by averaging the scans across each peak and subtracting the background from first 10 s of the TIC. Acquisition parameters: mode, ESI; drying gas flow, 11 L/min; nebulizer pressure, 45 psi; drying gas temperature, 325 °C; voltages: capillary, 4000 V; fragmentor, 160 V; skimmer, 65 V; octapole RF, 750 V; scan range, 100–1500 *m*/*z*; positive ion mode internal reference ions, *m*/*z* 121.050873 and 922.009798.

General Procedure 1 for the Iodo-acetoxylation of Alkynes. To a solution of $PhI(OAc)_2$ (1.0 mmol) in DCE (5 mL) containing 4Å molecular sieves (~1.0 g) was added I_2 (1.0 mmol). After stirring for 10 min, the alkyne (1.2 mmol) was added in one portion, and the resultant solution stirred at room temperature for 4 h. After this time, the molecular sieves were filtered off, and the reaction quenched by the addition of $Na_2S_2O_3$ (10% w/w aqueous, 10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic fractions were dried over $MgSO_4$ and filtered, and the solvent evaporated. The product was purified by either recrystallization or flash column chromatography as stated.

*(E)-2-Iodo-1,2-diphenylvinyl acetate (**2a**).*[5] General procedure 1 was followed using diphenylacetylene. Purification by recrystallization from ethanol afforded the title compound as a pale yellow solid (331 mg, 91%): mp = 142.8–145.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67–7.69 (m, 2H), 7.42–7.47 (m, 4H), 7.36–7.41 (m, 2H), 7.30 (tt, *J* = 1.4 and 7.4 Hz, 1H), 1.86 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.6, 147.3, 140.7, 137.1, 129.7, 129.3, 128.5, 128.4, 128.3, 128.1, 89.1, 20.4 ppm; HRMS (*m*/*z*) = $[C_{16}H_{13}O_2I + H]^+$ calcd 365.0033, found 365.0030.

*(E)-2-Iodo-2-(4-nitrophenyl)-1-phenylvinyl acetate (**2b**).* General procedure 1 was followed using 1-nitro-4-(phenylethynyl)benzene. Purification by column chromatography (1:1 PhMe/Pet. Sp. → 100% PhMe) afforded the title compound as a pale yellow amorphous solid (331 mg, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.21 (d, *J* = 9.0 Hz, 2H), 7.62–7.65 (m, 2H), 7.59 (d, *J* = 9.0 Hz, 2H), 7.41–7.44 (m, 3H), 1.87 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.2, 149.1, 147.3, 136.3, 129.83, 129.76, 129.5, 128.3, 123.6, 85.2, 20.4

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ppm; HRMS (m/z) = $[C_{16}H_{12}NO_4I + H]^+$ calcd 409.9884, found 409.9888.

*(E)-2-Iodo-2-(4-cyanophenyl)-1-phenylvinyl acetate (**2c**).* General procedure 1 was followed using 4-(phenylethynyl)benzonitrile. Purification by column chromatography (1:1 PhMe/Pet. Sp. → 100% PhMe) afforded the title compound as a pale yellow solid (339 mg, 87%): mp = 132.0−133.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.61−7.66 (m, 4H), 7.54 (d, J = 8.6 Hz, 2H), 7.40−7.44 (m, 3H), 1.86 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.2, 148.8, 145.4, 136.4, 132.1, 129.8, 129.5, 128.2, 118.4, 112.0, 85.7, 20.4 ppm; HRMS (m/z) = $[C_{17}H_{12}NO_2I + H]^+$ calcd 389.9985, found 389.9987.

*(E)-2-Iodo-2-phenyl-1-(p-tolyl)vinyl acetate (**2d**).*[15] General procedure 1 was followed using 1-methyl-4-(phenylethynyl)benzene. Purification by column chromatography (1:1 PhMe/Pet. Sp.) afforded the title compound as a white solid (321 mg, 85%): mp = 78.5−81.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 (d, J = 8.1 Hz, 2H), 7.33−7.35 (m, 2H), 7.23−7.28 (m, 2H), 7.18−7.20 (m, 1H), 7.11 (d, J = 7.9 Hz, 2H), 2.29 (s, 3H), 1.72 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.7, 147.4, 140.9, 139.4, 134.3, 129.5, 128.8, 128.5, 128.30, 128.26, 88.6, 21.5, 20.5 ppm; HRMS (m/z) = $[C_{17}H_{15}O_2I + H]^+$ calcd 379.0189, found 379.0184.

*(E)-4-Iodohex-3-en-3-yl acetate (**2e**).*[7] General procedure 1 was followed using 3-hexyne. Purification by column chromatography (1:19 EtOAc/Pet. Sp.) afforded the title compound as a pale yellow oil (217 mg, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.48 (q, J = 7.5 Hz, 2H), 2.26 (q, J = 7.4 Hz, 2H), 2.10 (s, 3H), 0.94 (t, J = 7.5 Hz, 3H), 0.93 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.4, 148.7, 96.1, 31.1, 29.8, 20.4, 14.0, 10.9 ppm; HRMS (m/z) = $[C_8H_{13}O_2I]^+$ calcd 267.9955, found 267.9958.

*(Z)-2-Iodo-1-(4-methoxyphenyl)-2-phenylvinyl acetate (**2f**).*[9] General procedure 1 was followed using 1-methoxy-4-(phenylethynyl)benzene. Purification by column chromatography (1:1 PhMe/Pet. Sp. → 100% PhMe) afforded the title compound as a pale yellow solid (367 mg, 93%): mp = 125.6−128.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.27−7.30 (m, 2H), 7.17−7.23 (m, 3H), 7.08 (d, J = 9.0 Hz, 2H), 6.64 (d, J = 9.0 Hz, 2H), 3.72 (s, 3H), 2.29 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.0, 159.6, 149.9, 140.8, 130.21, 130.17, 128.4, 128.1, 125.8, 113.5, 89.9, 55.2, 21.4 ppm; HRMS (m/z) = $[C_{17}H_{15}O_3I + Na]^+$ calcd 416.9958, found 416.9959.

*(Z)-1-(4-((Ethoxycarbonyl)amino)phenyl)-2-iodo-2-phenylvinyl acetate (**2g**).* General procedure 1 was followed using 1-(ethoxycarbonyl)amino-4-(phenylethynyl)benzene. Purification by recrystallization from ethanol afforded the title compound as a pale yellow solid (320 mg, 71%): mp = 161.4−164.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.18−7.22 (m, 2H), 7.10−7.16 (m, 3H), 7.07 (d, J = 8.8 Hz, 2H), 6.99 (dt, J = 2.2 and 8.8 Hz, 2H), 6.46 (brs, 1H), 4.12 (q, J = 7.1 Hz, 2H), 2.22 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.0, 153.2, 149.6, 140.6, 138.2, 130.2, 129.6, 128.4, 128.3, 117.7, 90.7, 61.4, 21.4, 14.5 ppm; HRMS (m/z) = $[C_{19}H_{18}NO_4I + H]^+$ calcd 452.0353, found 452.0358.

*(E)-2-Iodo-1-phenylpent-1-en-1-yl acetate (**2h**).* General procedure 1 was followed using 1-phenylpentyne. Purification by column chromatography (1:2 PhMe/Pet. Sp.) afforded the title compound as a pale yellow oil (258 mg, 78%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38−7.40 (m, 2H), 7.21−7.26 (m, 3H), 2.43 (t, J = 7.4 Hz, 2H), 2.00 (s, 3H), 1.52 (sext, J = 7.4 Hz, 2H), 0.88 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.3, 146.6, 137.6, 129.8, 128.9, 127.9, 96.7, 40.0, 22.4, 20.6, 13.2 ppm; HRMS (m/z) = $[C_{13}H_{15}O_2I + Na]^+$ calcd 353.0009, found 353.0008.

*(E)-2-Iodo-1-phenylhex-1-en-1-yl acetate (**2i**).* General procedure 1 was followed using 1-phenylhexyne. Purification by column chromatography (1:2 PhMe/Pet. Sp.) afforded the title compound as a pale yellow oil (289 mg, 84%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46−7.49 (m, 2H), 7.31−7.37 (m, 3H), 2.54 (t, J = 7.4 Hz, 2H), 2.11 (s, 3H), 1.53−1.61 (m, 2H), 1.33−1.43 (sext., J = 7.5 Hz, 2H), 0.96 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.3, 146.3, 137.6, 129.8, 128.9, 127.9, 96.9, 37.8, 31.1, 21.7, 20.6, 13.9 ppm; HRMS (m/z) = $[C_{14}H_{17}O_2I + Na]^+$ calcd 367.0165, found 367.0161.

*(E)-2-Iodo-1-phenylhept-1-en-1-yl acetate (**2j**).* General procedure 1 was followed using 1-phenylheptyne. Purification by column chromatography (1:2 PhMe/Pet. Sp.) afforded the title compound as a pale yellow oil (304 mg, 85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46−7.49 (m, 2H), 7.32−7.38 (m, 3H), 2.53 (t, J = 7.4 Hz, 2H), 2.11 (s, 3H), 1.55−1.63 (m, 2H), 1.32−1.38 (m, 4H), 0.92 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.3, 146.3, 137.6, 129.8, 128.9, 127.9, 96.9, 38.1, 30.7, 28.6, 22.4, 20.6, 14.0 ppm; HRMS (m/z) = $[C_{15}H_{19}O_2I + Na]^+$ calcd 381.0322, found 381.0317.

General Procedure 2 for the Iodo-acyloxylation of Alkynes. In a 100 mL RBF was combined iodobenzene diacetate (1.0 mmol), the carboxylic acid (2.0 mmol) and chlorobenzene (20 mL). The solution was then stirred on the rotary evaporator for 10 min at 50 °C, after which time the solvent was slowly evaporated over 30 min under reduced pressure. The resultant iodobenzene dicarboxylate was further dried on the high vacuum for an additional 30 min and then dissolved in DCE (5 mL) containing 4Å molecular sieves (∼1.0 g), and I_2 (1.0 mmol) added. After stirring for 10 min, diphenylacetylene (1.2 mmol) was added in one portion, and the resultant solution stirred at rt for 4 h. After this time, the molecular sieves were filtered off, and the reaction quenched by the addition of $Na_2S_2O_3$ (10% w/w aqueous, 10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic fractions were dried over $MgSO_4$ and filtered, and the solvent evaporated. The product was purified by either recrystallization or flash column chromatography as stated.

*(E)-2-Iodo-1,2-diphenylvinyl benzoate (**2n**).* General procedure 2 was followed using benzoic acid and diphenylacetylene. Purification by recrystallization from ethanol afforded the title compound as a white solid (358 mg, 84%): mp = 106.2−110.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.82 (dd, J = 1.3 and 8.4 Hz, 2H), 7.75 (dd, J = 1.4 and 8.2 Hz, 2H), 7.48−7.53 (m, 3H), 7.40−7.44 (m, 3H), 7.33−7.38 (m, 2H), 7.26−7.30 (m, 2H), 7.19 (dt, J = 1.3 and 8.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.3, 147.3, 140.6, 137.1, 133.5, 129.9, 129.8, 129.4, 128.9, 128.6, 128.4, 128.3, 128.2, 128.1, 89.3 ppm; HRMS (m/z) = $[C_{21}H_{15}O_2I + H]^+$ calcd 427.0189, found 427.0182.

*(E)-2-Iodo-1,2-diphenylvinyl 3-(trifluoromethyl)benzoate (**2o**).* General procedure 2 was followed using 3-trifluoromethylbenzoic acid and diphenylacetylene. Purification by column chromatography (1:1 PhMe/Pet. Sp.) afforded the title compound as a yellow solid (351 mg, 71%): mp = 120.2−121.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.04 (s, 1H), 7.97 (d, J = 7.8 Hz, 1H), 7.72−7.76 (m, 3H), 7.37−7.50 (m, 6H), 7.29 (t, J = 7.3 Hz, 2H), 7.19 (dt, J = 1.3 and 6.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.0, 146.9, 140.4, 136.7, 133.0, 129.9 (q, J = 3.6 Hz), 129.5, 129.1, 128.5, 128.4, 128.3, 128.2, 126.7 (q, J = 3.8 Hz), 89.6 ppm; ^{19}F NMR (400 MHz, $CDCl_3$) δ = −62.90 ppm; HRMS (m/z) = $[C_{22}H_{14}F_3O_2I + H]^+$ calcd 495.0063, found 495.0050.

*(E)-2-Iodo-1,2-diphenylvinyl 3,4-dimethylbenzoate (**2p**).* General procedure 2 was followed using 3,4-dimethylbenzoic acid and diphenylacetylene. Purification by column chromatography (1:1 PhMe/Pet. Sp.) afforded the title compound yellow oil that solidified upon standing (341 mg, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64−7.67 (m, 2H), 7.51 (s, 1H), 7.46 (dd, J = 1.7 and 7.9 Hz, 1H), 7.40−7.43 (m, 2H), 7.28−7.32 (m, 3H), 7.17−7.21 (m, 2H), 7.09 (tt, J = 1.3, 6.7, and 8.2 Hz, 1H), 7.01 (d, J = 7.8 Hz, 1H), 2.17 (s, 3H), 2.14 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.6, 147.4, 143.0, 140.7, 137.3, 136.8, 131.0, 129.75, 129.66, 129.3, 128.7, 128.23, 128.17, 128.0, 127.5, 126.4, 89.1, 20.0, 19.6 ppm; HRMS (m/z) = $[C_{23}H_{19}O_2I + H]^+$ calcd 455.0502, found 455.0500.

*(E)-2-Iodo-1,2-diphenylvinyl 3-phenylpropanoate (**2q**).* General procedure 2 was followed using 3-phenylpropanoic acid and diphenylacetylene. Purification by column chromatography (1:1 PhMe/Pet. Sp.) afforded the title compound as a clear oil (350 mg, 77%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.52−7.55 (m, 2H), 7.31−7.34 (m, 4H), 7.20−7.25 (m, 2H), 7.17−7.19 (m, 2H), 7.07−7.12 (3H), 6.91−6.93 (m, 2H), 2.57 (t, J = 7.5 Hz, 2H), 2.31−2.35 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.5, 147.2, 140.7, 139.9, 137.0, 129.7, 129.3, 128.54, 128.48, 128.4, 128.3, 128.14, 128.10, 126.3, 88.9, 35.2, 30.3 ppm; HRMS (m/z) = $[C_{23}H_{19}O_2I + H]^+$ calcd 455.0502, found 455.0495.

*(E)-2-Iodo-1,2-diphenylvinyl 2-((1S,4R)-bicyclo[2.2.1]heptan-2-yl)acetate (**2r**).* General procedure 2 was followed using 2-

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norbornaneacetic acid and diphenylacetylene. Purification by column chromatography (1:1 PhMe/Pet. Sp.) afforded the title compound as a clear oil (321 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.63−7.66 (m, 2H), 7.32−7.44 (m, 7H), 7.24−7.29 (m, 1H), 2.09 (s, 1H), 2.05 (dd, J = 8.0 and 15.2 Hz, 1H), 1.90 (dd, J = 7.6 and 15.2 Hz, 1H), 1.55−1.62 (m, 2H), 1.36−1.40 (m, 2H), 1.20−1.26 (m, 1H), 1.10 (dt, J = 1.8 and 9.9 Hz, 1H), 1.01−1.05 (m, 2H), 0.95−1.00 (m, 1H), 0.73−0.79 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.6, 147.4, 140.9, 137.2, 129.7, 129.2, 128.6, 128.3, 128.2, 128.0, 88.7, 40.85, 40.76, 38.0, 37.5, 36.6, 35.0, 29.7, 28.4 ppm; HRMS (m/z) = $[C_{23}H_{23}O_2I + H]^+$ calcd 459.0815, found 459.0811.

*(E)-2-Iodo-1,2-diphenylvinyl cyclopentanecarboxylate (**2s**).* General procedure 2 was followed using cylopentane carboxylic acid and diphenylacetylene. Purification by column chromatography (1:2 PhMe/Pet. Sp.) afforded the title compound as a pale yellow solid (289 mg, 69%): mp = 105.9−109.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64−7.67 (m, 2H), 7.35−7.43 (m, 5H), 7.32−7.34 (m, 2H), 7.24−7.29 (m, 1H), 2.49−2.57 (m, 1H), 1.58−1.63 (m, 2H), 1.39−1.49 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.1, 147.5, 140.9, 137.1, 129.6, 129.2, 128.5, 128.3, 128.2, 128.0, 88.3, 43.3, 29.3, 25.6 ppm; HRMS (m/z) = $[C_{20}H_{19}O_2I + H]^+$ calcd 419.0502, found 419.0494.

*(E)-2-Iodo-1,2-diphenylvinyl (S)-2-phenylpropanoate (**2t**).* General procedure 2 was followed using (*S*)-2-phenylpropanoic acid and diphenylacetylene. Purification by column chromatography (1:1 PhMe/Pet. Sp.) afforded the title compound as a pale yellow oil (372 mg, 82%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54−7.56 (m, 2H), 7.35−7.39 (m, 5H), 7.26−7.31 (m, 3H), 7.20−7.25 (m, 3H), 6.99−7.01 (m, 2H), 3.55 (q, J = 7.2 Hz, 1H), 1.28 (d, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.8, 147.1, 140.7, 139.0, 136.7, 129.6, 129.2, 128.6, 128.5, 128.24, 128.19, 127.9, 127.5, 127.1, 88.6, 45.1, 18.0 ppm; HRMS (m/z) = $[C_{23}H_{19}O_2I + H]^+$ calcd 455.0502, found 455.0492.

General Procedure 3 for the Iodo-acetoxylation of Ynamides. To a solution of $PhI(OAc)_2$ (1.0 mmol) in DCE (5 mL) containing 4Å molecular sieves (~1.0 g) was added I_2 (1.0 mmol). After stirring for 10 min, ynamide (1.2 mmol) was added in one portion, and the resultant solution stirred at 0 °C for 16 h. After this time, the molecular sieves were filtered off, and the reaction quenched by the addition of $Na_2S_2O_3$ (10% w/w aqueous, 10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic fractions were dried over $MgSO_4$ and filtered, and the solvent evaporated. The product was purified by flash column chromatography.

*(S,E)-2-Iodo-1-(4-isopropyl-2-oxooxazolidin-3-yl)-2-phenylvinyl acetate (**5a**).* General procedure 3 was followed using (*S*)-4-isopropyl-3-(phenylethynyl)oxazolidin-2-one. Purification by column chromatography (1:19 EtOAc/PhMe) afforded the title compound as a pale yellow oil (299 mg, 72%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.44−7.47 (m, 2H), 7.29−7.33 (m, 2H), 7.25−7.27 (m, 1H), 4.38 (t, J = 8.8 Hz, 1H), 4.19 (dd, J = 5.9 and 8.8 Hz, 1H), 4.07 (ddd, J = 4.0, 5.9, and 8.8 Hz, 1H), 2.11−2.19 (m, 1H), 1.87 (s, 3H), 1.06 (d, J = 6.8 Hz, 3H), 0.99 (d, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.8, 154.0, 139.1, 137.6, 128.8, 128.7, 128.3, 89.7, 64.0, 60.4, 29.7, 20.1, 18.3, 15.8 ppm; HRMS (m/z) = $[C_{16}H_{18}NO_4I + H]^+$ calcd 416.0353, found 416.0359.

*(S,Z)-2-Iodo-1-(4-isopropyl-2-oxooxazolidin-3-yl)-2-phenylvinyl acetate (**5a′**).* General procedure 3 was followed using (*S*)-4-isopropyl-3-(phenylethynyl)oxazolidin-2-one; however, the reaction was performed at 60 °C. Purification by column chromatography (1:19 EtOAc/PhMe) afforded the title compound as a pale yellow oil (266 mg, 64%, E/Z = 1:3). Major isomer (*cis*-**5a′**): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37−7.40 (m, 2H), 7.28−7.36 (m, 3H), 4.00 (t, J = 8.9 Hz, 1H), 3.93 (dd, J = 5.8 and 8.9 Hz, 1H), 3.40 (ddd, J = 3.3, 5.8, and 8.9 Hz, 1H), 2.28 (s, 3H), 1.93−2.04 (m, 1H), 0.72 (d, J = 7.0 Hz, 3H), 0.53 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.1, 155.6, 138.9, 138.3, 129.2, 128.8, 128.6, 91.0, 63.6, 60.5, 28.4, 21.1, 18.1, 14.2 ppm; HRMS (m/z) = $[C_{16}H_{18}NO_4I + H]^+$ calcd 416.0353, found 416.0357. Minor-isomer (*trans*-**5a**): see above.

*(S,E)-1-(4-Benzyl-2-oxooxazolidin-3-yl)-2-iodo-2-phenylvinyl acetate (**5b**).* General procedure 3 was followed using (*S*)-4-benzyl-3-(phenylethynyl)oxazolidin-2-one. Purification by column chromatography (1:19 EtOAc/PhMe) followed by recrystallization from ethanol afforded the title compound as white needle-like crystals (366 mg, 79%): mp = 121.4−123.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30−7.32 (m, 2H), 7.22−7.25 (m, 4H), 7.18−7.20 (m, 2H), 7.12−7.15 (m, 2H), 4.22−4.26 (m, 1H), 4.20 (t, J = 8.0 Hz, 1H), 4.11 (dd, J = 6.4 and 8.0 Hz, 1H), 3.46 (dd, J = 3.4 and 13.2 Hz, 1H), 2.86 (dd, J = 10.0 and 13.2 Hz, 1H), 1.80 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.9, 153.8, 138.9, 136.8, 135.6, 129.1, 129.0, 128.9, 128.7, 128.3, 127.3, 92.6, 68.2, 57.6, 39.2, 20.1 ppm; HRMS (m/z) = $[C_{20}H_{18}NO_4I + H]^+$ calcd 464.0353, found 464.0358.

*(S,E)-2-Iodo-1-(4-phenyl-2-oxooxazolidin-3-yl)-2-phenylvinyl acetate (**5c**).* General procedure 3 was followed using (*S*)-4-phenyl-3-(phenylethynyl)oxazolidin-2-one. Purification by column chromatography (1:19 EtOAc/PhMe) afforded the title compound as a pale yellow oil that solidified on standing (364 mg, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42−7.50 (m, 5H), 7.21−7.30 (m, 5H), 5.12 (dd, J = 6.5 and 8.7 Hz, 1H), 4.80 (t, J = 8.7 Hz, 1H), 4.32 (dd, J = 6.5 and 8.7 Hz, 1H), 1.57 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.6, 153.3, 138.7, 137.3, 137.1, 129.3, 129.1, 128.7, 128.2, 127.4, 90.3, 70.7, 60.3, 19.5 ppm; HRMS (m/z) = $[C_{19}H_{16}NO_4I + H]^+$ calcd 450.0197, found 450.0178.

*(E)-2-(3,5-Dimethylphenyl)-1,2-diphenylvinyl acetate (**6**).* To a degassed solution of vinyl iodide **2a** (728 mg, 2.0 mmol) in THF (10 mL) in a sealed tube was added $Pd(PPh_3)_4$ (5 mol %), Cs_2CO_3 (2.0 equiv. 5 M aqueous solution) and 3,5-dimethylphenyl boronic acid (450 mg, 3.0 mmol). The resultant solution was heated to 100 °C for 16 h. After this time the reaction mixture was diluted with EtOAc (10 mL) and washed with NH_4Cl (10 mL, sat. aq. solution) and brine (10 mL, sat. aq. solution). The organic phase was separated, dried over $MgSO_4$ and concentrated. Purification by column chromatography (1:1 PhMe/Pet. Sp.) afforded the title compound as a pale yellow oil that solidified upon standing (493 mg, 72%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.12−7.21 (m, 7H), 7.0−7.06 (m, 3H), 6.69 (s, 1H), 6.60 (brs, 2H), 2.019 (s, 3H), 2.018 (s, 3H), 1.85 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.9, 143.6, 140.4, 139.5, 137.5, 136.0, 132.3, 129.1, 129.0, 128.9, 128.6, 128.2, 128.0, 127.9, 127.4, 21.2, 21.0 ppm; HRMS (m/z) = $[C_{24}H_{22}O_2 + H]^+$ calcd 343.1693, found 343.1696.

*2-(3,5-Dimethylphenyl)-1,2-diphenylethan-1-one (**7**).*[18] To a solution of acetate **6** (342 mg, 1.0 mmol) in methanol (5 mL) was added NaOH (2.0 mmol, 2 M aqueous solution), and the resultant mixture stirred at room temperature for 16 h. After this time the volatiles were evaporated. The aqueous solution was then acidified to pH 5 using 1 M HCl and then extracted with EtOAc (4 × 5 mL). The combined organic phases were dried over $MgSO_4$ and concentrated. Purification by column chromatography (1:1 PhMe/Pet. Sp.) afforded the title compound as a clear oil (291 mg, 97%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 (dd, J = 1.4 and 8.5 Hz, 2H), 7.48 (dt, J = 1.3 and 6.8 Hz, 1H), 7.36−7.41 (m, 2H), 7.21−7.32 (m, 5H), 6.88 (s, 2H), 6.87 (s, 1H), 5.95 (s, 1H), 2.250 (s, 3H), 2.249 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 198.4, 139.3, 138.8, 138.3, 137.0, 133.0, 129.2, 128.99, 128.97, 128.64, 128.61, 127.1, 126.9, 59.4, 21.4 ppm; HRMS (m/z) = $[C_{22}H_{20}O + H]^+$ calcd 301.1587, found 301.1591.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra for all compounds and crystallographic data for compounds **2c**, **2n** and **5b**.[19] 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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(19) The crystallographic data for compounds **2c**, **2n** and **5b** have been deposited with the Cambridge Crystallographic Data Centre with reference numbers 1046658, 1046659 and 1046660, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

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