Direct Synthesis of α-Iodoenones by IPy$_2$BF$_4$-Promoted Rearrangement of Propargylic Esters.

Tatiana Suárez-Rodríguez, Ángel L. Suárez-Sobrino, and Alfredo Ballesteros*

Instituto Universitario de Química Organometálica “Enrique Moles” and Departamento de Química Orgánica e Inorgánica. Universidad de Oviedo, c/Julián Clavería 8. 33006 Oviedo, Spain.

**ABSTRACT:** A direct access to α-iodoenones from iodonium ion and propargylic tosylates or acetates is described. Bis(pyridine) iodonium tetrafluoroborate (IPy$_2$BF$_4$, Barluenga’s reagent) promotes the rearrangement of these propargylic alcohol derivatives in mild conditions. The transformation gives β-unsubstituted, β-monosubstituted and β,β-disubstituted α-iodoenones in high yields. β-Substituted-α-iodoenones are obtained with excellent (Z)-selectivity.

**INTRODUCTION**

The availability of propargylic alcohol derivatives and their ability to undergo rearrangement transformations to allenol derivatives, have recently inspired many researchers to use them as α-acylvinyl anion equivalents, and thereby as an alternative to the classical Morita-Baylis-Hillman reaction for the synthesis of α-substituted-α,β-unsaturated carbonyl compounds.$^1$

In this regard, it has been described recently the generation of metal allenolate species, ready to couple with different electrophiles, by rearrangement of α-hydroxypropargylsilanes,$^2$ or by bimetallic dual-catalyzed rearrangement/coupling reactions of propargylic alcohols$^3$ (Scheme 1, eq 1). Additionally, Au and Ag-catalyzed rearrangements of propargylic esters to allenyl carboxylates, followed by intramolecular cyclization
have been intensively studied.\textsuperscript{4} However, there are few examples of the intermolecular version of this reaction such as the Au-catalyzed coupling of propargylic esters with isochromane acetal analogs,\textsuperscript{5} in situ generated carbocations,\textsuperscript{6} arylboronic acids,\textsuperscript{7} or NIS (N-iodosuccinimide)\textsuperscript{8} (Scheme 1, eq 2).

Very recently, it was demonstrated that rearrangements of propargylic esters can be induced directly by a carbocation\textsuperscript{9} or an oxocarbenium ion\textsuperscript{10} to the direct formation of the coupling products without the use of a metal catalyst (Scheme 1, eq 3). In the other hand, we previously proposed that reactive iodonium ion, generated from bis(pyridine) iodonium tetrafluoroborate (IPy\textsubscript{2}BF\textsubscript{4}, Barluenga’s reagent),\textsuperscript{11} promotes the activation of the C-C triple bond moiety in the presence of nucleophiles.\textsuperscript{12} This led us to consider that this iodinating agent could mediate the rearrangement reaction of propargylic ester derivatives to provide directly α-iodoenones without the use of a metal catalyst (Scheme 1 eq 4).

\textbf{Scheme 1.} Examples of propargylic alcohol derivatives as α-acylvinyl equivalents.
α-Iodoenones are useful intermediates in synthesis because of their ability to undergo transition metal-catalyzed cross-coupling reactions that makes them good precursors of enones bearing different class of α-carbon substituents. In the past decade, some authors have described more efficient and versatile methods for the synthesis of α-iodoenones based in the rearrangement of propargylic alcohol derivatives, that improve the limitations from the use of enone derivatives as precursors. Interestingly, apart from some studies limited to tertiary propargylic alcohols using iodine and an oxidant, and a recent example through oxidation of internal alkynes in the presence of NIS, most general methods require the employment of at least one metal catalytic species to promote the reaction.

Considering this, we describe herein the rearrangement reaction of propargylic alcohol derivatives promoted by reactive iodonium ion, and its use as a new, versatile and general metal-free synthetic method of α-iodoenones.

**RESULTS AND DISCUSSION**

We include in our study, apart from the propargylic acetate derivatives, the corresponding tosylates since these compounds had been reported to participate in rearrangement reactions. Moreover, we first focused in the use of primary propargylic alcohols esters, taking into account the few examples described in the literature.

Thus, our preliminary study included the corresponding tosylate 1a (R = Ts), and acetate 2a (R = Ac) of 3-phenyl-2-propynol (Table 1). First, tosylate 1a was treated with different iodonium sources (I₂, ICl, NIS, IPy₂BF₄) in a 0.05M CH₂Cl₂ solution at rt, none conversion was observed after 14 h of reaction when NIS, I₂ and IPy₂BF₄ were used (entries 1-3). On the other hand, the reaction in the same conditions with ICl allowed to obtain iodoenone 3a in a low yield (17%, entry 4). Then, the use of HBF₄·OEt₂ (1.2 equiv) as acid additive at 0°C allowed to give iodoenone 3a after aqueous extraction and purification, with yields that go from 35% to 75% depending on the iodonium source (entries 5-7); as shown, IPy₂BF₄ resulted to be more efficient than NIS. This result could be improved using double amount of acid (2.4 eq, 93%, entry 8). Similar reaction conditions were employed as well for acetate derivative 2a, although the yield in this case was slightly lower.
(86%, entry 9). Other protic (HOTf, entry 10) or Lewis acids (BF$_3$·OEt$_2$, entry 11) did not show to improve the preliminary results.

### Table 1. Optimization studies

<table>
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<tr>
<th>Entry</th>
<th>I/2</th>
<th>Iodonium source</th>
<th>Additive (equiv)</th>
<th>t(h)</th>
<th>Yield(%)$^a$</th>
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<tr>
<td>1</td>
<td>1a</td>
<td>NIS</td>
<td>none</td>
<td>14$^b$</td>
<td>--</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>I$_2$</td>
<td>none</td>
<td>14$^b$</td>
<td>--</td>
</tr>
<tr>
<td>3</td>
<td>1a</td>
<td>IPy$_2$BF$_4$</td>
<td>none</td>
<td>14$^b$</td>
<td>--</td>
</tr>
<tr>
<td>4</td>
<td>1a</td>
<td>ICl</td>
<td>none</td>
<td>14$^b$</td>
<td>17$^c$</td>
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<tr>
<td>5</td>
<td>1a</td>
<td>NIS</td>
<td>HBF$_4$·OEt$_2$ (1.2)</td>
<td>0.5$^d$</td>
<td>35$^c$</td>
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<tr>
<td>6</td>
<td>1a</td>
<td>NIS</td>
<td>HBF$_4$·OEt$_2$ (1.2)</td>
<td>3$^d$</td>
<td>39$^c$</td>
</tr>
<tr>
<td>7</td>
<td>1a</td>
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<td>HBF$_4$·OEt$_2$ (1.2)</td>
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<td>75</td>
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<tr>
<td>8</td>
<td>1a</td>
<td>IPy$_2$BF$_4$</td>
<td>HBF$_4$·OEt$_2$ (2.4)</td>
<td>0.5$^d$</td>
<td>93</td>
</tr>
<tr>
<td>9</td>
<td>2a</td>
<td>IPy$_2$BF$_4$</td>
<td>HBF$_4$·OEt$_2$ (2.4)</td>
<td>0.5$^d$</td>
<td>86</td>
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<tr>
<td>10</td>
<td>1a</td>
<td>IPy$_2$BF$_4$</td>
<td>HOTf (2.4)</td>
<td>0.5$^d$</td>
<td>80</td>
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<tr>
<td>11</td>
<td>1a</td>
<td>IPy$_2$BF$_4$</td>
<td>BF$_3$·OEt$_2$ (2.4)</td>
<td>0.5$^d$</td>
<td>72</td>
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</table>

$^a$ Isolated yields. $^b$Reaction performed at room temperature. $^c$ Yields determined by $^1$H-NMR with 4-bromobenzaldehyde as internal standard. $^d$ Reaction performed at 0°C.

Next, we investigated the scope of the reaction using first primary tosylate derivatives 1. As shown in Table 2, the reaction takes place with good yields (80-94%) with aryl substituted primary propargylic alcohol tosylates 1a-e bearing either neutral (1a,b), electron-donating (1c) or electron-withdrawing substituents (1d,e).

The reaction also tolerates the presence of heterocyclic groups (1f), alkyl (1g,h) and other functions (1i). Thus, a variety of β-unsubstituted α-iodoenones 3a-i was obtained in good yields that could be reproducible in gram scale for 3a.
Then, we studied the behavior of secondary tosylates such as 3-alkyl substituted tosylates 1j,k (Table 2), these compounds required shorter reaction times (15 min) to give the corresponding β-substituted iodoenones 3j-k.
in good yields (77-82%) and excellent (Z)-selectivity. The (Z)-configuration of products 3j and 3k was determined by NOESY or NOE experiments respectively. Unfortunately, secondary 3-aryl substituted propargylic tosylates ($R^2 = Ar$) were unstable to reaction conditions, this limitation can also be extended to tertiary tosylates.

Table 3. IPy$_2$BF$_4$-promoted rearrangement reaction of propargylic acetates 2 to $\alpha$-iodoenones 3.

| 2a | 3a (86%) |
| 2d | 3d (76%) |
| 2l | 3l (75%) |
| 2m | 3m (86%) |
| 2n | 3n (71%$^{(a,b)}$) |
| 2o | 3o (54%$^{(c)}$) |
| 2p | 3p (80%$^{(d)}$) |
| 2q | 3q (60%$^{(e)}$) |
| 2r | 3r (66%$^{(d,f)}$) |

$^a$Z/E ratio > 20:1.$^b$Reaction time 5 min. $^c$Reaction performed with 2.0 equiv of acid at -20ºC.

$^d$1.2 equivalents of acid were used. $^e$2.2 equivalents of acid were used. $^f$Z/E ratio = 5:1.
As said above, propargylic acetates 2 can also undergo this reaction and thereby can be used as an alternative to the corresponding unstable tosylate derivatives. Table 3 shows the results employing acetates 2 derived from primary, secondary and tertiary propargylic alcohols. In this sense; apart from compounds 3a,d obtained previously from propargylic tosylates in better yields (see Table 2), new β-unsubstituted α-iodoenones 3l,m were synthesized (75-86% yield respectively), in those cases the reaction from the corresponding tosylate 1 failed.

We studied next the reaction in secondary and tertiary propargylic alcohol acetates 2n-r. In general, these compounds are also more sensitive to reaction conditions and some changes in the general experimental procedure were required (see Table 3). Contrary to its tosylate counterpart, 3-aryl substituted propargylic acetate 2n could undergo the iodonium-promoted rearrangement reaction to lead selectively to the (Z)-isomer (the configuration was determined by a NOE experiment) of β-substituted-α-iodoenone 3n in good yield (71%). Additionally, a variety of β,β-disubstituted α-iodoenones 3o-r, bearing alkyl and aryl groups or other functions, could be obtained from tertiary propargylic acetates 2o-r in moderate to good yields (54-80%). Acid equivalents and temperature should be controlled in some cases in order to prevent acetic acid elimination side reaction (see Table 3). For compound 3r the (Z/E) ratio fell to 5:1. The stereochemistry of the isomers was elucidated by a NOESY experiment.\(^{23}\)

In order to get some insight into the reaction course we analyzed the reaction crude by \(^1\)H NMR after running the reaction of 1a in CD\(_2\)Cl\(_2\). Thus, the presence of the corresponding iodoenone-BF\(_3\) complex 4a (R\(^1 =\) Ph) and tosylfluoride were detected (Scheme 2).\(^{24,25}\)

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**Scheme 2.** NMR experiment for 1a.

Moreover, activated enones 4a,s could be trapped when the reactions of propargylic tosylates 1a,s (Scheme 3) were quenched, before aqueous work up, with 1,3,5-trimethoxybenzene to furnish 1,4-nucleophylic adducts
5a,s in 72 and 70% yields respectively. On the other hand, adduct 5a was also obtained directly from enone 3a by treatment with BF$_3$·OEt$_2$ followed by the reaction with 1,3,5-trimethoxybenzene in 94% yield.

Scheme 3. In situ addition of 1,3,5-trimethoxybenzene to activated enones 4a,s.

According to previous mechanistic proposals for electrophile-induced rearrangement reactions of propargyl acetates,$^9,10$ a likely mechanism for tosylates 1 could be proposed as follows; the reaction would start from the activation of the alkynyl moiety by the iodonium cation to give complex A, followed by the intramolecular nucleophilic attack of the tosyl group oxygen to the activated alkyne, to furnish cation B. The addition of a fluoride anion to B provides intermediate C which, after C–O bond cleavage, eliminates tosylfluoride to yield BF$_3$-coordinated-enones 4 (Scheme 4). The hydrolysis of complexes 4 finally gives the corresponding enones 3. Furthermore, a similar pathway for acetates 2 could also be expected. In addition, Figure 1 shows a minimized 3D-model of the pseudochair conformation of intermediate B that would explain the (Z)-selectivity found in this transformation for secondary tosylates.
**CONCLUSIONS**

In conclusion, we have described a direct access to α-iodoenones, by treatment of propargylic tosylate or acetate derivatives with IPy$_2$BF$_4$. The reaction takes place in mild conditions and high yields with primary and secondary propargylic alcohol tosylates and alternatively with primary, secondary and tertiary propargylic alcohol acetates, to give rise to a variety of β-unsubstituted, β-substituted, and β,β-disubstituted-α-iodoenones respectively. Moreover, β-substituted iodoenones are obtained with excellent (Z)-selectivity. The reaction likely starts with the activation of the acetylene moiety by the iodonium cation, that promotes the rearrangement reaction to the final products.

**EXPERIMENTAL SECTION**

**General Remarks.** All reactions were carried out using oven-dried glassware under an atmosphere of nitrogen (99.99 %) or argon (99.999 %). Dichloromethane (DCM), was distilled from CaH$_2$ prior its use. The solvents used in column chromatography, hexane and ethyl acetate were obtained from commercial suppliers and used without further distillation. TLC was performed on aluminium-backed plates coated with silica gel 60 with F254 indicator (Merck), using UV light as a visualizing agent as well as phosphomolybdic acid in ethanol, potassium permanganate solution or p-anisaldehyde in ethanol as developing agents. Flash chromatography was performed on silica gel 60 (230-400 mesh). $^1$H NMR (300 MHz) and $^{13}$C NMR (75.5 MHz) spectra were measured in CDCl$_3$ at room temperature on a Bruker DPX-300, Bruker AV-300 MHz,
with TMS (δ = 0.0 ppm) as internal standard. Data are reported as follows: chemical shift (ppm), multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, quint; quintet, sext: sextet, septuplet: m: multiplet), coupling constants (J in Hz) and integration. Carbon multiplicities were assigned by DEPT techniques.

All common reagents and solvents were obtained from commercial suppliers and used without any further purification unless otherwise noted. IPy₂BF₄ was purified by precipitation from the addition of diethyl ether to a solution of IPy₂BF₄ in CH₂Cl₂.

High-resolution mass spectra (HRMS) were obtained by electron ionization techniques (EI) (70 eV) with a VG AutoSpec M mass Spectrometers and a microTOF focus (Bruker Daltonics, Bremen Germany).

Melting points (mp) of recrystallized samples were measured on a Buchi-Tottoli apparatus and were not corrected.

**Preparation of Starting materials 1 and 2.** Tosylates 1a, 1b, 1e, 1g, 1j, 1k, 1s, and acetates 2a, 2d, n were prepared according to the methods described in the literature.

**Preparation of tosylates 1c,d,f,h,i.** A propargyl alcohol (15 mmol) and tosyl chloride (15.75 mmol) were solved in diethyl ether (0.5-1.0 M); the solution was cooled to -50ºC and freshly powdered KOH (90 mmol) was added with vigorous stirring. The temperature of the mixture was allowed to rise to 0 ºC and the stirring was continued for 0.5-1 hour under the same experimental conditions. When the reaction finished (confirmed by TLC), it was poured into an ice-water mixture and extracted with diethyl ether (3 x 20 mL) and the combined extracts were washed with water and brine and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the crude purified by column chromatography or by recrystallization.

Characterization data and spectra for 1a,b,e, 1g, 1j, 1k, 1s, 2a, 2d, n, 2l, 2m, 2o, and 2p are available in the literature.

**3-(3-Methoxyphenyl)prop-2-yn-yl 4-methylbenzenesulfonate (1c).** Yield 4.08 g (86%), white solid, mp = 62-64 ºC; ¹H NMR δ = 2.41 (s, 3H), 3.80 (s, 3H), 4.97 (s, 2H), 6.78-6.81 (m, 1H), 6.84-6.93 (m, 2H), 7.17-7.25 (m, 1H), 7.35 (m, 2H), 7.88 (m, 2H); ¹³C NMR δ = 21.6 (C), 55.3 (CH₂), 58.6 (CH₃), 80.3 (C),
88.9 (C), 115.5 (CH), 116.8 (CH), 122.4 (C), 124.2 (CH), 128.2 (CH), 129.3 (CH), 129.8 (CH), 133.4 (C), 145.1 (C), 159.2 (C); HRMS calcd for C_{17}H_{16}O_{4}S [M]^+ 316.0769, found 316.0768.

3-(2-Bromophenyl)prop-2-yn-yl 4-methylbenzenesulfonate (1d). Yield 4.49 g (82%), white solid, mp = 68-70 °C; \(^1\)H NMR δ = 2.39 (s, 3H), 5.02 (s, 2H), 7.17-7.30 (m, 3H), 7.33 (d, J = 8.2, 2H), 7.54-7.60 (m, 1H), 7.88 (d, J = 8.2, 2H); \(^{13}\)C NMR δ = 21.6 (CH₃), 58.4 (CH₂), 85.0 (C), 87.2 (C), 123.7 (C), 125.4 (C), 126.9 (CH), 128.2 (CH), 129.8 (CH), 130.3 (CH), 132.4 (CH), 133.3 (C), 133.7 (CH), 145.1 (C); HRMS calcd for C_{18}H_{13}BrO_{3}S [M]^+ 363.9769, found 363.9771.

3-(Benzofuran-2-yl)prop-2-yn-yl 4-methylbenzenesulfonate (1f). Yield 3.67 g (75%), white solid, mp > 59 °C (decomposition); \(^1\)H NMR δ = 2.40 (s, 3H), 5.02 (s, 2H), 6.90 (s, 1H), 7.24-7.31 (m, 1H), 7.33-7.48 (m, 4H), 7.54-7.60 (m, 1H); 7.88 (d, J = 8.3, 2H); \(^{13}\)C NMR δ = 21.6 (CH₃), 57.9 (CH₂), 79.4 (C), 86.8 (C), 111.3 (CH), 113.4 (CH), 121.5 (CH), 123.5 (CH), 126.2 (CH), 127.1 (C), 128.2 (CH), 129.9 (CH), 133.0 (C), 137.0 (C), 145.3 (C), 154.9 (C); HRMS calcd for C_{18}H_{14}O_{4}S [M]^+ 326.0613, found 326.0615.

3-Cyclohexylprop-2-yn-yl 4-methylbenzenesulfonate (1h). Yield 3.99 g (91%), colorless oil; \(^1\)H NMR δ = 1.19-1.35 (m, 5H), 1.44-1.73 (m, 5H), 2.21-2.30 (m, 1H), 2.47 (s, 3H), 4.75 (d, J = 2.2, 2H), 7.36 (d, J = 8.2, 2H); \(^{13}\)C NMR δ = 21.6 (CH₃), 24.7 (CH₂), 25.7 (CH₂), 28.9 (CH), 2.0 (CH₂), 58.9 (CH₂), 71.7 (C), 94.4 (C), 128.1 (CH), 129.7 (CH), 133.5 (C), 144.8 (C); HRMS calcd for C_{16}H_{20}O_{3}S [M]^+ 292.1133, found 292.1154.

Hex-2-yne-1,6-diyl bis(4-methylbenzenesulfonate) (1i). Yield 4.69 g, (74%), white solid, mp = 64-66 °C; \(^1\)H NMR δ = 1.75 (quint, J = 6.5, 2H), 2.19 (tt, J = 6.5, 2.2, 2H), 2.47 (s, 3H), 2.48 (s, 3H), 4.04 (t, J = 6.5, 2H), 4.62 (t, J = 2.2, 2H), 7.33-7.41 (m, 4H), 7.75-7.85 (m, 4H); \(^{13}\)C NMR δ = 14.9 (CH₂), 21.7 (CH₃), 27.4 (CH₂), 58.3 (CH₂), 68.5 (CH₂), 73.1 (C), 87.9 (C), 127.9 (CH), 128.1 (CH), 129.8 (CH), 129.9 (CH), 132.8 (C), 133.2 (C), 144.9 (C), 145.0 (C); HRMS calcd for C_{20}H_{22}O_{6}S_{2} [M]^+ 422.0858, found 422.0860.

1-Benzyl-4-((4-fluorophenyl)ethyl)yl)piperidin-4-yl acetate (2q). Yield 4.22 g (80%), yellowish solid, mp = 45-47 °C; \(^1\)H NMR δ = 2.09 (s, 3H), 2.12-2.38 (m, 4H), 2.47-2.76 (m, 4H), 3.56 (s, 2H), 6.97-7.06 (t, J = 8.7, 2H), 7.25-7.38 (m, 5H), 7.39-7.47 (m, 2H); \(^{13}\)C NMR δ = 21.9 (CH₃), 36.7 (CH₂), 49.8 (CH₂), 62.7 (CH₂), 73.8 (C), 85.8 (C), 88.0 (C), 115.5 (d, J = 22.2, CH), 118.6 (d, J = 3.4, C), 127.1 (CH), 128.3
(CH), 129.1 (CH), 133.7 (d, J = 8.4, CH), 138.2 (C), 162.6 (d, J = 250 C), 169.3 (C); HRMS calcd for C_{22}H_{22}FNO_{2} [M]^+ 351.1635, found 351.1636.

3,4-Dimethyl-1-phenylpent-1-yne-3-yl acetate (2r). Yield 3.01 g (87%), yellow oil; \(^1\)H NMR \(\delta = 1.07\) (d, \(J = 6.6\), 3H), 1.11 (d, \(J = 6.6\), 3H), 1.73 (s, 3H), 2.06 (s, 3H), 2.28 (sept, \(J = 6.6\), 1H), 7.27–7.32 (m, 2H), 7.42–7.47 (m, 2H); \(^{13}\)C NMR \(\delta = 17.3\) (CH\(_3\)), 27.6 (CH\(_3\)), 22.0 (CH\(_3\)), 23.3 (CH\(_3\)), 37.5 (CH), 79.4 (C), 85.6 (C), 88.5 (C), 122.8 (C), 128.1 (CH), 128.2 (CH), 131.8 (CH), 169.3 (C). HRMS calcd for C\(_{15}\)H\(_{18}\)O\(_2\) [M]\(^+\) 230.1307, found 230.1305.

**General Procedure for the Synthesis of \(\alpha\)-Iodoenones 3.** Tosylates 1 or acetates 2 (0.25 mmol) and IPy\(_2\)BF\(_4\) (112 mg, 0.3 mmol, 1.2 equiv) were dissolved in anhydrous CH\(_2\)Cl\(_2\) (5 mL) under argon atmosphere. Then, HBF\(_4\)·Et\(_2\)O (82 \(\mu\)L, 0.6 mmol, 2.4 equiv) (1.2 equivalents for 3p and 3r; 2 equiv for 3o) was added at 0 °C (–20 °C for 3o) with vigorous stirring and the reaction maintained for 30 minutes (15 minutes for 3j and 3k; 5 minutes for 3n) at the same temperature. Next, H\(_2\)O (5 mL) was added and the mixture was extracted with CH\(_2\)Cl\(_2\) (3 x 5 mL). The organic layer was treated with a saturated solution of Na\(_2\)S\(_2\)O\(_3\) (5 mL), then dried over anhydrous Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 20:1 to 5:1) to give pure \(\alpha\)-iodoenones 3.

**Gram Scale Preparation of 3a.** Tosylate 1a (1.7 g, 6 mmol) and IPy\(_2\)BF\(_4\) (2.7 g, 7.2 mmol, 1.2 equiv) were dissolved in 120 mL of anhydrous CH\(_2\)Cl\(_2\) under argon atmosphere. Then, HBF\(_4\)·Et\(_2\)O (2 mL 14.4 mmol, 2.4 equiv) was added at 0 °C with vigorous stirring and the reaction maintained for 30 minutes at the same temperature. Next, H\(_2\)O (120 mL) was added and the mixture was extracted with CH\(_2\)Cl\(_2\) (3 x 50 mL). The organic layer was treated with a saturated solution of Na\(_2\)S\(_2\)O\(_3\) (120 mL), then dried over anhydrous Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 20:1) to give pure \(\alpha\)-iodoenone 3a (1.44 g, 94%).

2-Iodo-1-phenylprop-2-en-1-one (3a). Yield 59 mg, (from 1a, 93%), 55 mg (from 2a, 86%), yellow oil; \(^1\)H NMR \(\delta = 6.85\) (d, \(J = 2.2\), 1H), 6.89 (d, \(J = 2.2\), 1H), 7.48 (m, 2H), 7.60 (m, 1H), 7.84 (d, \(J = 7.6\), 2H); \(^{13}\)C NMR \(\delta = 107.9\) (C), 128.5 (CH), 129.8 (CH), 133.1 (CH), 133.8 (C), 138.2 (CH\(_2\)), 191.7 (C); HRMS calcd for C\(_9\)H\(_9\)IO [M]^+ 257.9543, found 257.9542.
2-Iodo-1-(p-tolyl)prop-2-en-1-one (3b). Yield 53 mg, (79%), yellow oil; $^1$H NMR δ =2.44 (s, 3H), 6.78 (d, $J = 2.2$, 1H), 6.84 (d, $J = 2.2$, 1H), 7.28 (d, $J = 8.4$, 2H), 7.78 (d, $J = 8.4$, 2H); $^{13}$C NMR δ = 21.7 (CH$_3$), 107.7 (C), 129.3 (CH), 130.2 (CH), 131.1 (C), 137.3 (CH$_2$), 144.3 (C), 191.5 (C); HRMS calcd for C$_{10}$H$_9$IO [M]$^+$ 271.9698, found 271.9698.

2-Iodo-1-(3-methoxyphenyl)prop-2-en-1-one (3c). Yield 58 mg, (81%), yellow oil; $^1$H NMR δ =3.87 (s, 3H), 6.84 (d, $J = 2.3$, 1H) 6.90 (d, $J = 2.3$, 1H), 7.11-7.18 (m, 1H), 7.33-7.36 (m, 1H), 7.37-7.41 (m, 2H); $^{13}$C NMR δ = 55.9 (CH$_3$), 108.2 (C), 114.6 (CH), 120.0 (CH), 123.0 (CH), 129.9 (CH), 135.4 (C), 138.8 (CH$_2$), 160.1 (C), 192.0 (C); HRMS calcd for C$_{10}$H$_9$IO$_2$ [M]$^+$ 287.9645, found 287.9647.

1-(2-Bromophenyl)-2-iodoprop-2-en-1-one (3d). Yield 71 mg (from 1d, 84%), 64 mg (from 2d, 76%), yellow oil; $^1$H NMR δ = 6.90 (d, $J = 2.2$, 1H), 7.05 (d, $J = 2.2$, 1H), 7.28-7.44 (m, 3H), 7.61-7.66 (m, 1H)); $^{13}$C NMR δ = 111.9 (C), 119.9 (C), 127.6 (CH), 129.2 (CH), 132.0 (CH), 133.6 (CH), 137.9 (C), 143.4 (CH$_2$), 191.5 (C); HRMS calcd for C$_9$H$_6$BrIO [M]$^+$ 335.8659, found 335.8647.

2-Iodo-1-(4-nitrophenyl)prop-2-en-1-one (3e). Yield 61 mg (80%), white solid, mp 87-89 °C; $^1$H NMR δ = 6.94 (d, $J = 2.5$, 1H), 6.99 (d, $J = 2.5$, 1H), 7.96 (d, $J = 8.9$, 2H), 8.35 (d, $J = 8.9$, 2H); $^{13}$C NMR δ = 107.6 (C), 124.1 (CH), 131.0 (CH), 139.6 (C), 140.6 (CH$_2$), 150.6 (C), 190.5 (C); HRMS calcd for C$_9$H$_5$NO$_3$ [M]$^+$ 302.9397, found 302.9392.

1-(Benzofuran-2-yl)-2-iodoprop-2-en-1-one (3f). Yield 23 mg (from 1f, 36%), 22 mg (from 2f, 34%), white solid, mp 82-83 °C (decomposition); $^1$H NMR δ = 6.92 (d, $J = 2.3$, 1H), 7.33-7.37 (m, 1H), 7.40 (d, $J = 2.3$, 1H), 7.51-7.58 (m, 1H), 7.60-7.66 (m, 2H), 7.73-7.78 (m, 1H); $^{13}$C NMR δ =106.0 (C), 112.6 (CH), 117.3 (CH), 123.5 (CH), 124.3 (CH), 126.7 (C), 128.9 (CH), 138.2 (CH$_2$), 148.4 (C), 156.3 (C), 179.8 (C); HRMS calcd for C$_{11}$H$_7$IO$_2$ [M]$^+$ 297.9492, found 297.9491.

2-IodoheX-1-en-3-one (3g). Yield 48 mg (85%), pale orange oil; $^1$H NMR δ = 0.98 (t, $J = 7.3$, 3H), 1.71 (sext, $J = 7.3$, 2H), 2.82 (t, $J = 7.3$, 2H), 6.83 (d, $J = 2.5$, 1H), 7.26 (d, $J = 2.5$, 1H); $^{13}$C NMR δ =14.1 (CH$_3$), 18.6 (CH$_2$), 38.9 (CH$_2$), 113.8 (C), 137.7 (CH$_2$), 195.5 (C); HRMS calcd for C$_8$H$_9$IO [M]$^+$ 223.9734, found 223.9736.

1-Cyclohexyl-2-iodoprop-2-en-1-one (3h). Yield 51 mg (77%), orange oil; $^1$H NMR δ = 1.18-1.53 (m, 5H), 1.67-1.76 (m, 1H), 1.77-1.90 (m, 4H), 3.15 (tt, $J = 11.3$, 3.2, 1H), 6.81 (d, $J = 2.4$, 1H), 7.23 (d, $J$ =
2.4, 1H); $^{13}$C NMR δ = 26.1 (CH$_2$), 26.15 (CH$_2$), 30.1 (CH$_2$), 44.6 (CH), 113.3 (C), 137.1 (CH$_2$), 199.0 (C); HRMS calcd for C$_9$H$_{13}$IO [M]$^+$ 264.0009, found 264.0011.

5-Iodo-4-oxohex-5-en-1-yl-4-methylbenzenesulfonate (3i). Yield 81 mg (82%), yellow oil; $^1$H NMR δ = 2.03 (m, 2H), 2.48 (s, 3H), 2.94 (t, J = 6.9, 2H), 4.10 (t, J = 2.2, 2H), 6.85 (d, J = 2.6, 1H), 7.25 (d, J = 2.6, 1H), 7.37 (d, J = 8.5, 2H), 7.79 (d, J = 8.5, 2H); $^{13}$C NMR δ = 21.7 (CH$_3$), 23.7 (CH$_2$), 31.9 (CH$_2$), 69.3 (CH$_2$), 112.2 (C), 127.8 (CH), 129.9 (CH), 132.8 (C), 138.1 (CH$_2$), 144.9 (C), 193.5 (C); HRMS calcd for C$_{13}$H$_{15}$IO$_4$S [M]$^+$ 393.9736, found 393.9737.

(Z)-4-Iodo-hex-4-en-3-one (3j). Yield 46 mg (82%), pale yellow oil; $^1$H NMR δ = 1.16 (t, J = 7.3, 3H), 2.08 (d, J = 7.3, 3H), 2.86 (q, J = 7.6, 2H), 7.14 (q, J = 6.6, 1H); $^{13}$C NMR δ = 9.1 (CH$_3$), 23.9 (CH$_3$), 31.2 (CH$_2$), 113.7 (C), 146.8 (CH), 195.3 (C); HRMS calcd for C$_9$H$_5$O [M]$^+$ 223.9699, found 223.9698.

(Z)-4-Iodo-2-methyl-3-en-5-one (3k). Yield 54 mg (77%), pale yellow oil; $^1$H NMR δ = 0.94 (t, J = 7.3, 3H), 1.13 (d, J = 6.7, 6H), 1.36 (sext., J = 7.3, 2H), 1.6 (quint., J = 7.3, 2H), 2.8 (t, J = 7.3, 2H), 2.78-2.92 (m, 1H), 6.74 (d, J = 8.8, 1H); $^{13}$C NMR δ = 13.9 (CH$_3$), 20.8 (CH$_3$), 22.3 (CH$_2$), 27.1 (CH$_2$), 37.4 (CH), 37.6 (CH$_2$), 109.7 (C), 157.2 (CH), 195.3 (C); HRMS calcd for C$_{10}$H$_{13}$O [M + H]$^+$ 281.0399, found 281.0397.

2-Iodo-1-(4-methoxyphenyl)prop-2-en-1-one (3l). Yield 54 mg (75%), pale yellow oil; $^1$H NMR δ = 3.90 (s, 3H), 6.69 (d, J = 2.2, 1H), 6.77 (d, J = 2.2, 1H), 6.96 (d, J = 9.0 Hz, 2H); 7.88 (d, J = 9.0, 2H); $^{13}$C NMR δ = 55.3 (CH$_3$), 106.8 (C), 113.9 (CH), 126.1 (C), 132.6 (CH), 135.8 (CH$_2$), 163.9 (C), 190.6 (C); HRMS calcd for C$_{10}$H$_{13}$O$_2$ [M]$^+$ 287.9645, found 287.9647.

2-Iodo-1-(thiophen-2-yl)prop-2-en-1-one (3m). Yield 57 mg (86%), orange oil; $^1$H NMR δ = 6.70 (d, J = 2.3, 1H), 6.99 (d, J = 2.3, 1H), 7.16 (t, J = 4.4, 1H), 7.72-7.78 (m, 2H); $^{13}$C NMR δ = 105.8 (C), 128.7 (CH), 135.6 (CH), 136.1 (CH), 136.4 (CH$_2$), 139.4 (C), 184.1 (C); HRMS calcd for C$_{7}$H$_5$IOS [M]$^+$ 263.9109, found 263.9106.

(Z)-2-Iodo-1-phenylpent-2-en-1-one (3n). Yield 51 mg (71%), pale orange oil; $^1$H NMR δ = 1.13 (t, J = 7.0, 3H), 2.48 (quint, J = 7.0, 2H), 6.64 (t, J = 7.0, 1H), 7.43-7.50 (m, 2H), 7.54-7.61 (m, 1H), 7.68-7.75 (m, 2H); $^{13}$C NMR δ = 12.0 (CH$_3$), 31.3 (CH$_2$), 107.9 (C), 128.4 (CH), 129.7 (CH), 132.4 (CH), 135.8 (C), 155.6 (CH), 192.0 (C); HRMS calcd for C$_{11}$H$_{11}$IO [M]$^+$ 285.9858, found 285.9855.
3-Iodo-2-methyloct-2-en-4-one (3o). Yield 36 mg (54%), pale yellow oil; $^1$H NMR $\delta = 0.94$ (t, $J = 7.3$, 1H), 1.28-1.44 (m, 2H), 1.55-1.69 (m, 2H), 1.97 (s, 3H), 2.04 (s, 3H), 2.82 (t, $J = 7.4$, 2H); $^{13}$C NMR $\delta =$13.9 (CH$_3$), 21.9 (CH$_3$), 22.3 (CH$_2$), 26.4 (CH$_2$), 30.3 (CH$_3$), 40.5 (CH$_2$), 95.4 (C), 144.3 (C), 202.3 (C); HRMS calcd for C$_9$H$_{15}$IO $[M]^+ 266.0203$, found 266.0201.

2-Cyclohexylidene-2-iodo-1-phenylethan-1-one (3p). Yield 65 mg (80%), pale yellow oil; $^1$H NMR $\delta = 1.41-1.51$ (m, 2H), 1.54-1.67 (m, 2H), 1.68-1.79 (m, 2H), 2.16-2.31 (m, 2H), 2.49-2.66 (m, 2H), 7.42-7.55 (m, 2H), 7.56-7.69 (m, 1H), 7.93-8.09 (m, 2H); $^{13}$C NMR $\delta =$26.2 (CH$_2$), 27.8 (CH$_2$), 28.0 (CH$_2$), 33.7 (CH$_2$), 39.3 (CH$_2$), 88.1 (C), 129.2 (CH), 130.4 (CH), 134.1 (CH), 134.4 (C), 150.0 (C), 193.6 (C); HRMS calcd for C$_{14}$H$_{15}$IO $[M]^+ 326.0165$, found 326.0168.

2-Iodo-3,4-dimethyl-1-phenylpent-en-1-one (3r). Yield 47 mg (66%), Z/E = 5:1, pale yellow oil; $^1$H NMR $\delta$ major isomer = 0.99 (d, $J = 6.8$, 6H), 2.04 (s, 3H), 2.53-2.85 (m, 1H), 7.43-7.55 (m, 2H), 7.56-7.67 (m, 1H) 7.93-8.03 (m, 2H), $\delta$ minor isomer = 1.14 (d, $J = 6.9$, 6H), 1.72 (s, 3H), 3.03-3.29 (m, 1H), 7.43-7.55 (m, 2H), 7.56-7.67 (m, 1H), 7.93-8.03 (m, 2H); $^{13}$C NMR $\delta$ major isomer $\delta =$19.8 (CH$_3$), 20.7 (CH$_3$), 33.9 (CH), 91.1 (C), 128.7 (CH), 130.0 (CH), 133.7 (CH), 133.8 (C), 151.0 (C), 193.2 (C); minor isomer = 14.7 (CH$_3$), 20.9 (CH$_3$), 39.2 (CH), 89.1 (C), 128.8 (CH), 129.9 (CH), 133.7 (CH), 133.8 (C), 149.7 (C), 193.0 (C); HRMS calcd for C$_9$H$_{15}$IO $[M]^+ 266.0203$, found 266.0201.

Preparation of $\alpha$-Iodoenone 3q. IPy$_2$BF$_4$ (112 mg, 0.3 mmol, 1.2 equiv) was dissolved under argon atmosphere of anhydrous CH$_2$Cl$_2$ (4 mL) at 0°C. Then, HBF$_4$·Et$_2$O (41 μL, 0.3 mmol, 1.2 equiv) were added with vigorous stirring, followed by a solution of 2q (0.25 mmol, 1 equiv) and HBF$_4$·Et$_2$O (34 μL, 0.25 mmol, 1 equiv) in anhydrous CH$_2$Cl$_2$ (1 mL). The stirring was maintained at the same temperature for 30 minutes. Next, H$_2$O (5 mL) was added and the mixture was extracted with CH$_2$Cl$_2$ (3 x 5 mL). The organic layer was treated with a saturated solution of Na$_2$S$_2$O$_3$ (5 mL), then dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 3:1) to give pure 3q (65 mg, 60%).

2-(1-Benzylpiperidin-4-ylidene)-1-(4-fluorophenyl)-2-idoethen-1-one (3p). Pale yellow oil; $^1$H NMR $\delta =$2.28-2.44 (m, 2H), 2.57-2.64 (m, 2H), 2.65-2.75 (m, 2H), 3.56 (s, 3H), 7.11-7.17 (m, 2H), 7.23-
7.37 (m, 5H), 7.81-8.01 (m, 2H); $^{13}$C NMR $\delta$ =33.1 (CH$_2$), 38.6 (CH$_2$), 54.0 (CH$_2$), 54.1 (CH$_2$), 62.7 (CH$_2$), 88.9 (CH), 116.5 (CH, d, $J$ = 9.4) 127.6 (CH), 128.7 (CH), 129.4 (CH), 130.7 (C, d, $J$ = 3.0), 133.1 (CH, d, $J$ = 9.4) 138.4 (C), 147.4 (C), 166.6 (C, d, $J$ = 257.7), 191.8 (C); HRMS calcd for C$_{20}$H$_{19}$FIONO [M]$^+$ 435.0486, found 435.0495.

**General Procedure for the Synthesis of products 5.** Tosylates 1 (0.25 mmol) and IPy$_2$BF$_4$ (112 mg, 0.3 mmol, 1.2 equiv) were dissolved in anhydrous CH$_2$Cl$_2$ (5 mL) under argon atmosphere. Then, HBF$_4$·Et$_2$O (82 µL, 0.6 mmol, 2.4 equiv) were added at 0 ºC with vigorous stirring and the reaction was maintained for 30 minutes at the same temperature. Then, 1,3,5-trimethoxybenzene (126 mg, 0.75 mmol, 1.5 equiv) was added at 0ºC and the mixture was stirred for 30 additional minutes. Then, H$_2$O (5 mL) was added and the mixture was extracted with CH$_2$Cl$_2$ (3 x 5 mL). The organic layer was treated with a saturated solution of Na$_2$S$_2$O$_3$ (5 mL), then dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by column chromatography previously deactivated with a 10:1 mixture of hexane/Et$_3$N (silica gel, hexane/ethyl acetate 10:1) to give compounds 5.

**Synthesis of 5a from α-Iodoenone 3a.** α-Iodoenone 3a (65 mg, 0.25 mmol, 1 equiv) was dissolved in CH$_2$Cl$_2$ (5 mL) under argon atmosphere and BF$_3$·Et$_2$O (31 µL, 0.25 mmol, 1 equiv) was added. The resulting solution was cooled to 0°C; then, 1,3,5-trimethoxybenzene (63 mg, 0.38 mmol, 1.5 equiv) was added and the mixture stirred for 30 minutes at the same temperature. Next, H$_2$O (5 mL) was added and the reaction extracted with CH$_2$Cl$_2$ (3 x 5 mL). The organic layer was treated with a saturated solution of Na$_2$S$_2$O$_3$ (5 mL), then dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 10:1) to give 5a (100 mg, 94%).

**2-Iodo-1-phenyl-3-(2,4,6-trimethoxyphenyl)propan-1-one (5a).** Yield 77 mg (72%), white solid, mp 110 ºC (decomposition); $^1$H NMR $\delta$ =3.32 (dd, $J$ = 14.5, 6.1, 1H), 3.63 (dd, $J$ = 14.5, 8.7, 1H), 3.82 (s, 9H), 5.84 (dd, $J$ = 8.7, 6.1, 1H), 6.14 (s, 2H), 7.42-7.50 (m, 2H), 7.53-7.60 (m, 1H), 7.94-8.02 (m, 2H); $^{13}$C NMR $\delta$ = 26.6 (CH), 28.4 (CH$_2$), 55.3 (CH$_3$), 55.7 (CH$_3$), 90.6 (CH), 108.1 (C), 128.6 (CH), 128.65 (CH), 133.1 (CH), 134.5 (C), 159.1 (C), 160.2 (C), 195.2 (C); HRMS calcd for C$_{18}$H$_{20}$IO$_4$ [M + H]$^+$ 427.0402, found 427.0401.
3-Iodo-4-(2,4,6-1-one (5s). Yield 65 mg (72%), white solid, mp 70 °C (decomposition); $^1$H NMR δ = 2.44 (s, 3H), 3.29 (dd, $J = 14.3$, 7.7, 1H), 3.35 (dd, $J = 14.3$, 7.7, 1H), 3.8 (s, 9H), 4.83 (t, $J = 7.7$, 1H), 6.12 (s, 2H); $^{13}$C NMR δ = 25.4 (CH), 29.0 (CH$_2$), 33.3 (CH$_3$), 55.4 (CH$_3$), 55.7 (CH$_3$), 90.7 (CH), 107.7 (C), 159.0 (C), 160.5 (C), 203.7 (C); HRMS calcd for C$_{13}$H$_{18}$IO$_4$ [M + H]$^+$ 365.0249, found 365.0244.

**ASSOCIATED CONTENT**

**Supporting Information**

The Supporting Information is available free of charge on the ACS Publications website.

Optimization studies. NMR study, and $^1$H and $^{13}$C NMR spectra (PDF).

**AUTHOR INFORMATION**

**Corresponding Author**

*Phone: +34-98-510-3506. E-mail: abg@uniovi.es*

**Notes**

The authors declare no competing financial interest.

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**REFERENCES**


(12) For intramolecular C-C bond formation see: (a) Barluenga, J.; González, J. M.; Campos, P. J.; Asensio, G. Iodine-induced stereoselective carbocyclizations: A new method for the synthesis of cyclohexane and


(22) At least two acid equivalents are needed to neutralize all pyridine moieties and liberate a more active iodonium ion.

(23) See Supporting Information

(24) To demonstrate the presence of 4a in the crude reaction mixture, this complex was prepared by *in situ* reaction of enone 3a with one equivalent of BF₃·OEt₂ in CD₂Cl₂. See Suporting Information.
(25) TsF could be isolated [36.1 mg, 83%, Rf (hexane / AcOEt 20:1) = 0.3] when the reaction is run according to the general procedure described in the experimental section at 0.25 mmol scale. See Supporting Information.


