

# Carbonylative Suzuki–Miyaura Coupling Reaction of Lactam-, Lactone-, and Thiolactone-Derived Enol Triflates for the Synthesis of Unsymmetrical Dienones

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A thorough study of the carbonylative Suzuki–Miyaura cross-coupling reaction of enol triflates with alkenylboronic acids for the synthesis of unsymmetrical dienones is reported. Conditions were found that enabled the coupling of structurally different enol triflates derived from lactams, lactones, and thiolactones (i.e., cyclic ketene aminal, acetal, and thioacetal triflates, respectively) with various alkenylboronic acids at

room temperature under 1 atm of CO pressure with 1–5% palladium catalyst; the carbonylated products were obtained in 50–86% overall yields. The methodology allows for a convergent and rapid preparation of substrates useful in conjugate additions and Nazarov reactions.

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## Introduction

Lactam- and lactone-derived enol triflates (Figure 1) and the corresponding phosphates are synthetically useful intermediates that have been widely used as electrophiles in metal-catalyzed coupling processes for the synthesis of natural products and heterocyclic compounds.<sup>[1,2]</sup> These compounds undergo palladium- and nickel-mediated coupling reactions with organotin-, -zinc, and -boron derivatives, as well as Sonogashira and Heck reactions, exchange with metals, and coupling with organocuprates.<sup>[3,4]</sup> Carbonylative coupling reactions are powerful synthetic tools, however, only methoxycarbonylation reactions have been carried out on these triflates so far.<sup>[1d,1e,1i,1j,5]</sup> Nevertheless, the possibility of forming new C–C bonds through carbonylative cross-coupling reactions involving organometallic reagents (Scheme 1) would certainly expand the utility and scope of these reactions in organic synthesis. Still carbonylative processes are well known and widely used, however, tin compounds are toxic and not many of them are commercially available.<sup>[6]</sup> Therefore, and also because of our previous experience of Suzuki–Miyaura coupling reactions of lactam-derived enol triflates,<sup>[7]</sup> we opted to investigate the carbonylative palladium-catalyzed coupling reactions of these triflates with boronic acids, which are safe, easily prepared, and widely available.

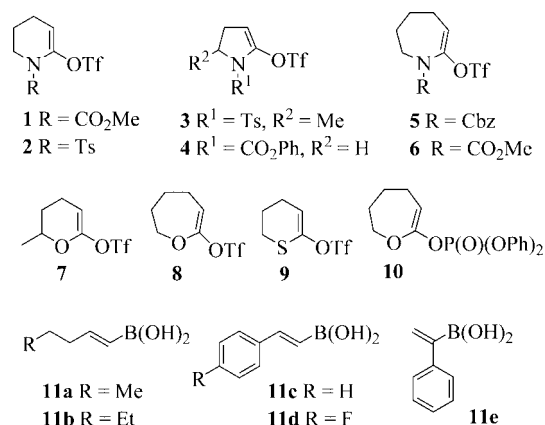
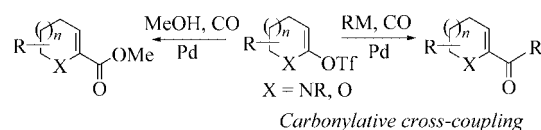


Figure 1. Enol triflates and boronic acids.



Scheme 1. Carbonylative processes involving enol triflates.

We started this study by evaluating the use of vinylboronic acids as coupling partners in the carbonylative reaction that leads to unsymmetrical divinyl ketones that we<sup>[1c,8]</sup> and others<sup>[9]</sup> have employed as substrates in the Nazarov reaction.<sup>[10]</sup> Quite surprisingly, a survey of the literature revealed that vinylboronic acids have never been used in carbonylative cross-coupling processes with a single exception in which arenediazonium salts were used as the electrophiles.<sup>[11]</sup> Moreover, only four papers dealing with the car-

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bonylative coupling of (carbocyclic) enol triflates with organoboron compounds such as sodium tetraphenylborate, 2-indolylborates,<sup>[12]</sup> and an arylboronic acid<sup>[13]</sup> have been published. In this manuscript we therefore disclose the results of our investigation of the carbonylative Suzuki–Miyaura reaction of structurally different enol triflates **1–8** (Figure 1) derived from lactams and lactones, (i.e., cyclic ketene aminal and acetal triflates, respectively) with vinylboronic acids for a convergent and rapid approach to unsymmetrical divinyl ketones.<sup>[14]</sup> We also report the extension of the methodology to thiolactone-derived enol triflate **9**, the simplest representative of a class of electrophiles that have never been used in any kind of metal-catalyzed coupling process.

## Results and Discussion

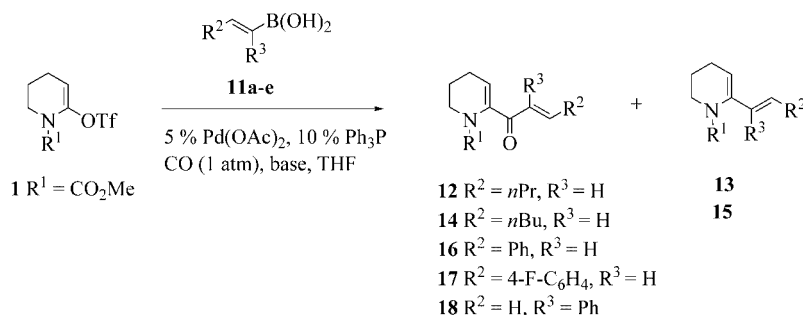
An initial survey (Table 1) of the conditions used for the carbonylative coupling of alkenylboronic acids with these triflates was carried out with cyclic ketene aminal triflate **1** (Figure 1) and revealed Pd(OAc)<sub>2</sub>/Ph<sub>3</sub>P to be the best catalyst system.<sup>[15]</sup>

While the reactions of cyclohexenyl triflates with lithium 2-indolylborates and sodium tetraphenylborate have been reported to require either medium CO pressure (15 atm) or

temperatures (60–90 °C) to occur,<sup>[12]</sup> with triflate **1** the rapid formation of the carbonylative coupling product **12** with (*E*)-pent-1-enylboronic acid (**11a**, Figure 1) was observed when carrying out the reaction at room temperature and under atmospheric pressure of carbon monoxide. In order to generate the negatively charged, four-coordinate boron “ate” complex that is required for the transmetalation step, KF was first used (Entry 1), but soon we found that CsF was by far superior for such a purpose (Entry 7). This is consistent with the observation that caesium salts are often the best choice in palladium-catalyzed coupling reactions involving organoboron compounds under anhydrous conditions.<sup>[16]</sup> We also tested some carbonates as the base but the results were worse. In particular, the reaction in the presence of 3 equiv. of Cs<sub>2</sub>CO<sub>3</sub> (Entry 4) furnished **12** in 39% yield after chromatography, whereas under the same conditions in the presence of CsF (Entry 3) the yield was 71% after chromatography.

All reactions were very fast with consumption (by TLC) of most of the triflate in the first 2 hours.<sup>[17]</sup> We tried two different protocols. In method A, triflate, boronic acid, CsF, and the catalyst [5% Pd(OAc)<sub>2</sub>/10% Ph<sub>3</sub>P] were mixed in anhydrous THF and the resulting mixture saturated with CO. In method B, a solution of the triflate was added to a CO-saturated mixture of the other reagents and the catalyst

Table 1. Carbonylative Suzuki–Miyaura reaction of vinyl triflate **1** with alkenylboronic acids.<sup>[a]</sup>



Entry	Boronic acid <sup>[b]</sup>	Amount of boronic acid (equiv.)	Base	Amount of base (equiv.)	Time [h]	<i>T</i> [°C]	Method <sup>[c]</sup>	Products (% yield) <sup>[d]</sup>
1	<b>11a</b>	2	KF	4	4	18	A	<b>12</b> (46)
2	<b>11a</b>	1.5	CsF	1.5	4	20	B	<b>12</b> (29)
3	<b>11a</b>	2	CsF	3	4	20	B	<b>12</b> (71), <b>13</b> (10) <sup>[e]</sup>
4	<b>11a</b>	2	Cs <sub>2</sub> CO <sub>3</sub>	3	3	20	B	<b>12</b> (39)
5	<b>11a</b>	1.5	CsF	2.25	4	20	A	<b>12</b> (66), <b>13</b> (12) <sup>[e]</sup>
6	<b>11a</b>	1.5	CsF	3	3	25	A	<b>12</b> (76), <sup>[f]</sup> <b>13</b> (15) <sup>[e,f]</sup>
7	<b>11a</b>	2	CsF	3	3	25	A	<b>12</b> (79), <b>13</b> (12) <sup>[e]</sup>
8	<b>11b</b>	2.2	CsF	3	4	25	A	<b>14</b> (46)
9	<b>11b</b> <sup>[g]</sup>	1.5	CsF	3	3	25	A	<b>14</b> (67), <b>15</b> (5) <sup>[e]</sup>
10	<b>11c</b>	1.5	CsF	3	3	25	A	<b>16</b> (76) <sup>[h]</sup>
11	<b>11c</b>	2.5	CsF	3.75	4	21	B	<b>16</b> (83) <sup>[f,h]</sup>
12	<b>11d</b>	2.5	CsF	3.75	4	18	B	<b>17</b> (70) <sup>[h]</sup>
13	<b>11e</b>	2.5	CsF	3	4	22	B	<b>18</b> (68) <sup>[h]</sup>

[a] Reactions carried out with 0.3–1.5 mmol of the substrates. [b] Commercial boronic acids were used. [c] Method A: The mixture prepared by mixing triflate, catalyst, and boronic acid in THF was flushed with CO and then left under static CO pressure (balloon). Method B: A mixture of boronic acid and catalyst in THF was flushed with CO and then a solution of triflate in THF was added, the solution flushed again with CO, and then left under static CO pressure. [d] Yield after chromatography. [e] Evaluated by <sup>1</sup>H NMR analysis of the crude reaction mixture. [f] Average yield of two runs. [g] Freshly prepared. [h] The relative amount of the non-carbonylated product could not be evaluated by <sup>1</sup>H NMR analysis of the crude reaction mixture.

in THF. This second protocol in general provided (slightly) higher yields as it prevents to a certain extent direct coupling before saturation of the mixture with CO. Two observations are worth mentioning. Degradation of either the triflate or the acyl-palladium intermediate complex could be the cause of the low yields obtained after chromatography in some cases (Entries 1, 2, 4, and 8). In particular, the water present in the commercial boronic acids can hydrolyze the acyl-palladium complex before transmetalation occurs.<sup>[12b]</sup> As an example, the reaction in Entry 8, which was carried out with a very moist commercial hex-1-enylboronic acid (**11b**), afforded **14** in 46% yield, whereas with a freshly prepared boronic acid<sup>[18]</sup> the yield increased to 67% (Entry 9). The second observation is that despite the reactions being carried out under 1 atm of CO, the non-carbonylative Suzuki–Miyaura coupling appears to be a minor problem with triflate **1** as non-carbonylated products were always obtained albeit in less than 15% yield. In most cases an excess of the commercial boronic acid was needed to give good yields and 2.5 equiv. were necessary to give the best yields in the case of arylvinylboronic acids **11c–e** (Entries 11–13). Steric hindrance had little effect on the reaction outcome because with  $\alpha$ -phenyl-substituted vinylboronic acid **11e** (Entry 13) the reaction provided the coupling product **18** in 68% yield. Also, the presence of electron-withdrawing substituents on the aromatic ring (fluorine in **11d**) is not detrimental to the success of the reaction.

In order to explore the scope of the reaction, we prepared a series of structurally different vinyl triflates by quenching with *N*-phenyltriflimide the enolates generated by treatment of lactams, lactones, and one thiolactone with KHMDS [potassium bis(trimethylsilyl)amide] (Figure 1). In contrast with six- and seven-membered lactam-derived vinyl triflates, which can be purified by chromatography, triflates **3**, **4**, **7** and **8** are unstable compounds that tend to decompose quickly. Therefore they were used without purification just after their preparation. With all these triflates we decided to apply protocol B using pent-1-enyl- (**11a**) and styrylboronic acid (**11c**) as representative boronic acids (in some cases also **11e**). The results are reported in Table 2.

The results of the carbonylative coupling of triflates **2–6** derived from differently protected (*N*-tosyl, *N*-Cbz, *N*-CO<sub>2</sub>Me, *N*-CO<sub>2</sub>Ph) five-, six-, and seven-membered lactams were satisfactory, although we had in some cases to optimize the reaction conditions. We were particularly pleased to obtain the coupling product between five-membered heterocyclic triflate **3** and pent-1-enylboronic acid (Entry 3) in 77% yield as this procedure could represent a better alternative to those previously proposed for the preparation of a roseophilin synthetic precursor.<sup>[1c]</sup> The reaction carried out on triflate **4** under the same conditions provided instead the carbonylated product **23** in low yield (31%) as a result of the very low thermal stability of the triflate (which in fact rapidly decomposes after its isolation and, presumably, during the reaction).

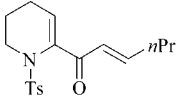
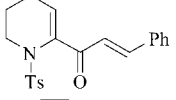
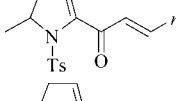
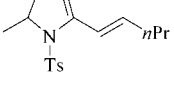
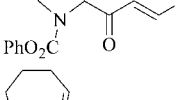
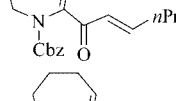
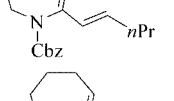
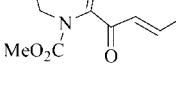
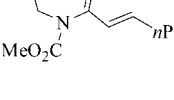
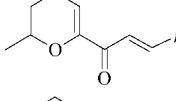
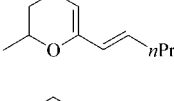
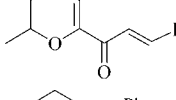
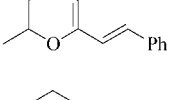
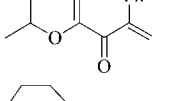
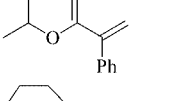
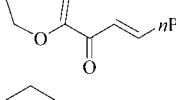
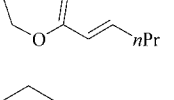
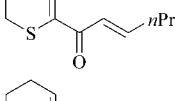
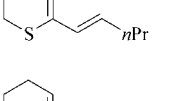
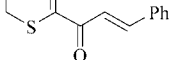
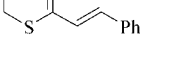
The yield of carbonylative coupling under standard conditions was barely acceptable with seven-membered ring triflate **5** (48%) as a relatively large amount of non-carbon-

ylated product **25** was formed (18%). With both triflates **5** and **6** we tried to suppress the unwanted, slower secondary process that leads to direct coupling products by decreasing the amount of catalyst to 1 mol-%. Although only the carbonylative process then apparently took place under these conditions, compounds **24** and **26** were obtained in low yields (46 and 41%, respectively) mainly as a result of the decomposition of the triflate back to the lactam. (In the case of the *N*-CO<sub>2</sub>Me-protected triflate **6** we determined that about 30% of the triflate was hydrolyzed to the corresponding lactam.) The reactions of triflates **5** and **6** with boronic acid **11a** were eventually carried out in the presence of dppf [1,1'-bis(diphenylphosphanyl)ferrocene] as ligand, which is reported to increase the relative amount of the carbonylated product in the Suzuki–Miyaura carbonylative process,<sup>[19]</sup> obtaining compounds **24** and **26** in good chromatographic yields (62 and 61%, respectively, Entries 5 and 6) together with smaller amounts of the byproducts **25** and **27** (11–13%).

The first attempt at carbonylative coupling of the crude reaction mixture containing cyclic ketene acetal triflate **7** was performed under standard conditions (Method B) with 5 mol-% Pd(OAc)<sub>2</sub>. The reaction with boronic acid **11a** was as fast as with the lactam derivatives but provided a smaller relative amount of the carbonylated product **28**, which was obtained in 42% yield after chromatography. (This experiment was repeated a number of times without appreciable variation of the reaction outcome.) Reducing the amount of catalyst (1 mol-%) did not change the product ratio. Thus the reaction was carried out in the presence of dppf as ligand (Entry 7) and with 2.5 equiv. of boronic acid, which provided, as in the case of *N*-heterocyclic triflates **5** and **6**, a higher ratio of **28** (50%) to **29** (6%). These conditions were applied to the coupling of **7** with boronic acids **11c** and **11e**; in both cases the carbonylated products were obtained in acceptable yields following chromatography after two steps (Entries 8 and 9). As for the seven-membered triflate **8**, this was best prepared according to Milne and Kocienski's procedure<sup>[4c]</sup> in which the aqueous work up is avoided. However, the carbonylative coupling of crude triflate **8** with boronic acid **11a** in the presence of dppf provided **34** in only 32% yield together with less than 6% of the non-carbonylated product (Entry 10). Considerable degradation of the unstable triflate **8** took place under these conditions. The corresponding phosphate **10** (Figure 1) did not react at all under these conditions.

Finally, carbonylative coupling of dihydrothiopyranyl triflate **9** with both boronic acids **11a** and **11c** under the conditions of protocol B provided an almost equimolar mixture of the carbonylative and non-carbonylative products.<sup>[20]</sup> Carbonylated products **36** and **38** were both obtained in 40% yield after chromatography and the corresponding non-carbonylative compounds in yields of 30–33%. Better results in terms of product ratio were obtained by using CsOAc as base (Entries 11 and 12) and compounds **36** and **38** could then be isolated in good overall yields (56 and 57%, respectively) after the two reaction steps.

Table 2. Carbonylative Suzuki–Miyaura reactions of lactam-, lactone-, and thiolactone-derived vinyl triflates with alkenylboronic acids.<sup>[a]</sup>

Entry	Reagents <sup>[b]</sup>	Product	% Yield <sup>[c]</sup>	Product	% Yield <sup>[c]</sup>	
1	<b>2</b> <b>11a</b>		<b>19</b>	69	n.d. <sup>[d]</sup>	
2	<b>2</b> <b>11c</b>		<b>20</b>	60	n.d. <sup>[d]</sup>	
3 <sup>[e]</sup>	<b>3</b> <b>11a</b>		<b>21</b>	77 <sup>[f]</sup>		<b>22</b> 13 <sup>[g]</sup>
4	<b>4</b> <b>11a</b>		<b>23</b>	31 <sup>[f]</sup>	n.d. <sup>[d]</sup>	
5 <sup>[e,h]</sup>	<b>5</b> <b>11a</b>		<b>24</b>	62		<b>25</b> 13
6 <sup>[e,h]</sup>	<b>6</b> <b>11a</b>		<b>26</b>	61		<b>27</b> 11
7 <sup>[e,h]</sup>	<b>7</b> <b>11a</b>		<b>28</b>	50 <sup>[i]</sup>		<b>29</b> 6 <sup>[g]</sup>
8 <sup>[e,h]</sup>	<b>7</b> <b>11c</b>		<b>30</b>	51 <sup>[f]</sup>		<b>31</b> 4 <sup>[g]</sup>
9 <sup>[e,h]</sup>	<b>7</b> <b>11e</b>		<b>32</b>	52 <sup>[f]</sup>		<b>33</b> 6 <sup>[g]</sup>
10 <sup>[e,h]</sup>	<b>8</b> <b>11a</b>		<b>34</b>	32 <sup>[f]</sup>		<b>35</b> 6 <sup>[g]</sup>
11 <sup>[i]</sup>	<b>9</b> <b>11a</b>		<b>36</b>	56 <sup>[f]</sup>		<b>37</b> 22
12 <sup>[i]</sup>	<b>9</b> <b>11c</b>		<b>38</b>	57 <sup>[f]</sup>		<b>39</b> 19 <sup>[g]</sup>

[a] Reactions carried out with 0.5–1.5 mmol of the substrates by method B at 18–22 °C in the presence of 5 mol-% of the catalyst Pd(OAc)<sub>2</sub>, 10 mol-% of Ph<sub>3</sub>P, 2 equiv. of the boronic acid, and 3 equiv. of CsF. All reactions were complete after 3–4 h by TLC. [b] Commercial boronic acids were used. [c] Yield after chromatography. [d] The relative amount of non-carbonylated product could not be evaluated by <sup>1</sup>H NMR analysis of the crude reaction mixture. [e] 2.5 Equiv. of boronic acid. [f] Overall yield over two steps after chromatography. [g] Conversion calculated by <sup>1</sup>H NMR analysis of the crude reaction mixture. [h] Reaction carried out in the presence of 6.25 mol-% of dppf as ligand. [i] Reaction carried out in the presence of CsOAc as base.

The results reported in Table 1 and Table 2 show that under standard conditions [5 mol-% of Pd(OAc)<sub>2</sub>, 10 mol-% of Ph<sub>3</sub>P, and 2–2.5 equiv. of pent-1-enylboronic acid] there is a noticeable difference in the ratio between carbonylated and non-carbonylated products obtained with triflates of six-membered lactams (e.g., **1**), lactones (**7**), and thio-

lactones (**9**), the highest ratios being observed with the N-heterocyclic triflates and the lowest with oxygen- and sulfur-containing vinyl triflates. In particular, we observed a carbonylated/non-carbonylated product ratio of 1.6 with triflate **7** (Table 3, Entry 2). This ratio grew to a value in excess of 7 with triflate **1** (Entry 1) and decreased to 1.3

with sulfur-containing triflate **9** (Entry 3). Thus it seems that the heteroatom has a certain influence on the reaction outcome.

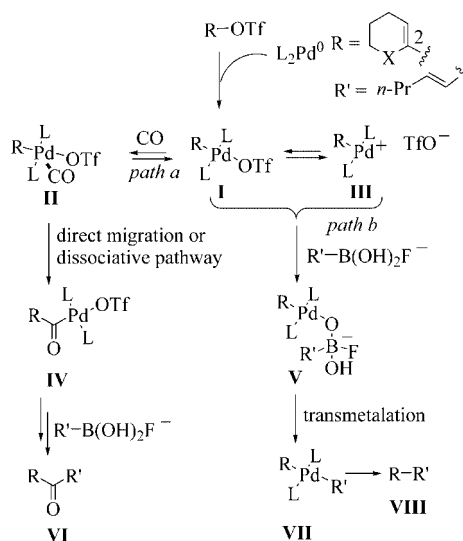
Table 3. Comparison of the carbonylative Suzuki–Miyaura reaction of vinyl triflates **1**, **7**, and **9** with boronic acid **11a**.<sup>[a]</sup>

Entry	Triflate	Products (Yield [%])	Product ratio
1	<b>1</b>	<b>12</b> (71)/ <b>13</b> (10)	7.1
2	<b>7</b>	<b>28</b> (42)/ <b>29</b> (27)	1.6
3	<b>9</b>	<b>36</b> (40)/ <b>37</b> (30)	1.3

[a] Reactions carried out with 0.5–1.5 mmol of substrates by method B at 18–22 °C in the presence of 5 mol-% of catalyst Pd(OAc)<sub>2</sub>, 10 mol-% of Ph<sub>3</sub>P, 2 equiv. of boronic acid, and 3 equiv. of CsF.

The mechanism of the carbonylative processes has been the subject of several studies.<sup>[19]</sup> The ratio between carbonylated product **VI** and non-carbonylated compound **VIII** depends on the relative rates of formation of the acyl-palladium complex **IV** (path a) and the transmetalated complex **VII** (path b), as reported in Scheme 2. The formation of a pentacoordinate intermediate after CO adsorption has been suggested and in some cases demonstrated with Ar–M–X complexes in which M is Ni<sup>II</sup>, Pd<sup>II</sup>, and Pt<sup>II</sup>.<sup>[21,22]</sup> This would lead to the formation of complex **II** which should be favored by the presence of an electronegative atom X in the R ring. The removal of electron density from the metal center by the heteroatom should stabilize **II** because the metal center can better accommodate another unshared electron pair from the new CO ligand.<sup>[21]</sup> As this effect should be primarily inductive, as shown by Garrou and Heck,<sup>[21]</sup> changing from sulfur (lowest electronegativity) to nitrogen and then to oxygen (highest electronegativity), as in this case, should greatly influence the equilibrium towards intermediate **II** and thus favor path a, leading to the carbonylated product **VI**. (The formation of the acyl-palladium complex **IV** could then occur either by direct migration of the alkenyl residue or by a dissociative process.)<sup>[21–23]</sup> The same inductive effect could also favor the coordination of the boronic acid to complex **I** and consequently the formation of the non-carbonylated product **VIII** through path b. However, formation of **V** is likely to be preceded by dissociation of the triflate anion to form cationic complex **III**<sup>[24]</sup> which should be less favored in the presence of an electronegative atom in R such as nitrogen and oxygen.

On the other hand, too low an electron density on the C-2 carbon atom of R, as in **7**, due to the high electronegativity of the heterocyclic oxygen atom could be detrimental to the rate of migration of the R group to form the acyl-palladium complex **IV**, in accordance with the observation that for aromatic halides the migration step that forms the acyl-palladium complex is critically influenced by the electron density of the aryl moiety.<sup>[19,21,23]</sup> Thus the migration step that leads to **VI** is retarded and either degradation of the acyl-palladium complex or direct coupling to give **29** becomes competitive. Instead, in the coupling of sulfur-containing triflate **9**, the higher electron density on C-2 retards the adsorption of CO and the relative amount of the non-



Scheme 2. Mechanism of the carbonylative coupling reaction.

carbonylated product increases. As the best ratios in favor of the carbonylated products are obtained with N-heterocycle triflates **1** and **2** (and **3**), there must be in these cases an optimal electron density on C-2 such that CO adsorption is still fast and migration of R to form the acyl-palladium complex is not too slow.<sup>[25]</sup>

From a practical point of view, direct transmetalation (path b) could be retarded by reducing the reactivity of the boronic acid with a consequential increase in the relative amount of the carbonylated product. This actually occurred with thiolactone-derived triflate **9** when CsOAc was used as base (Entries 11 and 12, Table 2) which is less efficient in boron quaternization than CsF. Also, reducing the amount of catalyst in some cases helped to suppress the unwanted secondary pathway, although in this case degradation of the triflate occurred. Finally, bidentate ligands with a large bite angle such as dppf were effective in increasing the rate of the carbonylation reaction (path a) of the lactone-derived triflate **7** (Table 2, Entries 7–9) as well as seven-membered N-heterocycle derivatives (Table 2, Entries 5 and 6).

## Conclusions

In conclusion, the carbonylative Suzuki–Miyaura coupling reaction of structurally different vinyl triflates derived from lactams, lactones, and thiolactones with alkenyl-boronic acids occur at room temperature and under 1 atm of CO pressure, that is, under operationally simple conditions, using 5 mol-% of Pd(OAc)<sub>2</sub> and either 10 mol-% of Ph<sub>3</sub>P or 6.25 mol-% of dppf as ligand to give unsymmetrical dienones. Good-to-excellent yields (60–86%) were obtained in particular with N-heterocyclic vinyl triflates. Good overall yields over two steps (50–57%) were also obtained with lactone- and thiolactone-derived enol triflates. We observed that the relative amounts of the carbonylated products (with respect to the corresponding non-carbonylated ones) could be related to the electron density on C-2,

which in turn greatly depends on the electronegativity of the heteroatom present in the ring. The highest ratios were obtained with five- and six-membered N-heterocyclic vinyl triflates. In the case of the six-membered O-heterocycle **7**, the low electron density on C-2 could retard the migration step that generates the acyl-palladium complex. With sulfur-containing heterocyclic triflate **9**, the high electron density on C-2 could instead slow down the adsorption of CO by the palladium complex. This methodology allows for the rapid preparation of unsymmetrical divinyl ketones which are useful as substrates for a variety of reactions such as conjugate additions and Nazarov reactions.

## Experimental Section

<sup>1</sup>H NMR spectra were recorded at 200 and 400 MHz at 25 °C. <sup>13</sup>C NMR spectra were recorded at 50.33 MHz at 25 °C. Mass spectra were carried out by EI at 70 eV. Chromatographic separations were performed under pressure on silica gel using flash column chromatographic techniques; *R<sub>f</sub>* values refer to TLC carried out on 0.25 mm silica gel plates with the same eluent as indicated for column chromatography. Boronic acids were purchased or prepared as reported previously.<sup>[18]</sup> THF was distilled from Na/benzophenone. Dichloromethane and 1,2-dichloroethane were distilled from CaH<sub>2</sub>.

**Methyl 6-(Trifluoromethylsulfonyloxy)-1,2,3,4-tetrahydropyridine-1-carboxylate (1):**<sup>[26]</sup> A solution of methyl 2-oxopiperidine-1-carboxylate (1.76 g, 11.2 mmol) in THF (20 mL) was added to a solution prepared by diluting a 0.5 M solution of KHMDS [potassium bis(trimethylsilyl)amide] in toluene (28 mL, 14 mmol), cooled to –78 °C and under nitrogen, with THF (70 mL) and the resulting mixture was stirred for 1.5 h. Afterwards a solution of PhNTf<sub>2</sub> (14 mmol) in THF (20 mL) was added dropwise and after 1 h the reaction mixture was warmed to room temperature. After 16 h, water (100 mL) was added, the mixture was extracted with Et<sub>2</sub>O (3 × 60 mL), and the combined organic layers were washed with 10% NaOH (100 mL) and dried for 1 h with anhydrous K<sub>2</sub>CO<sub>3</sub>. After filtration and evaporation of the solvent the crude oil was purified by chromatography (EtOAc/petroleum ether 1:8, 1.5% Et<sub>3</sub>N, *R<sub>f</sub>* = 0.38) providing **1** as a colorless oil (2.57 g, 79%). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 5.32 (t, *J* = 3.8 Hz, 1 H, C=CH), 3.80 (s, 3 H, CO<sub>2</sub>CH<sub>3</sub>), 3.67 (m, 2 H, N-CH<sub>2</sub>), 2.28 (m, 2 H, C=CH-CH<sub>2</sub>), 1.80 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm.

**1-(4-Methylphenylsulfonyl)-1,4,5,6-tetrahydropyridin-2-yl Trifluoromethanesulfonate (2):**<sup>[3c]</sup> A solution of 1-(toluene-4-sulfonyl)piperidin-2-one (547 mg, 2.16 mmol) in THF (8 mL) was added dropwise to a solution prepared by diluting a 0.5 M solution of KHMDS in toluene (5.8 mL, 2.9 mmol), cooled to –78 °C and under nitrogen, with THF (14 mL) and the resulting mixture was stirred for 1.5 h. Afterwards a solution of PhNTf<sub>2</sub> (2.68 mmol) in THF (4 mL) was added dropwise and after 1 h the reaction mixture was warmed to room temperature. After 16 h, water (50 mL) was added, the mixture was extracted with Et<sub>2</sub>O (3 × 30 mL), and the combined organic layers were washed with 10% NaOH (50 mL) and dried for 1 h with anhydrous K<sub>2</sub>CO<sub>3</sub>. After filtration and evaporation of the solvent the crude oil was purified by chromatography (EtOAc/petroleum ether 1:4, 1.5% Et<sub>3</sub>N, *R<sub>f</sub>* = 0.31) providing **2** as a white solid (666 mg, 80%). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 7.78 (d, *J* = 8.14 Hz, 2 H, CH<sub>arom</sub>), 7.34 (d, *J* = 8.14 Hz, 2 H, CH<sub>arom</sub>), 5.45 (t, *J* = 4.0 Hz, 1 H, C=CH), 3.68–3.61 (m, 2 H, N-CH<sub>2</sub>), 2.45 (s, 3 H, CH<sub>3</sub>-C<sub>arom</sub>), 2.18–2.08 (m, 2 H, C=CH-CH<sub>2</sub>), 1.52–1.41 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm.

**5-Methyl-1-(4-methylphenylsulfonyl)-4,5-dihydro-1H-pyrrol-2-yl Trifluoromethanesulfonate (3):**<sup>[8b]</sup> A solution of 5-methyl-*N*-tosylpyrrolidin-2-one (253 mg, 1.0 mmol) in THF (2 mL) was added to a solution of KHMDS (2.5 mL of a 0.5 M solution in toluene, 1.25 mmol) in THF (5.5 mL), cooled to –78 °C and under nitrogen, and the resulting mixture was stirred for 1.5 h. Afterwards a solution of PhNTf<sub>2</sub> (447 mg, 1.25 mmol) in THF (1.5 mL) was quickly added and the mixture was stirred for 1 h at –78 °C before the temperature was allowed to rise to 0 °C. Then a 10% NaOH solution (10 mL) was added, the mixture was extracted with Et<sub>2</sub>O (3 × 10 mL), washed with water (10 mL) and brine (2 × 10 mL), and then dried with anhydrous K<sub>2</sub>CO<sub>3</sub>. After filtration and evaporation of the solvent, crude vinyl triflate **3** was obtained as a yellowish oil and used directly in the next coupling reaction. *This triflate must be stored in a refrigerator and used within 24 h of its preparation.* <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 7.76 (d, *J* = 8.1 Hz, 2 H, CH<sub>arom</sub>), 7.35 (d, *J* = 8.1 Hz, 2 H, CH<sub>arom</sub>), 5.09 (br. s, 1 H, C=CH), 4.19 (m, 1 H, N-CH), 2.46 (s, 3 H, CH<sub>3</sub>-C<sub>arom</sub>), 2.27 (td, *J* = 7.3, 2.2 Hz, 1 H, CH-CH<sub>2</sub>), 1.87 (dt, *J* = 16.8, 2.9 Hz, 1 H, CH-CH<sub>2</sub>), 1.39 (d, *J* = 6.6 Hz, 3 H, CH<sub>3</sub>-CH) ppm.

**Benzyl 7-(Trifluoromethylsulfonyloxy)-2,3,4,5-tetrahydro-1H-azepine-1-carboxylate (5):**<sup>[7a]</sup> A solution of benzyl 2-oxoazepane-1-carboxylate (988 mg, 4 mmol) in THF (8 mL) was added to a solution of KHMDS (10 mL of a 0.5 M solution in toluene, 5 mmol) in THF (22 mL) cooled to –78 °C and under nitrogen and the resulting mixture was stirred for 1.5 h. Afterwards a solution of PhNTf<sub>2</sub> (1.786 g, 5 mmol) in THF (6 mL) was quickly added and then left to stir for 1 h at –78 °C before allowing the temperature to rise to 0 °C. Then a 10% NaOH solution (40 mL) was added, the mixture was extracted with Et<sub>2</sub>O (3 × 40 mL), washed with water (40 mL) and brine (2 × 40 mL), and then dried with anhydrous K<sub>2</sub>CO<sub>3</sub>. After filtration and evaporation of the solvent, the crude reaction mixture was purified by chromatography (EtOAc/petroleum ether 1:2, 1.5% Et<sub>3</sub>N, *R<sub>f</sub>* = 0.90) providing **5** as a colorless oil (951 mg, 82%). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 7.43–7.25 (m, 5 H, CH<sub>arom</sub>), 5.71 (t, *J* = 6.2 Hz, 1 H, C=CH), 5.22 (s, 2 H, CH<sub>2</sub>Ph), 3.80–3.45 (m, 2 H, N-CH<sub>2</sub>), 2.21–2.05 (m, 2 H, C=CH-CH<sub>2</sub>), 1.82–1.65 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>), 1.48–1.64 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>) ppm.

**Methyl 7-(Trifluoromethylsulfonyloxy)-2,3,4,5-tetrahydro-1H-azepine-1-carboxylate (6):** A solution of methyl 2-oxoazepane-1-carboxylate (822 mg, 4.8 mmol) in THF (8 mL) was added to a solution of KHMDS (12 mL of a 0.5 M solution in toluene, 6 mmol) in THF (30 mL) cooled to –78 °C and under nitrogen and the resulting mixture was stirred for 1.5 h. Afterwards a solution of PhNTf<sub>2</sub> (2.14 g, 6 mmol) in THF (7 mL) was quickly added and left to stir for 1 h at –78 °C before allowing the temperature to rise to 0 °C. Then a 10% NaOH solution (40 mL) was added, the mixture was extracted with Et<sub>2</sub>O (3 × 40 mL), washed with water (40 mL) and brine (2 × 40 mL), and then dried with anhydrous K<sub>2</sub>CO<sub>3</sub>. After filtration and evaporation of the solvent, the crude reaction mixture was purified by chromatography (EtOAc/petroleum ether 1:4, 1.5% Et<sub>3</sub>N, *R<sub>f</sub>* = 0.53) providing **6** as a colorless oil (880 mg, 60%). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 5.70 (t, *J* = 6.6 Hz, 1 H, C=CH), 3.79 (s, 3 H, CO<sub>2</sub>CH<sub>3</sub>), 3.75–3.37 (m, 2 H, N-CH<sub>2</sub>), 2.29–2.04 (m, 2 H, C=CH-CH<sub>2</sub>), 1.90–1.69 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>), 1.66–1.41 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>) ppm.

**2-Methyl-3,4-dihydro-2H-pyran-6-yl Trifluoromethanesulfonate (7):**<sup>[8b]</sup> A 0.5 M solution of KHMDS in toluene (3.8 mL, 1.88 mmol) was added dropwise in about 10 min to a solution of 6-methyltetrahydropyran-2-one (171 mg, 1.5 mmol) in anhydrous THF (3 mL) cooled to –78 °C and under nitrogen. Afterwards a solution of PhNTf<sub>2</sub> (672 mg, 1.88 mmol) in THF (1.5 mL) was added and the

resulting mixture left to stir at  $-78\text{ }^{\circ}\text{C}$  for 2 h before allowing the temperature to rise to  $0\text{ }^{\circ}\text{C}$ . Then a 10% NaOH solution (6 mL) was added and the mixture was extracted with  $\text{Et}_2\text{O}$  ( $3 \times 6\text{ mL}$ ) and dried with anhydrous  $\text{K}_2\text{CO}_3$  for about 30 min. After filtration, the solution of crude triflate **7** was concentrated under vacuum to a small volume (about 1.5 mL) and immediately used in the next coupling step. *It is important not to remove the solvent completely, as the triflate quickly decomposes if exposed to air.*<sup>[4d]</sup>  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta = 4.75$  (t,  $J = 2.5\text{ Hz}$ , 1 H,  $\text{C}=\text{CH}$ ), 4.31–4.15 (m, 1 H,  $\text{O}-\text{CH}$ ), 2.25–2.15 (m, 2 H,  $\text{C}=\text{CH}-\text{CH}_2$ ), 1.94–1.77 (m, 1 H,  $=\text{CHCH}_2\text{CH}_2$ ), 1.69–1.47 (m, 1 H,  $=\text{CHCH}_2\text{CH}_2$ ), 1.35 (d,  $J = 6.5\text{ Hz}$ , 3 H,  $\text{CH}_3-\text{CH}$ ) ppm.

**3,4-Dihydro-2H-thiopyran-6-yl Trifluoromethanesulfonate (9):** A solution of tetrahydrothiopyran-2-one<sup>[27]</sup> (348 mg, 3 mmol) in THF (6 mL) was added to a solution of KHMDS (7.5 mL of a 0.5 M solution in toluene, 3.75 mmol) in THF (16.5 mL) cooled to  $-78\text{ }^{\circ}\text{C}$  and under nitrogen and the resulting mixture was stirred for 1.5 h. Afterwards a solution of  $\text{PhNTf}_2$  (1.340 g, 3.75 mmol) in THF (4.5 mL) was quickly added and then left to stir for 1 h at  $-78\text{ }^{\circ}\text{C}$  before allowing the temperature to rise to room temperature. Then a 10% NaOH solution (30 mL) was added, the mixture was extracted with  $\text{Et}_2\text{O}$  ( $3 \times 30\text{ mL}$ ), washed with water (30 mL) and brine ( $2 \times 30\text{ mL}$ ), and then dried with anhydrous  $\text{K}_2\text{CO}_3$ . After filtration and evaporation of the solvent, crude triflate **9** (762 mg) was obtained as a pale yellowish oil and used directly in the next step.  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta = 5.84$  (t,  $J = 4.4\text{ Hz}$ , 1 H,  $\text{C}=\text{CH}$ ), 3.06–3.01 (m, 2 H,  $\text{S}-\text{CH}_2$ ), 2.41–2.32 (m, 2 H,  $\text{C}=\text{CH}-\text{CH}_2$ ), 2.06–1.95 (m, 2 H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 154.3$  (s), 114.9 (d), 29.2 (t), 23.7 (t), 21.7 (t) ppm.

**Methyl 6-[(2E)-Hex-2-enoyl]-1,2,3,4-tetrahydropyridine-1-carboxylate (12):**  $\text{Pd}(\text{OAc})_2$  (5.6 mg, 0.025 mmol),  $\text{Ph}_3\text{P}$  (13 mg, 0.05 mmol), (*E*)-pent-1-enylboronic acid (**11a**) (115 mg, 1.0 mmol), and CsF (228 mg, 1.5 mmol) were added to a solution of triflate **1** (145 mg, 0.5 mmol) in anhydrous THF (8 mL) under nitrogen. The flask was flushed with CO and then stirred under a static pressure of CO (1 atm). After 3 h,  $\text{Et}_2\text{O}$  (30 mL) was added to the dark orange solution which was washed with water (20 mL). The aqueous phase was extracted with  $\text{Et}_2\text{O}$  (20 mL) and the combined organic layers were dried with  $\text{Na}_2\text{SO}_4$ . After filtration and evaporation of the solvent, the crude oil was purified by chromatography ( $\text{EtOAc}$ /petroleum ether 1:3,  $R_f = 0.40$ ) yielding **12** (94 mg, 79%) as a pale yellow oil.  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta = 6.87$  (dt,  $J = 15.8, 6.6\text{ Hz}$ , 1 H,  $\text{COCH}=\text{CH}$ ), 6.23 (dt,  $J = 15.8, 1.5\text{ Hz}$ , 1 H,  $\text{COCH}=\text{CH}$ ), 5.83 (t,  $J = 4.0\text{ Hz}$ , 1 H,  $\text{C}=\text{CH}$ ), 3.67–3.58 (m, 2 H,  $\text{N}-\text{CH}_2$ ), 3.61 (s, 3 H,  $\text{CO}_2\text{CH}_3$ ), 2.29–2.08 (m, 4 H,  $\text{C}=\text{CH}-\text{CH}_2$ ,  $\text{CH}_3\text{CH}_2\text{CH}_2$ ), 1.89–1.73 (m, 2 H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.56–1.35 (m, 2 H,  $\text{CH}_3\text{CH}_2\text{CH}_2$ ), 0.89 (t,  $J = 6.9\text{ Hz}$ , 3 H,  $\text{CH}_3\text{CH}_2\text{CH}_2$ ) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 188.2$  (s), 154.3 (s), 147.6 (d), 139.6 (s), 126.3 (d), 120.9 (d), 52.8 (q), 43.5 (t), 34.7 (t), 23.0 (t), 22.7 (t), 21.4 (t), 13.7 (q) ppm. MS:  $m/z$  (%) = 237 (24)  $[\text{M}]^+$ , 208 (22), 194 (57), 55 (100).  $\text{C}_{13}\text{H}_{19}\text{NO}_3$  (237.29): calcd. C 65.80, H 8.07, N 5.90; found C 65.69, H 7.93, N 5.95.

**Methyl 6-[(2E)-Hept-2-enoyl]-1,2,3,4-tetrahydropyridine-1-carboxylate (14):** Prepared as reported above for **12** starting from **1** (87 mg, 0.3 mmol) and freshly prepared (*E*)-hex-1-enylboronic acid (**11b**) (56 mg, 0.45 mmol). Chromatography ( $\text{EtOAc}$ /petroleum ether 1:3,  $R_f = 0.34$ ) afforded **14** (58 mg) in 67% yield.  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta = 6.90$  (dt,  $J = 16.1, 6.6\text{ Hz}$ , 1 H,  $\text{COCH}=\text{CH}$ ), 6.24 (d,  $J = 16.1\text{ Hz}$ , 1 H,  $\text{COCH}=\text{CH}$ ), 5.84 (t,  $J = 3.7\text{ Hz}$ , 1 H,  $\text{C}=\text{CH}$ ), 3.71–3.57 (m, 2 H,  $\text{N}-\text{CH}_2$ ), 3.63 (s, 3 H,  $\text{CO}_2\text{CH}_3$ ), 2.33–2.12 (m, 4 H,  $\text{C}=\text{CH}-\text{CH}_2$ ,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.92–1.73 (m, 2 H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.59–1.18 (m, 4 H,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$ ),

$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$ ), 0.88 (t,  $J = 6.6\text{ Hz}$ , 3 H,  $\text{CH}_3\text{CH}_2\text{CH}_2-\text{CH}_2$ ) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 188.2$  (s), 154.2 (s), 148.0 (d), 139.6 (s), 126.3 (d), 121.0 (d), 52.8 (q), 43.6 (t), 32.5 (t), 30.3 (t), 23.0 (t), 22.7 (t), 22.3 (t), 13.9 (q) ppm. MS:  $m/z$  (%) = 251 (20)  $[\text{M}]^+$ , 208 (24), 194 (84), 55 (100).  $\text{C}_{14}\text{H}_{21}\text{NO}_3$  (251.32): calcd. C 66.91, H 8.42, N 5.57; found C 66.71, H 8.13, N 5.36.

**Methyl 6-[(2E)-3-Phenylprop-2-enoyl]-1,2,3,4-tetrahydropyridine-1-carboxylate (16):** A suspension prepared by mixing (*E*)-styrylboronic acid (**11c**) (370 mg, 2.5 mmol),  $\text{Pd}(\text{OAc})_2$  (11 mg, 0.05 mmol),  $\text{Ph}_3\text{P}$  (26 mg, 0.1 mmol), and CsF (570 mg, 3.75 mmol) in anhydrous THF (10 mL) was flushed with CO whilst stirring. After 10 min, a solution of triflate **1** (290 mg, 1 mmol) in THF (6 mL) was slowly added by syringe, the resulting mixture was flushed again with CO, and finally left under static pressure of CO (1 atm) for 4 h at room temperature. Usual work up gave a crude oil which was purified by chromatography ( $\text{EtOAc}$ /petroleum ether 1:3,  $R_f = 0.23$ ) to give **16** (233 mg) in 86% yield as a pale yellow oil.  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.67$  (d,  $J = 15.8\text{ Hz}$ , 1 H,  $\text{COCH}=\text{CH}$ ), 7.61–7.47 (m, 2 H,  $\text{CH}_{\text{arom}}$ ), 7.46–7.32 (m, 3 H,  $\text{CH}_{\text{arom}}$ ), 6.92 (d,  $J = 15.8\text{ Hz}$ , 1 H,  $\text{COCH}=\text{CH}$ ), 5.98 (t,  $J = 3.7\text{ Hz}$ , 1 H,  $\text{C}=\text{CH}$ ), 3.75–3.66 (m, 2 H,  $\text{N}-\text{CH}_2$ ), 3.64 (s, 3 H,  $\text{CO}_2\text{CH}_3$ ), 2.36–2.23 (m, 2 H,  $\text{C}=\text{CH}-\text{CH}_2$ ), 1.95–1.79 (m, 2 H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 187.9$  (s), 154.5 (s), 143.2 (d), 139.8 (s), 134.6 (s), 130.2 (d), 128.7 (d, 2 C), 128.2 (d, 2 C), 122.5 (d), 121.6 (d), 53.0 (q), 43.6 (t), 23.0 (t), 22.6 (t) ppm. MS:  $m/z$  (%) = 271 (64)  $[\text{M}]^+$ , 212 (41), 131 (40), 103 (67), 77 (100), 59 (44), 51 (64).  $\text{C}_{16}\text{H}_{17}\text{NO}_3$  (271.31): calcd. C 70.83, H 6.32, N 5.16; found C 70.99, H 6.01, N 4.87.

**Methyl 6-[(2E)-3-(4-Fluorophenyl)prop-2-enoyl]-1,2,3,4-tetrahydropyridine-1-carboxylate (17):** Prepared as reported above for **16**. A suspension prepared by mixing boronic acid **11d** (415 mg, 2.5 mmol),  $\text{Pd}(\text{OAc})_2$  (11 mg, 0.05 mmol),  $\text{Ph}_3\text{P}$  (26 mg, 0.1 mmol), and CsF (570 mg, 3.75 mmol) in anhydrous THF (10 mL) was flushed with CO whilst stirring. After 10 min, a solution of triflate **1** (290 mg, 1 mmol) in THF (6 mL) was slowly added by syringe, the resulting mixture was flushed again with CO, and finally left under static pressure of CO (1 atm) for 4 h at room temperature. Usual work up gave a crude oil which was purified by chromatography ( $\text{EtOAc}$ /petroleum ether 1:2,  $R_f = 0.32$ ) to give **17** (202 mg) in 70% yield as a pale yellow oil.  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.64$  (d,  $J = 16.1\text{ Hz}$ , 1 H,  $\text{COCH}=\text{CH}$ ), 7.57–7.47 (m, 2 H,  $\text{CH}_{\text{arom}}$ ), 7.11–6.99 (m, 2 H,  $\text{CH}_{\text{arom}}$ ), 6.83 (d,  $J = 16.1\text{ Hz}$ , 1 H,  $\text{COCH}=\text{CH}$ ), 5.98 (t,  $J = 3.7\text{ Hz}$ , 1 H,  $\text{C}=\text{CH}$ ), 3.75–3.66 (m, 2 H,  $\text{N}-\text{CH}_2$ ), 3.64 (s, 3 H,  $\text{CO}_2\text{CH}_3$ ), 2.35–2.22 (m, 2 H,  $\text{C}=\text{CH}-\text{CH}_2$ ), 1.95–1.77 (m, 2 H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 187.6$  (s), 166.1 and 161.1 (both d,  $^1J_{\text{CF}} = 251.0\text{ Hz}$ , 1 C), 154.5 (s), 141.8 (d), 139.8 (s), 130.8 (s), 130.1 and 129.9 (both d,  $^3J_{\text{CF}} = 8.4\text{ Hz}$ , 2 C), 122.2 (d), 121.7 (d), 116.0 and 115.6 (both d,  $^2J_{\text{CF}} = 22.1\text{ Hz}$ , 2 C), 53.0 (q), 43.6 (t), 23.1 (t), 22.7 (t) ppm. MS:  $m/z$  (%) = 289 (69)  $[\text{M}]^+$ , 261 (15), 230 (56), 214 (58), 149 (100), 121 (54).  $\text{C}_{16}\text{H}_{16}\text{FNO}_3$  (289.30): calcd. C 66.43, H 5.57, N 4.84; found C 66.11, H 5.62, N 4.71.

**Methyl 6-(2-Phenylprop-2-enoyl)-1,2,3,4-tetrahydropyridine-1-carboxylate (18):** Prepared as reported above for **16**. A suspension prepared by mixing boronic acid **11e** (185 mg, 1.25 mmol),  $\text{Pd}(\text{OAc})_2$  (5.6 mg, 0.025 mmol),  $\text{Ph}_3\text{P}$  (13 mg, 0.05 mmol), and CsF (228 mg, 1.5 mmol) in anhydrous THF (5 mL) was flushed with CO whilst stirring. After 10 min, a solution of triflate **1** (145 mg, 0.5 mmol) in THF (3 mL) was slowly added by syringe, the resulting mixture was flushed again with CO, and finally left under static pressure of CO (1 atm) for 4 h at room temperature. Usual work up gave a crude oil which was purified by chromatography ( $\text{EtOAc}$ /petroleum

ether 1:2, 0.5% Et<sub>3</sub>N, R<sub>f</sub> = 0.4) to give **18** (92 mg) in 68% yield as a pale yellow oil. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 7.50–7.30 (m, 5 H, CH<sub>arom</sub>), 5.93 (s, 1 H, C=CH<sub>2</sub>), 5.91 (t, *J* = 3.7 Hz, 1 H, C=CH-CH<sub>2</sub>), 5.85 (s, 1 H, C=CH<sub>2</sub>), 3.59 (s, 3 H, CO<sub>2</sub>CH<sub>3</sub>), 3.53–3.47 (m, 2 H, N-CH<sub>2</sub>), 2.30–2.21 (m, 2 H, C=CH-CH<sub>2</sub>), 1.89–1.80 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 191.5 (s), 153.8 (s), 146.5 (s), 139.0 (s), 136.6 (s), 128.0 (d, 2 C), 127.9 (d, 2 C), 127.4 (d), 123.1 (t), 122.4 (d), 52.9 (q), 42.9 (t), 23.0 (t), 22.5 (t) ppm. MS: *m/z* (%) = 271 (100) [M]<sup>+</sup>, 226 (29), 198 (25), 168 (42), 154 (60), 103 (43), 77 (58). C<sub>16</sub>H<sub>17</sub>NO<sub>3</sub> (271.31): calcd. C 70.83, H 6.32, N 5.16; found C 70.71, H 5.99, N 4.98.

**(2E)-1-[1-(4-Methylphenylsulfonyl)-1,4,5,6-tetrahydropyridin-2-yl]-hex-2-en-1-one (19):** A suspension prepared by mixing boronic acid **11a** (114 mg, 1 mmol), Pd(OAc)<sub>2</sub> (6 mg, 0.025 mmol), Ph<sub>3</sub>P (13 mg, 0.05 mmol), and CsF (228 mg, 1.5 mmol) in anhydrous THF (5 mL) was flushed with CO whilst stirring. After 10 min, a solution of triflate **2** (193 mg, 0.5 mmol) in THF (3 mL) was slowly added by syringe, the resulting mixture was flushed with CO, and finally left under static pressure of CO (1 atm) for 3 h at room temperature. Usual work up gave a crude oil which was purified by chromatography (EtOAc/petroleum ether 1:2, 0.5% Et<sub>3</sub>N, R<sub>f</sub> = 0.48) to give **19** (115 mg, 69%) as a pale yellow oil. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 7.69 (d, *J* = 8.4 Hz, 2 H, CH<sub>arom</sub>), 7.26 (d, *J* = 8.4 Hz, 2 H, CH<sub>arom</sub>), 7.02–6.87 (dt, *J* = 16.1, 7.3 Hz, 1 H, COCH=CH), 6.51 (d, *J* = 16.1 Hz, 1 H, COCH=CH), 6.03 (t, *J* = 3.7 Hz, 1 H, C=CH), 3.45–3.39 (m, 2 H, N-CH<sub>2</sub>), 2.37 (s, 3 H, CH<sub>3</sub>-C<sub>arom</sub>), 2.19 (q, *J* = 7.0 Hz, 2 H, C=CH-CH<sub>2</sub>), 2.06–1.98 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.57–1.38 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.32–1.08 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 0.91 (t, *J* = 7.3 Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 188.6 (s), 147.4 (d), 143.9 (s), 139.1 (s), 135.2 (s), 129.6 (d, 2 C), 127.7 (d, 2 C), 127.1 (d), 125.2 (d), 44.9 (q), 34.5 (t), 22.3 (t), 21.5 (t), 21.3 (t), 19.3 (t), 13.7 (q) ppm. MS: *m/z* (%) = 333 (15) [M]<sup>+</sup>, 290 (66), 226 (64), 178 (82), 135 (56), 97 (50), 91 (88), 65 (44), 55 (100). C<sub>18</sub>H<sub>23</sub>NO<sub>3</sub>S (333.45): calcd. C 64.84, H 6.95, N 4.20; found C 64.91, H 6.69, N 4.31.

**(2E)-1-[1-(4-Methylphenylsulfonyl)-1,4,5,6-tetrahydropyridin-2-yl]-3-phenylprop-2-en-1-one (20):** A suspension prepared by mixing boronic acid **11c** (148 mg, 1 mmol), Pd(OAc)<sub>2</sub> (6 mg, 0.025 mmol), Ph<sub>3</sub>P (13 mg, 0.05 mmol), and CsF (228 mg, 1.5 mmol) in anhydrous THF (5 mL) was flushed with CO whilst stirring. After 10 min, a solution of triflate **2** (193 mg, 0.5 mmol) in THF (3 mL) was slowly added by syringe, the resulting mixture was flushed with CO, and finally left under static pressure of CO (1 atm) for 3 h at room temperature. Usual work up gave a crude oil which was purified by chromatography (EtOAc/petroleum ether 1:2, 0.5% Et<sub>3</sub>N, R<sub>f</sub> = 0.52) to give **20** (110 mg, 60%) as a pale yellow oil. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 7.75–7.68 (m, 3 H, COCH=CH, CH<sub>arom</sub>), 7.61–7.56 (m, 2 H, CH<sub>arom</sub>), 7.37–7.25 (m, 5 H, CH<sub>arom</sub>), 7.20 (d, *J* = 16.1 Hz, 1 H, COCH=CH), 6.17 (t, *J* = 3.7 Hz, 1 H, C=CH), 3.54–3.49 (m, 2 H, N-CH<sub>2</sub>), 2.40 (s, 3 H, CH<sub>3</sub>-C<sub>arom</sub>), 2.15–2.06 (m, 2 H, C=CH-CH<sub>2</sub>), 1.39–1.22 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 188.2 (s), 144.0 (d), 142.3 (d), 139.4 (s), 135.2 (s), 134.8 (s), 130.1 (d), 129.6 (d, 2 C), 128.6 (d, 2 C), 128.3 (d, 2 C), 127.8 (d, 2 C), 125.7 (d), 123.4 (d), 45.1 (q), 22.4 (t), 21.5 (t), 19.3 (t) ppm. MS: *m/z* (%) = 367 (4) [M]<sup>+</sup>, 303 (19), 212 (100), 131 (43), 103 (43), 91 (50), 77 (38), 65 (22). C<sub>21</sub>H<sub>21</sub>NO<sub>3</sub>S (367.46): calcd. C 68.64, H 5.76, N 3.81; found C 68.52, H 5.48, N 4.02.

**(2E)-1-[5-Methyl-1-(4-methylphenylsulfonyl)-4,5-dihydro-1H-pyrrol-2-yl]hex-2-en-1-one (21):** A suspension prepared by mixing boronic acid **11a** (284 mg, 2.5 mmol), Pd(OAc)<sub>2</sub> (11.2 mg, 0.05 mmol), Ph<sub>3</sub>P (26.2 mg, 0.1 mmol), and CsF (455.7 mg, 3.0 mmol) in anhydrous

THF (10 mL) was flushed with CO whilst stirring. After 10 min, a solution of crude triflate **3** (1 mmol) in THF (6 mL) was slowly added by syringe, the resulting mixture was flushed with CO, and finally left under static pressure of CO (1 atm) for 18 h at room temperature. Usual work up gave a crude oil which was purified by chromatography (EtOAc/petroleum ether 1:4, 0.5% Et<sub>3</sub>N, R<sub>f</sub> = 0.42) to give **21** (256 mg, 77%) as a pale yellow oil. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 7.66 (d, *J* = 8.4 Hz, 2 H, CH<sub>arom</sub>), 7.29 (d, *J* = 8.4 Hz, 2 H, CH<sub>arom</sub>), 7.06 (dt, *J* = 15.8, 6.8 Hz, 1 H, COCH=CH), 6.58 (dt, *J* = 15.8, 1.4 Hz, 1 H, COCH=CH), 5.95 (t, *J* = 3.3 Hz, 1 H, C=CH), 4.25–4.06 (m, 1 H, N-CH), 2.41 (s, 3 H, CH<sub>3</sub>-C<sub>arom</sub>), 2.26 (qd, *J* = 7.4, 1.4 Hz, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.10 (ddd, *J* = 18.0, 8.4, 2.2 Hz, 1 H, =CHCH<sub>2</sub>CH), 1.82 (ddd, *J* = 18.0, 3.3, 2.6 Hz, 1 H, =CHCH<sub>2</sub>CH), 1.63–1.44 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.31 (d, *J* = 6.6 Hz, 3 H, CH<sub>3</sub>-CH-N), 0.96 (t, *J* = 7.4 Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 185.4 (s), 148.4 (d), 143.9 (s), 143.4 (s), 133.2 (s), 129.4 (d, 2 C), 127.9 (d), 127.6 (d), 125.3 (d), 58.9 (d), 36.2 (t), 34.7 (t), 22.6 (q), 21.7 (q), 21.5 (t), 13.8 (q) ppm. MS: *m/z* (%) = 333 (66) [M]<sup>+</sup>, 290 (85), 178 (99), 91 (100). C<sub>18</sub>H<sub>23</sub>NO<sub>3</sub>S (333.45): calcd. C 64.84, H 6.95, N 4.20; found C 64.71, H 7.12, N, 3.86.

**Phenyl 5-[(2E)-Hex-2-enoyl]-2,3-dihydro-1H-pyrrole-1-carboxylate (23):** A solution of phenyl 2-oxopyrrolidine-1-carboxylate (205 mg, 1.0 mmol) in THF (2 mL) was added to a solution of KHMDS (2.5 mL of a 0.5 M solution in toluene, 1.25 mmol) in THF (5.5 mL) cooled to –78 °C and under nitrogen and the resulting mixture was stirred for 1.5 h. Afterwards a solution of PhNTf<sub>2</sub> (447 mg, 1.25 mmol) in THF (1.5 mL) was quickly added and the mixture was left to stir for 1 h at –78 °C before allowing the temperature to rise to 0 °C. Then a 10% NaOH solution (10 mL) was added, the mixture was extracted with Et<sub>2</sub>O (3 × 10 mL), washed with water (10 mL) and brine (2 × 10 mL), and dried with anhydrous K<sub>2</sub>CO<sub>3</sub> for 30 min. After filtration and evaporation of the solvent, crude vinyl triflate **4** was dissolved in anhydrous THF (2 mL) and added to a CO-saturated suspension prepared by mixing boronic acid **11a** (228 mg, 2.0 mmol), Pd(OAc)<sub>2</sub> (11 mg, 0.05 mmol), Ph<sub>3</sub>P (26 mg, 0.1 mmol), and CsF (456 mg, 3 mmol) in anhydrous THF (8 mL). The resulting mixture was flushed with CO and finally left under static pressure of CO (1 atm) for 18 h at room temperature. Usual work up gave a crude oil which was purified by chromatography (EtOAc/petroleum ether 1:5, 0.5% Et<sub>3</sub>N, R<sub>f</sub> = 0.14) to give **23** (88 mg, 31%) as a colorless oil. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 7.37–7.07 (m, 5 H, CH<sub>arom</sub>), 6.95 (dt, *J* = 15.8, 7.0 Hz, 1 H, COCH=CH), 6.31 (d, *J* = 15.8 Hz, 1 H, COCH=CH), 5.79 (t, *J* = 3.3 Hz, 1 H, C=CH), 4.14 (t, *J* = 8.8 Hz, 2 H, N-CH<sub>2</sub>), 2.78 (td, *J* = 8.8, 3.3 Hz, 2 H, C=CH-CH<sub>2</sub>), 2.28–2.13 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.58–1.40 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 0.91 (t, *J* = 7.3 Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 185.5 (s), 150.5 (s), 149.4 (d), 147.6 (s), 142.7 (s), 129.1 (d, 2 C), 128.6 (d), 125.3 (d), 121.2 (d, 2 C), 119.7 (d), 48.7 (t), 34.6 (t), 28.7 (t), 21.4 (t), 13.8 (q) ppm. MS: *m/z* (%) = 285 (5) [M]<sup>+</sup>, 192 (69), 138 (96), 55 (100). C<sub>17</sub>H<sub>19</sub>NO<sub>3</sub> (285.34): calcd. C 71.56, H 6.71, N 4.91; found C 71.33, H 7.02, N 4.53.

**Benzyl 7-[(2E)-Hex-2-enoyl]-2,3,4,5-tetrahydro-1H-azepine-1-carboxylate (24):** A suspension prepared by mixing boronic acid **11a** (114 mg, 1 mmol), Pd(OAc)<sub>2</sub> (1 mg, 0.005 mmol), Ph<sub>3</sub>P (2.6 mg, 0.01 mmol), and CsF (228 mg, 1.5 mmol) in anhydrous THF (6 mL) was flushed with CO whilst stirring. After 10 min, a solution of triflate **5** (190 mg, 0.5 mmol) in THF (2 mL) was slowly added by syringe, the resulting mixture was flushed with CO, and finally left under static pressure of CO (1 atm) for 3 h at room temperature. Usual work up gave an oil which was purified by



chromatography (EtOAc/petroleum ether 1:4, 0.5% Et<sub>3</sub>N) to give **24** ( $R_f = 0.31$ , 78 mg, 48%) as a pale yellow oil.

The same reaction was carried out also as follows: A suspension prepared by mixing boronic acid **11a** (228 mg, 2 mmol), Pd(OAc)<sub>2</sub> (9 mg, 0.04 mmol), dppf [1,1'-bis(diphenylphosphanyl)ferrocene] (27 mg, 0.05 mmol), and CsF (374 mg, 2.46 mmol) in anhydrous THF (6 mL) was flushed with CO whilst stirring. After 10 min, a solution of triflate **5** (303 mg, 0.8 mmol) in THF (2 mL) was slowly added by syringe, the resulting mixture was flushed with CO, and finally left under static pressure of CO (1 atm) for 4 h at room temperature. Usual work up and chromatography gave **24** (162 mg, 62%) and **25** ( $R_f = 0.67$ , 31 mg, 13%).

**24**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) (3:1 mixture of rotamers):  $\delta$  (major rotamer) = 7.30–7.20 (m, 5 H, CH<sub>arom</sub>), 6.86 (dt,  $J = 15.4$ , 7.0 Hz, 1 H, COCH=CH), 6.54 (t,  $J = 6.6$  Hz, 1 H, C=CH), 6.31 (d,  $J = 15.4$  Hz, 1 H, COCH=CH), 5.04 (s, 2 H, CH<sub>2</sub>Ph), 3.53–3.65 (m, 2 H, N-CH<sub>2</sub>), 2.38–2.28 (m, 2 H, C=CH-CH<sub>2</sub>), 2.21–2.04 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.90–1.79 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>), 1.59–1.50 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.50–1.32 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>), 0.89 (t,  $J = 7.7$  Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta = 187.4$  (s), 154.1 (s), 148.7 (d), 143.5 (s), 135.7 (s), 133.8 (d), 127.9 (d, 2 C), 127.7 (d, 2 C), 127.6 (d), 124.9 (d), 67.4 (t), 47.8 (t), 34.5 (t), 29.3 (t), 27.3 (t), 23.3 (t), 21.3 (t), 13.7 (q) ppm. MS:  $m/z$  (%) = 327 (1) [M]<sup>+</sup>, 240 (19), 91 (100). C<sub>20</sub>H<sub>25</sub>NO<sub>3</sub> (327.42): calcd. C 73.37, H 7.70, N 4.28; found C 72.98, H 7.56, N 4.11.

**25**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) (3:1 mixture of rotamers):  $\delta$  (major rotamer) = 7.30–7.20 (m, 5 H, CH<sub>arom</sub>), 5.92 (d,  $J = 15.4$  Hz, 1 H, =C-CH=CH), 5.72–5.42 (m, 1 H, 1 H, C=CH, =C-CH=CH), 5.11 (s, 2 H, CH<sub>2</sub>Ph), 3.50–3.30 (m, 2 H, N-CH<sub>2</sub>), 2.20–2.09 (m, 2 H, C=CH-CH<sub>2</sub>), 2.09–1.94 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.89–1.81 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>), 1.60–1.20 (m, 4 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>), 0.84 (t,  $J = 7.3$  Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta = 154.2$  (s), 147.5 (s), 143.0 (s), 136.8 (d), 129.5 (d), 128.1 (d, 2 C), 127.6 (d, 2 C), 126.7 (d), 125.9 (d), 66.7 (t), 47.4 (t), 34.3 (t), 29.8 (t), 26.8 (t), 24.6 (t), 22.4 (t), 13.8 (q) ppm. MS:  $m/z$  (%) = 299 (7) [M]<sup>+</sup>, 208 (10), 164 (26), 91 (100).

**Methyl 7-[(2E)-Hex-2-enoyl]-2,3,4,5-tetrahydro-1H-azepine-1-carboxylate (26)**: A suspension prepared by mixing boronic acid **11a** (114 mg, 1 mmol), Pd(OAc)<sub>2</sub> (1 mg, 0.005 mmol), Ph<sub>3</sub>P (2.6 mg, 0.01 mmol), and CsF (228 mg, 1.5 mmol) in anhydrous THF (6 mL) was flushed with CO whilst stirring. After 10 min, a solution of triflate **6** (152 mg, 0.5 mmol) in THF (2 mL) was slowly added by syringe, the resulting mixture was flushed with CO, and finally left under static pressure of CO (1 atm) for 18 h at room temperature. Usual work up gave an oil which was purified by chromatography (EtOAc/petroleum ether 1:8, 0.5% Et<sub>3</sub>N) to give **26** ( $R_f = 0.13$ , 52 mg, 41%) as a pale yellow oil.

The same reaction was carried out also as follows: A suspension prepared by mixing boronic acid **11a** (228 mg, 2 mmol), Pd(OAc)<sub>2</sub> (9 mg, 0.04 mmol), dppf (27 mg, 0.05 mmol), and CsF (374 mg, 2.46 mmol) in anhydrous THF (6 mL) was flushed with CO whilst stirring. After 10 min, a solution of triflate **6** (244 mg, 0.8 mmol) in THF (2 mL) was slowly added by syringe, the resulting mixture was flushed with CO, and finally left under static pressure of CO (1 atm) for 4 h at room temperature. Usual work up and chromatography gave **26** (122 mg, 61%) and **27** ( $R_f = 0.45$ , 19 mg, 11%).

**26**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta = 6.94$  (dt,  $J = 15.5$ , 7.0 Hz, 1 H, COCH=CH), 6.54 (t,  $J = 6.6$  Hz, 1 H, C=CH), 6.36 (d,  $J = 15.5$  Hz, 1 H, COCH=CH), 3.58 (s, 3 H, CO<sub>2</sub>CH<sub>3</sub>), 3.62–3.50 (m, 2 H, N-CH<sub>2</sub>), 2.37–2.27 (m, 2 H, C=CH-CH<sub>2</sub>), 2.23–2.10 (m, 2 H,

CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.89–1.74 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>), 1.65–1.38 (m, 4 H, CH<sub>2</sub>CH<sub>2</sub>, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 0.91 (t,  $J = 7.7$  Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta = 187.4$  (s), 154.8 (s), 148.7 (d), 143.6 (s), 133.7 (d), 124.8 (d), 52.8 (q), 47.9 (t), 34.7 (t), 29.4 (t), 27.4 (t), 23.3 (t), 21.6 (t), 13.8 (q) ppm. MS:  $m/z$  (%) = 251 (16) [M]<sup>+</sup>, 208 (98), 136 (44), 55 (100). C<sub>14</sub>H<sub>21</sub>NO<sub>3</sub> (251.32): calcd. C 66.91, H 8.42, N 5.57; found C 70.22, H 8.78, N 5.33.

**27**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta = 5.91$  (d,  $J = 15.4$  Hz, 1 H, =C-CH=CH), 5.65 (t,  $J = 6.6$  Hz, 1 H, C=CH), 5.51 (dt,  $J = 15.4$ , 6.6 Hz, 1 H, =C-CH=CH), 3.64 (s, 3 H, CO<sub>2</sub>CH<sub>3</sub>), 3.60–3.40 (br. s, 2 H, N-CH<sub>2</sub>), 2.10–1.95 (m, 4 H, C=CH-CH<sub>2</sub>, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.83–1.71 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>), 1.60–1.32 (m, 4 H, CH<sub>2</sub>CH<sub>2</sub>, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 0.88 (t,  $J = 7.7$  Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta = 143.0$  (s), 129.5 (d), 126.6 (d), 125.9 (d), 52.6 (q), 47.4 (t), 34.3 (t), 29.9 (t), 26.9 (t), 24.6 (t), 22.6 (t), 13.7 (q) ppm. MS:  $m/z$  (%) = 223 (39) [M]<sup>+</sup>, 164 (100).

**(2E)-1-(2-Methyl-3,4-dihydro-2H-pyran-6-yl)hex-2-en-1-one (28)**: A suspension prepared by mixing boronic acid **11a** (342 mg, 3 mmol), Pd(OAc)<sub>2</sub> (17 mg, 0.075 mmol), Ph<sub>3</sub>P (39 mg, 0.15 mmol), and CsF (684 mg, 4.5 mmol) in anhydrous THF (15 mL) was flushed with CO whilst stirring. After 10 min, a solution of crude triflate **7** (1.5 mmol) in THF (9 mL) was slowly added by syringe, the resulting mixture was flushed with CO, and finally left under static pressure of CO (1 atm) for 18 h at room temperature. Usual work up gave an oil which was purified by chromatography (EtOAc/petroleum ether 1:10, 0.5% Et<sub>3</sub>N) to give **28** ( $R_f = 0.31$ , 116 mg, 42%) as a colorless oil and **29** ( $R_f = 0.91$ , 65 mg, 27%) as a pale yellow oil.

The same reaction was carried out as follows: A suspension prepared by mixing boronic acid **11a** (285 mg, 2.5 mmol), Pd(OAc)<sub>2</sub> (11.2 mg, 0.05 mmol), dppf (34.6 mg, 0.0625 mmol), and CsF (456 mg, 3 mmol) in anhydrous THF (8 mL) was flushed with CO whilst stirring. After 10 min, a solution of crude triflate **7** (1 mmol) in THF (1.3 mL) was slowly added by syringe, the resulting mixture was flushed with CO, and finally left under static pressure of CO (1 atm) for 18 h at room temperature. Usual work up and chromatography afforded **28** (97 mg, 50%) and **29** (10 mg, 6%).

**28**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta = 6.98$  (dt,  $J = 15.4$ , 6.9 Hz, 1 H, COCH=CH), 6.66 (d,  $J = 15.4$  Hz, 1 H, COCH=CH), 5.97 (t,  $J = 3.7$  Hz, 1 H, C=CH), 4.05–3.95 (m, 1 H, O-CH), 2.28–2.12 (m, 4 H, C=CH-CH<sub>2</sub>, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.90–1.76 (m, 1 H, =CHCH<sub>2</sub>CH<sub>2</sub>), 1.65–1.40 (m, 3 H, =CHCH<sub>2</sub>CH<sub>2</sub>, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.36 (d,  $J = 6.2$  Hz, 3 H, CH<sub>3</sub>-CH), 0.92 (t,  $J = 7.3$  Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta = 185.5$  (s), 151.4 (s), 148.4 (d), 124.2 (d), 109.7 (d), 72.2 (d), 34.8 (t), 28.4 (t), 21.6 (t), 21.1 (t), 20.9 (q), 13.9 (q) ppm. MS:  $m/z$  (%) = 194 (2) [M]<sup>+</sup>, 97 (65), 55 (100). C<sub>12</sub>H<sub>18</sub>O<sub>2</sub> (194.27): calcd. C 74.19, H 9.34; found C 74.47, H 9.01.

**29**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta = 5.96$  (dt,  $J = 15.4$ , 6.6 Hz, 1 H, =C-CH=CH), 5.74 (d,  $J = 15.4$  Hz, 1 H, =C-CH=CH), 4.67 (t,  $J = 4.0$  Hz, 1 H, C=CH), 4.02–3.90 (m, 1 H, O-CH), 2.20–2.00 (m, 4 H, C=CH-CH<sub>2</sub>, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.90–1.75 (m, 1 H, =CHCH<sub>2</sub>CH<sub>2</sub>), 1.63–1.40 (m, 3 H, =CHCH<sub>2</sub>CH<sub>2</sub>, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.33 (d,  $J = 6.2$  Hz, 3 H, CH<sub>3</sub>-CH), 0.92 (t,  $J = 7.3$  Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta = 150.6$  (s), 128.3 (d), 125.8 (d), 99.1 (d), 71.5 (d), 34.6 (t), 29.4 (t), 22.5 (t), 21.2 (q), 13.9 (q) ppm. MS:  $m/z$  (%) = 166 (3) [M]<sup>+</sup>, 55 (100).

**(2E)-1-(2-Methyl-3,4-dihydro-2H-pyran-6-yl)-3-phenylprop-2-en-1-one (30)**: A suspension prepared by mixing boronic acid **11c** (555 mg, 3.75 mmol), Pd(OAc)<sub>2</sub> (17 mg, 0.075 mmol), dppf (52 mg, 0.094 mmol), and CsF (684 mg, 4.5 mmol) in anhydrous THF

(12 mL) was flushed with CO whilst stirring. After 10 min, a solution of crude triflate **7** (1.5 mmol) in THF (2 mL) was slowly added by syringe, the resulting mixture flushed with CO, and finally left under static pressure of CO (1 atm) for 18 h at room temperature. Usual work up gave an oil which was purified by chromatography (EtOAc/petroleum ether 1:10, 0.5% Et<sub>3</sub>N) to give **30** (*R*<sub>f</sub> = 0.22, 176 mg, 51%) as a colorless oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 7.75 (d, *J* = 16.1 Hz, 1 H, COCH=CH), 7.62–7.58 (m, 2 H, CH<sub>arom</sub>), 7.45–7.25 (m, 3 H, CH<sub>arom</sub>), 7.36 (d, *J* = 16.1 Hz, 1 H, COCH=CH), 6.10 (t, *J* = 4.03 Hz, 1 H, C=CH), 4.19–4.01 (m, 1 H, O-CH), 2.30–2.12 (m, 2 H, C=CH-CH<sub>2</sub>), 1.97–1.81 (m, 1 H, =CHCH<sub>2</sub>CH<sub>2</sub>), 1.68–1.50 (m, 1 H, =CHCH<sub>2</sub>CH<sub>2</sub>), 1.41 (d, *J* = 6.2 Hz, 3 H, CH<sub>3</sub>-CH) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 185.2 (s), 151.5 (s), 143.4 (d), 134.8 (s), 130.0 (d), 128.6 (d, 2 C), 128.2 (d, 2 C), 120.5 (d), 109.7 (d), 72.2 (d), 28.4 (t), 21.0 (q), 20.9 (t) ppm. MS: *m/z* (%) = 228 (59) [M]<sup>+</sup>, 200 (22), 131 (100), 103 (62), 77 (45). C<sub>15</sub>H<sub>16</sub>O<sub>2</sub> (228.29): calcd. C 78.92, H 7.06; found C 79.16, H 6.88.

**1-(2-Methyl-3,4-dihydro-2H-pyran-6-yl)-2-phenylprop-2-en-1-one (32)**: A suspension prepared by mixing boronic acid **11e** (370 mg, 2.5 mmol), Pd(OAc)<sub>2</sub> (11.2 mg, 0.05 mmol), dppf (34.6 mg, 0.0625 mmol), and CsF (456 mg, 3 mmol) in anhydrous THF (8 mL) was flushed with CO whilst stirring. After 10 min, a solution of crude triflate **7** (1 mmol) in THF (1.3 mL) was slowly added by syringe, the resulting mixture flushed with CO, and finally left under static pressure of CO (1 atm) for 18 h at room temperature. Usual work up gave an oil which was purified by chromatography (EtOAc/petroleum ether 1:10, 0.5% Et<sub>3</sub>N) to give **32** (*R*<sub>f</sub> = 0.13, 118 mg, 52%) as a colorless oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 7.40–7.23 (m, 5 H, CH<sub>arom</sub>), 6.00 (t, *J* = 7.8 Hz, 1 H, C=CH), 5.86 (s, 1 H, C=CH<sub>2</sub>), 5.58 (s, 1 H, C=CH<sub>2</sub>), 4.02–3.94 (m, 1 H, O-CH), 2.29–2.01 (m, 2 H, C=CH-CH<sub>2</sub>), 1.94–1.78 (m, 1 H, =CHCH<sub>2</sub>CH<sub>2</sub>), 1.69–1.45 (m, 1 H, =CHCH<sub>2</sub>CH<sub>2</sub>), 1.33 (d, *J* = 6.2 Hz, 3 H, CH<sub>3</sub>-CH-O) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 192.2 (s), 151.1 (s), 147.2 (s), 136.8 (s), 128.3 (d, 2 C), 128.0 (d), 126.3 (d, 2 C), 118.9 (t), 116.6 (d), 72.3 (d), 28.2 (t), 21.3 (d), 20.7 (q) ppm. MS: *m/z* (%) = 228 (69) [M]<sup>+</sup>, 174 (65), 156 (59), 103 (100), 77 (54). C<sub>15</sub>H<sub>16</sub>O<sub>2</sub> (228.29): calcd. C 78.92, H 7.06; found C 78.73, H 7.48.

**(2E)-1-(4,5,6,7-Tetrahydrooxepin-2-yl)hex-2-en-1-one (34)**: A solution of ε-caprolactone (114 mg, 1.0 mmol) and PhNTf<sub>2</sub> (429 mg, 1.2 mmol) in anhydrous THF (5 mL) was added dropwise, in about 60 min, to a cooled (–78 °C) solution of KHMDS (0.5 M in toluene, 2.8 mL, 1.40 mmol) in THF (3.5 mL) whilst stirring and under nitrogen. The resulting mixture was left to stir at –78 °C for 15 min before allowing the temperature to rise to –10 °C. Then the solution was concentrated under vacuum to about 1/3 of the original volume and used directly in the coupling step as follows: A suspension prepared by mixing boronic acid **11a** (285 mg, 2.5 mmol), Pd(OAc)<sub>2</sub> (11.2 mg, 0.05 mmol), dppf (34.6 mg, 0.0625 mmol), and CsF (456 mg, 3 mmol) in anhydrous THF (8 mL) was flushed with CO whilst stirring. After 10 min, the above solution of crude triflate **8** (≈1 mmol) was slowly added by syringe, the resulting mixture flushed with CO, and finally left under static pressure of CO (1 atm) for 2 h at room temperature. Usual work up gave an oil which was purified by chromatography (EtOAc/petroleum ether 1:10, 0.5% Et<sub>3</sub>N) to give **34** (*R*<sub>f</sub> = 0.33, 61 mg, 32%) as a colorless oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 6.97 (dt, *J* = 15.7, 7.0 Hz, 1 H, COCH=CH), 6.70 (d, *J* = 15.7 Hz, 1 H, COCH=CH), 6.30 (t, *J* = 6.2 Hz, 1 H, C=CH), 4.00 (t, *J* = 5.1 Hz, 2 H, O-CH<sub>2</sub>), 2.40–2.11 (m, 4 H, C=CH-CH<sub>2</sub>, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.98–1.79 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>), 1.76–1.57 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.56–1.40 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>), 0.92 (t, *J* = 7.3 Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 187.1 (s), 156.9 (s), 148.6 (d), 124.5 (d), 120.2 (d), 72.7 (t), 34.8 (t), 31.4 (t), 26.5 (t), 24.8 (t), 21.5 (t), 13.8 (t) ppm.

MS: *m/z* (%) = 194 (17) [M]<sup>+</sup>, 151 (75), 97 (64), 55 (100). C<sub>12</sub>H<sub>18</sub>O<sub>2</sub> (194.27): calcd. C 74.19, H 9.34; found C 74.44, H 9.08.

**(2E)-1-(3,4-Dihydro-2H-thiopyran-6-yl)hex-2-en-1-one (36)**: A suspension prepared by mixing boronic acid **11a** (80 mg, 0.7 mmol), Pd(OAc)<sub>2</sub> (3.9 mg, 0.0175 mmol), Ph<sub>3</sub>P (9.2 mg, 0.035 mmol), and CsOAc (202 mg, 1.05 mmol) in anhydrous THF (3.5 mL) was flushed with CO whilst stirring. After 10 min, a solution of crude triflate **9** (0.35 mmol) in THF (2 mL) was slowly added by syringe, the resulting mixture flushed with CO, and finally left under static pressure of CO (1 atm) for 3 h at room temperature. Usual work up gave an oil which was purified by chromatography (EtOAc/petroleum ether 1:8, 0.5% Et<sub>3</sub>N) to give **36** (*R*<sub>f</sub> = 0.33, 38 mg, 56%) as a pale yellow oil and **37** (*R*<sub>f</sub> = 0.68, 13 mg, 22%) as a pale yellow oil. Both compounds tend to be quickly oxidized on exposure to air.

**36**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 6.95 (dt, *J* = 15.4, 7.0 Hz, 1 H, COCH=CH), 6.91 (t, *J* = 4.7 Hz, 1 H, C=CH), 6.62 (dt, *J* = 15.4, 1.47 Hz, 1 H, COCH=CH), 2.92–2.86 (m, 2 H, S-CH<sub>2</sub>), 2.40 (q, *J* = 6.2 Hz, 2 H, C=CH-CH<sub>2</sub>), 2.28–2.15 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.5–1.93 (m, 2 H, =CHCH<sub>2</sub>CH<sub>2</sub>), 1.60–1.42 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 0.94 (t, *J* = 7.4 Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 187.3 (s), 148.4 (d), 136.9 (s), 132.3 (d), 123.5 (d), 34.8 (t), 26.3 (t), 25.2 (t), 21.6 (t), 21.5 (t), 13.8 (q) ppm. MS: *m/z* (%) = 196 (15) [M]<sup>+</sup>, 167 (21), 153 (20), 97 (23), 55 (100). C<sub>11</sub>H<sub>16</sub>OS (196.31): calcd. C 67.30, H 8.22; found C 67.66, H 8.13.

**37**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 6.04 (d, *J* = 15.4 Hz, 1 H, =C-CH=CH), 5.76 (dt, *J* = 15.4, 6.6 Hz, 1 H, =C-CH=CH), 5.73 (t, *J* = 4.0 Hz, 1 H, C=CH), 2.92–2.85 (m, 2 H, S-CH<sub>2</sub>), 2.30–2.10 (m, 2 H), 2.10–1.91 (m, 4 H), 1.52–1.33 (m, 2 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 0.91 (t, *J* = 7.0 Hz, 3 H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 130.6 (d), 130.5 (s), 129.2 (d), 121.1 (d), 76.4 (t), 34.8 (t), 26.6 (t), 24.8 (t), 22.8 (t), 22.6 (t), 13.8 (q) ppm. MS: *m/z* (%) = 168 (7) [M]<sup>+</sup>, 139 (19), 55 (100).

**(2E)-1-(3,4-Dihydro-2H-thiopyran-6-yl)-3-phenylprop-2-en-1-one (38)**: A suspension prepared by mixing boronic acid **11c** (444 mg, 2.0 mmol), Pd(OAc)<sub>2</sub> (11.2 mg, 0.05 mmol), Ph<sub>3</sub>P (26.2 mg, 0.1 mmol), and CsOAc (577 mg, 3 mmol) in anhydrous THF (10 mL) was flushed with CO whilst stirring. After 10 min, a solution of crude triflate **9** (1.0 mmol) in THF (6 mL) was slowly added by syringe, the resulting mixture flushed with CO, and finally left under static pressure of CO (1 atm) for 3 h at room temperature. Usual work up gave an oil which was purified by chromatography (EtOAc/petroleum ether 1:7, 0.5% Et<sub>3</sub>N) to give **38** (*R*<sub>f</sub> = 0.47, 131 mg, 57%) as a pale yellow oil. Compound **38** tends to be quickly oxidized on exposure to air. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 7.70 (d, *J* = 15.4 Hz, 1 H, COCH=CH), 7.61–7.56 (m, 2 H, CH<sub>arom</sub>), 7.42–7.37 (m, 3 H, CH<sub>arom</sub>), 7.28 (d, *J* = 15.4 Hz, 1 H, COCH=CH), 7.05 (t, *J* = 4.4 Hz, 1 H, C=CH), 2.96–2.91 (m, 2 H, S-CH<sub>2</sub>), 2.51–2.41 (m, 2 H, C=CH-CH<sub>2</sub>), 2.09–1.97 (m, 2 H, =CHCH<sub>2</sub>CH<sub>2</sub>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 187.2 (s), 143.8 (d), 134.5 (s), 134.8 (s), 132.7 (d), 130.3 (d), 128.8 (d, 2 C), 128.3 (d, 2 C), 119.8 (d), 26.4 (t), 25.2 (t), 21.5 (t) ppm. MS: *m/z* (%) = 230 (77) [M]<sup>+</sup>, 131 (100), 103 (80), 77 (70). C<sub>14</sub>H<sub>14</sub>OS (230.33): calcd. C 73.01, H 6.13; found C 72.82, H 5.77.

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