Alkyl Tosylates as Alkylating Reagents in the Catellani Reaction

Qianwen Gao*  
Ze-Shui Liua  
Yu Huab  
Siwei Zhoua  
Hong-Gang Cheng*a  
Qianghui Zhou*a,b

* Sauvage Center for Molecular Sciences, Engineering Research Center of Organosilicon Compounds Materials, Wuhan University, 430072 Wuhan, P. R. of China  
qhzhou@whu.edu.cn  
hgcheng@whu.edu.cn

b The Institute for Advanced Studies, Wuhan University, 430072 Wuhan, P. R. of China

Abstract A cooperative catalytic system involving a Pd/XPhos complex and inexpensive S-norbornene-2-carbonitrile that enables the use of alkyl tosylates as alkylating reagents in the Catellani reaction has been developed. This mild, scalable protocol is compatible with a range of readily available functionalized aryl iodides and alkyl tosylates, as well as terminating olefins (45 examples, up to 97% yield).

Key words Catellani reaction, cooperative catalysis, alkyl tosylates, S-norbornene-2-carbonitrile, polysubstituted arenes

The development of straightforward strategies to assemble complex molecular scaffolds represents one of the central tasks in modern organic synthesis.1 Therein, the transition-metal-catalyzed C–H functionalization of arenes is among the most attractive strategies.2 It can build various transition-metal-catalyzed C–H functionalization of arenes has been well studied.6 However, the development of electrophilic reagents for ortho C–H functionalization was relatively lagging behind until 2018, and was mainly limited to alkyl halides,3j,4 aryl halides,7 azirines,8 O-benzoylhydroxylamines,9 and various carboxylic acid derivatives.10 Since 2018, rapid progress has been made in this direction. For instance, epoxides and aziridines were successfully employed as alkylating reagents in Catellani-type reactions by Dong,11 Liang,12 and our group.13 Moreover, hexamethylidisilane, hexamethylgermane, and hexabutyldistannane as electrophilic reagents were also reported by the Cheng group (Scheme 1a).14 Later, the Dong and Gu groups independently reported an ortho-thiolation reaction via rational design of S-containing electrophiles.15

Recently, our group reported a dual-tasked methylation of aryl iodides through Pd/NBE cooperative catalysis, with inexpensive methyl tosylate and trimethyl phosphate as the methylating reagent (Scheme 1b).16 It was found that the iodide ion17 can react with methyl tosylate to slowly release iodomethane in situ,18 and significantly reduce the possible side reactions. The Dong group also utilized similar methylation of aryl bromides or alkyl triflates using methyl 4-nitrobenzenesulphonate19 or phenyltrimethylammonium salt20 as the methylating reagent, respectively. Inspired by this chemistry, we envisaged whether alkyl tosylates generally can serve as alkylating reagents to react with aryl iodides and olefins in a Catellani-type process. The use of alkyl tosylates instead of alkyl halides has several advantages. Firstly, they can be easily prepared from inexpensive and abundant alcohols, which are feedstock chemicals. Secondly, the generation of halide-containing waste would be reduced, thereby decreasing the environmental impact. Lastly, the slow release mechanism would maintain a low concentration of the active alkyl iodides, thus diminishing the potential competitive side reactions. As part of our continuing efforts in exploring novel Catellani-type reactions,12,21 herein we describe the development of an ortho-C–H
Qianwen Gao received her B.Sc. degree in chemistry from Hunan Normal University in 2016. In the fall of 2016, she began graduate study at Wuhan University under the direction of Prof. Qianghui Zhou. Her research focuses on synthetic methodology developments and asymmetric catalysis.

Ze-Shui Liu received his B.S. degree from Yangtze University in 2011. After earning his M.S. degree from China West Normal University in 2015, he pursued and received his Ph.D. in 2018, under the guidance of Prof. Qianghui Zhou at Wuhan University. Currently, he is working as a postdoctoral fellow in the group of Prof. Qianghui Zhou. His research interests include synthetic methodology developments and asymmetric catalysis.

Yu Hua received his B.Sc. degree from Guangxi University in 2017. In the fall of 2017, he began graduate study at Wuhan University under the direction of Prof. Qianghui Zhou. His research focuses on synthetic methodology developments and asymmetric catalysis.

Siwei Zhou has studied at Wuhan University, where he will receive his B.Sc. degree in 2020. Currently, he is undertaking his graduation project under the guidance of Prof. Qianghui Zhou. His research interest focuses on the synthesis of biological active molecules.

Hong-Gang Cheng received his Ph.D. from Central China Normal University in 2014, under the supervision of Prof. Wen-jing Xiao. Then, he conducted his postdoctoral research at the University of Tokyo with Prof. Shū Kobayashi, at Wuhan University with Prof. Qianghui Zhou, and at RWTH Aachen University with Prof. Franziska Schoenebeck. He is currently an associate professor at Wuhan University. His research interests include the development of new synthetic methodologies and the synthesis of bioactive natural products.

Qianghui Zhou received his B.S. degree from Peking University in 2005. He pursued graduate study under the guidance of Prof. Dawei Ma at Shanghai Institute of Organic Chemistry and earned his Ph.D. in 2010. He then took up a postdoctoral position in the lab of Prof. Phil S. Baran at The Scripps Research Institute. In June 2015, he began his independent career in the College of Chemistry and Molecular Sciences of Wuhan University. His lab currently focuses on developing novel methodologies for the synthesis of biologically important molecules.
alkylation of aryl iodides via Pd/NBE cooperative catalysis, using alkyl tosylates as the new generation alkylating reagent (Scheme 1c).

Initially, our efforts commenced with a model reaction using readily available 1-iodonaphthalene (1a), n-butyl tosylate (2a), and tert-butyl acrylate (3a) as the reactants (Table 1). After extensive survey of the reaction parameters, the optimal conditions were identified to be: Pd$_2$(dba)$_3$ as the catalyst (2.5 mol%), XPhos$^{23}$ as the ligand (2.5 mol%), the inexpensive NBE derivative 5-norbornene-2-carbonitrile as the mediator ($N_1$, 20 mol%), Cs$_2$CO$_3$ as the base (2.5 equiv), and CH$_3$CN as the solvent, where the desired product 4a was obtained in 98% yield at 80 °C under argon (entry 1). A series of control experiments were subsequently conducted

<table>
<thead>
<tr>
<th>Entry</th>
<th>Change from the standard conditions</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>no change</td>
<td>98 (86)$^c$</td>
</tr>
<tr>
<td>2</td>
<td>no Pd$_2$(dba)$_3$</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>no $N_1$</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>no XPhos</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>$N_2$ instead of $N_1$</td>
<td>45</td>
</tr>
<tr>
<td>6</td>
<td>$K_2$CO$_3$ instead of Cs$_2$CO$_3$</td>
<td>41</td>
</tr>
<tr>
<td>7</td>
<td>toluene instead of CH$_3$CN</td>
<td>11</td>
</tr>
<tr>
<td>8</td>
<td>1a (1.0 equiv) and 3a (1.2 equiv) instead of 1a (1.2 equiv) and 3a (1.0 equiv)</td>
<td>63</td>
</tr>
</tbody>
</table>

$^a$ All reactions were performed on a 0.1 mmol scale.
$^b$ GC yield with biphenyl as an internal standard.
$^c$ Isolated yield in parentheses.
to investigate the role of each component. In the absence of either Pd catalyst or mediator, no desired product 4a was observed (entries 2, 3). In contrast, product 4a can be produced in the absence of phosphine ligand, albeit in a lower yield (entry 4). On the other hand, using simple NBE (Nf) resulted in a significantly lower yield (entry 5). The use of potassium carbonate instead of cesium carbonate as the base dramatically decreased the yield (entry 6). The polarity of the reaction solvent is also important, since the switching of CH3CN to toluene led to sluggish results (entry 7). Notably, when aryl iodide 1a was used as the limiting reagent, dramatically lower yield was observed (entry 8).

With the above optimal conditions in hand, we firstly examined the scope of aryl iodides 1, with n-butyl tosylate (2a) and tert-butyl acrylate (3a) as the reaction partners. As shown in Scheme 2a, bicyclic aryl iodides (4a, b), as well as ones bearing a methyl (4c, 4h–o), ethyl (4d), trifluoromethyl (4f), phenyl (4g), and even sterically hindered isopropyl group (4e) at the ortho position, were suitable substrates, affording the corresponding products in 42–91% yield. This reaction exhibited high chemoselectivity, as a variety of functional groups were well tolerated, including bromide (4b and 4l),24 fluoride (4i and 4k), methyl ester (4m and 4p), amide (4n), nitro (4o), benzyloxy (4p and 4q), and methoxy (4r), providing opportunities for further diversifications. Notably, densely functionalized aryl iodides (4p and 4q) and heteroaryl iodide (4r) also reacted well to afford the desired products in moderate yields.

Then, the scope of olefins 3 was explored. As shown in Scheme 2b, an array of monosubstituted olefins with electron-withdrawing groups, such as acrylates (4a′, b′), methyl vinyl ketone (4c′), and acrylaldehyde (4d′), as well as the Weinreb amide derivative of acrylic acid (4e′), are suitable substrates to provide the corresponding products in moderate to excellent yields (42–92%). Notably, acrylonitrile afforded the product 4f′′ as a mixture of geometrical isomers in 79% yield (Z/E = 1:6:1). Interestingly, simple styrene and 4-nitrostyrene were also competent substrates to generate products 4g′′ and 4h′′ in 54% and 74% yield, respectively.

We subsequently examined the scope of alkyl tosylates 2 (Scheme 3). The reactions with tosylates containing a pure aliphatic chain gave the desired products 4a″–c″ in excellent yields (90–95%). Other tosylates with various functional groups, including ester (4d″), trifluoromethyl (4e″), protected amino group (4f″), phenyl (4g″), and naphthyl (4h″), afforded the corresponding products 4d–h″ in good

---

**Scheme 2** Substrate scope with respect to aryl iodides 1 and olefins 3. All reactions were performed on a 0.2 mmol scale. Isolated yields are reported.
to excellent yields. Interestingly, in the case of 3-bromopropyl tosylate, a mixture of inseparable bromo/iodo-substituted product 4i′′ was obtained in 56% yield (ratio of Br/I = 1:1.3), which may be attributed to partial iodo/bromo exchange during the reaction. Moreover, cyclopentylmethyl (4j′′), cyclobutylmethyl (4k′′), and benzyl (4l′′) tosylates were also tolerated. It is noteworthy that the alkyl benzene sulfonate, alkyl 4-nitrobenzenesulfonate, and alkyl mesylate could also participate in the reaction smoothly to provide product 4h′′ in 74–84% yield. However, secondary alkyl tosylates furnished the corresponding products in very low yield (4m′′ and 4n′′).

Scheme 3  Substrate scope with respect to tosylates 2. All reactions were performed on a 0.2 mmol scale. Isolated yields are reported. * 2-(Naphthalen-1-yl)ethyl benzenesulfonate was applied. ** 2-(Naphthalen-1-yl)ethyl 4-nitrobenzenesulfonate was applied. *** 2-(Naphthalen-1-yl)ethyl mesylate was applied. **** Pd2(dba)3 (5 mol%), XPhos (5 mol%), and N1 (50 mol%) were applied.

Scheme 4  Synthetic applications and scale-up experiment
To illustrate the synthetic utility of this protocol, an annihilation process was explored by incorporation of an aryl iodide 1 and an olefin-containing tosylate 5 (Scheme 4A). It was found that 1a reacted with the bifunctional olefinic ester-containing tosylates 5a and 5b to afford the benzofused products 6a and 6b, both in 87% yield. When olefinic alcohol-containing tosylates 5c–e were employed, a consecutive intermolecular Catellani-type C–H alkylation followed by an intramolecular redox-relay Heck termination occurred, providing the corresponding five-, six-, and seven-membered carbocycles 6c–e with a diversifiable carbonyl functionality in 43–86% yield. The practicality of this protocol was investigated by running the reaction on a larger scale (3a, 4.0 mmol), which led to an intriguing gram-scale preparation of product 4d** (1.44 g, 91% yield) (Scheme 4B).

In summary, we have developed a cooperative catalytic system involving a Pd/XPhos complex and 5-norbornene-2-carbonitrile that enables the use of alkyl tosylates as alkylation reagents in the Catellani reaction, providing a valuable complement to state-of-the-art transformations. This mild, scalable protocol is compatible with a wide range of readily available functionalized aryl iodides and alkyl tosylates, as well as terminating olefins. The inexpensive reagent 5-norbornene-2-carbonitrile acts as a catalytic mediator for the process, and only 20 mol% is required to achieve satisfactory results. Further studies on the application of alkyl tosylates as alkylation reagents in other Catellani-type reactions are currently ongoing in our laboratory.

All reactions dealing with air- or moisture-sensitive compounds were performed by standard Schlenk techniques in oven-dried reaction vessels under argon atmosphere. Unless otherwise noted, all solvents were dried with a JC Meyer Solvent Drying System. Most reagents were purchased from commercial sources and used without further purification, unless otherwise stated. Reactions were monitored by TLC carried out on 0.2 mm commercial silica gel plates, using UV light and visualization agent or a basic solution of KMnO₄ or an acidic solution of p-anisaldehyde and heat as the developing agent. †H NMR and 13C NMR spectra were recorded with a Bruker DMX 400 spectrometer (400 MHz, 1H at 400 MHz, 13C at 100 MHz). Chemical shifts are reported in parts per million (ppm, δ) downfield from TMS (δ = 0.00 ppm) and were referenced to residual solvent [CDCl₃, δ = 7.26 ppm (1H) and 77.16 ppm (13C)]. All 13C chemical shifts were not referenced. Coupling constants are reported in hertz (Hz). Data for †H NMR spectra are reported as follows: chemical shift (ppm, referenced to protium), multiplicity (standard abbreviations), coupling constant (Hz), and integration. Gas chromatography was recorded with an Agilent 7890 instrument with biphenyl as internal standard. High-resolution mass spectra (HRMS) were recorded with a Bruker Compact TOF mass spectrometer system.

Compounds 4; General Procedure
A 25-mL oven-dried Schlenk tube equipped with a magnetic stir bar was charged with Pd2(dba)3 (4.6 mg, 0.005 mmol, 0.025 equiv), XPhos (2.4 mg, 0.005 mmol, 0.025 equiv), Cs₂CO₃ (162.9 mg, 0.5 mmol, 0.25 equiv), and anhydrous CH₂CN (1.0 mL). After stirring for about 15 min at r.t. under argon, aryl iodide 1 (0.24 mmol, 1.2 equiv), alkyl tosylate 2 (0.4 mmol, 2.0 equiv), olefin 3 (0.2 mmol, 1.0 equiv), and 5-norbornene-2-carbonitrile (4.8 mg, 0.04 mmol, 0.2 equiv) were added, then the mixture was heated to 80 °C and stirred for 15 h. After completion of the reaction (monitored by TLC), the mixture was cooled to r.t., filtered through a thin pad of Celite, eluting with EtOAc (10 mL), and the combined filtrate was concentrated in vacuo. The residue was directly purified by column chromatography on silica gel or purified by PTLC to give the desired product.

tert-Butyl (E)-3-(2-Butynaphthalen-1-yl)acrylate (4a)
Yield: 53.4 mg (86%); colorless oil. Rf = 0.6 (5% EtOAc in petroleum).
1H NMR (400 MHz, CDCl₃): δ = 8.11–8.05 (m, 2 H), 7.82–7.80 (m, 1 H), 7.75 (d, J = 8.4 Hz, 1 H), 7.51–7.41 (m, 2 H), 7.35 (d, J = 8.5 Hz, 1 H), 6.15 (d, J = 16.3 Hz, 1 H), 2.83–2.79 (m, 2 H), 1.63–1.61 (m, 2 H), 1.59 (s, 9 H), 1.44–1.37 (m, 2 H), 0.95 (t, J = 7.3 Hz, 3 H).
13C NMR (100 MHz, CDCl₃): δ = 166.02, 141.66, 138.94, 132.20, 131.55, 130.91, 128.51, 128.31, 128.00, 127.59, 126.45, 125.30, 125.24, 80.85, 33.72, 33.56, 28.39, 22.71, 14.09.
HRMS (ESI): m/z calcd for C₁₁H₁₉NaO₃ [M + Na+]: 333.1825; found: 333.1828.

tert-Butyl (E)-3-(4-Bromo-2-butylnaphthalen-1-yl)acrylate (4b)
Yield: 64.0 mg (82%); light yellow oil. Rf = 0.6 (5% EtOAc in petroleum).
1H NMR (400 MHz, CDCl₃): δ = 8.23–8.21 (m, 1 H), 8.04–7.98 (m, 2 H), 7.68 (s, 1 H), 7.56–7.52 (m, 2 H), 6.11 (d, J = 16.3 Hz, 1 H), 2.78–2.74 (m, 2 H), 1.64–1.61 (m, 2 H), 1.58 (s, 9 H), 1.44–1.35 (m, 2 H), 0.95 (t, J = 7.3 Hz, 3 H).
13C NMR (100 MHz, CDCl₃): δ = 165.72, 140.90, 139.47, 132.77, 131.83, 131.13, 130.62, 128.22, 127.51, 127.20, 126.68, 125.71, 125.34, 81.07, 33.39, 28.36, 22.66, 14.03.
HRMS (ESI): m/z calcd for C₁₁H₁₃BrNaO₂ [M + Na+]: 311.0693; found: 311.0695.

tert-Butyl (E)-3-(2-Butyl-6-methylphenyl)acrylate (4c)
Yield: 41.0 mg (75%); light yellow oil. Rf = 0.6 (5% EtOAc in petroleum).
1H NMR (400 MHz, CDCl₃): δ = 7.77 (d, J = 16.4 Hz, 1 H), 7.16–7.12 (m, 1 H), 7.06–7.05 (m, 2 H), 5.96 (d, J = 16.3 Hz, 1 H), 2.65–2.61 (m, 2 H), 2.34 (s, 3 H), 1.55 (s, 9 H), 1.52–1.49 (m, 2 H), 1.40–1.34 (m, 2 H), 0.92 (t, J = 7.3 Hz, 3 H).
13C NMR (100 MHz, CDCl₃): δ = 166.20, 142.45, 141.62, 136.39, 134.06, 128.23, 128.09, 127.16, 125.92, 80.66, 33.57, 33.39, 28.35, 22.69, 21.46, 14.05.
HRMS (ESI): m/z calcd for C₁₈H₂₆NaO₂ [M + Na+]: 297.1825; found: 297.1829.

tert-Butyl (E)-3-(2-Butyl-6-ethylphenyl)acrylate (4d)
Yield: 46.0 mg (80%); light yellow oil. Rf = 0.6 (5% EtOAc in petroleum).
1H NMR (400 MHz, CDCl₃): δ = 7.78 (d, J = 16.3 Hz, 1 H), 7.21–7.17 (m, 1 H), 7.10–7.05 (m, 2 H), 5.94 (d, J = 16.3 Hz, 1 H), 2.67–2.60 (m, 4 H), 1.55 (s, 9 H), 1.53–1.49 (m, 2 H), 1.39–1.30 (m, 2 H), 1.18 (t, J = 7.5 Hz, 3 H), 0.92 (t, J = 7.3 Hz, 3 H).

© 2020. Thieme. All rights reserved. Synthesis 2020, 52, 834–846
**tert-Butyl (E)-3-(2-Butyl-6-isopropenylphenyl)acrylate (4e)**

Yield: 45.8 mg (76%); light yellow oil.

\( R_f = 0.6 \) (5% EtOAc in petroleum).

\( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.80 \) (d, \( J = 16.2 \) Hz, 1 H), 7.24–7.20 (m, 1 H), 7.17–7.15 (m, 1 H), 7.06–7.04 (m, 1 H), 5.88 (d, \( J = 16.3 \) Hz, 1 H), 3.16–3.12 (m, 1 H), 2.61–2.57 (m, 2 H), 1.55 (s, 9 H), 1.53–1.47 (m, 2 H), 1.38–1.33 (m, 2 H), 1.19 (d, \( J = 6.8 \) Hz, 6 H), 0.91 (t, \( J = 7.3 \) Hz, 3 H).

\( ^{13}C \) NMR (100 MHz, CDCl\(_3\)): \( \delta = 165.95, 146.87, 143.00, 140.80, 133.57, 128.19, 126.75, 126.32, 122.95, 80.73, 33.69, 33.36, 30.05, 28.36, 24.08, 22.75, 14.03.


**tert-Butyl (E)-3-(6-Butyl-3-fluoro-2-methylphenyl)acrylate (4i)**

Yield: 32.0 mg (56%); light yellow oil.

\( R_f = 0.6 \) (5% EtOAc in petroleum).

\( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.69 \) (d, \( J = 16.3 \) Hz, 1 H), 7.01–6.97 (m, 1 H), 6.93–6.89 (m, 1 H), 5.93 (d, \( J = 16.3 \) Hz, 1 H), 2.59–2.55 (m, 2 H), 2.23 (d, \( J = 2.4 \) Hz, 3 H), 1.55 (s, 9 H), 1.52–1.45 (m, 2 H), 1.37–1.31 (m, 2 H), 0.91 (t, \( J = 7.3 \) Hz, 3 H).

\( ^{13}C \) NMR (100 MHz, CDCl\(_3\)): \( \delta = 165.83, 159.73 \) (d, \( J = 241.6 \) Hz, 1 H), 141.42 (d, \( J = 2.9 \) Hz, 3 H), 136.93 (d, \( J = 3.6 \) Hz, 1 H), 135.95 (d, \( J = 4.3 \) Hz, 1 H), 127.71 (d, \( J = 8.6 \) Hz, 1 H), 126.94, 123.08 (d, \( J = 16.5 \) Hz, 1 H), 114.61 (d, \( J = 23.0 \) Hz, 1 H), 80.89, 33.34, 33.08, 28.32, 22.57, 14.02, 12.60 (d, \( J = 5.5 \) Hz).

\( ^{19}F \) NMR (377 MHz, CDCl\(_3\)): \( \delta = -118.90 \).

HRMS (ESI): \( m/z \) calcd for C\(_{18}\)H\(_{23}\)F\(_3\)NaO\(_2\) [M + Na\(^+\)]: 315.1731; found: 315.1740.

**tert-Butyl (E)-3-(2-Butyl-4,6-dimethylphenyl)acrylate (4j)**

Yield: 32.0 mg (56%); light yellow oil.

\( R_f = 0.6 \) (5% EtOAc in petroleum).

\( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.76 \) (d, \( J = 16.4 \) Hz, 1 H), 6.88 (s, 2 H), 5.95 (d, \( J = 16.3 \) Hz, 1 H), 2.63–2.59 (m, 2 H), 2.32 (s, 3 H), 2.29 (s, 3 H), 1.55 (s, 9 H), 1.54–1.48 (m, 2 H), 1.41–1.34 (m, 2 H), 0.93 (t, \( J = 7.3 \) Hz, 3 H).

\( ^{13}C \) NMR (100 MHz, CDCl\(_3\)): \( \delta = 166.41, 142.37, 141.87, 137.98, 136.53, 130.96, 129.23, 128.07, 125.26, 80.54, 33.62, 33.54, 28.37, 22.76, 21.51, 21.26, 14.07.

HRMS (ESI): \( m/z \) calcd for C\(_{18}\)H\(_{25}\)FNaO\(_2\) [M + Na\(^+\)]: 311.1892; found: 311.1896.

**tert-Butyl (E)-3-(2-Butyl-4-fluoro-6-methylphenyl)acrylate (4k)**

Yield: 44.0 mg (75%); light yellow oil.

\( R_f = 0.6 \) (5% EtOAc in petroleum).

\( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.68 \) (d, \( J = 16.3 \) Hz, 1 H), 6.76 (d, \( J = 9.5 \) Hz, 2 H), 5.92 (d, \( J = 16.3 \) Hz, 1 H), 2.63–2.59 (m, 2 H), 2.33 (s, 3 H), 1.54 (s, 9 H), 1.53–1.48 (m, 2 H), 1.48–1.31 (m, 2 H), 0.92 (t, \( J = 7.3 \) Hz, 3 H).

\( ^{13}C \) NMR (100 MHz, CDCl\(_3\)): \( \delta = 166.08, 162.15 \) (d, \( J = 246.9 \) Hz, 1 H), 144.25 (d, \( J = 7.7 \) Hz, 1 H), 144.16, 139.00 (d, \( J = 8.1 \) Hz, 1 H), 129.95 (d, \( J = 3.0 \) Hz, 1 H), 126.08, 114.91 (d, \( J = 21.0 \) Hz, 1 H), 113.70 (d, \( J = 20.7 \) Hz, 1 H), 80.75, 33.61, 33.60 (d, \( J = 1.8 \) Hz, 1 H), 28.34, 22.58, 21.61 (d, \( J = 1.7 \) Hz, 14.02.

\( ^{19}F \) NMR (377 MHz, CDCl\(_3\)): \( \delta = -114.58 \).

HRMS (ESI): \( m/z \) calcd for C\(_{18}\)H\(_{23}\)FNaO\(_2\) [M + Na\(^+\)]: 315.1753; found: 315.1745.

**tert-Butyl (E)-3-(4-Bromo-2-butyl-6-methylphenyl)acrylate (4l)**

Yield: 55.7 mg (79%); light yellow oil.

\( R_f = 0.6 \) (5% EtOAc in petroleum).

\( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.65 \) (d, \( J = 16.3 \) Hz, 1 H), 7.20 (s, 2 H), 5.94 (d, \( J = 16.3 \) Hz, 1 H), 2.60–2.56 (m, 2 H), 2.30 (s, 3 H), 1.54 (s, 9 H), 1.52–1.46 (m, 2 H), 1.39–1.31 (m, 2 H), 0.92 (t, \( J = 7.3 \) Hz, 3 H).
### Methyl 4-((E)-(3-tert-Butoxy-3-oxoprop-1-en-1-yl)-3-butyl-5-methylbenzoate (4m)

Yield: 57.6 mg (87%); light yellow oil.

R<sub>f</sub> = 0.3 (5% EtOAc in petroleum).

1H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.74–7.70 (m, 3 H), 7.97 (d, J = 16.4 Hz, 1 H), 3.90 (s, 3 H), 2.35 (s, 3 H), 1.54 (s, 9 H), 1.52–1.49 (m, 2 H), 1.38–1.32 (m, 2 H), 0.91 (t, J = 7.3 Hz, 3 H).

13C NMR (100 MHz, CDCl<sub>3</sub>): 138.92, 136.59, 129.29, 129.05, 128.10, 126.98, 80.97, 52.23, 33.45, 33.17, 28.30, 22.64, 21.33, 14.00.

HRMS (ESI): m/z calcd for C<sub>18</sub>H<sub>25</sub>BrNaO<sub>2</sub> [M + Na<sup>+</sup>]: 342.1676; found: 342.1681.

### 1-(tert-Butyl) (E)-(3-tert-Butoxy-3-oxoprop-1-en-1-yl)-3-butyl-5-methylbenzoate (4n)

Yield: 44.0 mg (42%); light yellow solid; mp 80–85 °C.

R<sub>f</sub> = 0.3 (5% EtOAc in petroleum).

1H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.70 (d, J = 16.2 Hz, 1 H), 7.44–7.32 (m, 10 H), 6.63 (s, 1 H), 6.59 (d, J = 16.1 Hz, 1 H), 5.15 (s, 2 H), 4.85 (s, 2 H), 3.86 (s, 3 H), 2.72–2.68 (m, 2 H), 1.57–1.48 (m, 11 H), 1.37–1.31 (m, 2 H), 0.92 (t, J = 7.3 Hz, 3 H).

13C NMR (100 MHz, CDCl<sub>3</sub>): δ = 167.02, 166.74, 156.24, 156.19, 146.97, 136.59, 136.47, 136.42, 128.85, 128.67, 128.56, 128.40, 128.07, 127.02, 124.72, 120.61, 118.01, 110.28, 80.32, 76.50, 70.50, 52.62, 34.21, 33.29, 28.34, 22.52, 14.05.

HRMS (ESI): m/z calcd for C<sub>18</sub>H<sub>25</sub>NaO<sub>2</sub> [M + Na<sup>+</sup>]: 354.2040; found: 354.2047.

### tert-Butyl (E)-3-(5-(Benzyloxy)-2,2-dimethyl-4-oxo-4H-benzo[d][1,3]dioxin-6-yl)acrylate (4q)

Yield: 49.0 mg (53%); light yellow oil.

R<sub>f</sub> = 0.4 (10% EtOAc in petroleum).

1H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.98 (d, J = 5.2 Hz, 1 H), 7.75 (d, J = 16.0 Hz, 1 H), 6.75 (d, J = 5.2 Hz, 1 H), 6.70 (d, J = 16.0 Hz, 1 H), 4.00 (s, 3 H), 2.75–2.71 (m, 2 H), 1.59–1.54 (m, 2 H), 1.53 (s, 9 H), 1.43–1.32 (m, 2 H), 0.93 (t, J = 7.3 Hz, 3 H).

13C NMR (100 MHz, CDCl<sub>3</sub>): δ = 167.31, 167.24, 154.20, 146.33, 135.30, 124.95, 118.89, 116.29, 80.48, 53.81, 32.93, 32.81, 28.36, 22.66, 14.01.

HRMS (ESI): m/z calcd for C<sub>20</sub>H<sub>28</sub>NaO<sub>4</sub> [M + Na<sup>+</sup>]: 553.2561; found: 553.2575.
Yield: 40.7 mg (81%); light yellow oil.

**13C NMR (100 MHz, CDCl3):** δ = 166.49, 143.50, 139.13, 136.10, 132.20, 131.44, 130.53, 128.82, 128.75, 128.41, 128.36, 128.00, 126.60, 125.38, 125.08, 66.62, 33.80, 33.61, 22.75, 14.10.

**HRMS (ESI):** m/z calcd for C9H9NaO2 [M + Na+]: 167.2235; found: 167.2231.

**[E]-4-(2-Butynaphthalen-1-yl)but-3-en-2-one (4c)**

Yield: 40.0 mg (67%); light yellow oil.

**Rf = 0.3 (5% EtOAc in petroleum).**

**1H NMR (400 MHz, CDCl3):** δ = 8.06–7.99 (m, 2 H), 7.93 (dd, J = 7.3, 2.0 Hz, 1 H), 7.78 (d, J = 8.4 Hz, 1 H), 7.51–7.47 (m, 2 H), 7.37 (d, J = 8.5 Hz, 1 H), 6.51 (d, J = 16.5 Hz, 1 H), 2.83–2.79 (m, 2 H), 2.48 (s, 3 H), 1.64–1.58 (m, 2 H), 1.44–1.35 (m, 2 H), 0.94 (t, J = 7.3 Hz, 3 H).

**13C NMR (100 MHz, CDCl3):** δ = 198.28, 141.54, 139.15, 134.75, 132.25, 131.37, 130.58, 128.93, 128.45, 128.04, 126.65, 125.45, 124.97, 33.87, 33.60, 27.88, 22.77, 14.11.

**HRMS (ESI):** m/z calcd for C18H18NaO2 [M + Na+]: 310.1288; Found: 310.1288.

**[(E)-4-(2-Butynaphthalen-1-yl)-1-naphthalene (4g)]**

Yield: 31.0 mg (54%); light yellow oil.

**Rf = 0.8 (petroleum).**

**1H NMR (400 MHz, CDCl3):** δ = 8.17–8.15 (m, 1 H), 7.82–7.78 (m, 1 H), 7.72 (d, J = 8.4 Hz, 1 H), 7.59–7.58 (m, 2 H), 7.50–7.31 (m, 7 H), 6.75 (d, J = 16.6 Hz, 1 H), 2.87–2.84 (m, 2 H), 1.68–1.61 (m, 2 H), 1.43–1.34 (m, 2 H), 0.92 (t, J = 7.3 Hz, 3 H).

**13C NMR (100 MHz, CDCl3):** δ = 138.40, 137.59, 135.66, 133.58, 132.41, 132.37, 128.89, 128.21, 128.08, 127.86, 127.27, 126.55, 125.95, 125.80, 125.02, 33.85, 33.59, 22.82, 14.20.


**2-Butyl-[(E)-1-styryl]naphthalene (4h)**

Yield: 49.0 mg (74%); yellow solid; mp 96–100°C.

**Rf = 0.4 (5% EtOAc in petroleum).**

**1H NMR (400 MHz, CDCl3):** δ = 8.28 (d, J = 8.5 Hz, 2 H), 8.12–8.10 (m, 1 H), 7.86–7.84 (m, 1 H), 7.78 (d, J = 8.4 Hz, 1 H), 7.71–7.66 (m, 3 H), 7.51–7.45 (m, 2 H), 7.41 (d, J = 8.4 Hz, 1 H), 6.84 (d, J = 16.5 Hz, 1 H), 2.88–2.84 (m, 2 H), 1.70–1.62 (m, 2 H), 1.45–1.38 (m, 2 H), 0.94 (t, J = 7.3 Hz, 3 H).

**13C NMR (100 MHz, CDCl3):** δ = 147.05, 143.82, 138.71, 133.55, 132.36, 132.00, 130.80, 128.40, 128.07, 128.05, 126.94, 126.31, 125.30, 125.26, 124.33, 33.84, 33.57, 22.77, 14.15.

**HRMS (ESI):** m/z calcd for C18H16NaO2 [M + Na+]: 354.1465; Found: 354.1474.

**tert-Butyl (E)-3-(2-Hexynaphthalen-1-yl)acrylate (4a)**

Yield: 60.7 mg (90%); light yellow oil.

**Rf = 0.6 (5% EtOAc in petroleum).**

**1H NMR (400 MHz, CDCl3):** δ = 8.12–8.05 (m, 2 H), 7.83–7.90 (m, 1 H), 7.75 (d, J = 8.4 Hz, 1 H), 7.51–7.43 (m, 2 H), 7.35 (d, J = 8.4 Hz, 1 H), 6.15 (d, J = 16.3 Hz, 1 H), 2.82–2.78 (m, 2 H), 1.65–1.61 (m, 2 H), 1.60 (s, 9 H), 1.40–1.35 (m, 2 H), 1.34–1.30 (m, 4 H), 0.90 (t, J = 6.3 Hz, 3 H).

**13C NMR (100 MHz, CDCl3):** δ = 166.00, 141.67, 138.98, 132.20, 131.55, 130.90, 128.51, 128.31, 127.98, 125.77, 126.44, 125.29, 125.24, 80.82, 34.05, 31.75, 31.38, 29.30, 28.39, 22.72, 14.24.

**HRMS (ESI):** m/z calcd for C19H18NaO2 [M + Na+]: 361.2138; Found: 361.2141.

**t-Butyl (E)-3-(2-Dodecylnaphthalen-1-yl)acrylate (4b)**

Yield: 87.6 mg (93%); light yellow oil.

**Rf = 0.6 (5% EtOAc in petroleum).**

**1H NMR (400 MHz, CDCl3):** δ = 8.11–8.05 (m, 2 H), 7.83–7.80 (m, 1 H), 7.75 (d, J = 8.4 Hz, 1 H), 7.49–7.44 (m, 2 H), 7.35 (d, J = 8.5 Hz, 1 H), 6.15 (d, J = 16.3 Hz, 1 H), 2.82–2.78 (m, 2 H), 1.66–1.62 (m, 2 H), 1.59 (s, 9 H), 1.36–1.26 (m, 18 H), 0.88 (t, J = 6.8 Hz, 3 H).
**tert-Butyl (E)-3-(2-(Methylpentyl)naphthalen-1-yl)acrylate (4c)**

Yield: 64.2 mg (95%); light yellow oil.

**tert-Butyl (E)-3-(2-(3-Methylpentyl)naphthalen-1-yl)acrylate (4d)**

Yield: 72.7 mg (82%); light yellow oil.

**tert-Butyl (E)-3-(2-(4,4,4-Trifluorobutyl)naphthalen-1-yl)acrylate (4e)**

Yield: 65.0 mg (89%); light yellow oil.

**tert-Butyl (E)-3-(2-(2-(Naphthalen-1-yl)ethyl)naphthalen-1-yl)-3-oxoprop-1-en-1-yl)naphthalen-2-yl)hexanoate (4f)**

Yield: 72.6 mg (97%); colorless oil.

**tert-Butyl (E)-3-(2-(2-(Naphthalen-1-yl)ethyl)naphthalen-1-yl)-3-oxoprop-1-en-1-yl)naphthalen-2-yl)hexanoate (4g)**

Yield: 69.3 mg (85%); white solid; mp 84–87 °C.

**tert-Butyl (E)-3-(2-(3-Bromopropyl)naphthalen-1-yl)acrylate, tert-Butyl (E)-3-(2-(2-(Naphthalen-1-yl)ethyl)naphthalen-1-yl)-3-oxoprop-1-en-1-yl)naphthalen-2-yl)hexanoate (4h)**

Yield: 69.3 mg (85%); white solid; mp 84–87 °C.

**tert-Butyl (E)-3-(2-(3-Iodopropyl)naphthalen-1-yl)acrylate (4i)**

Yield: 45.0 mg (56%); light yellow oil.

**HRMS (ESI):** 
- m/z calc'd for C_{28}H_{27}NNaO_{4} [M + Na^+]: 464.1832; found: 464.1837.
- m/z calc'd for C_{29}H_{42}KO_{2} [M + K^+]: 461.2816; found: 461.2817.

© 2020. Thieme. All rights reserved. Synthesis 2020, 52, 834–846.

**Feature**

- **13C NMR** (100 MHz, CDCl3): δ = 141.67, 139.00, 132.20, 131.55, 130.90, 128.51, 128.31, 128.00, 127.57, 126.45, 125.30, 125.25, 80.83, 34.07, 32.07, 31.46, 29.83, 29.80, 29.79, 29.75, 29.69, 29.63, 29.51, 28.40, 22.85, 14.29.
- **HRMS (ESI):** 
  - m/z calc'd for C_{39}H_{42}KO_{2} [M + K^+]: 461.2816; found: 461.2817.

**t-Butoxy-3-oxoprop-1-en-1-yl)naphthalen-2-yl)hexanoate (4f)**

Yield: 72.6 mg (92%); light yellow oil.

**tert-Butyl (E)-3-(2-(1,3-Dioxoisindolin-2-yl)propyl)naphthalen-1-yl)acrylate (4f)**

Yield: 72.7 mg (82%); light yellow oil.

**Ethyl 6-{1-[(E)-3-tert-Butoxy-3-oxoprop-1-en-1-yl]naphthalen-2-yl}hexanoate (4f)**

Yield: 72.6 mg (92%); light yellow oil.

**tert-Butyl (E)-3-(2-(4,4,4-Trifluorobutyl)naphthalen-1-yl)acrylate (4f)**

Yield: 72.6 mg (92%); light yellow oil.

© 2020. Thieme. All rights reserved. Synthesis 2020, 52, 834–846.
**tert-Butyl (E)-3-(2-(Cyclopentylmethyl)naphthalen-1-yl)acrylate (4f)**

Yield: 57.5 mg (85%); light yellow oil.

Rf = 0.6 (5% EtOAc in petroleum).

1H NMR (400 MHz, CDCl3): δ = 8.12–8.07 (m, 2 H), 7.83–7.78 (m, 1 H), 7.75 (d, J = 8.4 Hz, 1 H), 7.49–7.44 (m, 2 H), 7.36 (d, J = 8.0 Hz, 1 H), 6.15 (d, J = 16.3 Hz, 1 H), 2.83 (d, J = 7.3 Hz, 2 H), 2.18–2.10 (m, 1 H), 1.74–1.64 (m, 4 H), 1.60 (s, 9 H), 1.55–1.50 (m, 2 H), 1.27–1.24 (m, 2 H).

13C NMR (100 MHz, CDCl3): δ = 131.49, 131.06, 128.80, 128.25, 128.01, 126.37, 125.57, 125.38, 123.93, 80.93, 37.43, 30.86, 28.42, 22.10, 12.39.

**Ethyl (E)-2-(2,3-Dihydrophenanthren-4(1H)-ylidene)acetate (6a)**

Base: Cs2CO3; yield: 46.5 mg (87%); yellow oil.

Rf = 0.5 (5% EtOAc in petroleum).

1H NMR (400 MHz, CDCl3): δ = 8.36 (d, J = 8.4 Hz, 1 H), 7.83 (d, J = 7.9 Hz, 1 H), 7.73 (d, J = 8.3 Hz, 1 H), 7.52–7.48 (m, 1 H), 7.46–7.42 (m, 1 H), 7.27 (d, J = 6.5 Hz, 1 H), 6.25 (t, J = 1.9 Hz, 1 H), 4.25 (q, J = 7.2 Hz, 2 H), 3.32 (td, J = 6.9, 1.9 Hz, 2 H), 2.82 (t, J = 6.2 Hz, 2 H), 1.94–1.87 (m, 2 H), 1.33 (t, J = 7.1 Hz, 3 H).

13C NMR (100 MHz, CDCl3): δ = 167.09, 154.04, 139.44, 133.39, 133.26, 130.27, 128.85, 128.60, 126.64, 125.56, 125.30, 125.14, 119.24, 59.95, 30.64, 28.73, 22.36, 14.52.


**Ethyl (E)-2-(7,8,9,10-Tetrahydro-11-ylidene)acetaldehyde (6c)**

Base: K2CO3; yield: 18.0 mg (43%); brown oil.

Rf = 0.4 (5% EtOAc in petroleum).

1H NMR (400 MHz, CDCl3): δ = 7.98–7.95 (m, 1 H), 7.84–7.79 (m, 1 H), 7.72 (d, J = 8.3 Hz, 1 H), 7.48–7.41 (m, 2 H), 7.30 (d, J = 8.3 Hz, 1 H), 5.83 (s, 1 H), 4.29–4.24 (m, 2 H), 3.84–3.79 (m, 1 H), 3.01–2.94 (m, 1 H), 2.50–2.40 (m, 1 H), 2.06–2.01 (m, 1 H).

13C NMR (100 MHz, CDCl3): δ = 165.78, 141.48, 140.74, 136.51, 132.42, 131.87, 131.60, 129.03, 128.71, 128.59, 128.54, 128.37, 128.00, 126.63, 124.26, 124.69, 125.35, 80.90, 39.86, 28.36.

Acknowledgment

We are grateful to the National Natural Science Foundation of China (Grants 21602161, 21871213, and 21801193), for the startup funding from Wuhan University, and to the China Postdoctoral Science Foundation (No. 2018M642894, Z.-S. Liu) for financial support.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690801.

References


(6) See ref. 3, and references cited therein.


(17) The iodide ion is gradually generated from the aryl iodide after its oxidative addition with Pd(0) catalyst: Maestri, G.; Motti, E.;


(22) See the Supporting Information for optimization details.


(24) Aryl bromides survived this reaction, but are actually reactive under the conventional Pd/XPhos conditions; see ref. 21 and: Bruno, N. C.; Niljianskul, N.; Buchwald, S. L. J. Org. Chem. 2014, 79, 4161.

(25) For one example using methyl 4-nitrobenzenesulfonate as the electrophile, see ref. 19.