Synthesis F. Li et al. Feature

Photocatalytic Generation of π-Allyltitanium Complexes from Butadiene via a Radical Strategy

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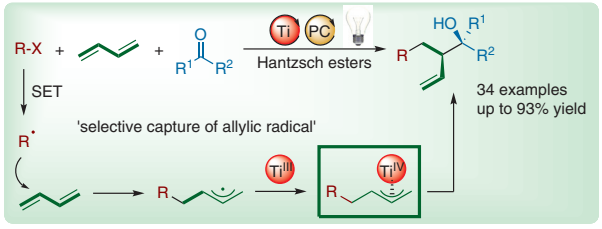

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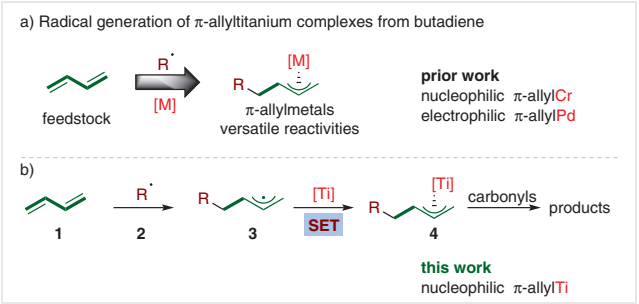
Abstract The direct conversion of industrial feedstock chemicals into highly valuable fine chemical intermediates is of great appeal to the synthetic community as well as industrial applications. This study reports a conceptually new radical strategy for the photocatalytic generation of π-allyltitanium complexes from butadiene. This novel and environmentally benign strategy enables the direct three-component allylation of carbonyls with 1,3-butadiene and α-bromocarboxylates, providing rapid access to valuable homoallylic alcohols with exceptional regio- and diastereoselectivity control.

Key words photocatalysis, allylation, radical, butadiene, π-allyltitanium

The direct conversion of industrial feedstock chemicals into highly valuable fine chemical intermediates is of great appeal to the synthetic community as well as industrial applications. Homoallylic alcohols are important building blocks in synthetic chemistry. The addition of allylmetallic reagents to carbonyls is the most common route to homoallylic alcohols.[1–4] 1,3-Butadiene is one of the most convenient industrial raw material produced as a by-product of ethylene production from steam crackers.[5–7] In recent years, breakthroughs in transition-metal catalysis have enabled the utilization of butadiene as surrogates for stoichiometric allylmetallic reagents for the homoallylic alcohol synthesis.[8–15] In these processes, various π-allylmetal complexes are usually generated via the addition of a metal hydride species to butadiene (ionic approach).[16]

Over the last few decades, radical-based transformations have been increasingly used in organic synthesis due to their outstanding features, such as ease of generation, mild reaction conditions, and broad functional group compatibility. Recently, the combination of π-allylmetal chemistry with radical chemistry of butadiene emerged as a distinct new option for the generation of π-allylmetal complexes. Specifically, in situ formed transient allylic radicals through the addition of alkyl radicals to butadiene were trapped by reductive metals and generate π-allylmetal complexes (Scheme 1a). Based on this strategy, Takai et al. first reported the generation of nucleophilic π-allylchromium complexes from butadiene.[10,12] Another example for the generation of electrophilic π-allylpalladium complexes via the addition of a hybrid alkyl-Pd(I) radical to butadiene was reported by Glorius and Gevorgyan, respectively.[17–20]



Scheme 1 Concept of merging π-allylmetal chemistry with radical chemistry of butadiene

Titanium is an earth-abundant, low-cost transition metal and in general nontoxic and environmentally friendly. These features and its rich redox properties make titanium especially attractive for organic transformations.[21,22] Metallaphotoredox catalysis is a new and rapidly growing research subject.[23–27] In this backdrop, our group developed the first dual titanium and photoredox catalysis for the radical opening/cyclization of epoxides.[28] The same catalyst system was then applied for the photocatalytic Barbier-type allylation of aldehydes and ketones with allyl bromide.[29,30] Interestingly, mechanistic studies indicated that the allyl radical was produced from allyl bromide through SET reduction by a photocatalyst. The resulting allyl radical

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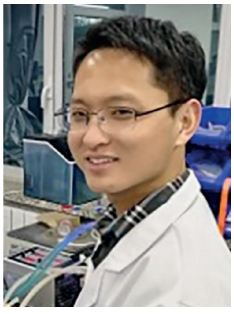
was rapidly trapped/reduced by $Cp_2Ti^{III}Cl$ (Nugent–RajanBabu reagent,[31] a powerful and mild single-electron reductant) via SET process to form key nucleophilic π-allyltitanium complexes. Inspired by this work, we anticipated that a three-component allylation of carbonyls with butadiene and alkyl halides might be viable for a dual photoredox and titanium catalysis (Scheme 1b). We envisioned that Ti^{III} and the alkyl radicals would be generated under photoreduction conditions. The addition of the alkyl radicals to butadiene would produce transient allyl radicals that are expected to be rapidly trapped by single-electron reductant Ti^{III}. The resulting nucleophilic π-allyltitanium complexes could be successively coupled with carbonyls. However, two challenges complicate this reaction, 1) highly reactive allyl

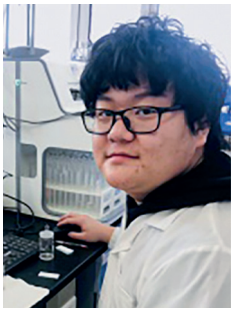
Biographical Sketches

Lei Shi received his master's degree under the supervision of Professor Kuiling Ding and Ph.D. degree from the University of Edinburgh (U.K.) in 2011 under the supervision of Professor Michael Greaney. Then he worked as a postdoctoral associate with Professor K. C. Nicolaou at The Scripps Research Institute. He is currently a professor at Dalian University of Technology, and his research interest is photoredox and transition metal catalysis.



Fusheng Li was born in 1990 in Jiangxi, China. He received his bachelor's degree from Hainan University in 2014. Later he completed a master's degree in 2017 at Tianjin University of Technology. Now he is a fourth year Ph.D. candidate under the guidance of Prof. Lei Shi at Dalian University of Technology. His research focuses on photoredox and transition-metal-catalyzed carbonyls allylation reaction.

Shuangjie Lin was born in 1989 in Hubei, China. He obtained his bachelor's degree from Beijing University of Chemical Technology in 2011 and master's degree from Jiangxi Science & Technology Normal University in 2017, respectively. Now he is working as a Ph.D. candidate under the guidance of Prof. Lei Shi at Dalian University of Technology. His research focuses on photoredox and transition-metal-catalyzed carbonyls allylation reaction.



Xiyu Li is an undergraduate student majoring in applied chemistry at Dalian University of Technology. Currently, he is conducting national college innovation and entrepreneurship program under the guidance of Prof. Lei Shi. The research focuses on the difunctionalizations of butadiene by dual photoredox and titanium catalysis.

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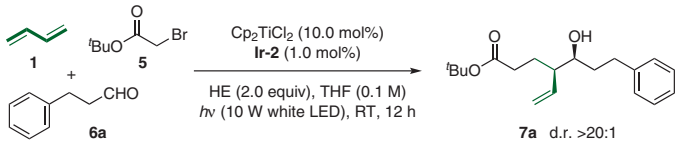
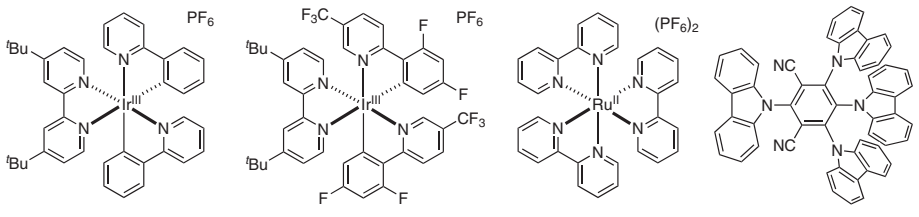
radicals intermediates are readily polymerized through a radical chain reaction, (main method for the production of synthetic rubber in the industry); and 2) Ti^{III} has to selectively react with allyl radicals without touching alkyl radicals. Furthermore, reductive Ti^{III} or photocatalyst can result in pinacol formation of aromatic aldehydes and ketones. With the aforementioned challenges in mind, in this study, we report the successful execution of this idea and present a simple, broadly applicable, one-step protocol for the three-component allylation of aldehydes and ketones with butadiene by dual photoredox and titanium catalysis.

We began our study by examining butadiene (**1**), aldehyde **6a**, and *tert*-butyl bromoacetate (**5a**) as the radical precursor. After a systematic variation of different reaction parameters, we were pleased to identify the optimal reaction conditions in which a mixture of Cp_2TiCl_2 (10.0 mol%), $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (**Ir-2**; 1.0 mol%, $E_{1/2}^{IV/III*}$ = –0.96 V vs SCE in MeCN), Hantzsch ester (HE, 2.0 equiv), and aldehyde **6a** (1.0 equiv) in THF at room temperature with irradiation by a 10 W white light-emitting diode (LED) lamp for 12 hours afforded the desired product **7a** in an excellent yield of 81% (d.r. >20:1, Table 1, entry 1). Using 10 W 450 nm LED instead of white LED led to a low yield of 62%. Further screening of other photosensitizers including $Ir(ppy)_2(dtbbpy)PF_6$ (**Ir-1**), $Ru(bpy)_3(PF_6)_2$ (**Ru-1**), and cheap and readily obtained organic dye 4CzIPN resulted in lower yields (entries 3–5). Various solvents, including DCE, MeCN, and toluene were tested, and they all resulted in less yields but did not affect the diastereoselectivity (entries 7–9). The use of other organic electron donors, such as *N*,*N*-diisopropylethylamine (DIPEA) instead of HE, resulted in no product (entry 10). Importantly, the reaction did not proceed in the

Table 1 Reaction Optimization for Aldehydes[a,b,c]



Entry	Variation from standard conditions	Yield (%)
1	none	81
2	450 nm LED instead white LED	62
3	$Ir(ppy)_2(dtbbpy)PF_6$ (**Ir-1**) instead of **Ir-2**	51
4	4CzIPN instead of **Ir-2**	36
5	$Ru(bpy)_3Cl_2$ (**Ru-1**) instead of **Ir-2**	0
6	0.2 M instead of 0.1 M	63
7	DCE instead of THF	54
8	MeCN instead of THF	41
9	toluene instead of THF	40
10	DIPEA instead of HE	0
11	no Cp_2TiCl_2	0
12	no HE	0
13	no photocatalyst	0
14	no light	0



[a] Reaction conditions: **6a** (1.0 mmol scale).
[b] Yields were determined by ^1H NMR spectroscopy versus an internal standard.
[c] Diastereomeric ratios were determined by ^1H NMR spectroscopy.

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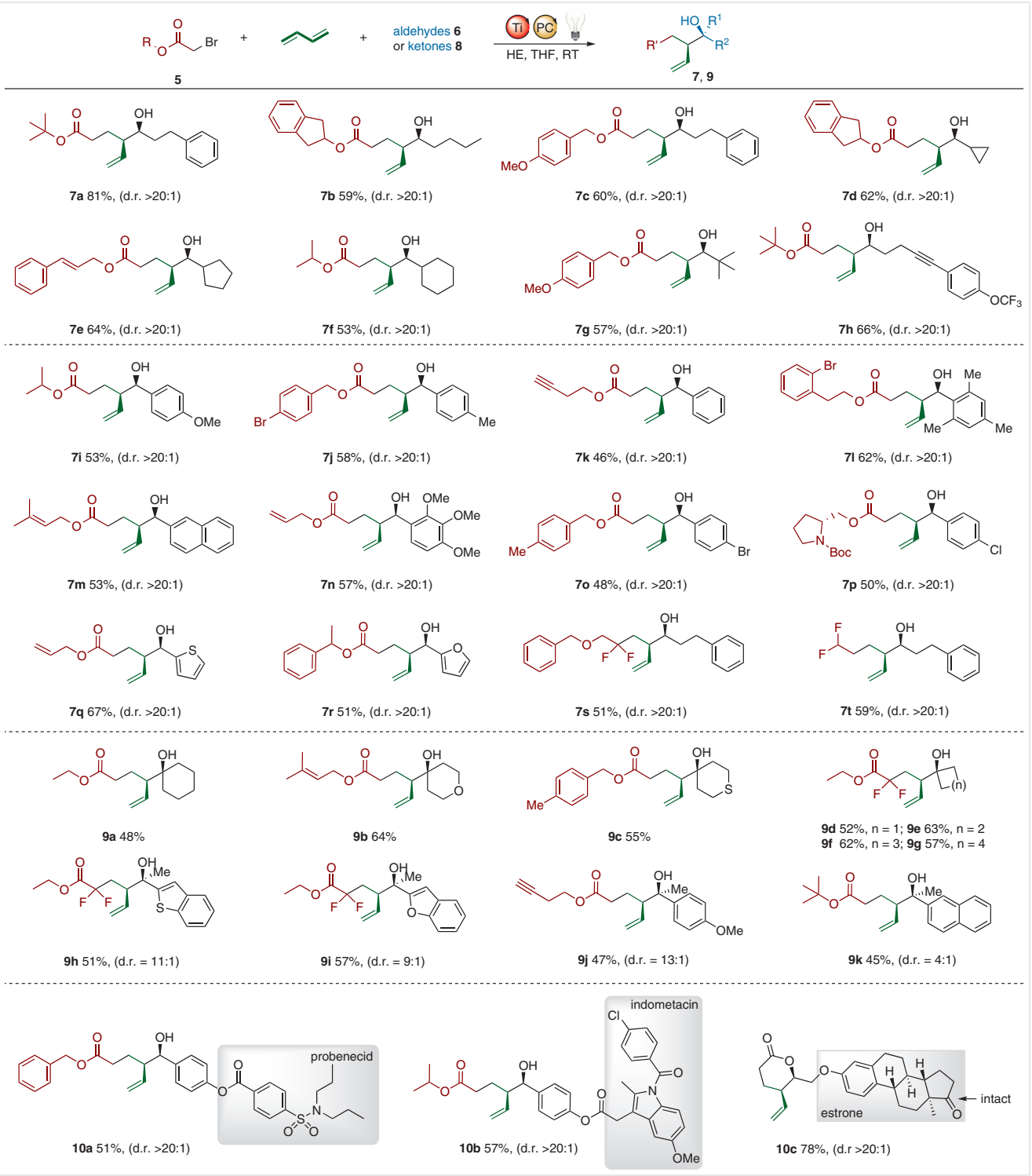
absence of Cp_2TiCl_2, HE, the photocatalyst, or visible light (entries 11–14).

With satisfactory reaction conditions established, we then explored the scope of the cyclization reaction using **Ir-2** as the photosensitizer. Remarkably, the reaction worked



Scheme 2 Scope of the reaction. *Reagents and conditions*: **6** or **8** (1.0 mmol scale). Yields were determined by ^{1}H NMR spectroscopy versus an internal standard. Diastereomeric ratios were determined by ^{1}H NMR spectroscopy. 2 equiv of LiCl were added for the preparation of **9h**,**i**.

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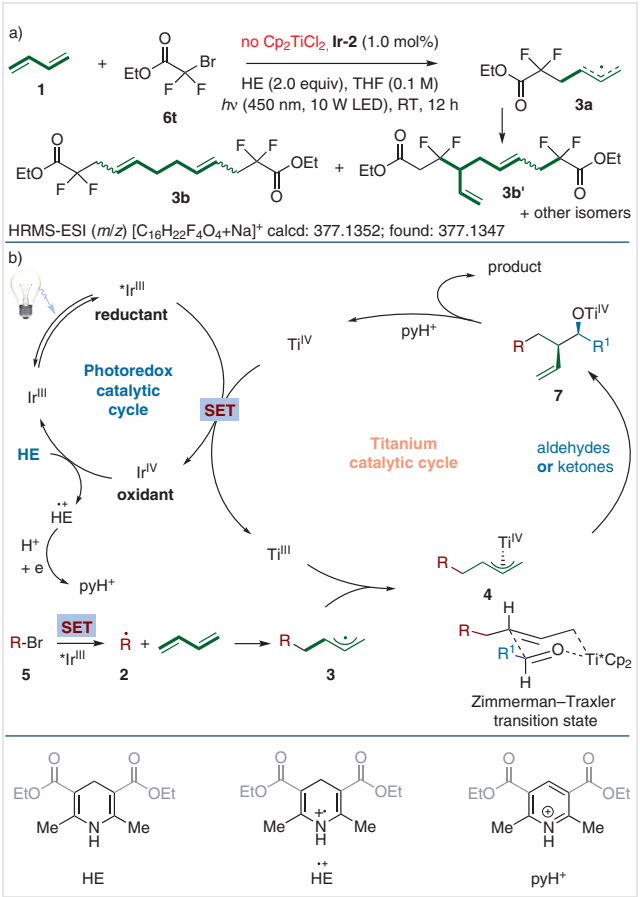
well with various aldehydes, ketones, and various ester groups, affording the desired homoallylic alcohols in generally good yield with remarkably high regio- and diastereoselectivity (Scheme 2). Generally, ketones showed lower reactivity. In these cases, high Ti catalyst loading and prolonged reaction were required for better yields. The sterically hindered substrates such as pivaldehyde and mesitaldehyde worked smoothly and gave desired products **7g** and **7l** in satisfactory yields. Cyclic ketones with 4–7-membered ring sizes were tested and they all produced the desired products **9a–g** in good yields. Heteroatoms, such as oxygen and sulfur did not interfere with the catalytic cycle (**9b** and **9c**). Importantly, various heteroarenes, the most widely used core structures in pharmaceutical synthesis, were also compatible with this dual catalysis, including furan **7r**, thiophene **7q**, benzothiophene **9h**, and benzofuran **9i**. Because of the extremely mild conditions, photocatalysis demonstrated broad compatibility with plentiful synthetically important and sensitive functional groups. These included alkene **7m**, alkyne **7k**, ether **7n**, and bromobenzene **7o**. To show the potential applicability of our strategy in late-stage functionalization, probenecid, indomethacin, and lithocholic acid derivatives were used and the desired products **10a**, **10b**, and **10c** were obtained in good yields. This novel photocatalytic approach provides access to a broad range of novel and valuable homoallylic alcohols with adjacent stereocenter, which could be of considerable interest to a wide community of synthetic and medicinal chemists.

To further investigate the mechanism of the reactions, Stern–Volmer luminescence quenching studies were performed. These studies proved that HE, Cp_2TiCl_2, and ethyl bromodifluoroacetate (**6t**) can quench the excited state photocatalyst. The reaction is light-dependent as indicated by the on-off-light experiment, and the quantum yield of the reaction was calculated to be 0.08. Therefore the radical-chain mechanism is unlikely. To determine whether the difluoroacetate radical can be added to butadiene before further reduction by a photocatalyst, the reactions were performed in the absence of titanium and carbonyls. In this case, the allyl radical dimerization product, together with isomeric products, were isolated in significant amount (Scheme 3a). Thus the proposed radical addition pathway is indeed operative in the photocatalytic reaction independent of the Cp_2TiCl_2 catalyst. Additionally, the absence of a cyclopropane-opening compound in the allylation of cyclopropanecarboxaldehyde (Scheme 2, 7d) suggested that the ketyl radical intermediates are not likely involved in the process.

Based on these results, we tentatively propose the following catalytic cycle (Scheme 3b). First, α-bromocarboxylates are reduced by the **Ir^{III}** complex to produce the radical **2**, which can rapidly add to butadiene to form the allyl radical **3**. Ti^{III} can trap allyl radicals **3** to form nucleophilic **4** that later couples with carbonyls. After hydrolysis by **pyH$^+$**, the



Scheme 3 a) The existence of an allyl radical **3a** and its dimerization. b) Proposed catalytic mechanism.

homoallylic alcohols would be obtained and free Ti^{IV} is released. Resulting Ti^{IV} is reduced by an excited **Ir^{III}** to Ti^{III} using HE as the terminal reductant and produce HE$^{\bullet+}$, which can further participate in electron transfer events and eventually produce **pyH$^+$**. The *anti*-selectivity of homoallylic alcohols can be explained by Zimmerman–Traxler transition state.

Chemoselectivity is a desirable property for organic synthesis. Therefore a competing experiment was performed and the result clearly indicated that our approach could discriminate between aldehydes and ketones (Scheme 4a). This advantage might be useful for the selective allylation of aldehydes in the presence of ketones. In order to show the difference between the photocatalytic system and the traditional metal reduction approach, the crotylation reaction was carried out with the same substrates (Scheme 4b). Although the two approaches gave a similar yield of allylic alcohols, exceptional diastereoselectivity was only obtained under the photocatalytic condition. These results clearly show the inherent advantages of the photocatalytic approach. For the comparison of the photocatalytic titanium catalysis with the well-known Cr-catalyzed

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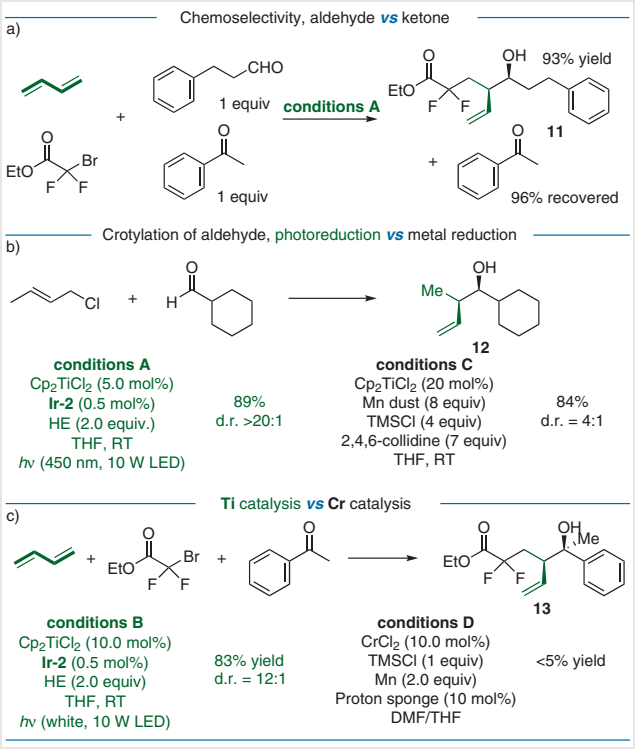

Scheme 4 a) Chemoselective allylation of aldehyde in the presence of ketone. b) Comparison of the photoreductive approach with the metal reductive approach. c) Comparison of Ti-catalysis with Cr-catalysis.

Nozaki–Hiyama–Kishi allylation reaction, acetophenone was used as substrate (Scheme 4c). The results clearly showed that the Ti catalytic approach produced the allylic alcohol in 83% yield (d.r. = 12:1). In contrast, less than 5% yield of product was formed when Cr was used instead of Ti under the same conditions. Therefore, the photocatalytic titanium catalysis developed in this study complements the classical Cr catalysis.

In summary, a novel, eco-friendly, and operationally simple three-component allylation reaction with feedstock butadiene was developed based on the dual photoredox and nontoxic metal titanium catalysis. This method provides a strategically distinct way for the rapid assembly of valuable homoallylic with exceptional regio- and diastereoselectivity with outstanding functional group compatibility. Mechanistic studies revealed that the key to the success of such a photocatalytic system is a highly efficient and selective capture of a reactive allyl radical by Ti^{III} and subsequent formation of a nucleophilic allyl-Ti^{IV} complex. This approach of dual photoredox and titanium catalysis will undoubtedly constitute a valuable addition to the current portfolio of allylation of carbonyl compounds with feedstock butadiene.

All reactions were conducted in flame-dried glassware under a N_2 atmosphere using anhydrous solvent. Commercially available reagents were used without further purification. TLC was performed using Huanghai TLC silica gel plates HSG F254 and visualized using UV light, anisaldehyde or $KMnO_4$. The photocatalytic reactions were performed on WATTCAS Parallel Light Reactor (WP-TEC-1020L) with 10W LEDs. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker 400M spectrometer. Chemical shifts in ^1H NMR spectra were reported in parts per million (ppm) on the δ scale from an internal standard of residual $CDCl_3$ (7.26 ppm). Data for ^1H NMR were reported as follows: chemical shift, multiplicity (standard abbreviations), coupling constant in hertz (Hz), and integration. Data for ^{13}C NMR spectra were reported in terms of chemical shift in ppm from the central peak of $CDCl_3$ (77.00 ppm). IR spectra were recorded on a Thermo Scientific Nicolet 6700 Flex FT-IR spectrophotometer. ESI mass spectra were obtained from an TOF LCMS or LTQ Orbitrap XL mass spectrometer using MeCN as the mobile phase. UV/Vis spectra were recorded on an HP 8453 spectrometer. The fluorescence emission spectra were recorded on an Edinburgh FS920 spectrometer.

Three-Component Allylation of Aldehydes with 1,3-Butadiene and α-Bromocarboxylates; General Procedure

To a solution of aldehyde **6** (1.0 mmol, 1.0 equiv), HE (2.0 mmol, 2.0 equiv), Cp_2TiCl_2 (10.0 mol%), and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**Ir-2**, 1 mol%) in THF was added 1,3-butadiene (**1**; 2.0 M in THF, 2.0 mmol, 2.0 equiv) and α-bromocarboxylate **5** (2.0 mmol, 2.0 equiv). The reaction mixture was stirred at RT using 10 W white LED for 12 h. The mixture was concentrated under reduced pressure to give the crude residue, which was purified by silica gel chromatography to afford **7**.

Three-Component Allylation of Ketones with 1,3-Butadiene and α-Bromocarboxylates; General Procedure

To a solution of ketone **8** (1.0 mmol, 1.0 equiv), HE (2.0 mmol, 2.0 equiv), Cp_2TiCl_2 (20.0 mol%), and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**Ir-2**, 1 mol%) in THF was added 1,3-butadiene (**1**; 2.0 M in THF, 2.0 mmol, 2.0 equiv) and α-bromocarboxylate **5** (2.0 mmol, 2.0 equiv). The reaction mixture was stirred at RT using 10 W white LED for 12 h. The mixture was concentrated under reduced pressure to give the crude residue, which was purified by silica gel chromatography to afford **9**.

Compounds 10–13

For the preparation of compounds **10**–**13**, see Schemes 2 and 4.

7a

Yield: 246 mg (81%); colorless oil.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.35 (m, 2 H), 7.33–7.27 (m, 3 H), 5.74 (ddd, *J* = 17.2, 10.3, 9.3 Hz, 1 H), 5.30 (dd, *J* = 10.3, 2.0 Hz, 1 H), 5.20 (dd, *J* = 17.2, 1.5 Hz, 1 H), 3.69–3.51 (m, 1 H), 2.98–2.86 (m, 1 H), 2.82–2.69 (m, 1 H), 2.44–2.31 (m, 1 H), 2.31–2.19 (m, 1 H), 2.19–2.09 (m, 1 H), 1.98–1.77 (m, 4 H), 1.74–1.58 (m, 1 H), 1.53 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.11, 142.13, 137.66, 128.43, 128.34, 125.75, 118.62, 80.22, 72.63, 50.05, 36.52, 33.27, 32.13, 28.07, 25.88.

HRMS-ESI: *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{28}O_3Na$: 327.1936; found: 327.1936.

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7b

Yield: 186 mg (59%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.15 (m, 4 H), 5.67–5.55 (m, 1 H), 5.53 (m, 1 H), 5.17 (dd, *J* = 10.3, 1.9 Hz, 1 H), 5.05 (dd, *J* = 17.1, 1.7 Hz, 1 H), 3.46 (m, 1 H), 3.31 (ddd, *J* = 16.8, 6.4, 1.7 Hz, 2 H), 2.99 (dd, *J* = 16.9, 3.0 Hz, 2 H), δ 2.39–2.27 (m, 1 H), 2.28–2.15 (m, 1 H), 2.07–1.92 (m, 1 H), 1.91–1.76 (m, 1 H), 1.68–1.55 (m, 2 H), 1.52–1.24 (m, 6 H), 0.90 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.69, 140.37, 137.57, 126.74, 124.59, 118.59, 75.18, 73.44, 49.77, 39.56, 39.54, 34.39, 32.34, 27.87, 25.87, 22.68, 14.05.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{28}O_3Na$: 339.1936; found: 339.1925.

7c

Yield: 220 mg (60%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (dd, *J* = 7.7, 5.9 Hz, 4 H), 7.20 (d, *J* = 7.3 Hz, 3 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 5.62 (dt, *J* = 17.2, 9.8 Hz, 1 H), 5.19 (dd, *J* = 10.3, 1.9 Hz, 1 H), 5.08 (dd, *J* = 17.3, 1.9 Hz, 1 H), 5.05 (s, 2 H), 3.80 (s, 3 H), 3.56–3.47 (m, 1 H), 2.86–2.74 (m, 1 H), 2.70–2.57 (m, 1 H), 2.44–2.34 (m, 1 H), 2.33–2.22 (m, 1 H), 2.09–1.98 (m, 1 H), 1.93–1.83 (m, 1 H), 1.82–1.70 (m, 2 H), 1.69–1.58 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.53, 159.59, 142.06, 137.35, 130.08, 128.40, 128.33, 128.05, 125.75, 118.80, 113.89, 72.73, 66.00, 55.22, 49.88, 36.52, 32.11, 32.07, 25.82.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{28}O_4Na$: 391.1885; found: 391.1874.

7d

Yield: 186 mg (62%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.21 (m, 2 H), 7.21–7.16 (m, 2 H), 5.68 (dt, *J* = 17.2, 9.8 Hz, 1 H), 5.53 (m, 1 H), 5.17 (dd, *J* = 10.3, 1.9 Hz, 1 H), 5.09 (dd, *J* = 17.2, 1.7 Hz, 1 H), 3.31 (dd, *J* = 16.9, 6.6 Hz, 2 H), 2.99 (dd, *J* = 16.9, 3.0 Hz, 2 H), 2.71 (dd, *J* = 8.8, 5.3 Hz, 1 H), 2.41–2.11 (m, 3 H), 2.06–1.91 (m, 1 H), 1.72–1.54 (m, 1 H), 0.98–0.82 (m, 1 H), 0.59–0.44 (m, 2 H), 0.33–0.17 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.66, 140.40, 138.11, 126.73, 124.58, 118.30, 78.81, 75.13, 50.68, 39.57, 32.40, 25.79, 15.62, 3.38, 2.38.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{24}O_3Na$: 323.1623; found: 323.1613.

7e

Yield: 210 mg (64%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (t, *J* = 7.3 Hz, 2 H), 7.29 (d, *J* = 7.3 Hz, 1 H), 7.25–7.20 (m, 2 H), 6.67 (d, *J* = 11.7 Hz, 1 H), 5.80 (dt, J = 11.7, 6.6 Hz, 1 H), 5.76–5.65 (m, 1 H), 5.18 (dd, *J* = 10.3, 2.0 Hz, 1 H), 5.08 (dd, *J* = 17.3, 2.0 Hz, 1 H), 4.84 (dd, *J* = 6.6, 1.7 Hz, 2 H), 3.31 (ddd, *J* = 8.4, 5.0, 3.6 Hz, 1 H), 2.48–2.23 (m, 2 H), 2.20–2.07 (m, 1 H), 2.00–1.72 (m, 4 H), 1.70–1.61 (m, 2 H), 1.58–1.47 (m, 3 H), 1.40–1.28 (m, 1 H), 1.22–1.09 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.59, 137.21, 136.00, 132.97, 128.70, 128.36, 127.50, 125.80, 118.09, 78.19, 61.35, 48.06, 43.97, 32.12, 29.02, 28.85, 26.67, 25.54, 25.50.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{28}O_3Na$: 351.1936; found: 351.1921.

7f

Yield: 142 mg (53%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.66 (dt, *J* = 17.3, 9.8 Hz, 1 H), 5.19 (dd, *J* = 10.3, 1.9 Hz, 1 H), 5.08 (dd, *J* = 17.3, 1.8 Hz, 1 H), 5.05–4.95 (m, 1 H), 3.17 (dt, *J* = 6.6, 4.9 Hz, 1 H), 2.38–2.27 (m, 1 H), 2.27–2.16 (m, 2 H), 1.91–1.81 (m, 1 H), 1.82–1.70 (m, 3 H), 1.69–1.58 (m, 3 H), 1.58–1.51 (m, 1 H), 1.47–1.33 (m, 1 H), 1.22 (d, *J* = 6.3 Hz, 6 H), 1.18–0.96 (m, 4 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.29, 137.65, 118.32, 77.56, 67.53, 46.21, 40.46, 32.48, 29.52, 27.72, 26.43, 26.29, 26.24, 25.97, 21.83.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{28}O_3Na$: 291.1936; found: 291.1930.

7g

Yield: 182 mg (57%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8.7 Hz, 2 H), 6.88 (d, *J* = 8.7 Hz, 2 H), 5.80 (dt, *J* = 17.4, 9.9 Hz, 1 H), 5.11 (dd, *J* = 10.4, 1.9 Hz, 1 H), 5.04 (s, 2 H), 4.98 (dd, *J* = 17.5, 1.7 Hz, 1 H), 3.81 (s, 3 H), 3.20 (dd, *J* = 6.7, 2.1 Hz, 1 H), 2.45–2.19 (m, 3 H), 1.79 (q, *J* = 7.5 Hz, 2 H), 1.55 (d, *J* = 6.7 Hz, 1 H), 0.89 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.66, 159.59, 137.81, 130.11, 128.16, 117.18, 113.91, 81.77, 65.95, 55.27, 44.98, 35.87, 32.05, 29.23, 26.61.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{28}O_4Na$: 343.1885; found: 343.1876.

7h

Yield: 272 mg (66%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (d, *J* = 8.0 Hz, 2 H), 7.12 (d, *J* = 8.0 Hz, 2 H), 5.65 (dt, *J* = 18.9, 9.7 Hz, 1 H), 5.21 (d, *J* = 10.1 Hz, 1 H), 5.12 (d, *J* = 17.2 Hz, 1 H), 3.73–3.58 (m, 1 H), 2.62–2.46 (m, 2 H), 2.31 (dt, *J* = 14.9, 6.6 Hz, 1 H), 2.18 (dt, *J* = 15.9, 7.7 Hz, 1 H), 2.10–1.97 (m, 2 H), 1.92–1.74 (m, 2 H), 1.70 (s, 1 H), 1.66–1.53 (m, 1 H), 1.42 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1, 148.3, 137.5, 132.9, 122.6, 120.4 (d, *J* = 257.8 Hz), 120.7, 118.7, 90.7, 80.3, 79.5, 72.1, 49.9, 33.4, 33.1, 28.0, 25.8, 15.9.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –57.85.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{27}F_3O_4Na$: 435.1759; found: 435.1755.

7i

Yield: 155 mg (53%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.3 Hz, 2 H), 6.88 (d, *J* = 8.7 Hz, 2 H), 5.64 (dt, *J* = 17.1, 9.8 Hz, 1 H), 5.27 (dd, *J* = 10.2, 1.8 Hz, 1 H), 5.19 (dd, *J* = 17.1, 1.4 Hz, 1 H), 4.94 (m, 1 H), 4.39 (d, *J* = 7.8 Hz, 1 H), 3.80 (s, 3 H), 2.36–2.20 (m, 2 H), 2.17–2.05 (m, 1 H), 1.60–1.50 (m, 1 H), 1.49–1.37 (m, 1 H), 1.18 (d, *J* = 6.3 Hz, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.95, 159.17, 138.47, 134.17, 128.05, 119.53, 113.72, 76.25, 67.48, 55.24, 52.26, 32.36, 25.57, 21.80, 21.77.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{24}O_4Na$: 315.1572; found: 315.1571.

7j

Yield: 233 mg (58%); colorless oil.

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^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.4 Hz, 2 H), 7.22–7.12 (m, 6 H), 5.62 (dt, *J* = 17.1, 10.1 Hz, 1 H), 5.25 (dd, *J* = 10.2, 1.8 Hz, 1 H), 5.16 (dd, *J* = 17.2, 1.4 Hz, 1 H), 4.99 (s, 2 H), 4.40 (dd, *J* = 7.6, 2.4 Hz, 1 H), 2.41–2.32 (m, 4 H), 2.33–2.15 (m, 2 H), 2.12 (d, *J* = 2.5 Hz, 1 H), 1.67–1.42 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.10, 138.97, 138.21, 137.48, 134.94, 131.64, 129.84, 129.03, 126.76, 122.19, 119.53, 76.48, 65.27, 52.04, 32.00, 25.50, 21.13.

HRMS-ESI: *m*/*z* [M – OH]$^+$ calcd for $C_{21}H_{22}BrO_2^+$: 385.0798; found: 385.0808.

7k

Yield: 125 mg (46%); colorless oil.

^{1}H NMR (400 MHz, acetone-d_6): δ = 7.37–7.26 (m, 4 H), 7.24–7.17 (m, 1 H), 5.69 (ddd, *J* = 17.3, 10.3, 9.3 Hz, 1 H), 5.02 (dd, *J* = 10.3, 2.2 Hz, 1 H), 4.90 (dd, *J* = 17.5, 2.4 Hz, 1 H), 4.67 (t, *J* = 4.7 Hz, 1 H), 4.15 (d, *J* = 4.2 Hz, 1 H), 4.11 (t, *J* = 6.7 Hz, 2 H), 2.50 (td, *J* = 6.7, 2.7 Hz, 2 H), 2.40 (t, *J* = 2.7 Hz, 1 H), 2.38–2.20 (m, 2 H), 1.86–1.73 (m, 1 H), 1.67–1.55 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.12, 142.03, 138.04, 128.32, 127.79, 126.86, 119.62, 80.04, 76.62, 69.85, 61.94, 52.05, 31.90, 25.49, 18.90.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{20}O_3Na$: 295.1310; found: 295.1304.

7l

Yield: 275 mg (62%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 8.0 Hz, 1 H), 7.24–7.13 (m, 2 H), 7.12–7.06 (m, 1 H), 6.82 (s, 2 H), 5.65 (dt, *J* = 17.0, 9.8 Hz, 1 H), 5.32 (dd, *J* = 10.2, 1.8 Hz, 1 H), 5.26 (dd, *J* = 17.1, 1.6 Hz, 1 H), 4.85 (dd, *J* = 9.9, 1.9 Hz, 1 H), 4.23 (td, *J* = 7.0, 1.5 Hz, 2 H), 3.01 (t, *J* = 7.0 Hz, 2 H), 2.72 (dd, *J* = 9.6, 5.1 Hz, 1 H), 2.41 (s, 6 H), 2.31–2.16 (m, 4 H), 2.11 (dt, *J* = 16.1, 8.0 Hz, 1 H), 1.94 (s, 1 H), 1.47–1.32 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.13, 139.66, 137.12, 136.83, 133.91, 132.85, 130.98, 128.29, 127.39, 124.58, 119.69, 72.71, 63.10, 49.94, 35.16, 32.16, 25.41, 21.07, 20.74.

HRMS-ESI: *m*/*z* [M – OH]$^+$ calcd for $C_{24}H_{28}BrO_2^+$: 427.1267; found: 427.1280.

7m

Yield: 179 mg (53%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.80 (m, 3 H), 7.77 (s, 1 H), 7.50–7.43 (m, 3 H), 5.68 (dt, *J* = 17.1, 9.9 Hz, 1 H), 5.32–5.15 (m, 3 H), 4.62 (dd, *J* = 7.5, 2.6 Hz, 1 H), 4.49 (d, *J* = 7.2 Hz, 2 H), 2.50–2.38 (m, 1 H), 2.37–2.27 (m, 2 H), 2.22–2.11 (m, 1 H), 1.72 (s, 3 H), 1.66 (s, 3 H), 1.60–1.50 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.40, 139.48, 139.02, 138.03, 133.11, 128.17, 127.96, 127.65, 126.07, 126.03, 125.86, 124.55, 119.68, 118.48, 76.69, 61.23, 52.01, 32.08, 25.71, 25.66, 17.94.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{26}O_3Na$: 361.1780; found: 361.1772.

7n

Yield: 199 mg (57%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.00 (d, *J* = 8.6 Hz, 1 H), 6.67 (d, *J* = 8.6 Hz, 1 H), 5.94–5.81 (m, 1 H), 5.69 (dt, *J* = 17.4, 9.8 Hz, 1 H), 5.35–5.06 (m, 4 H), 4.74–4.63 (m, 1 H), 4.52 (d, *J* = 5.5 Hz, 2 H), 3.92 (s, 3 H), 3.85 (s, 6 H), 2.46–2.31 (m, 3 H), 2.30–2.17 (m, 1 H), 1.66–1.57 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.11, 153.08, 151.45, 141.78, 138.49, 132.19, 127.83, 122.01, 118.90, 118.06, 107.21, 71.55, 64.91, 61.10, 60.66, 55.92, 51.36, 31.99, 25.93.

HRMS-ESI: *m*/*z* [M – OH]$^+$ calcd for $C_{19}H_{25}O_5^+$: 333.1697; found: 333.1695.

7o

Yield: 193 mg (48%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 8.4 Hz, 2 H), 7.22–7.13 (m, 6 H), 5.59 (dt, *J* = 17.1, 9.8 Hz, 1 H), 5.24 (dd, *J* = 10.2, 1.6 Hz, 1 H), 5.13 (dd, *J* = 17.0, 1.9 Hz, 1 H), 5.02 (s, 2 H), 4.41 (dd, *J* = 7.2, 2.4 Hz, 1 H), 2.35 (s, 3 H), 2.30–2.14 (m, 3 H), 1.66–1.55 (m, 1 H), 1.56–1.43 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.15, 141.03, 138.12, 137.51, 132.84, 131.38, 129.21, 128.54, 128.40, 121.53, 120.00, 75.90, 66.16, 52.00, 31.98, 25.48, 21.18.

HRMS-ESI: *m*/*z* [M – OH]$^+$ calcd for $C_{21}H_{22}BrO_2^+$: 385.0798; found: 385.0806.

7p

Yield: 218 mg (50%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (d, *J* = 8.4 Hz, 2 H), 7.24 (d, *J* = 8.5 Hz, 2 H), 5.65–5.53 (m, 1 H), 5.24 (d, *J* = 10.2 Hz, 1 H), 5.13 (d, *J* = 17.1 Hz, 1 H), 4.44 (d, *J* = 7.1 Hz, 1 H), 4.16–3.82 (m, 3 H), 3.41–3.24 (m, 2 H), 2.48–2.37 (m, 1 H), 2.38–2.24 (m, 2 H), 2.21–2.12 (m, 1 H), 1.99–1.67 (m, 4 H), 1.64–1.55 (m, 1 H), 1.43 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.08, 154.49, 140.58, 137.60, 133.31, 128.38, 128.17, 119.76, 79.69, 75.83, 64.63, 55.40, 52.09, 52.04, 46.45, 31.90, 28.41, 25.38, 25.35.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{32}ClNO_5Na$: 460.1867; found: 460.1851.

7q

Yield: 178 mg (67%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.20 (m, 1 H), 7.03–6.89 (m, 2 H), 5.96–5.79 (m, 1 H), 5.67 (ddd, *J* = 17.1, 10.2, 9.3 Hz, 1 H), 5.35–5.13 (m, 4 H), 4.76 (dd, *J* = 7.4, 3.0 Hz, 1 H), 4.54 (d, *J* = 5.7 Hz, 2 H), 2.45–2.30 (m, 3 H), 2.30–2.16 (m, 1 H), 1.79–1.66 (m, 1 H), 1.62–1.49 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.00, 145.83, 137.61, 132.13, 126.44, 125.02, 124.94, 119.98, 118.20, 72.59, 65.02, 52.45, 31.87, 25.62.

HRMS-ESI: *m*/*z* [M – OH]$^+$ calcd for $C_{14}H_{17}O_2S^+$: 249.0944; found: 249.0947.

7r

Yield: 160 mg (51%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.27 (m, 6 H), 6.36–6.30 (m, 1 H), 6.27 (d, *J* = 3.2 Hz, 1 H), 5.86 (q, *J* = 6.6 Hz, 1 H), 5.71–5.51 (m, 1 H), 5.30–5.12 (m, 2 H), 4.50 (dt, *J* = 7.7, 4.0 Hz, 1 H), 2.61–2.46 (m, 1 H), 2.42–2.22 (m, 2 H), 2.19–2.12 (m, 1 H), 1.75–1.54 (m, 2 H), 1.51 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.55, 154.53, 142.06, 141.64, 137.55, 128.43, 127.81, 126.06, 126.03, 119.62, 119.57, 110.13, 107.50, 72.22, 70.13, 49.37, 32.17, 25.49, 22.17.

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HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{22}O_4Na$: 337.1416; found: 337.1405.

7s

Yield: 183 mg (51%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.26 (m, 7 H), 7.22–7.15 (m, 3 H), 5.73 (dt, *J* = 17.3, 9.7 Hz, 1 H), 5.19–5.05 (m, 2 H), 4.58 (d, *J* = 2.3 Hz, 2 H), 3.68–3.51 (m, 3 H), 2.80 (ddd, *J* = 13.7, 9.8, 5.8 Hz, 1 H), 2.65 (ddd, *J* = 13.7, 9.6, 6.7 Hz, 1 H), 2.44 (tt, *J* = 9.0, 4.5 Hz, 1 H), 2.29–2.00 (m, 2 H), 1.84–1.65 (m, 2 H), 1.60 (d, *J* = 5.1 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 141.90, 137.33, 137.11, 128.50, 128.41, 128.03, 127.88, 125.87, 118.02, 73.70, 72.85, 70.59 (t, *J* = 32.7 Hz), 43.94 (t, *J* = 3.2 Hz), 36.42, 34.99 (t, *J* = 22.9 Hz), 32.20.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –100.33 to –101.35 (m, 1 F), –101.45 to –102.44 (m, 1 F).

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{26}F_2O_2Na$: 383.1799; found: 383.1797.

(7t)

Yield: 150 mg (59%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (t, *J* = 7.6 Hz, 2 H), 7.25–7.15 (m, 3 H), 5.87 (dt, *J* = 56.8, 3.4 Hz, 1 H), 5.72–5.55 (m, 1 H), 5.25 (d, *J* = 10.3 Hz, 1 H), 5.14 (d, *J* = 17.2 Hz, 1 H), 3.53 (dd, *J* = 7.4, 3.9 Hz, 1 H), 2.91–2.76 (m, 1 H), 2.74–2.60 (m, 1 H), 2.05 (hept, *J* = 4.9, 4.1 Hz, 1 H), 1.90–1.58 (m, 5 H), 1.55–1.42 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 141.93, 137.32, 128.42, 125.88, 119.04, 117.67 (t, *J* = 238.9 Hz), 73.01, 49.88, 36.57, 32.12, 32.08 (t, *J* = 20.7 Hz), 23.11.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –115.96 (dtd, *J* = 56.8, 17.6, 5.0 Hz, 2 F).

HRMS-ESI: *m*/*z* [M – OH]$^+$ calcd for $C_{15}H_{19}F_2$: 237.1449; found: 237.1450.

9a

Yield: 115 mg (48%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.60 (dt, *J* = 17.1, 10.0 Hz, 1 H), 5.16 (dd, *J* = 10.2, 2.1 Hz, 1 H), 5.04 (dd, *J* = 17.1, 2.1 Hz, 1 H), 4.11 (q, *J* = 7.1 Hz, 2 H), 2.39–2.28 (m, 1 H), 2.24–2.10 (m, 1 H), 2.06–1.95 (m, 1 H), 1.95–1.86 (m, 1 H), 1.64–1.40 (m, 10 H), 1.37 (s, 1 H), 1.24 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.84, 137.89, 118.63, 76.68, 72.34, 60.19, 54.91, 35.02, 34.76, 32.67, 25.79, 23.10, 21.73, 14.23.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{24}O_3Na$: 263.1623; found: 263.1616.

9b

Yield: 180 mg (64%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.58 (dt, *J* = 17.1, 10.0 Hz, 1 H), 5.32 (t, *J* = 7.9 Hz, 1 H), 5.21 (dd, *J* = 10.2, 1.9 Hz, 1 H), 5.08 (dd, *J* = 17.1, 1.9 Hz, 1 H), 4.55 (d, *J* = 7.2 Hz, 2 H), 3.81–3.69 (m, 4 H), 2.43–2.32 (m, 1 H), 2.26–2.14 (m, 1 H), 2.05–1.96 (m, 1 H), 1.97–1.87 (m, 1 H), 1.83–1.77 (m, 1 H), 1.75 (s, 3 H), 1.70 (s, 3 H), 1.57–1.46 (m, 2 H), 1.41 (d, *J* = 13.8 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.64, 139.10, 136.89, 119.58, 118.52, 70.03, 63.62, 63.55, 61.28, 55.24, 35.46, 35.23, 32.35, 25.73, 22.68, 17.98.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{26}O_4Na$: 305.1729; found: 305.1718.

9c

Yield: 184 mg (55%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (d, *J* = 8.0 Hz, 2 H), 7.17 (d, *J* = 7.9 Hz, 2 H), 5.56 (dt, *J* = 17.1, 10.0 Hz, 1 H), 5.20 (dd, *J* = 10.2, 1.9 Hz, 1 H), 5.11–5.00 (m, 3 H), 3.08–2.95 (m, 2 H), 2.44–2.33 (m, 6 H), 2.29–2.17 (m, 1 H), 2.07–1.96 (m, 1 H), 1.91–1.76 (m, 4 H), 1.74–1.66 (m, 1 H), 1.55–1.43 (m, 1 H), 1.40 (s, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.40, 138.15, 136.87, 132.90, 129.23, 128.49, 119.95, 70.86, 66.17, 55.98, 36.02, 35.58, 32.42, 23.95, 23.89, 23.01, 21.17.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{26}O_3SNa$: 357.1500; found: 357.1487.

9d

Yield: 129 mg (52%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.68 (ddd, *J* = 17.2, 10.3, 9.1 Hz, 1 H), 5.21–5.00 (m, 2 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 2.46–2.32 (m, 1 H), 2.34–2.22 (m, 1 H), 2.22–2.08 (m, 2 H), 2.02–1.92 (m, 1 H), 1.88–1.71 (m, 3 H), 1.61–1.47 (m, 1 H), 1.32 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.13 (t, *J* = 32.9 Hz), 135.81, 118.55, 116.16 (dd, *J* = 4.3, 2.1 Hz), 62.62, 56.58, 45.54 (dd, *J* = 4.7, 2.3 Hz), 34.51, 34.17, 33.47 (t, *J* = 23.0 Hz), 13.83, 11.54.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –100.35 to –102.76 (m, 1 F), –104.58 to –108.17 (m, 1 F).

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{18}F_2O_3Na$: 271.1122; found: 271.1117.

9e

Yield: 165 mg (63%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.70 (ddd, *J* = 19.3, 10.1, 5.8 Hz, 1 H), 5.18–5.03 (m, 2 H), 4.26 (q, *J* = 7.1 Hz, 2 H), 2.48–2.21 (m, 3 H), 1.89–1.71 (m, 2 H), 1.69–1.47 (m, 6 H), 1.33 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.17 (t, *J* = 33.3 Hz), 137.18, 118.23, 116.69 (dd, *J* = 496.6, 421.5 Hz), 83.77, 62.61, 47.43 (dd, *J* = 5.0, 2.3 Hz), 38.27, 38.23, 35.05 (t, *J* = 22.8 Hz), 23.78, 13.87.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –100.62 to –101.54 (m, 1 F), –104.88 to –105.86 (m, 1 F).

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{20}F_2O_3Na$: 285.1278; found: 285.1271.

9f

Yield: 171 mg (62%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.63 (dt, *J* = 17.1, 9.8 Hz, 1 H), 5.23–4.99 (m, 2 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 2.48 (dt, *J* = 17.9, 15.0 Hz, 1 H), 2.32–2.06 (m, 2 H), 1.67–1.42 (m, 8 H), 1.40–1.34 (m, 1 H), 1.32 (t, *J* = 7.3 Hz, 3 H), 1.23–1.09 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.19 (t, *J* = 32.9 Hz), 136.90, 118.69, 116.94 (dd, *J* = 248.7, 245.8 Hz), 72.17, 62.56, 48.60 (dd, *J* = 7.5, 1.6 Hz), 35.30, 33.91, 33.68 (t, *J* = 23.3 Hz), 25.56, 21.70, 21.56, 13.86.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –100.48 to – 101.52 (m, 1 F), –104.62 to –105.80 (m, 1 F).

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{22}F_2O_3Na$: 299.1435; found: 299.1425.

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9g

Yield: 165 mg (57%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.63 (dt, *J* = 16.9, 9.9 Hz, 1 H), 5.18–5.03 (m, 2 H), 4.26 (q, *J* = 7.1 Hz, 2 H), 2.57–2.39 (m, 1 H), 2.35–2.06 (m, 2 H), 1.81–1.40 (m, 12 H), 1.34 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.21 (t, *J* = 32.3 Hz), 137.12, 118.81, 118.09 (dd, *J* = 292.3, 256.4 Hz), 75.93, 62.59, 49.85 (dd, *J* = 4.5, 2.1 Hz), 39.48, 38.05, 34.12 (t, *J* = 22.7 Hz), 29.34, 29.32, 22.45, 22.24, 13.89.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –100.51 to –101.68 (m, 1 F), –104.48 to –105.62 (m, 1 F).

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{24}F_2O_3Na$: 313.1591; found: 313.1591.

9h

Yield: 180 mg (51%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89–7.77 (m, 1 H), 7.77–7.65 (m, 1 H), 7.40–7.27 (m, 2 H), 7.15 (s, 1 H), 5.69 (dt, *J* = 17.2, 9.8 Hz, 1 H), 5.30–5.19 (m, 2 H), 4.19 (m, 2 H), 2.78–2.65 (m, 1 H), 2.60–2.44 (m, 1 H), 2.43 (s, 1 H), 2.19–1.98 (m, 1 H), 1.68 (s, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.95 (t, *J* = 32.8 Hz), 150.24, 139.48, 139.43, 136.08, 124.28, 124.20, 123.45, 122.19, 120.72, 120.37, 116.00 (dd, *J* = 252.2, 249.4 Hz), 74.76, 62.67, 50.15 (dd, *J* = 4.3, 3.0 Hz), 34.57 (t, *J* = 23.1 Hz), 27.58, 13.75.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –101.51 (ddd, *J* = 261.1, 16.7, 13.4 Hz, 1 F), –104.41 (ddd, *J* = 260.3, 19.0, 15.3 Hz, 1 F).

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{20}F_2O_3SNa$: 377.0999; found: 377.0999.

9i

Yield: 192 mg (57%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.41 (m, 1 H), 7.43–7.33 (m, 1 H), 7.25–7.09 (m, 2 H), 6.58 (s, 1 H), 5.65–5.46 (m, 1 H), 5.22–4.99 (m, 2 H), 4.16 (ddt, *J* = 18.4, 14.1, 7.1 Hz, 2 H), 2.91–2.73 (m, 1 H), 2.51–2.29 (m, 1 H), 2.24 (s, 1 H), 2.18–1.83 (m, 1 H), 1.54 (s, 3 H), 1.20 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.01 (t, *J* = 32.1 Hz), 159.96, 154.79, 135.92, 127.91, 124.28, 122.94, 121.07, 119.93, 116.03 (dd, *J* = 249.6, 238.1 Hz), 111.31, 103.49, 72.99, 62.71, 48.14 (dd, *J* = 4.6, 3.0 Hz), 34.59 (t, *J* = 23.1 Hz), 24.78, 13.83.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –100.49 to –102.24 (m, 1 F), –103.82 to –104.98 (m, 1 F).

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{20}F_2O_4Na$: 361.1227; found: 361.1205.

9j

Yield: 148 mg (47%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 8.9 Hz, 2 H), 6.86 (d, *J* = 8.9 Hz, 2 H), 5.53 (dt, *J* = 17.1, 9.9 Hz, 1 H), 5.21 (dd, *J* = 10.2, 2.0 Hz, 1 H), 5.14 (dd, *J* = 17.1, 1.7 Hz, 1 H), 4.12 (t, *J* = 6.8 Hz, 2 H), 3.80 (s, 3 H), 2.48 (td, *J* = 6.8, 2.7 Hz, 2 H), 2.33–2.22 (m, 2 H), 2.18–2.07 (m, 1 H), 2.02 (s, 1 H), 1.98 (t, *J* = 2.7 Hz, 1 H), 1.89–1.77 (m, 1 H), 1.55 (s, 3 H), 1.39–1.25 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.34, 158.42, 138.04, 137.83, 127.05, 119.55, 113.19, 80.13, 75.11, 69.82, 61.90, 56.27, 55.20, 32.35, 26.16, 23.99, 18.91.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{24}O_4Na$: 339.1572; found: 339.1563.

9k

Yield: 153 mg (45%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (s, 1 H), 7.86–7.79 (m, 3 H), 7.58 (dd, *J* = 8.7, 1.9 Hz,1 H), 7.50–7.43 (m, 2 H), 5.59 (dt, *J* = 17.1, 10.0 Hz, 1 H), 5.21 (dd, *J* = 10.3, 1.9 Hz, 1 H), 5.15 (dd, *J* = 17.1, 1.6 Hz, 1 H), 2.45–2.36 (m, 1 H), 2.26 (s, 1 H), 2.22–2.14 (m, 1 H), 2.07–1.95 (m, 1 H), δ 1.90–1.77 (m, 1 H), 1.68 (s, 3 H), 1.60 (d, *J* = 1.2 Hz, 1 H), 1.37 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.94, 143.68, 137.78, 132.96, 132.34, 128.24, 127.52, 127.39, 125.90, 125.72, 124.53, 124.35, 119.56, 80.07, 75.61, 55.87, 33.55, 28.04, 26.17, 23.95.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{28}O_3Na$: 363.1936; found: 363.1924.

10a

Yield: 302 mg (51%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 8.5 Hz, 2 H), 7.95 (d, *J* = 8.6 Hz, 2 H), 7.43–7.27 (m, 7 H), 7.20 (d, *J* = 8.6 Hz, 2 H), 5.63 (dt, *J* = 17.2, 9.8 Hz, 1 H), 5.26 (dd, *J* = 10.2, 1.6 Hz, 1 H), 5.16 (dd, *J* = 15.9, 1.5 Hz, 1 H), 5.07 (s, 2 H), 4.50 (dd, *J* = 7.3, 2.3 Hz, 1 H), 3.20–3.06 (m, 4 H), 2.42–2.25 (m, 2 H), 2.22 (d, *J* = 2.5 Hz, 1 H), 1.73–1.47 (m, 7 H), 0.89 (t, *J* = 7.4 Hz, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.16, 163.74, 150.04, 144.89, 140.11, 137.66, 135.90, 132.80, 130.75, 128.52, 128.23, 128.04, 127.15, 121.29, 119.88, 75.99, 66.19, 52.07, 49.91, 31.99, 25.50, 21.92, 11.14.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{39}NO_7SNa$: 616.2345; found: 616.2331.

10b

Yield: 352 mg (57%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.5 Hz, 2 H), 7.48 (d, *J* = 8.5 Hz, 2 H), 7.32 (d, *J* = 8.5 Hz, 2 H), 7.05 (d, *J* = 8.4 Hz, 3 H), 6.89 (d, *J* = 9.0 Hz, 1 H), 6.69 (dd, *J* = 9.0, 2.5 Hz, 1 H), 5.62 (dt, *J* = 17.2, 9.8 Hz, 1 H), 5.25 (dd, *J* = 10.2, 1.7 Hz, 1 H), 5.15 (dd, *J* = 17.1, 1.4 Hz, 1 H), 4.94 (pent, *J* = 6.2 Hz, 1 H), 4.52–4.41 (m, 1 H), 3.90 (s, 2 H), 3.84 (s, 3 H), 2.45 (s, 3 H), 2.33–2.06 (m, 4 H), 1.54–1.44 (m, 1 H), 1.18 (d, *J* = 6.3 Hz, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.87, 169.19, 168.30, 156.12, 150.14, 139.84, 139.34, 137.81, 136.20, 133.82, 131.20, 130.83, 130.49, 129.14, 127.88, 121.20, 119.77, 115.01, 111.99, 111.82, 101.17, 75.99, 67.56, 55.73, 52.12, 32.29, 30.57, 25.48, 21.79, 21.78, 13.42.

HRMS-ESI: *m*/*z* [M – OH]$^+$ calcd for $C_{35}H_{35}ClNO_6^+$: 600.2147; found: 600.2147.

10c

Yield: 318 mg (78%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19 (d, *J* = 8.6 Hz, 1 H), 6.70 (dd, *J* = 8.6, 2.7 Hz, 1 H), 6.63 (d, *J* = 2.5 Hz, 1 H), 5.85 (ddd, *J* = 17.0, 10.4, 8.7 Hz, 1 H), 5.29–5.16 (m, 2 H), 4.66 (dt, *J* = 9.4, 3.6 Hz, 1 H), 4.21–3.98 (m, 2 H), 2.93–2.82 (m, 2 H), 2.65–2.57 (m, 2 H), 2.55–2.45 (m, 1 H), 2.43–2.33 (m, 1 H), 2.27–1.93 (m, 8 H), 1.91–1.82 (m, 1 H), 1.65–1.44 (m, 7 H), 0.91 (s, 3 H).

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^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.47, 156.66, 137.82, 134.29, 132.29, 126.37, 118.63, 114.39, 112.17, 78.20, 77.20, 63.48, 50.40, 48.00, 43.96, 40.04, 38.35, 35.86, 32.73, 31.57, 29.63, 27.06, 26.52, 25.90, 24.66, 21.57, 13.84.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{34}O_4Na$: 445.2355; found: 445.2352.

11

Yield: 290 mg (93%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.27 (m, 2 H), 7.24–7.17 (m, 3 H), 5.71 (dt, *J* = 17.2, 9.8 Hz, 1 H), 5.23–5.08 (m, 2 H), 4.28 (q, *J* = 7.1 Hz, 2 H), 3.62 (dt, *J* = 8.3, 4.2 Hz, 1 H), 2.88–2.58 (m, 2 H), 2.51–2.41 (m, 1 H), 2.40–2.24 (m, 2 H), 2.01 (s, 1 H), 1.84–1.65 (m, 2 H), 1.34 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.08 (t, *J* = 33.0 Hz), 141.62, 135.77, 128.35, 128.29, 125.84, 118.55, 116.57 (dd, *J* = 249.2, 248.7 Hz), 72.91, 62.67, 43.59 (dd, *J* = 4.3, 2.3 Hz), 36.24, 35.89 (t, *J* = 22.7 Hz), 32.05, 13.73.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –101.44 (dt, *J* = 261.5, 15.0 Hz, 1 F), –105.06 (dt, *J* = 260.7, 17.9 Hz, 1 F).

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{22}F_2O_3Na$: 335.1435; found: 335.1431.

12

Yield: 149 mg (89%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.84–5.68 (m, 1 H), 5.13–5.01 (m, 2 H), 3.08 (t, *J* = 6.3, 5.3 Hz, 1 H), 2.36 (m, 1 H), 1.85–1.69 (m, 3 H), 1.68–1.57 (m, 2 H), 1.51 (s, 1 H), 1.44–1.33 (m, 1 H), 1.29–1.05 (m, 5 H), 1.01 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 140.34, 116.01, 78.77, 40.49, 40.29, 29.94, 27.02, 26.46, 26.41, 26.09, 16.93.

13

Yield: 247 mg (83%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.25 (m, 4 H), 7.24–7.15 (m, 1 H), 5.43 (dt, *J* = 18.4, 9.5 Hz, 1 H), 5.17–5.01 (m, 2 H), 4.13 (qd, *J* = 7.1, 3.4 Hz, 2 H), 2.63–2.48 (m, 1 H), 2.33 (tdd, *J* = 16.2, 14.6, 2.1 Hz, 1 H), 1.91 (s, 1 H), 1.89–1.74 (m, 1 H), 1.51 (s, 3 H), 1.21 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.34 (t, *J* = 32.7 Hz), 144.62, 136.80, 128.07, 127.19, 125.81, 119.44, 116.16 (dd, *J* = 249.4, 237.7 Hz), 75.03, 62.58, 49.89 (dd, *J* = 4.6, 2.8 Hz), 34.24 (t, *J* = 22.9 Hz), 26.85, 13.81.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –100.07 to –101.84 (m, 1 F), –104.26 to –105.78 (m, 1 F).

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{20}F_2O_3Na$: 321.1278; found: 321.1281.

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Supporting Information

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