Synthesis K. Rode et al. Feature

Aerobic Allylation of Alcohols with Non-Activated Alkenes Enabled by Light-Driven Selenium-π-Acid Catalysis

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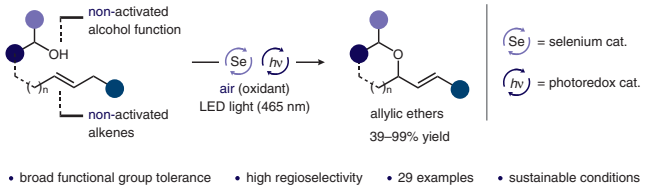

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Abstract A new organocatalytic protocol for the aerobic dehydrogenative allylation of alcohols using non-activated alkenes as the allylating reagent and ambient air as the terminal oxidant is established. Mechanistically, the procedure relies on the interplay of a diselane and a photoredox catalyst by means of a light-induced electron transfer process. Under optimized conditions, a broad range of both cyclic and acyclic ethers is accessed with very high functional group tolerance and excellent regioselectivity.

Key words alcohols, allylations, alkenes, oxidations, photoredox catalysis, selenium-π-acids

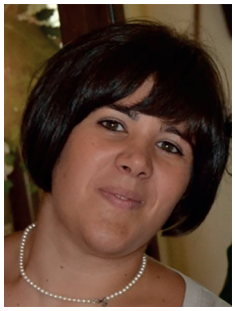
Ethers play pivotal roles in a number of chemical, biological, and industrial contexts. In nature, ethers are, *inter alia*, found as functional motifs in bioactive substances such as polyether antibiotics[1] or as skeletal elements in lignifying plants.[2] In addition, ethers are very frequently encountered in the realm of technical and medicinal applications. Representative examples include excipients,[3] cosmetics,[4] and binders for the production of ceramics.[5] Traditional protocols for the construction of simple non-epoxydic ethers rely on the redox-neutral conversion of alcohols or alkoxides with different electrophiles such as alkyl and aryl halides (e.g., Williamson ether synthesis, Ullmann condensation, Buchwald–Hartwig coupling, etc.).[6] An efficient alternative strategy for the formation of ethers under particularly mild conditions is the catalytic conversion of alcohols with discrete[7] or latent allylic electrophiles.[8] In the latter case, the carbon–carbon double bond of a simple alkene is directly activated under oxidative conditions in such a way that it will react with an unactivated alcohol to furnish the corresponding ether derivative. Typical oxidants for such transformations include, for instance, Cu(II) salts, benzoquinones, *N*-fluorinated compounds, λ^3-iodanes, and neat oxygen.[8] From an environmental and atom-economic viewpoint,[9] the use of O_2 is particularly appealing due to the low-polluting profile of its reduction by-products (i.e., H_2O and H_2O_2). Despite the fact that aerobic allylic etherifications of alcohols with simple alkenes—in particular catalyzed by palladium complexes—have experienced substantial progress and reached remarkable levels of efficiency over recent years, there are still significant limitations associated with these processes. For instance, although the use of ambient air as a gratuitous reagent would be highly desirable, aerobic Pd-catalyzed alkene etherifications generally require the presence of neat oxygen to maintain a proper catalytic turnover and to avoid the formation of inactive Pd(0) species.[10,11] In conceptually related reactions, it was even shown that the use of air led to significantly inferior results in comparison to pure O_2.[12] Another critical aspect concerning intermolecular Pd-catalyzed aerobic allylic etherifications of alkenes correlates with the substitution pattern on the olefin. In the cases reported thus far, predominantly terminal alkenes were presented as suitable substrates.[8,13]

Against this background, the demand for alternative catalytic concepts that allow aerobic etherification reactions to be conducted under an atmosphere of ambient air and with a broadened scope in terms of internal alkenes becomes vividly evident. In this context, selenium-catalyzed etherifications of alkenes were shown to be sufficiently tolerant toward higher substitution patterns on the olefinic entity.[8a,h,14] Irrespective of these important contributions, the generalized utilization of air as the terminal oxidant in Se-catalyzed, inter- and intramolecular dehydrogenative allylic etherifications of simple alcohols with alkenes has remained elusive thus far.[15] In the course of our research program on the design of oxidative alkene functionalizations catalyzed by selenium-π-acids,[16] we recently discovered that these reactions can be driven by visible light, using

Biographical Sketches

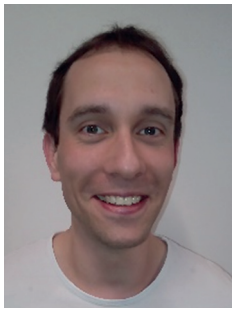
Alexander Breder was born in 1978 in Halle, Germany. In 2005, he received his diploma degree from the University of Bielefeld. He then moved to the Swiss Federal Institute of Technology Zurich (ETH), Switzerland, where he was a Ph.D. student in the group of Prof. Erick M. Carreira. Upon completion of his Ph.D. in 2009, he joined the group of Prof. Barry M. Trost at Stanford University as a postdoctoral fellow. Since December 2011, he pursues an independent research career at the Institute for Organic and Biomolecular Chemistry at the Georg-August-University Göttingen, Germany. His research program is focused on the investigation of novel concepts on dual photoredox/selenium catalysis in the context of method development and the synthesis of biologically relevant molecules.

Katharina Rode studied chemistry at the Georg-August-University Göttingen, Germany. In 2014, she finished her master's degree with a thesis on the synthesis of chiral thioamides for oxidative alkene functionalizations. Her Ph.D. studies, in the group of Dr. Alexander Breder, are directed toward the development of new selenium-π-acid-catalyzed reactions.



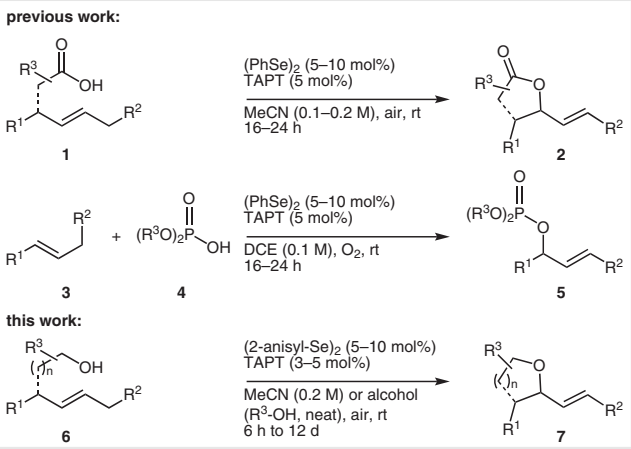
Martina Palomba studied chemistry at the University of Perugia, Italy. In 2014, she completed her master's degree with a thesis on the addition and elimination reactions of vinyl selenones with Prof. Luana Bagnoli and Prof. Francesca Marini, and has continued with her Ph.D. studies in the same group. During a research stay at the University of Göttingen, Germany in the group of Dr. Breder in 2017, she became interested in selenium-π-acid-catalyzed functionalizations of olefins.

Stefan Ortgies studied chemistry at the Georg-August-University Göttingen, Germany. In 2013, he finished his master's degree with a thesis on the synthesis of chiral diselenides for asymmetric oxidative alkene functionalizations. During his Ph.D. in the group of Dr. Alexander Breder, he has worked on the development of new selenium-catalyzed reactions with a focus on aerobic photoredox reactions.



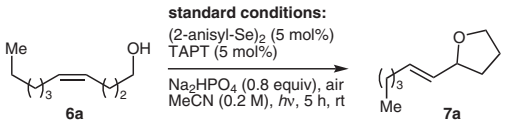
Rene Rieger studied chemistry at the Georg-August-University Göttingen, Germany. In 2016, he obtained his master's degree in chemistry with a thesis on the oxidative lactonization of alkenoic acids using dual selenium catalysis. He is currently working on his dissertation in the group of Dr. Alexander Breder. His work focuses on selenium-catalyzed oxidative functionalizations of olefins.

ambient air or neat O_2 as the sole oxidant and an organic photoredox co-catalyst (Scheme 1).[17,18] Since in these preceding investigations the aerobic conversion of simple alkenes with carboxylic acids and hydrogen phosphates was found to be facile,[18] we surmised that a similar catalytic regime would potentially also be applicable to the cognate conversion of alkenes with alcohols.



Scheme 1 Aerobic functionalizations of alkenes facilitated by dual photoredox/selenium-π-acid catalysis. TAPT = 2,4,6-tris(4-anisyl)pyrylium tetrafluoroborate

Table 1 Optimization of the Reaction Conditions



Entry	Deviation from standard conditions	Yield (%)[a]
1	none	69
2	DMTA instead of TAPT	31
3	$[Ru(bpz)_3](PF_6)_2$ instead of TAPT	9
4	TAPT (3 mol% instead of 5 mol%)	65
5	DCE instead of MeCN	29
6	acetone instead of MeCN	9
7	THF instead of MeCN	0
8	1,4-dioxane instead of MeCN	0
9	$MeNO_2$ instead of MeCN	42
10	$(PhSe)_2$ (10 mol%) instead of (2-anisyl-Se)$_2$ (5 mol%)	27
11	O_2 and molecular sieves, 3 mol% TAPT	67
12	argon instead of air	0
13	no irradiation	0
14	no TAPT	0

[a] Yields were determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene or $(Cl_2HC)_2$ as internal standards.

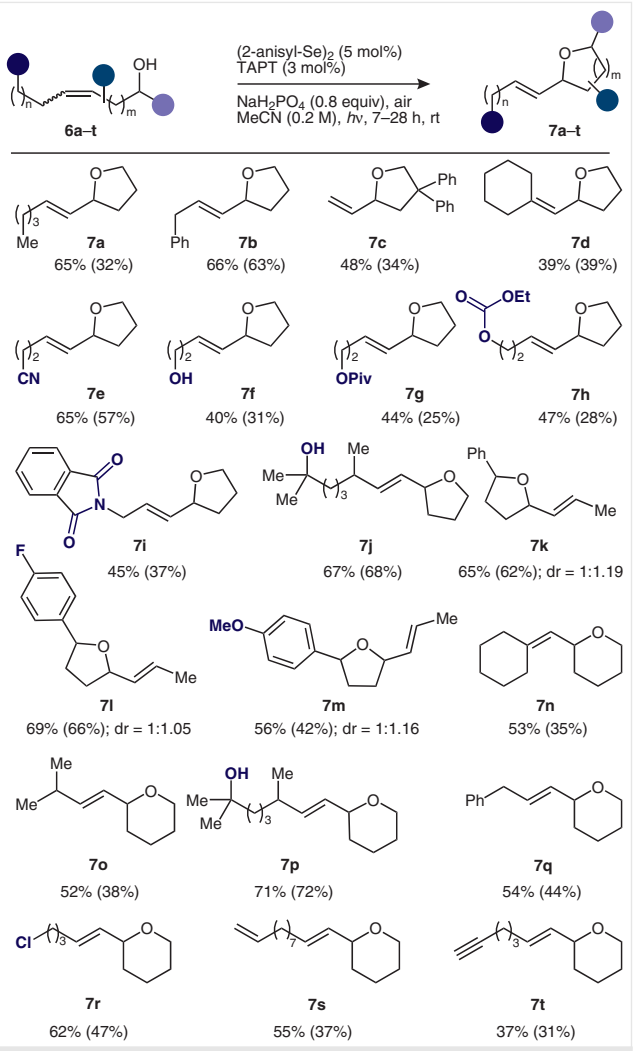
As a result of these considerations, we present herein the first generalized dual-catalytic allylation of alcohols using simple alkenes as latent allylating reagents and air as the terminal oxidant mediated by a selenium-π-acid and a photoredox catalyst.

In preceding investigations, we screened a number of selenium catalysts for their ability to quench the fluorescence of common photocatalysts.[19] From these experiments we were able to identify combinations of certain pyrylium and acridinium salts with electron-neutral and electron-rich diselenides as promising catalyst pairs for the title procedure. Comparison of the catalytic activities of 2,4,6-tris(4-anisyl)pyrylium tetrafluoroborate (TAPT), 10-(3,5-dimethoxyphenyl)-9-mesityl-1,3,6,8-tetramethoxyacridinium tetrafluoroborate) (DMTA)[20] and $[Ru(bpz)_3](PF_6)_2$ (each 5 mol%) in the aerobic cycloetherification of (*Z*)-dec-4-en-1-ol (**6a**) revealed that TAPT was the most efficient co-catalyst (Table 1, entries 1–3).

Lowering of the photocatalyst loading by 40% (i.e., from 5 mol% to 3 mol%) resulted in a tolerable yield reduction of only four percent (Table 1, entry 4). On the other hand, changing from acetonitrile to different solvents such as 1,2-dichloroethane, acetone, 1,4-dioxane, THF, and nitromethane invariably led to significantly inferior results (entries 5–9). Likewise, the use of $(PhSe)_2$ instead of its anisyl analogue resulted in a markedly lower yield (entry 10). We also investigated the impact of the atmosphere and the presence or absence of light on the reaction outcome (entries 11–14). Changing from ambient air to neat oxygen using 3 mol% of the TAPT photocatalyst resulted in a comparable yield of 67%. However, when the reaction was attempted under argon, no product formation was recorded, which indicates that oxygen is indeed serving as the sole oxidant in this process. Furthermore, when the reaction mixture was deprived of light irradiation (465 nm) (entry 13) or the photocatalyst (entry 14), we did not detect any of the cyclization product. These results indicate that light indeed serves as an indispensable energy source solely made available by the photocatalyst.[19]

With an operative set of conditions in hand, we began to determine the scope and limitations of the title protocol (Scheme 2). In the early phase of this part of the investigation we noticed that in some reactions NaH_2PO_4 provided slightly better yields than Na_2HPO_4.

Therefore, we decided to use NaH_2PO_4 as the base for all subsequent experiments. In general, the intramolecular aerobic cycloetherification of unsaturated alcohols **6a–t** furnished the corresponding tetrahydrofuran and tetrahydropyran derivatives **7a–t** in moderate to good isolated yields (up to 71%, shown in parentheses). With regard to the, in part, significant discrepancies between the isolated and the crude yields, we suspect that in some cases the high volatility of the ether products causes significant material

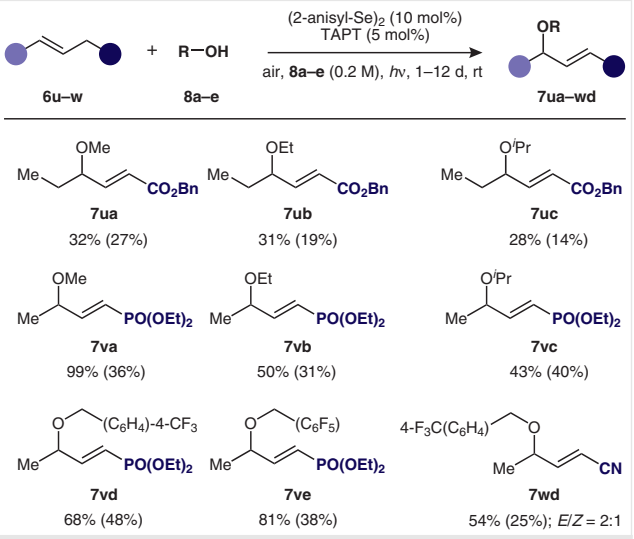


Scheme 2 Reactions were carried out on a 1.0 mmol scale under an atmosphere of ambient air (balloon pressure) with LED irradiation at 465 nm. Isolated yields are given in parentheses and crude yields were determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene or $(Cl_2HC)_2$ as an internal standard

losses during the purification process (e.g., compounds **7a**, **7n** and **7o**). Nonetheless, the method turned out to be very tolerant of various functionalities such as nitrile, ester, halogen, carbonate, ether, imide, and unprotected hydroxy groups. Furthermore, we were able to show that the newly formed double bond within the products could be obtained in a mono-, di-, or trisubstituted fashion, emphasizing the structural flexibility of our etherification protocol. In addition to primary alcohols, the title method also proved effective for the conversion of secondary alcohols such as substrates **6k–m**, providing access to 2,5-disubstituted tetrahydrofurans **7k–m** as mixtures of diastereomers in isolated yields ranging from 42–66%. Most notably, even additional non-aromatic carbon–carbon multiple bonds within the substrate structures (e.g., dienol **6s** and enynol **6t**) remained intact throughout the cyclization event. These results underscore the high degree of site-selectivity which can be rationalized on the basis of kinetic differences between the observed 6-*exo*-trig cyclization and the non-competitive macrocyclization reactions.

Our investigations continued with the intermolecular reactions of alcohols with alkenes. In contrast to the aerobic cycloetherifications, which proceeded within 7–28 hours, the reaction times for the cognate intermolecular process were found to be in the range of many days. We attributed this observation to the moderate nucleophilicity of alcohols compared to other nucleophiles such as carboxylates and phosphates.[18] An additional problem that particularly occurred under prolonged reaction times was the Schenck-ene reaction,[21] which led to significant loss of the olefinic starting material.

In order to perform the target process in a reasonable time frame and thereby reduce any undesired side reactions, we were forced to use the corresponding alcohols **8a–e** as the solvent, incorporate electron-withdrawing groups in allylic positions within the olefinic substrates **6u–w**, and increase the loadings of the selenium catalyst and the photocatalyst to 10 mol% and 5 mol%, respectively (Scheme 3). Furthermore, we noticed that under these conditions the presence of a base was no longer necessary for the conversion to take place. Consequently, we were able to synthesize a series of allylic ethers **7ua–wd** in moderate isolated yields (14–48%), however, with excellent regioselectivity. As was already observed in the intramolecular etherifications (see Scheme 2), the catalyst system was tolerant of various functional groups such as ester, halide, nitrile and phosphonate. We also noticed that unfunctionalized alkanols such as ethanol (**8b**), isopropanol (**8c**), and *n*-butanol (not shown in Scheme 3) most often resulted in low yields (e.g., **7uc**). Alkanols with electron-withdrawing groups at the α-position provided somewhat improved yields (e.g., **7vd** and **7ve**). We suspect that the latter set of alcohols is more readily deprotonated by the anionic reduction products derived from O_2 and therefore lead to slightly better results. This rationale is corroborated by the observation that more acidic alcohols typically reacted faster than unsubstituted examples. It should be pointed out that in certain cases (e.g., **7va**, **7vd**, and **7ve**), the differences between the isolated and crude yields were due to difficulties encountered during chromatographic purification of the respective products, thus, the isolated yields are in these cases not reflective of the actual efficiency of the title procedure.



Scheme 3 Reactions were carried out on a 1.0 mmol scale under an atmosphere of ambient air (balloon pressure) with LED irradiation at 465 nm. Isolated yields are depicted in parentheses and crude yields were determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene, benzaldehyde, phthalide or $(Cl_2HC)_2$ as an internal standard

In conclusion, we have developed an efficient and generalized procedure for the aerobic dual photoredox/selenium-π-acid-catalyzed cycloetherification of unsaturated alcohols. This method gives access to various cyclic allylic ethers typically in reasonable isolated yields. The corresponding intermolecular process is characterized by a rather sluggish reactivity of the alcohol nucleophiles, which entails prolonged reaction times and diminished yields due to undesired side reactions. Nonetheless, the overall title process is characterized by very high functional group tolerance and excellent regioselectivity. Furthermore, the process is believed to proceed through the transient photoredox catalytic formation of oligomeric, Lewis acidic selenonium species $[(PhSe)_n^{m+}]$, which will immediately react with the olefinic π-system to afford a seleniranium intermediate.[18] Subsequent attack of the seleniranium ion by the corresponding alcohol nucleophile followed by oxidative elimination of the selenium residue presumably results in the formation of the ether products. Future endeavors will be focused on the application of the aerobic etherification in the total synthesis of biologically relevant natural products and the design of asymmetric variants of this reaction.

Unless stated otherwise, all catalytic reactions were carried out under an atmosphere of air. Chemicals were obtained from commercial sources and were used without further purification. Yields correspond to those of isolated compounds unless indicated otherwise. Purity is estimated to be ≥95% based on ^{1}H NMR spectroscopic analysis.

Irradiation experiments were performed at λ = 465 nm using commercially available blue LED strips. The light intensity applied was in the range of 9000 lx. TLC: Merck Silica Gel 60 F_{254}. Visualization of the developed chromatogram was performed by fluorescence quenching at 254 nm and staining with *p*-anisaldehyde or potassium permanganate. Chromatography: Separations were carried out on Merck Silica 60 (0.063–0.200 mm, 70–230 mesh ASTM) using forced flow. NMR (^{1}H, ^{13}C) spectra were recorded at 300, 400 or 500 MHz (^{1}H), and 76, 101, or 126 [^{13}C, APT (attached proton test)], respectively, on VARIAN Unity-300, AMX 300 and Inova 500 instruments in $CDCl_3$ solution at 298 K, unless specified otherwise. On the same machines NMR (^{19}F) and (^{31}P) spectra were recorded respectively at 282 or 376 MHz and 162 MHz. Chemical shifts (δ) are given in ppm. Multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, sept = septet, m = multiplet). High-resolution mass spectrometry (HRMS): APEX IV 7T FTICR, BRUKER Daltonics.

Tetrahydrofurans and Tetrahydropyrans 7a–t; General Procedure

To a solution of the respective alcohol **6a–t** (1.00 mmol, 1.0 equiv) in MeCN (0.2 M) were added (2-anisyl)$_2$Se$_2$ (18.6 mg, 0.05 mmol, 0.05 equiv), TAPT (14.6 mg, 0.03 mmol, 0.03 equiv) and NaH_2PO_4 (96 mg, 0.8 mmol, 0.8 equiv). The mixture was subjected to irradiation at λ = 465 nm and stirred vigorously using a cross-shaped stir bar (750 rpm) under ambient air. The solvent was removed under reduced pressure and the residue purified on silica gel to afford the title compound.

(*E*)-2-(Hex-1-en-1-yl)tetrahydrofuran (7a)

Reaction time: 7 h; eluting with *n*-pentane/Et_2O (9:1).

Yield: 49 mg, 0.32 mmol (32%); colorless liquid; ^{1}H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 65%; R_f = 0.31 (*n*-pentane/Et_2O, 9:1).

IR (neat): 2957, 2926, 2857, 1459, 1377, 1153, 1054, 966, 731 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.67 (dtd, *J* = 15.2, 6.7, 0.9 Hz, 1 H), 5.44 (ddt, *J* = 15.3, 7.2, 1.4 Hz, 1 H), 4.22 (q, *J* = 7.1 Hz, 1 H), 3.89 (ddd, *J* = 8.3, 7.3, 6.3 Hz, 1 H), 3.75 (td, *J* = 7.9, 6.1 Hz, 1 H), 2.08–1.98 (m, 3 H), 1.97–1.79 (m, 2 H), 1.65–1.51 (m, 2 H), 1.33 (tddd, *J* = 10.0, 8.7, 7.0, 4.3 Hz, 3 H), 0.88 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 133.0, 130.7, 80.2, 68.0, 32.4, 32.0, 31.4, 26.1, 22.4, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{19}O$: 155.1430; found: 155.1433.

(*E*)-2-(3-Phenylprop-1-en-1-yl)tetrahydrofuran (7b)

Reaction time: 8 h; eluting with *n*-pentane/EtOAc (6:4).

Yield: 119 mg, 0.63 mmol (63%); yellow liquid; ^{1}H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 66%; R_f = 0.53 (*n*-pentane/EtOAc, 60:40).

IR (neat): 3026, 2971, 2870, 1672, 1602, 1495, 1452, 1369, 1178, 1048, 968, 919, 745, 697, 587, 485 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.22 (m, 2 H), 7.22–7.04 (m, 3 H), 5.89–5.76 (m, 1 H), 5.53 (ddt, *J* = 15.2, 7.0, 1.6 Hz, 1 H), 4.27 (q, *J* = 7.0 Hz, 1 H), 3.94–3.84 (m, 1 H), 3.76 (td, *J* = 7.9, 6.2 Hz, 1 H), 3.37 (d, *J* = 6.7 Hz, 2 H), 2.19–1.77 (m, 3 H), 1.68–1.52 (m, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.2, 132.4, 130.9, 128.7, 128.5, 126.1, 79.8, 68.1, 38.8, 32.4, 26.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{16}NaO$: 211.1093; found: 211.1089.

4,4-Diphenyl-2-vinyltetrahydrofuran (7c)

Reaction time: 9 h; eluting with *n*-pentane/CH_2Cl_2 (5:95 to 15:85).

Yield: 86 mg, 0.34 mmol (34%); colorless liquid; ^{1}H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 48%; R_f = 0.45 (*n*-pentane/EtOAc, 60:40).

IR (neat): 3083, 3059, 3026, 2980, 2938, 2925, 2864, 1598, 1493, 1446, 1335, 1056, 988, 925, 873, 843, 773, 756, 732, 696, 670, 582 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.27 (m, 6 H), 7.25–7.17 (m, 4 H), 5.91 (ddd, *J* = 17.1, 10.2, 6.9 Hz, 1 H), 5.25 (ddd, *J* = 17.1, 1.6, 1.1 Hz, 1 H), 5.11 (ddd, *J* = 10.2, 1.7, 1.0 Hz, 1 H), 4.68 (dd, *J* = 8.7, 1.2 Hz, 1 H), 4.51–4.39 (m, 1 H), 4.17 (d, *J* = 8.7 Hz, 1 H), 2.67 (ddd, *J* = 12.1, 6.0, 1.2 Hz, 1 H), 2.46 (dd, *J* = 12.2, 9.7 Hz, 1 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 146.1, 145.7, 138.9, 128.6, 128.5, 127.30, 127.26, 126.6, 126.5, 116.0, 79.8, 79.8, 56.3, 45.3.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{18}O$: 250.1358; found: 250.1356.

2-(Cyclohexylidenemethyl)tetrahydrofuran (7d)

Reaction time: 8 h; eluting with *n*-pentane/CH_2Cl_2 (5:95 to 10:90).

Yield: 65 mg, 0.39 mmol (39%); yellow liquid; ^{1}H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 39%; R_f = 0.32 (*n*-pentane/EtOAc, 60:40).

IR (neat): 2924, 2852, 1670, 1599, 1446, 1337, 1234, 1171, 1049, 983, 935, 855, 751, 637, 470, 381 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.11 (dt, *J* = 8.5, 1.3 Hz, 1 H), 4.51 (td, *J* = 8.3, 6.0 Hz, 1 H), 3.86 (dt, *J* = 8.1, 6.9 Hz, 1 H), 3.77–3.65 (m, 1 H), 2.32–1.77 (m, 7 H), 1.73–1.32 (m, 7 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 143.1, 122.5, 74.8, 67.6, 37.0, 32.8, 29.2, 28.3, 27.8, 26.7, 26.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{18}NaO$: 189.1250; found: 189.1253.

(*E*)-5-(Tetrahydrofuran-2-yl)pent-4-enenitrile (7e)

Reaction time: 9 h; eluting with *n*-pentane/EtOAc (95:5 to 80:20).

Yield: 86 mg, 0.57 mmol (57%); colorless liquid; ^{1}H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 65%; R_f = 0.67 (*n*-pentane/EtOAc, 60:40).

IR (neat): 2973, 2867, 2244, 1444, 1372, 1179, 1049, 967, 921, 868 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.75–5.54 (m, 2 H), 4.26 (q, *J* = 6.7 Hz, 1 H), 3.88 (ddd, *J* = 8.2, 7.3, 6.3 Hz, 1 H), 3.76 (td, *J* = 7.9, 6.2 Hz, 1 H), 2.49–2.31 (m, 4 H), 2.03 (dddd, *J* = 12.0, 8.1, 6.7, 5.1 Hz, 1 H), 1.99–1.80 (m, 2 H), 1.59 (ddt, *J* = 12.1, 8.4, 7.4 Hz, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 134.3, 127.2, 119.2, 79.1, 68.2, 32.2, 28.1, 25.9, 17.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_9H_{14}NO$: 152.1070; found: 152.1068.

(*E*)-4-(Tetrahydrofuran-2-yl)but-3-en-1-ol (7f)

Reaction time: 28.5 h; eluting with *n*-pentane/EtOAc (2:1 to 1:1).

Yield: 44 mg, 0.31 mmol (31%); colorless liquid; ^{1}H NMR yield using 1,1,2,2-tetrachloroethane as the internal standard: 40%; R_f = 0.29 (*n*-pentane/EtOAc, 2:1).

IR (neat): 3387, 2944, 2871, 1444, 1373, 1039, 967, 921, 864, 596 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.67 (dt, *J* = 15.4, 6.4 Hz, 1 H), 5.61–5.51 (m, 1 H), 4.29–4.20 (m, 1 H), 3.94–3.84 (m, 1 H), 3.80–3.71 (m, 1 H), 3.65 (t, *J* = 6.3 Hz, 2 H), 2.40–2.19 (m, 2 H), 2.16–1.79 (m, 4 H), 1.66–1.52 (m, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 133.9, 128.4, 79.8, 68.1, 61.9, 35.8, 32.4, 26.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_8H_{15}O_2$: 143.1067; found: 143.1064.

(*E*)-4-(Tetrahydrofuran-2-yl)but-3-en-1-yl Pivalate (7g)

Alcohol **6g** (585 µmol) was used; reaction time: 11 h; eluting with *n*-pentane/EtOAc (7:1).

Yield: 33 mg, 0.15 mmol (25%); colorless liquid; ^{1}H NMR yield using 1,1,2,2-tetrachloroethane as the internal standard: 44%; R_f = 0.29 (*n*-pentane/EtOAc, 7:1).

IR (neat): 2970, 2872, 1726, 1480, 1460, 1398, 1366, 1283, 1150, 1052, 967, 869, 770 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.69–5.59 (m, 1 H), 5.58–5.49 (m, 1 H), 4.29–4.18 (m, 1 H), 4.09 (t, *J* = 6.7 Hz, 2 H), 3.88 (ddd, *J* = 8.0, 7.1, 6.3 Hz, 1 H), 3.81–3.71 (m, 1 H), 2.59–2.16 (m, 2 H), 2.08–1.96 (m, 1 H), 1.96–1.80 (m, 2 H), 1.66–1.50 (m, 1 H), 1.18 (s, 9 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.4, 133.7, 127.3, 79.6, 68.1, 63.5, 38.9, 32.4, 31.9, 27.4, 26.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{23}O_3$: 227.1642; found: 227.1643.

(*E*)-Ethyl [4-(Tetrahydrofuran-2-yl)but-3-en-1-yl] Carbonate (7h)

Alcohol **6h** (524 µmol) was used; reaction time: 7 h; eluting with *n*-pentane/EtOAc (7:1).

Yield: 31 mg, 0.14 mmol (28%); colorless liquid; ^{1}H NMR yield using 1,1,2,2-tetrachloroethane as the internal standard: 47%; R_f = 0.23 (*n*-pentane/EtOAc, 7:1).

IR (neat): 2978, 2868, 1741, 1464, 1384, 1366, 1247, 1091, 1051, 1007, 968, 873, 791 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.70–5.60 (m, 1 H), 5.61–5.51 (m, 1 H), 4.29–4.20 (m, 1 H), 4.20–4.11 (m, 4 H), 3.93–3.84 (m, 1 H), 3.82–3.70 (m, 1 H), 2.51–2.30 (m, 2 H), 2.14–1.76 (m, 3 H), 1.69–1.49 (m, 1 H), 1.30 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 155.1, 134.1, 126.6, 79.6, 68.1, 67.1, 64.0, 32.3, 31.8, 26.1, 14.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{19}O_4$: 215.1278; found: 215.1281.

(*E*)-2-[3-(Tetrahydrofuran-2-yl)allyl]isoindoline-1,3-dione (7i)

Reaction time: 7.5 h; eluting with *n*-pentane/EtOAc (4:1).

Yield: 85 mg, 0.33 mmol (37%); yellow liquid; ^{1}H NMR yield using 1,1,2,2-tetrachloroethane as the internal standard: 45%; R_f = 0.19 (*n*-pentane/EtOAc, 4:1).

IR (neat): 2972, 2868, 1770, 1705, 1613, 1467, 1428, 1391, 1188, 1112, 1087, 1050, 939, 854, 794, 718, 614, 529, 444 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87–7.81 (m, 2 H), 7.76–7.66 (m, 2 H), 5.84–5.62 (m, 2 H), 4.39–4.13 (m, 3 H), 3.87 (ddd, *J* = 8.3, 7.1, 6.4 Hz, 1 H), 3.80–3.69 (m, 1 H), 2.08–1.96 (m, 1 H), 1.95–1.78 (m, 2 H), 1.63–1.51 (m, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 167.9, 135.1, 134.0, 132.2, 124.2, 123.3, 78.7, 68.2, 39.2, 32.2, 25.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{16}NO_3$: 258.1125; found: 258.1124.

(*E*)-2,6-Dimethyl-8-(tetrahydrofuran-2-yl)oct-7-en-2-ol (7j)

Reaction time: 7 h; eluting with *n*-pentane/EtOAc (2:3).

Yield: 154 mg, 680 µmol (68%); yellow liquid; 1:1 mixture of diastereomers (see the ^{13}C NMR spectrum); ^{1}H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 67%; R_f = 0.21 (*n*-pentane/EtOAc, 2:3).

IR (neat): 3442, 2965, 2868, 1460, 1375, 1160, 1053, 968, 938, 910, 865, 764, 551 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.69–5.46 (m, 1 H), 5.40 (ddd, *J* = 15.3, 6.8, 0.7 Hz, 1 H), 4.22 (q, *J* = 6.9 Hz, 1 H), 3.97–3.83 (m, 1 H), 3.80–3.69 (m, 1 H), 2.25–1.74 (m, 4 H), 1.66–1.52 (m, 1 H), 1.47–1.23 (m, 7 H), 1.19 (s, 6 H), 0.98 (dd, *J* = 6.7, 3.4 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.3, 138.2, 129.14, 129.06, 80.14, 80.10, 71.14, 71.11, 68.00, 67.99, 44.2, 44.1, 37.5, 37.4, 36.5, 32.6, 32.5, 29.5, 29.4, 26.14, 26.10, 22.2, 22.1, 20.58, 20.56.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{26}NaO_2$: 249.1825; found: 249.1827.

(*E*)-2-Phenyl-5-(prop-1-en-1-yl)tetrahydrofuran (7k)

Reaction time: 16 h; eluting with *n*-pentane/EtOAc (20:1).

Yield: 117 mg, 621 µmol (62%); colorless liquid; inseparable mixture of diastereomers (dr = 1:1.19); ^{1}H NMR yield using 1,1,2,2-tetrachloroethane as the internal standard: 65%; R_f = 0.41 (*n*-pentane/EtOAc, 20:1).

IR (neat): 2966, 2867, 1493, 1449, 1355, 1043, 1027, 962, 931, 877, 751, 697 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.28 (m, 4.27 H), 7.28–7.18 (m, 1.12 H), 5.88–5.49 (m, 2 H), 5.14–5.00 (m, 0.60 H), 4.93 (td, *J* = 7.1, 3.5 Hz, 0.49 H), 4.61 (ddddd, *J* = 7.2, 6.6, 5.5, 1.4, 0.7 Hz, 0.46 H), 4.43 (dtd, *J* = 7.3, 6.7, 0.6 Hz, 0.39 H), 2.53–2.27 (m, 1.18 H), 2.24–2.04 (m, 1.37 H), 2.01–1.76 (m, 1.86 H), 1.78–1.69 (m, 3.72 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 143.8, 143.4, 132.3, 132.1, 128.30, 128.26, 128.3, 127.9, 127.6, 127.15, 127.08, 125.9, 125.6, 80.9, 80.7, 80.6, 80.5, 35.6, 34.7, 33.3, 32.3, 18.0, 17.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{17}O$: 189.1274; found: 189.1278.

(*E*)-2-(4-Fluorophenyl)-5-(prop-1-en-1-yl)tetrahydrofuran (7l)

Reaction time: 16 h; eluting with *n*-pentane/EtOAc (20:1).

Yield: 137 mg, 664 µmol (66%); colorless liquid, inseparable mixture of diastereomers (dr = 1:1.05); ^{1}H NMR yield using 1,1,2,2-tetrachloroethane as the internal standard: 69%; R_f = 0.44 (*n*-pentane/EtOAc, 20:1).

IR (neat): 2967, 2864, 1605, 1509, 1449, 1352, 1294, 1221, 1155, 1045, 963, 931, 831, 782 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.27 (m, 1.78 H), 7.11–6.80 (m, 1.84 H), 5.89–5.46 (m, 2 H), 5.07–4.94 (m, 0.62 H), 4.88 (t, *J* = 6.9 Hz, 0.63 H), 4.66–4.53 (m, 0.53 H), 4.41 (tdt, *J* = 7.2, 6.5, 0.6 Hz, 0.50 H), 2.64–2.26 (m, 1.10 H), 2.25–2.05 (m, 1.24 H), 1.99–1.77 (m, 1.66 H), 1.77–1.64 (m, 3.10 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 162.03 (d, *J* = 244.3 Hz), 161.99 (d, *J* = 244.1 Hz), 139.4 (d, *J* = 3.0 Hz), 139.1 (d, *J* = 2.9 Hz), 132.2, 131.9, 128.1, 127.7, 127.5 (d, *J* = 8.1 Hz), 127.3 (d, *J* = 7.9 Hz), 115.10 (d, *J* = 21.3 Hz), 115.07 (d, *J* = 21.3 Hz), 80.9, 80.7, 80.3, 80.0, 35.7, 34.7, 33.3, 32.2, 18.0, 17.9.

^{19}F NMR (282 MHz, $CDCl_3$): δ = −115.9 (tt, *J* = 8.9, 5.5 Hz), −116.0 (tt, *J* = 8.7, 5.5 Hz).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{16}OF$: 207.1180; found: 207.1182.

(*E*)-2-(4-Methoxyphenyl)-5-(prop-1-en-1-yl)tetrahydrofuran (7m)

Reaction time: 16 h; eluting with *n*-pentane/EtOAc (20:1).

Yield: 91 mg, 0.42 mmol (42%); colorless liquid; inseparable mixture of diastereomers (dr = 1.1.16); ^{1}H NMR yield using 1,1,2,2-tetrachloroethane as the internal standard: 56%; R_f = 0.25 (*n*-pentane/EtOAc, 20:1).

IR (neat): 2937, 1612, 1512, 1462, 1301, 1242, 1172, 1032, 963, 931, 828, 540 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51–7.22 (m, 2.32 H), 6.98–6.66 (m, 2.16 H), 5.85–5.48 (m, 2 H), 4.99 (dq, *J* = 8.1, 6.4 Hz, 0.53 H), 4.91–4.79 (m, 0.66 H), 4.63–4.52 (m, 0.40 H), 4.45–4.34 (m, 0.47 H), 3.80 (s, 3.49 H), 2.45–1.97 (m, 2.25 H), 1.96–1.75 (m, 1.67 H), 1.75–1.66 (m, 3.67 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 158.84, 158.80, 135.7, 135.4, 132.4, 132.2, 127.8, 127.5, 127.2, 127.0, 113.8, 113.7, 80.8, 80.7, 80.5, 80.3, 55.4, 35.5, 34.6, 33.4, 32.4, 18.0, 17.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{19}O_2$: 219.1380; found: 219.1382.

2-(Cyclohexylidenemethyl)tetrahydro-2*H*-pyran (7n)

Reaction time: 17 h; eluting with *n*-pentane/CH_2Cl_2 (1:9).

Yield: 62 mg, 0.35 mmol (35%); colorless liquid; ^{1}H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 53%; R_f = 0.43 (*n*-pentane/CH_2Cl_2, 1:9).

IR (neat): 2926, 2851, 1446, 1204, 1174, 1084, 1051, 1033, 992, 901, 846 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.11 (dquin, *J* = 8.0, 1.2 Hz, 1 H), 4.29–3.87 (m, 2 H), 3.47 (td, *J* = 11.4, 2.5 Hz, 1 H), 2.35–1.94 (m, 5 H), 1.88–1.75 (m, 1 H), 1.69–1.26 (m, 10 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 142.7, 123.3, 74.3, 68.4, 37.1, 32.9, 29.7, 28.6, 28.1, 26.9, 26.1, 23.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{21}O$: 181.1587; found: 181.1588.

(*E*)-2-(3-Methylbut-1-en-1-yl)tetrahydro-2*H*-pyran (7o)

Reaction time: 7 h; eluting with *n*-pentane/Et_2O (9:1).

Yield: 58 mg, 0.38 mmol (38%); colorless liquid; ^{1}H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 52%; R_f = 0.43 (*n*-pentane/Et_2O, 9:1).

IR (neat): 2955, 2934, 2841, 1464, 1362, 1263, 1204, 1176, 1085, 1051, 1035, 968, 896, 847 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.64 (ddd, *J* = 15.6, 6.4, 1.1 Hz, 1 H), 5.41 (ddd, *J* = 15.6, 6.2, 1.4 Hz, 1 H), 4.06–3.95 (m, 1 H), 3.73 (dddd, *J* = 10.8, 6.2, 2.1, 1.1 Hz, 1 H), 3.55–3.42 (m, 1 H), 2.39–2.20 (m, 1 H), 1.92–1.77 (m, 1 H), 1.70–1.29 (m, 5 H), 0.98 (dd, *J* = 6.7, 0.9 Hz, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.8, 128.4, 78.5, 68.5, 32.5, 30.9, 26.1, 23.7, 22.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{19}O$: 155.1430; found: 155.1436.

(*E*)-2,6-Dimethyl-8-(tetrahydro-2*H*-pyran-2-yl)oct-7-en-2-ol (7p)

Reaction time: 7 h; eluting with *n*-pentane/Et_2O (1:1).

Yield: 172 mg, 717 µmol (71%); yellow liquid; mixture of diastereomers (see the ^{13}C NMR spectrum); ^1H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 72%; R_f = 0.19 (*n*-pentane/Et_2O, 1:1).

IR (neat): 3437, 2934, 2845, 1463, 1374, 1203, 1175, 1083, 1049, 1033, 968, 938, 895, 754 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.53 (dddd, *J* = 15.7, 8.4, 7.4, 1.0 Hz, 1 H), 5.42 (dddd, *J* = 15.6, 6.2, 2.3, 0.9 Hz, 1 H), 4.00 (ddt, *J* = 11.6, 4.0, 1.6 Hz, 1 H), 3.80–3.68 (m, 1 H), 3.53–3.41 (m, 1 H), 2.16–2.04 (m, 1 H), 1.90–1.77 (m, 1 H), 1.72–1.22 (m, 12 H), 1.19 (s, 6 H), 0.98 (dd, *J* = 6.7, 3.4 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.4, 137.3, 129.9, 129.7, 78.5, 78.3, 71.2, 71.1, 68.5, 44.10, 44.08, 37.4, 37.3, 36.52, 36.46, 32.6, 32.5, 29.41, 29.38, 29.36, 26.03, 26.01, 23.6, 22.1, 22.0, 20.6, 20.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{29}O_2$: 241.2162; found: 241.2160.

(*E*)-2-(3-Phenylprop-1-en-1-yl)tetrahydro-2*H*-pyran (7q)

Reaction time: 7 h; eluting with *n*-pentane/CH_2Cl_2 (1:9).

Yield: 90 mg, 0.44 mmol (44%); yellow liquid; ^1H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 54%; R_f = 0.43 (*n*-pentane/CH_2Cl_2, 1:9).

IR (neat): 2933, 2841, 1495, 1453, 1438, 1204, 1175, 1083, 1048, 1033, 967, 894, 745, 697, 580, 543, 497, 456 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.24 (m, 2 H), 7.24–7.03 (m, 3 H), 5.83 (dtd, *J* = 15.4, 6.7, 1.2 Hz, 1 H), 5.54 (ddt, *J* = 15.4, 6.1, 1.5 Hz, 1 H), 4.09–3.95 (m, 1 H), 3.84–3.73 (m, 1 H), 3.59–3.42 (m, 1 H), 3.41–3.24 (m, 2 H), 1.94–1.78 (m, 1 H), 1.74–1.30 (m, 5 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.2, 132.8, 130.2, 128.7, 128.4, 126.1, 78.1, 68.5, 39.0, 32.4, 26.1, 23.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{19}O$: 203.1430; found: 203.1434.

(*E*)-2-(5-Chloropent-1-en-1-yl)tetrahydro-2*H*-pyran (7r)

Alcohol **6r** (818 µmol) was used; reaction time: 7 h; eluting with *n*-pentane/CH_2Cl_2 (1:9).

Yield: 88 mg, 0.47 mmol (47%); yellow liquid; ^1H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 62%; R_f = 0.44 (*n*-pentane/CH_2Cl_2, 1:9).

IR (neat): 2934, 2844, 1440, 1265, 1204, 1083, 1049, 1034, 968, 895, 726, 653 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.64 (dtd, *J* = 15.5, 6.3, 0.8 Hz, 1 H), 5.52 (ddt, *J* = 15.5, 5.8, 1.0 Hz, 1 H), 4.08–3.95 (m, 1 H), 3.82–3.68 (m, 1 H), 3.53 (t, *J* = 6.6 Hz, 2 H), 2.18 (dddd, *J* = 8.0, 7.0, 6.0, 0.8 Hz, 2 H), 2.03–1.74 (m, 3 H), 1.73–1.23 (m, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 132.8, 129.4, 78.1, 68.5, 44.6, 32.4, 32.1, 29.6, 26.1, 23.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{17}ClONa$: 211.0860; found: 211.0865.

(*E*)-2-(Undeca-1,10-dien-1-yl)tetrahydro-2*H*-pyran (7s)

Reaction time: 17 h; eluting with *n*-pentane/Et_2O (20:1).

Yield: 86 mg, 0.37 mmol (37%); colorless liquid; ^1H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 55%; R_f = 0.23 (*n*-pentane/Et_2O, 20:1).

IR (neat): 2924, 2852, 1727, 1640, 1463, 1439, 1371, 1263, 1203, 1175, 1085, 1035, 966, 907, 861, 843, 810, 723 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.80 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1 H), 5.66 (dtd, *J* = 15.5, 6.6, 1.1 Hz, 1 H), 5.45 (ddt, *J* = 15.5, 6.2, 1.4 Hz, 1 H), 5.04–4.88 (m, 2 H), 4.00 (ddt, *J* = 11.6, 4.1, 1.8 Hz, 1 H), 3.73 (ddd, *J* = 9.2, 4.5, 1.9 Hz, 1 H), 3.56–3.40 (m, 1 H), 2.02 (qdd, *J* = 6.9, 5.4, 1.2 Hz, 4 H), 1.90–1.76 (m, 1 H), 1.70–1.19 (m, 15 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.3, 131.9, 131.3, 114.2, 78.4, 68.5, 34.0, 32.5, 32.4, 29.5, 29.4, 29.31, 29.28, 29.1, 26.1, 23.7.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{28}ONa$: 259.2032; found: 259.2034.

(*E*)-2-(Hept-1-en-6-yn-1-yl)tetrahydro-2*H*-pyran (7t)

Reaction time: 14.5 h; eluting with *n*-pentane/Et_2O (30:1).

Yield: 54 mg, 0.31 mmol (31%); colorless liquid; ^1H NMR yield using 1,1,2,2-tetrachloroethane as the internal standard: 37%; R_f = 0.11 (*n*-pentane/Et_2O, 30:1).

IR (neat): 3304, 2933, 2843, 1439, 1344, 1263, 1203, 1175, 1083, 1049, 1034, 967, 896, 842, 810 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.64 (dtd, *J* = 15.5, 6.5, 0.9 Hz, 1 H), 5.50 (ddt, *J* = 15.5, 6.0, 1.2 Hz, 1 H), 4.06–3.95 (m, 1 H), 3.81–3.68 (m, 1 H), 3.53–3.40 (m, 1 H), 2.37–2.04 (m, 4 H), 1.93 (t, *J* = 2.6 Hz, 1 H), 1.89–1.79 (m, 1 H), 1.68–1.23 (m, 7 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 132.3, 130.3, 84.4, 78.2, 68.52, 68.49, 32.4, 31.4, 28.1, 26.1, 23.6, 18.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{19}O$: 179.1430; found: 179.1429.

Intermolecular Etherification; General Procedure

To a solution of the respective alkene **6u–w** (1.00 mmol, 1.0 equiv) in the respective alcohol **8a–e** (0.2 M) were added (2-anisyl)$_2Se_2$ (0.10 mmol, 0.10 equiv) and TAPT (24.0 mg, 0.05 mmol, 0.05 equiv). The mixture was subjected to irradiation at λ = 465 nm and stirred vigorously using a cross-shaped stir bar (750 rpm) under ambient air. The solvent was removed under reduced pressure and the residue purified on silica gel to afford the title compound.

Benzyl (*E*)-4-Methoxyhex-2-enoate (7ua)

Alkene **6u** (500 µmol), MeOH (2.5 mL), (2-anisyl)$_2Se_2$ (18 mg, 50 µmol, 0.1 equiv) and TAPT (12.0 mg, 0.025 mmol, 0.05 equiv) were employed; reaction time: 70.5 h; eluting with *n*-pentane/EtOAc (25:1).

Yield: 32 mg, 136 µmol (27%); colorless liquid; ^1H NMR yield using 1,1,2,2-tetrachloroethane as the internal standard: 32%; R_f = 0.43 (*n*-pentane/EtOAc 10:1).

IR (neat): 2968, 2933, 2878, 2824, 1717, 1657, 1455, 1377, 1355, 1266, 1198, 1159, 1127, 1087, 981, 846, 737, 696 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.47–7.30 (m, 5 H), 6.85 (dd, *J* = 15.8, 6.4 Hz, 1 H), 6.04 (dd, *J* = 15.8, 1.3 Hz, 1 H), 5.20 (s, 2 H), 3.67 (qd, *J* = 6.3, 1.3 Hz, 1 H), 3.31 (s, 3 H), 1.89–1.36 (m, 2 H), 0.92 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 166.2, 148.9, 136.0, 128.7, 128.4, 128.4, 121.9, 81.9, 66.4, 57.2, 27.7, 9.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{18}O_3Na$: 257.1148; found: 257.1146.

Benzyl (*E*)-4-Ethoxyhex-2-enoate (7ub)

(*o*-MeOPh)$_2$Se$_2$ (36 mg, 100 µmol, 0.1 equiv) was employed; reaction time: 92 h; eluting with *n*-pentane/EtOAc (50:1).

Yield: 48 mg, 0.19 mmol (19%); colorless liquid; ^{1}H NMR yield using 1,1,2,2-tetrachloroethane as the internal standard: 31%; R_f = 0.31 (*n*-pentane/EtOAc 50:1).

IR (neat): 2972, 2932, 2875, 1719, 1658, 1456, 1377, 1338, 1268, 1164, 1126, 1092, 983, 748, 697 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47–7.30 (m, 5 H), 6.87 (dd, *J* = 15.8, 6.2 Hz, 1 H), 6.03 (dd, *J* = 15.8, 1.3 Hz, 1 H), 5.19 (d, *J* = 0.5 Hz, 2 H), 3.77 (qd, *J* = 6.2, 1.4 Hz, 1 H), 3.53 (dq, *J* = 9.3, 7.0 Hz, 1 H), 3.38 (dqd, *J* = 9.2, 7.0, 0.9 Hz, 1 H), 1.69–1.49 (m, 2 H), 1.20 (t, *J* = 7.0 Hz, 3 H), 1.08–0.79 (m, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 166.2, 149.5, 136.1, 128.6, 128.32, 128.30, 121.3, 80.1, 66.4, 64.9, 28.1, 15.6, 9.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{20}O_3Na$: 271.1305; found: 271.1303.

Benzyl (*E*)-4-Isopropoxyhex-2-enoate (7uc)

Reaction time: 63 h; eluting with CH_2Cl_2.

Yield: 37 mg, 149 µmol (14%); colorless liquid; ^{1}H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 28%; R_f = 0.20 (CH_2Cl_2).

IR (neat): 2970, 2933, 2876, 2362, 2323, 1717, 1655, 1498, 1457, 1377, 1330, 1268, 1161, 1121, 1062, 1005, 983, 913, 861, 737, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.29 (m, 5 H), 6.90 (dd, *J* = 15.7, 5.8 Hz, 1 H), 6.04 (dd, *J* = 15.7, 1.4 Hz, 1 H), 5.28–5.09 (m, 2 H), 3.86 (qd, *J* = 6.0, 1.4 Hz, 1 H), 3.58 (sept, *J* = 6.1 Hz, 1 H), 1.68–1.49 (m, 2 H), 1.29–1.04 (m, 6 H), 0.93 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.4, 150.4, 136.1, 128.7, 128.4, 128.3, 120.8, 77.5, 70.1, 66.4, 28.4, 23.3, 21.9, 9.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{22}NaO_3$: 285.1461; found: 285.1460.

Diethyl (*E*)-(3-Methoxybut-1-en-1-yl)phosphonate (7va)

Reaction time: 8 d; eluting with CH_2Cl_2/acetone (20:1 + 1% AcOH).

Yield: 81 mg, 0.36 mmol (36%); yellow liquid; ^{1}H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: >99%; R_f = 0.07 (CH_2Cl_2/acetone, 20:1 + 1% AcOH).

IR (neat): 2980, 2933, 2905, 2871, 2826, 1744, 1722, 1635, 1444, 1392, 1369, 1337, 1248, 1216, 1112, 1049, 1020, 956, 858, 826, 789, 746 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.66 (ddd, *J* = 22.4, 17.2, 5.3 Hz, 1 H), 5.85 (ddd, *J* = 20.5, 17.2, 1.4 Hz, 1 H), 4.08 (dqt, *J* = 8.4, 7.1, 1.1 Hz, 4 H), 3.87 (qddd, *J* = 6.6, 5.3, 2.4, 1.4 Hz, 1 H), 3.31 (s, 3 H), 1.32 (t, *J* = 7.1 Hz, 6 H), 1.26 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 153.5 (d, *J* = 4.3 Hz), 116.9 (d, *J* = 187.8 Hz), 77.4, 61.9 (dd, *J* = 5.6, 2.1 Hz), 56.9, 20.3 (d, *J* = 1.9 Hz), 16.5 (d, *J* = 6.2 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ = 18.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_9H_{20}O_4P$: 223.1094; found: 223.1095.

Diethyl (*E*)-(3-Ethoxybut-1-en-1-yl)phosphonate (7vb)

Reaction time: 8.5 d; eluting with CH_2Cl_2/acetone (30:1 + 1% AcOH).

Yield: 73 mg, 0.31 mmol (31%); yellow liquid; ^{1}H NMR yield using phthalide as the internal standard: 50%; R_f = 0.10 (CH_2Cl_2/acetone, 30:1 + 1% AcOH).

IR (neat): 2978, 2934, 2904, 2872, 1721, 1634, 1444, 1392, 1369, 1336, 1245, 1206, 1163, 1094, 1050, 1020, 957, 855, 828, 749 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.68 (ddd, *J* = 22.4, 17.2, 5.2 Hz, 1 H), 5.85 (ddd, *J* = 20.8, 17.2, 1.4 Hz, 1 H), 4.16–4.02 (m, 4 H), 3.98 (dddd, *J* = 6.6, 5.2, 2.5, 1.4 Hz, 1 H), 3.46 (dqd, *J* = 9.2, 7.0, 2.1 Hz, 2 H), 1.32 (tt, *J* = 7.1, 0.3 Hz, 6 H), 1.26 (d, *J* = 6.6 Hz, 3 H), 1.20 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 154.2 (d, *J* = 4.4 Hz), 116.4 (d, *J* = 188.1 Hz), 75.5 (d, *J* = 21.9 Hz), 64.6, 61.9 (dd, *J* = 5.6, 2.5 Hz), 20.7 (d, *J* = 2.1 Hz), 16.5 (d, *J* = 6.4 Hz), 15.5.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 18.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{22}O_4P$: 237.1250; found: 237.1257.

Diethyl (*E*)-(3-Isopropoxybut-1-en-1-yl)phosphonate (7vc)

Reaction time: 12 d; eluting with CH_2Cl_2/acetone (30:1 + 1% AcOH).

Yield: 101 mg, 402 µmol (40%); yellow liquid; ^{1}H NMR yield using benzaldehyde as the internal standard: 43%; R_f = 0.10 (CH_2Cl_2/acetone, 30:1 + 1% AcOH).

IR (neat): 1975, 1934, 1909, 1872, 1722, 1633, 1445, 1369, 1247, 1121, 1020, 958, 851, 802, 751 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.70 (ddd, *J* = 22.2, 17.2, 4.9 Hz, 1 H), 5.86 (ddd, *J* = 21.1, 17.2, 1.5 Hz, 1 H), 4.14–4.01 (m, 5 H), 3.60 (quin, *J* = 6.1 Hz, 1 H), 1.32 (td, *J* = 7.1, 0.5 Hz, 6 H), 1.23 (d, *J* = 6.6 Hz, 3 H), 1.14 (dd, *J* = 6.1, 3.2 Hz, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 155.1 (d, *J* = 4.5 Hz), 115.8 (d, *J* = 188.3 Hz), 72.8 (d, *J* = 21.7 Hz), 70.1, 62.0 (dd, *J* = 5.6, 3.0 Hz), 23.1, 22.1, 21.3 (d, *J* = 2.1 Hz), 16.5 (d, *J* = 6.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ = 18.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{24}O_4P$: 251.1407; found: 251.1400.

Diethyl (*E*)-(3-{[4-(Trifluoromethyl)benzyl]oxy}but-1-en-1-yl)phosphonate (7vd)

Alkene **6v** (700 µmol), [4-(trifluoromethyl)phenyl]methanol (3.5 mL), Ph_2Se_2 (22 mg, 70 µmol, 0.1 equiv) and TAPT (17.0 mg, 0.035 mmol, 0.05 equiv) were employed; reaction time: 73 h; eluting with CH_2Cl_2/acetone (30:1 + 1% AcOH).

Yield: 123 mg, 0.34 mmol (48%); brown liquid; ^{1}H NMR yield using 1,3,5-trimethoxybenzene as the internal standard: 68%; R_f = 0.21 (CH_2Cl_2/acetone, 30:1 + 1% AcOH).

IR (neat): 2987, 2935, 2871, 1623, 1444, 1424, 1392, 1369, 1325, 1248, 1161, 1121, 1066, 1051, 1017, 956, 823 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.53 (m, 2 H), 7.55–7.40 (m, 2 H), 6.72 (ddd, *J* = 22.4, 17.2, 5.4 Hz, 1 H), 5.92 (ddd, *J* = 20.2, 17.2, 1.4 Hz, 1 H), 4.61 (d, *J* = 12.5 Hz, 1 H), 4.51 (d, *J* = 12.5 Hz, 1 H), 4.26–3.87 (m, 5 H), 1.37–1.30 (m, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 153.0 (d, *J* = 4.5 Hz), 142.4, 130.0 (d, *J* = 32.3 Hz), 127.6, 125.6 (q, *J* = 271.8 Hz), 125.5 (q, *J* = 3.8 Hz), 117.4 (d, *J* = 188.1 Hz), 75.6 (d, *J* = 22.1 Hz), 70.2, 61.7–62.4 (m), 20.6 (d, *J* = 1.9 Hz), 16.5 (d, *J* = 6.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = −62.5.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 17.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{23}F_3O_4P$: 367.1281; found: 367.1283.

Diethyl (*E*)-{3-[(Perfluorophenyl)methoxy]but-1-en-1-yl}phosphonate (7ve)

Reaction time: 8.5 d; eluting with CH_2Cl_2/acetone (30:1 + 1% AcOH).

Yield: 148 mg, 381 µmol (38%); yellow liquid; ^{1}H NMR yield using benzaldehyde as the internal standard: 81%; R_f = 0.25 (CH_2Cl_2/acetone, 30:1 + 1% AcOH).

IR (neat): 2983, 2936, 2909, 2875, 1750, 1722, 1656, 1636, 1522, 1504, 1393, 1305, 1248, 1123, 1046, 1022, 957, 936, 848, 821, 787, 753, 673 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.67 (ddd, *J* = 22.4, 17.2, 5.4 Hz, 1 H), 5.90 (ddd, *J* = 20.0, 17.2, 1.4 Hz, 1 H), 4.60 (dt, *J* = 11.0, 1.9 Hz, 1 H), 4.52 (dt, *J* = 11.2, 1.9 Hz, 1 H), 4.26–3.96 (m, 5 H), 1.33 (td, *J* = 7.1, 1.3 Hz, 6 H), 1.29 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 152.4 (d, *J* = 4.8 Hz), 145.7 (dddt, *J* = 249.3, 11.9, 8.2, 3.9 Hz), 141.6 (dtt, *J* = 255.0, 13.4, 5.3 Hz), 137.6 (m), 117.6 (d, *J* = 188.0 Hz), 111.3 (td, *J* = 18.0, 3.8 Hz), 76.3 (d, *J* = 22.3 Hz), 62.1 (dd, *J* = 5.6, 2.1 Hz), 58.0 (d, *J* = 2.9 Hz), 20.7 (d, *J* = 2.0 Hz), 16.5 (d, *J* = 6.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –143.0 (m), –153.5 (m), –161.8 (m).

^{31}P NMR (162 MHz, $CDCl_3$): δ = 17.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{19}F_5O_4P$: 389.0936; found: 389.0933.

(*E*/*Z*)-4-{[4-(Trifluoromethyl)benzyl]oxy}pent-2-enenitrile (7wd)

Reaction time: 1 d; eluting with *n*-pentane/EtOAc (30:1).

Yield: 63 mg, 0.25 mmol (25%) (*E*/*Z* = 2:1); yellow liquid; ^{1}H NMR yield using 1,1,2,2-tetrachloroethane as the internal standard: 54% (*E*/*Z* = 2:1); R_f = 0.10 (*n*-pentane/EtOAc).

IR (neat): *E* isomer: 2982, 2936, 2869, 2360, 2341, 2226, 1729, 1621, 1421, 1325, 1163, 1121, 1065, 1018, 965, 824 cm^{-1}; *Z* isomer: 2984, 2934, 2872, 2360, 2341, 1326, 1163, 1122, 1066, 1019, 824 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*E* isomer) = 7.74–7.55 (m, 2 H), 7.47–7.35 (m, 2 H), 6.70 (dd, *J* = 16.3, 5.2 Hz, 1 H), 5.63 (dd, *J* = 16.4, 1.6 Hz, 1 H), 4.59 (d, *J* = 12.4 Hz, 1 H), 4.54 (d, *J* = 12.5 Hz, 1 H), 4.12 (qdd, *J* = 6.6, 5.2, 1.6 Hz, 1 H), 1.35 (d, *J* = 6.5 Hz, 3 H); δ (*Z* isomer) = 7.66–7.55 (m, 2 H), 7.49–7.44 (m, 2 H), 6.45 (dd, *J* = 11.1, 8.6 Hz, 1 H), 5.48 (dd, *J* = 11.1, 0.9 Hz, 1 H), 4.59 (d, *J* = 12.2 Hz, 1 H), 4.52 (d, *J* = 12.0 Hz, 1 H), 4.50 (m, 1 H), 1.39 (d, *J* = 6.4 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (*E* isomer) = 155.5, 141.8, 130.3 (q, *J* = 32.4 Hz), 127.6, 125.6 (q, *J* = 3.8 Hz), 124.2 (q, *J* = 272.0 Hz), 117.0, 100.0, 74.4, 70.3, 203.; δ (*Z* isomer) = 155.4, 141.9, 130.2 (d, *J* = 32.4 Hz), 127.8, 125.6 (q, *J* = 3.9 Hz), 125.3 (m), 115.2, 100.9, 74.2, 70.6, 20.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{13}F_3NO$: 256.0944; found: 256.0938.

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Supporting Information

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