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Diastereoselective Synthesis of Dihydropyrans via Prins Cyclization of Enol Ethers: Total Asymmetric Synthesis of (+)-Civet Cat Compound

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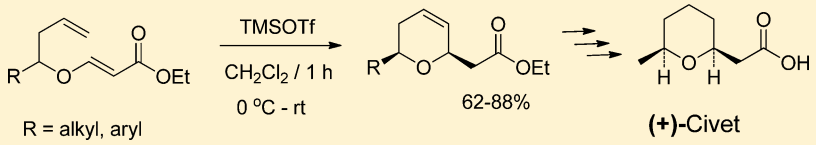
Supporting Information



ABSTRACT: Trimethylsilyl trifluoromethanesulfonate (TMSOTf) can be efficiently used for Prins cyclization of acrylyl enol ethers to 5,6-dihydro-2*H*-pyran-2-acetates stereo- and regioselectively in good yields. The methodology was used for the total synthesis of natural product (+)-civet.

Dihydropyrans are important structural units found in many biologically active natural products such as laulimalide[1] and aspergillide C (Figure 1).[2] This is also important from a synthetic point of view because of the fact that the C=C functionality of the dihydropyrans can be modified to generate polyfunctional tetrahydropyrans by various oxidation and reduction reactions.[3] They can also be used as synthetic intermediates for the preparation of homoallylic alcohols.[4] Apart from these synthetic applications, substituted dihydropyrans are used as a flavoring material for food and beverages.[5] The dihydropyrans are generally synthesized by hetero-Diels–Alder reactions,[6] olefin metathesis,[7] base-promoted cyclizations of sulfenyl dienols,[8] oxonium-ene reactions,[9] [4 + 2] annulations of crotylsilanes,[10] and Prins cyclization reactions.[11] The Prins cyclization is an important reaction for the synthesis of dihydro- and tetrahydropyrans because of its diastereoselectivity.[11] Generally, Prins cyclization reactions of homoallylic/homopropargylic alcohols and aldehydes are conducted under Lewis acidic conditions to form dihydropyrans. The drawback of this type of reaction is the formation of 4-hydroxy tetrahydropyrans and corresponding ethers.[12] In most cases, the reaction is not regioselective.[12] To circumvent this problem, several groups introduced the silyl-Prins reaction.[13] We now present a methodology for the stereo- and regioselective synthesis of 5,6-dihydro-2*H*-pyran-2-acetates using the Prins enol-ether cyclization reaction.

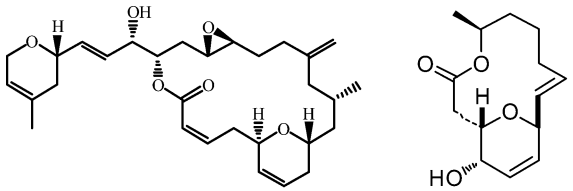


Figure 1. Structures of natural products.

In continuation of our interest in the synthesis of dihydropyrans,[9,11g] we were in search of a stereo- and regioselective methodology for the synthesis of dihydropyrans. Initially, we investigated the reactions of enol-ether **1b**, which was prepared according to a literature procedure[14b] with $BF_3 \cdot Et_2O$ (entry 1) in dry dichloromethane at room temperature. Although the reaction gave the desired 5,6-dihydropyran product **2b** in 25% yield, it also generated 4-chlorobenzaldehyde **3** and alcohol **4**[15] as side products. The reaction was then carried out with different Lewis acids and solvents, and the results are summarized in Table 1. It was concluded from the results in Table 1 that $FeCl_3$, $Sc(OTf)_3$, and $Bi(OTf)_3$ (entries 2, 3, and 6) are not suitable reagents for this transformation because they instead generated the aldehyde and alcohol. However, $In(OTf)_3$ and $InCl_3$ (entries 4 and 5) did not provide any products. The reaction with triflic acid (TfOH) resulted in an intractable mixture containing minor amounts of dihydropyran (see the Supporting Information). TMSOTf (entry 7) was found to be a good reagent for the cyclization reaction, with a 66% yield. The reaction was performed at −20 °C (entry 9) but gave only a 54% yield. The reaction was also performed in acetonitrile (entry 10) and benzene. Although there was no reaction in acetonitrile, an inseparable 3:2 mixture (76%) of 4-phenyl tetrahydropyrans **5** and 5,6-dihydropyran **2b** was formed in benzene (Scheme 1).

The reaction was generalized with different substituents in the homoallyl alcohol component, and the results are summarized in Table 2. The reaction gave only one diastereomer, **2**, with 2,6-cis configurations, which was

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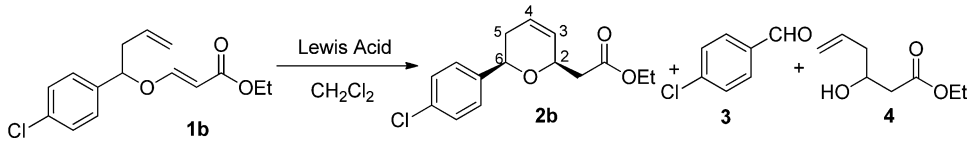
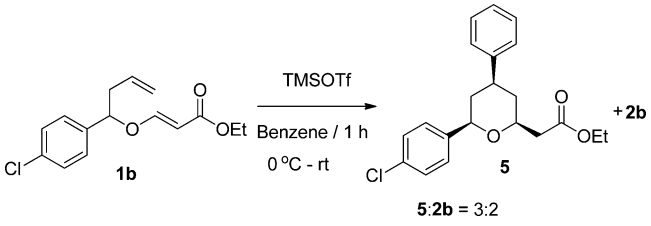
Table 1. Optimization of the Reaction



entry	Lewis acid	temp.	solvents	products (% yield)[a]			
1	$BF_3{\cdot}Et_20$	0 °C to rt	CH_2Cl_2	**2b** (25)	**3** (21)	**4** (19)	**1b** (31)
2	$FeCl_3$	0 °C to rt	CH_2Cl_2		**3** (26)	**4** (16)	**1b** (44)
3	$Sc(OTf)_3$	0 °C to rt	CH_2Cl_2		**3** (30)	**4** (27)	**1b** (23)
4	$ln(OTf)_3$	0 °C to rt	CH_2Cl_2				**1b** (90)
5	$lnCl_3$	0 °C to rt	CH_2Cl_2				**1b** (94)
6	$Bi(OTf)_3$	0 °C to rt	CH_2Cl_2		**3** (33)	**4** (28)	**1b** (26)
7	TMSOTf	0 °C to rt	CH_2Cl_2	**2b** (66)	trace	trace	
8	TMSOTf	rt	CH_2Cl_2	**2b** (64)	trace	trace	
9	TMSOTf	−20 °C	CH_2Cl_2	**2b** (54)	trace	trace	**1b** (35)
10	TMSOTf	0 °C to rt	CH_3CN				**1b** (95)

[a]Yields refer to isolated yield. The compounds were characterized by IR, NMR, and mass spectrometry.

Scheme 1. Reaction in Benzene



confirmed by ^1H and ^{13}C NMR and NOE experiments (see the Supporting Information). The reaction gave good yields with both aromatic and aliphatic substituents. The reaction with an aromatic group having a highly electron-withdrawing group such as a nitro group on the aromatic ring gave decomposed products (entry h). However, *p*-tolyl-substituted substrate **1m** gave **2m** in 30% yield and cross-over product diethyl 5,6-dihydro-2*H*-pyran-2,6-diacetate **2m′** in 33% yield. The reaction is also regiospecific, and only the 5,6-dihydropyran regioisomers were formed in the reactions. The olefin regiochemistry was proved in one case by converting **2a** to the corresponding known methyl ester.[16] The ^1H and ^{13}C NMR spectra of this material were clearly different from those reported for the methyl ester of regioisomeric 3,6-dihydropyran.[13f,16] This contrasts with the formation of benzyl 2-(6-methyl-dihydropyranyl)acetate as a mixture of olefin regioisomers in the indium triflate-promoted reaction of pent-4-en-2-ol with benzyl 3-oxopropanoate.[12]

The proposed mechanism is shown in Scheme 2. Lewis acid activation of the carbonyl group of the ester functionality of enol ether **1** leads to the formation of oxocarbenium ion **7**, which after Prins cyclization forms tetrahydropyranyl cation **8**. The side-chain enolate abstracts a proton from C-3 of the tetrahydropyranyl carbocation **8**, which is acidic in nature because of the presence of a positive charge in the α position, via a second six-membered cyclic transition state to form the 3,4-double bond in final compound **2**.[17] Another possibility is that the bulky equatorial silyl-enol ether and axial hydrogen at C-3 of carbocation **8′** experiences a steric constraint. To release this steric constraint, the axial hydrogen at C-3 eliminates to give the selective elimination product **2**.[18] This explains the formation of a single regioisomer.

The formation of aldehyde **3** and alcohol **4** (Table 1) can be explained by fragmentation reactions from intermediate cation **8**. A generalized mechanism for these types of crossover products is shown in Scheme 3. The tetrahydropyranyl cation **8** undergoes retro-Prins fragmentation in two different pathways, **A** and **B**, to give aldehydes **10** and **13** and alcohols **11** and **14**, respectively, after hydrolysis of **9** and **12**. Alcohol **11** and aldehyde **13** combine under these reaction conditions to give cross-over product **2m′**, as shown in Table 1.

The methodology was utilized for the asymmetric synthesis of *cis*-6-methyltetrahydropyran-2-yl acetic acid, or civet, which was isolated from the glandular secretions of the civet cat by Maurer in 1979 and used as an additive by the perfumery industry.[19]

The synthetic strategy was related to that used in Nussbaumer and Frater's synthesis of racemic **20**.[14a] The synthesis started with (2*S*)-pent-4-en-2-ol (**15**) as shown in Scheme 4. (2*S*)-Pent-4-en-2-ol was O-alkylated with ethyl propiolate (**16**) in the presence of *N*-methyl morpholine (NMM) in dichloromethane to give enol ether **17** in 80% yield. Prins cyclization of enol ether **17** and subsequent hydrogenation with palladium on charcoal gave tetrahydropyran **19**, which was then hydrolyzed with methanolic sodium hydroxide to give the civet cat compound in 85% yield and in 17% yield over four steps. The specific rotation of the synthesized civet cat compound was found to be $[\alpha]_D^{20}$ +22.4° (*c* 0.25, $CHCl_3$), which compares favorably with the literature data: lit.[20a] $[\alpha]_D^{20}$ +22.0° (*c* 1.23, $CHCl_3$), lit.[20b] $[\alpha]_D^{20}$ +21.0° (*c* 0.3, $CHCl_3$), and lit.[20c] $[\alpha]_D^{20}$ +21.9° (*c* 1.108, $CHCl_3$). The ^1H and ^{13}C NMR spectral data are in good agreement with those previously reported for the civet cat secretion.[20] The good agreement of the specific rotation with the reported data indicates that under these reaction conditions the product does not undergo racemization[11g,21] (Scheme 4).

In conclusion, we have developed a methodology for the synthesis of 5,6-dihydro-2*H*-pyran-2-acetates from enol ethers using the Prins cyclization reaction. The reaction is diastereo- and regioselective and proceeds in good yields in most cases. The utility of this methodology was demonstrated by a short asymmetric synthesis of a natural product (+)-civet cat secretion from (*S*)-pent-4-en-2-ol n in good yield.

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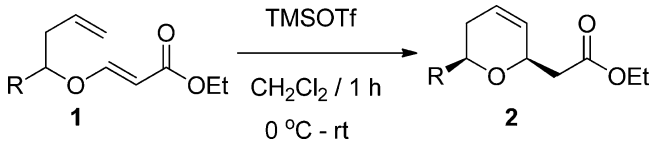
Table 2. Synthesis of Dihydropyrans



Entry	Substrate R =	Product 2	% Yield[a]
a	Ph	**2a**	60
b	4-Cl-Ph	**2b**	66
c	2-Cl-Ph	**2c**	67
d	4-Br-Ph	**2d**	69
e	3-Br-Ph	**2e**	72
f	4-MeO_2C-Ph	**2f**	64
g	2-Naphthyl	**2g**	62
h	4-NO_2-Ph	**2h**	dp
i	$PhCH_2$	**2i**	64
j	$(CH_3)_2CHCH_2$	**2j**	81
k	*n*-C_6H_{13}	**2k**	79
l	*cyclo*-C_6H_{11}	**2l**	66
m	4-Me-Ph	**2m**	30
		2m'	33

[a]Yields refer to isolated yield. dp, decomposed products. The compounds were characterized by IR, NMR, and mass spectrometry.

EXPERIMENTAL SECTION

General Experimental Section. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on 600, 400, and (150, 100, 75) MHz NMR spectrometer, respectively, using TMS as an internal standard. Chiral (*S*)-pent-4-ene-2-ol (**15**) was purchased from a chemical supplier. Compounds **1a** and **1k** are known compounds that were prepared according to a literature procedure.[14c] Their IR, NMR, and HRMS data agreed well with the reported data. The same procedure[14c] was used to prepare compounds **1b**−**1j**, **1l**, and **1m**. Compounds **19** and **20** are also known, and their preparations were carried out according to literature procedures. The IR, NMR, and HRMS data for these compounds agree well with the respective literature data.

*(E)-Ethyl 3-((1-(4-Chlorophenyl)but-3-en-1-yl)oxy)acrylate (**1b**).* Pale-yellow oil (235 mg, 84%). ^1H NMR (400 MHz, $CDCl_3$): δ 1.23 (t, J = 7.2 Hz, 3H), 2.48−2.55 (m, 1H), 2.64−2.71 (m, 1H), 4.11 (q, J = 7.2 Hz, 2H), 4.87 (t, J = 6.0 Hz, 1H), 5.06−5.10 (m, 2H), 5.19 (d, J = 12.8 Hz, 1H), 5.64−5.75 (m, 1H), 7.21 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 12.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 41.7, 59.7, 83.0, 98.8, 118.6, 127.6, 128.9, 132.5, 134.0, 138.1, 161.0, 167.4. IR (KBr, neat): 2983, 2935, 1710, 1634, 1487, 1368, 1132, 1043, 829, 744 cm^{-1}. HRMS (APCI) calcd for $C_{15}H_{18}ClO_3$ $(M + H)^+$, 281.0939; found, 281.0949.

*(E)-Ethyl 3-((1-(2-Chlorophenyl)but-3-en-1-yl)oxy)acrylate (**1c**).* Pale-yellow oil (232 mg, 83%). ^1H NMR (400 MHz, $CDCl_3$): δ 1.15 (t, J = 7.2 Hz, 3H), 2.53 (dd, J = 6.8 and 5.6 Hz, 2H), 4.06 (q, J =

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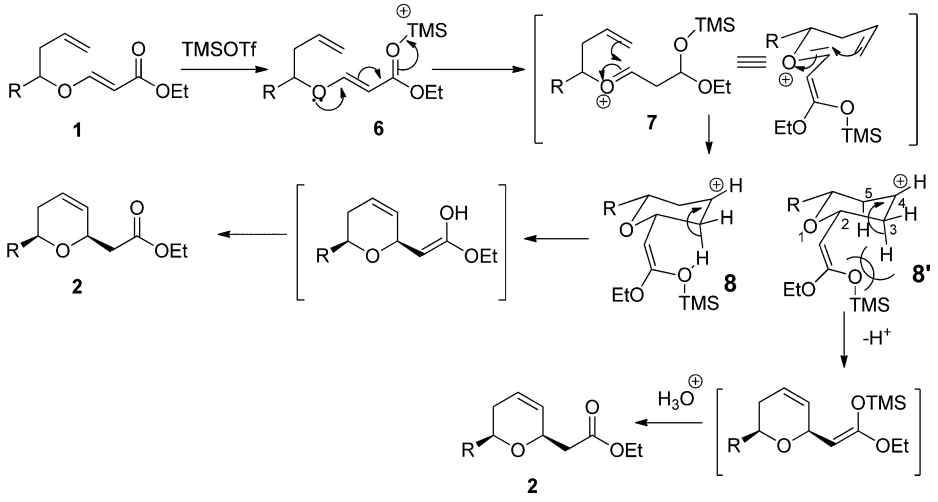
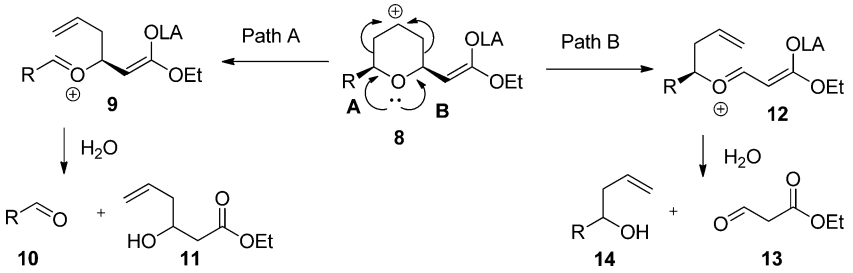
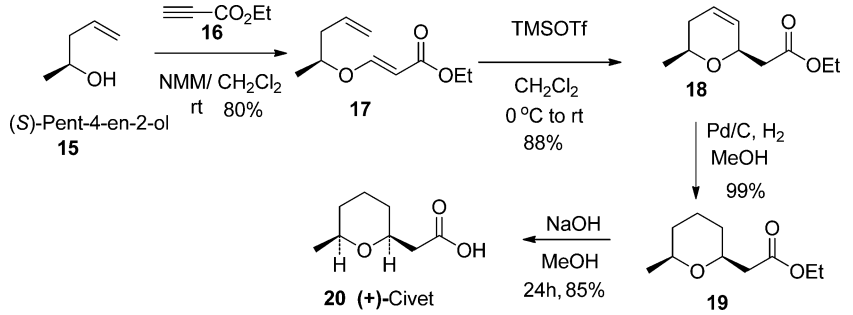
Scheme 2. Mechanism of the Reaction



Scheme 3. Mechanism for the Formation of Alcohols 11 and 14 and Aldehydes 10 and 13



Scheme 4. Short Synthesis of (+)-Civet



7.2 Hz, 2H), 5.02−5.06 (m, 2H), 5.09 (d, J = 12.4 Hz, 1H), 5.30 (t, J = 6.0 Hz, 1H), 5.68−5.79 (m, 1H), 7.14−7.32 (m, 4H), 7.43 (d, J = 12.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 40.2, 59.7, 79.7, 98.7, 118.5, 127.2, 127.4, 129.3, 129.4, 129.6, 132.7, 137.2, 161.1, 167.5. IR (KBr, neat): 2983, 2939, 1710, 1633, 1470, 1320, 1132, 1043, 830, 755 cm^{-1}. HRMS (APCI) calcd for $C_{15}H_{18}ClO_3$ $(M + H)^+$, 281.0939; found, 281.0949.

*(E)-Ethyl 3-((1-(4-Bromophenyl)but-3-en-1-yl)oxy)acrylate (**1d**).* Colorless oil (288 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (t, J = 7.2 Hz, 3H), 2.48−2.55 (m, 1H), 2.63−2.70 (m, 1H), 4.01−4.16 (m, 2H), 4.85 (t, J = 7.2 Hz, 1H), 5.06−5.11 (m, 2H), 5.18 (d, J = 12.8 Hz, 1H), 5.64−5.75 (m, 1H), 7.14 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 12.8 Hz, 1H), 7.49 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 41.7, 59.8, 83.0, 98.9, 118.7, 122.2, 127.9, 131.9, 132.5, 138.6, 161.0, 167.5. IR (KBr, neat): 2983, 2940, 1712, 1632, 1480, 1132, 1055, 828, 743 cm^{-1}. HRMS (APCI) calcd for $C_{15}H_{18}BrO_3$ $(M + H)^+$, 325.0434; found, 325.0442.

*(E)-Ethyl 3-((1-(3-Bromophenyl)but-3-en-1-yl)oxy)acrylate (**1e**).* Colorless oil (278 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (t, J = 7.2 Hz, 3H), 2.51−2.59 (m, 1H), 2.66−2.73 (m, 1H), 4.06−4.15 (m, 2H), 4.96 (dd, J = 7.2 and 5.6 Hz, 1H), 5.05−5.10 (m, 2H), 5.19 (d, J = 12.8 Hz, 1H), 5.63−5.75 (m, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 12.8 Hz, 1H), 8.04 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 41.7, 59.8, 82.9, 98.9, 118.8, 122.8, 124.8, 129.1, 130.3, 131.4, 132.4, 141.9, 161.0, 167.5. IR (KBr, neat): 2982, 2937, 1707, 1634, 1471, 1194, 1043, 831, 742 cm^{-1}. HRMS (APCI) calcd for $C_{15}H_{18}BrO_3$ $(M + H)^+$, 325.0434; found, 325.0442.

*(E)-Methyl 4-(1-((3-Ethoxy-3-oxoprop-1-en-1-yl)oxy)but-3-en-1-yl)benzoate (**1f**).* Pale-yellow oil (273 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (t, J = 7.2 Hz, 3H), 2.51−2.59 (m, 1H), 2.66−2.73 (m, 1H), 3.91 (s, 3H), 4.06−4.15 (m, 2H), 4.96 (dd, J = 7.2 and 5.6 Hz, 1H), 5.05−5.10 (m, 2H), 5.19 (d, J = 12.8 Hz, 1H), 5.63−5.75 (m, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 12.8 Hz, 1H), 8.04 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 41.8, 52.3, 59.9, 83.2, 99.1, 118.9, 126.3, 130.1, 130.2, 132.5, 144.7, 161.1, 166.7, 167.6. IR (KBr, neat): 2985, 1720, 1635, 1445, 1282, 1129, 1044, 829, 770 cm^{-1}. HRMS (APCI) calcd for $C_{17}H_{21}O_5$ $(M + H)^+$, 305.1384; found, 305.1397.

*(E)-Ethyl 3-((1-(Naphthalen-2-yl)but-3-en-1-yl)oxy)acrylate (**1g**).* Colorless oil (230 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18 (t, J = 7.2 Hz, 3H), 2.57−2.65 (m, 1H), 2.73−2.79 (m, 1H), 4.01−4.13 (m,

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2H), 5.01−5.12 (m, 3H), 5.24 (d, J = 12.4 Hz, 1H), 5.68−5.79 (m, 1H), 7.37 (dd, J = 8.8 and 1.6 Hz, 1H), 7.46−7.51 (m, 2H), 7.53 (d, J = 12.4 Hz, 1H), 7.70 (s, 1H), 7.80−7.85 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 41.8, 59.8, 84.1, 98.8, 118.5, 123.8, 125.7, 126.4, 126.5, 127.9, 128.1, 128.9, 133.0, 133.2, 133.3, 137.0, 161.4, 167.8. IR (KBr, neat): 2981, 2934, 1706, 1633, 1324, 1130, 1045, 824, 749 cm^{-1}. HRMS (APCI) calcd for $C_{19}H_{21}O_3$ (M + H)$^+$, 297.1485; found, 297.1500.

(E)-Ethyl 3-((1-(4-Nitrophenyl)but-3-en-1-yl)oxy)acrylate (**1h**). Colorless solid, mp 109−110 °C (238 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.25 (t, J = 7.2 Hz, 3H), 2.56−2.61 (m, 1H), 2.67−2.72 (m, 1H), 4.07−4.14 (m, 2H), 5.04 (t, J = 6.8 Hz, 1H), 5.05−5.11 (m, 2H), 5.20 (d, J = 12.8 Hz, 1H), 5.68−5.75 (m, 1H), 7.46 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 12.8 Hz, 1H), 8.24 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 41.6, 60.0, 82.4, 99.4, 119.4, 124.0, 127.1, 131.9, 146.8, 147.8, 166.1, 167.3. IR (KBr, neat): 2983, 2929, 1711, 1615, 1524, 1341, 1189, 1132, 1042, 848, 745 cm^{-1}. HRMS (APCI) calcd for $C_{15}H_{17}NO_5$ (M + H)$^+$, 292.1179; found, 292.1178.

(E)-Ethyl 3-((1-Phenylpent-4-en-2-yl)oxy)acrylate (**1i**). Colorless oil (236 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.25 (t, J = 7.2 Hz, 3H), 2.37 (t, J = 7.2 Hz, 2H), 2.86−2.95 (m, 2H), 4.10−4.19 (m, 3H), 5.09−5.17 (m, 2H), 5.24 (d, J = 12.4 Hz, 1H), 5.75−5.82 (m, 1H), 7.17 (d, J = 6.8 Hz, 2H), 7.23−7.31 (m, 3H), 7.41 (d, J = 12.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 38.2, 40.3, 59.8, 83.9, 97.6, 118.8, 126.9, 128.7, 129.6, 133.1, 137.1, 162.2, 168.1. IR (KBr, neat): 2982, 2933, 1703, 1641, 1322, 1132, 1025, 832, 701 cm^{-1}. HRMS (APCI) calcd for $C_{16}H_{21}O_3$ (M + H)$^+$, 261.1485; found, 261.1489.

(E)-Ethyl 3-((6-Methylhept-1-en-4-yl)oxy)acrylate (**1j**). Pale-yellow oil (164 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (d, J = 6.4 Hz, 3H), 0.89 (d, J = 6.4 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H), 1.28−1.34 (m, 1H), 1.51−1.58 (m, 1H), 1.62−1.72 (m, 1H), 2.31 (t, J = 5.6 Hz, 2H), 3.95−4.01 (m, 1H), 4.12 (q, J = 7.2 Hz, 2H), 5.05−5.11 (m, 2H), 5.21 (d, J = 12.4 Hz, 1H), 5.66−5.77 (m, 1H), 7.48 (d, J = 12.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 21.7, 22.7, 24.1, 38.8, 42.6, 59.1, 81.1, 96.8, 118.0, 132.8, 162.0, 167.5. IR (KBr, neat): 2955, 1711, 1633, 1463, 1376, 1207, 1130, 1043, 832, 742 cm^{-1}. HRMS (APCI) calcd for $C_{13}H_{23}O_3$ (M + H)$^+$, 227.1642; found, 227.1658.

(E)-Ethyl 3-((1-Cyclohexylbut-3-en-1-yl)oxy)acrylate (**1l**). Pale-yellow oil (179 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90−1.07 (m, 3H), 1.10−1.27 (m, 6H), 1.49−1.69 (m, 5H), 1.76−2.10 (m, 1H), 2.22−2.28 (m, 1H), 4.08 (q, J = 7.2 Hz, 2H), 4.14−4.21 (m, 1H), 5.00−5.07 (m, 2H), 5.15 (d, J = 12.8 Hz, 1H), 5.63−5.81 (m, 1H), 7.41 (d, J = 12.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 26.0, 26.1, 26.4, 28.1, 28.9, 35.9, 41.4, 59.6, 88.5, 96.7, 118.1, 133.7, 163.5, 169.4. IR (KBr, neat): 2928, 2856, 1711, 1632, 1450, 1244, 1132, 1042, 832, 743 cm^{-1}. HRMS (APCI) calcd for $C_{15}H_{25}O_3$ (M + H)$^+$, 253.1798; found, 253.1798.

(E)-Ethyl 3-((1-(p-Tolyl)but-3-en-1-yl)oxy)acrylate (**1m**). Pale-yellow oil (241 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18 (t, J = 7.2 Hz, 3H), 2.30 (s, 3H), 2.46−2.54 (m, 1H), 2.63−2.71 (m, 1H), 4.02−4.10 (m, 2H), 4.84 (dd, J = 7.2 and 6.4 Hz, 1H), 5.04−5.10 (m, 2H), 5.21 (d, J = 12.8 Hz, 1H), 5.65−5.78 (m, 1H), 7.00−7.18 (m, 4H), 7.50 (d, J = 12.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 21.0, 41.7, 59.5, 83.3, 98.3, 118.0, 126.1, 129.3, 133.1, 136.5, 137.9, 161.3, 167.5. IR (KBr, neat): 2983, 2932, 1709, 1635, 1452, 1318, 1132, 819, 750 cm^{-1}. HRMS (APCI) calcd for $C_{16}H_{21}O_3$ (M + H)$^+$, 261.1485; found, 261.1480.

Synthesis of Ethyl-2-(6-phenyl-5,6-dihydro-2H-pyran-2-yl)acetate (**2a**). To a solution of (*E*)-ethyl-3-((1-phenylbut-3-en-1-yl)oxy)-acrylate (246 mg, 1.00 mmol) in dry dichloromethane (2 mL) at 0 °C was added trimethylsilyl trifluoromethane sulfonate (0.18 mL, 1.00 mmol) under a N_2 atmosphere. The temperature was slowly brought to room temperature. The reaction mixture was stirred at room temperature for 1 h. The progress of the reaction was monitored by TLC with ethyl acetate and hexane (EtOAc/hexane 1:9) as eluents. After the completion of the reaction, the solvent was removed on a rotary evaporator and quenched with a saturated solution of $NaHCO_3$ (3 mL). The product was extracted with ethyl acetate (2 × 15 mL) and then washed with brine solution (3 mL). The organic layer was dried (Na_2SO_4) and evaporated to give the crude product, which was purified by short column chromatography over silica gel (EtOAc/hexane 1:9) to give **2a** (147 mg, 60%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (t, J = 7.2 Hz, 3H), 2.25−2.29 (m, 2H), 2.55 (dd, J = 15.2 and 6.4 Hz, 1H), 2.68 (dd, J = 15.2 and 7.6 Hz, 1H), 4.16 (dq, J = 7.2 and 2.4 Hz, 2H), 4.64 (dd, J = 8.8 and 5.2 Hz, 1H), 4.73−4.78 (m, 1H), 5.76 (ddd, J = 9.6, 3.6, and 1.6 Hz, 1H), 5.76 (ddd, J = 9.6, 4.8, and 2.4 Hz, 1H), 7.23−7.29 (m, 2H), 7.31−7.42 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 32.9, 40.9, 60.7, 72.5, 75.7, 125.8, 127.5, 128.5, 128.7, 129.0, 142.6, 171.3. IR (KBr, neat): 2921, 2847, 1730, 1602, 1453, 1382, 1285, 1172, 1070, 1026, 752, 696 cm^{-1}. HRMS (APCI) calcd for $C_{15}H_{19}O_3$ (M + H)$^+$, 247.1329; found, 247.1332. Compound **2a** was transesterified using trimethylsilyl chloride in methanol, as per a literature procedure,[22] to the corresponding methyl ester, methyl 2-((2*S*,6*S*)-6-phenyl-5,6-dihydro-2*H*-pyran-2-yl)acetate **2a′** as a colorless oil (150 mg, 65%). The NMR, IR, and HRMS data agreed well with the reported data (see the Supporting Information for spectra).[16]

Ethyl-2-(6-(4-chlorophenyl)-5,6-dihydro-2H-pyran-2-yl)acetate (**2b**). Colorless oil (184 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (t, J = 7.2 Hz, 3H), 2.20−2.25 (m, 2H), 2.54 (dd, J = 15.2 and 7.5 Hz, 1H), 2.67 (dd, J = 15.2 and 7.5 Hz, 1H), 4.14−4.20 (m, 2H), 4.61 (dd, J = 8.8 and 5.2 Hz, 1H), 4.72−4.80 (m, 1H), 5.74−5.79 (m, 1H), 5.91−5.96 (m, 1H), 7.22−7.35 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 32.9, 40.9, 60.7, 72.5, 74.9, 125.6, 127.2, 128.6, 129.1, 133.1, 141.2, 171.2. IR (KBr, neat): 2981, 2925, 1735, 1655, 1492, 1393, 1166, 1163, 1085, 1030, 823 cm^{-1}. HRMS (APCI) calcd for $C_{15}H_{17}ClO_3$ (M + H)$^+$, 281.0939; found, 281.0949.

Ethyl-2-(6-(2-chlorophenyl)-5,6-dihydro-2H-pyran-2-yl)acetate (**2c**). Colorless oil (187 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (t, J = 7.2 Hz, 3H), 2.40−2.50 (m, 2H), 2.56 (dd, J = 15.2 and 6.4 Hz, 1H), 2.68 (dd, J = 15.2 and 7.6 Hz, 1H), 4.11−4.22 (m, 2H), 4.74−4.84 (m, 1H), 4.98 (dd, J = 10.4 and 3.2 Hz, 1H), 5.75−5.79 (m, 1H), 5.92−5.98 (m, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 7.6 Hz, 1H), 7.30 (d, J = 7.6 Hz, 1H), 7.57 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 31.4, 41.0, 60.7, 72.6, 72.7, 125.9, 127.2, 127.3, 128.5, 128.8, 129.2, 131.6, 140.4, 171.2. IR (KBr, neat): 2979, 2925, 1735, 1585, 1473, 1380, 1172, 1079, 1037, 756 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{17}ClNaO_3$ (M + Na)$^+$, 303.0758; found, 303.0756.

Ethyl-2-(6-(4-bromoophenyl)-5,6-dihydro-2H-pyran-2-yl)acetate (**2d**). Colorless oil (223 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.27 (t, J = 7.2 Hz, 3H), 2.20−2.27 (m, 2H), 2.54 (dd, J = 15.2 and 6.4 Hz, 1H), 2.67 (dd, J = 15.2 and 7.6 Hz, 1H), 4.11−4.21 (m, 2H), 4.60 (dd, J = 8.4 and 4.8 Hz, 1H), 4.72−4.79 (m, 1H), 5.74−5.79 (m, 1H), 5.90−5.96 (m, 1H), 7.23 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 32.9, 40.9, 60.7, 72.5, 75.0, 121.3, 125.6, 127.6, 129.1, 131.5, 141.7, 171.2. IR (KBr, neat): 2923, 2850, 1733, 1647, 1483, 1382, 1169, 1077, 1023, 678 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{17}BrNaO_3$ (M + Na)$^+$, 347.0253; found, 347.0251 (major) and 349.0207 (minor).

Ethyl-2-(6-(3-bromoophenyl)-5,6-dihydro-2H-pyran-2-yl)acetate (**2e**). Colorless oil (233 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (t, J = 7.2 Hz, 3H), 2.21−2.27 (m, 2H), 2.54 (dd, J = 14.8 and 6.0 Hz, 1H), 2.67 (dd, J = 14.8 and 7.6 Hz, 1H), 4.12−4.22 (m, 2H), 4.61 (dd, J = 9.2 and 5.2 Hz, 1H), 4.71−4.79 (m, 1H), 5.74−5.79 (m, 1H), 5.90−5.96 (m, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.26 (d, J = 7.6 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.53 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 32.7, 40.8, 60.7, 72.4, 74.7, 122.5, 124.3, 125.4, 128.8, 128.9, 129.9, 130.4, 144.9, 171.1. IR (KBr, neat): 2923, 2850, 1733, 1569, 1381, 1170, 1078, 1029, 781, 695 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{17}BrNaO_3$ (M + Na)$^+$, 347.0253; found, 347.0251 (major) and 349.0207 (minor).

Methyl-4-(6-(2-ethoxy-2-oxoethyl)-3,6-dihydro-2H-pyran-2-yl)-benzoate (**2f**). Colorless liquid (194 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (t, J = 7.2 Hz, 3H), 2.21−2.30 (m, 2H), 2.56 (dd, J = 15.2 and 6.4 Hz, 1H), 2.69 (dd, J = 15.2 and 7.6 Hz, 1H), 3.91 (s, 3H), 4.11−4.23 (m, 2H), 4.70 (dd, J = 10.0 and 4.0 Hz, 1H), 4.74−4.80 (m, 1H), 5.75−5.80 (m, 1H), 5.93−5.98 (m, 1H), 7.43 (d, J = 8.0 Hz, 2H), 7.99 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 32.8, 40.8, 52.2, 60.7, 72.4, 75.1, 125.5, 125.6, 129.0, 129.1, 129.7, 147.7, 167.1, 171.2. IR (KBr, neat): 2945, 2850, 1727, 1617, 1438,

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1382, 1174, 1105, 1025, 764, 702 cm^{-1}. HRMS (APCI) calcd for $C_{17}H_{20}O_5$ $(M + H)^+$, 305.1384; found, 305.1394.

*Ethyl 2-(6-(naphthalen-1-yl)-5,6-dihydro-2H-pyran-2-yl)acetate (**2g**).* Colorless oil (183 mg, 62%). ^1H NMR (400 MHz, $CDCl_3$): δ 1.27 (t, J = 7.2 Hz, 3H), 2.31−2.37 (m, 2H), 2.58 (dd, J = 14.8 and 6.4 Hz, 1H), 2.73 (dd, J = 14.8 and 7.6 Hz, 1H), 4.12−4.21 (m, 2H), 4.77−4.90 (m, 2H), 5.78−5.82 (m, 1H), 5.94−6.0 (m, 1H), 7.41−7.64 (m, 3H), 7.79−7.98 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 32.9, 41.0, 60.7, 72.6, 75.8, 124.3, 124.4, 125.8 (2C), 126.2, 127.8, 128.2 (2C), 129.1, 133.0, 133.5, 140.1, 171.3. IR (KBr, neat): 2945, 2850, 1727, 1617, 1438, 1382, 1174, 1105, 1025, 764, 702 cm^{-1}. HRMS (ESI) calcd for $C_{19}H_{20}NaO_3$ $(M + Na)^+$, 319.1305; found, 319.1317.

*Ethyl-2-(6-benzyl-5,6-dihydro-2H-pyran-2-yl)acetate (**2i**).* Colorless oil (166 mg, 64%). ^1H NMR (600 MHz, $CDCl_3$): δ 1.24 (t, J = 7.2 Hz, 3H), 1.86−1.92 (m, 1H), 2.00−2.07 (m, 1H), 2.44 (dd, J = 15.0 and 6.0 Hz, 1H), 2.55 (dd, J = 15.0 and 8.4 Hz, 1H), 2.68 (dd, J = 14.0 and 6.0 Hz, 1H), 2.93 (dd, J = 14.0 and 6.8 Hz, 1H), 3.77−3.80 (m, 1H), 4.07−4.17 (m, 2H), 4.50−4.55 (m, 1H), 5.62−5.66 (m, 1H), 5.78−5.83 (m, 1H), 7.17−7.29 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 30.7, 41.0, 42.4, 60.6, 72.0, 75.0, 125.7, 126.3, 128.3, 128.9, 129.7, 138.7, 171.3. IR (KBr, neat): 2923, 2848, 1734, 1596, 1376, 1170, 1085, 1033, 741, 696 cm^{-1}. HRMS (APCI) calcd for $C_{16}H_{20}O_3$ $(M + H)^+$, 261.1485; found, 261.1489.

*Ethyl 2-(6-Isobutyl-5,6-dihydro-2H-pyran-2-yl)acetate (**2j**).* Colorless oil (183 mg, 81%). ^1H NMR (400 MHz, $CDCl_3$): δ 0.84 (d, J = 6.4 Hz, 3H), 0.85 (d, J = 6.4 Hz, 3H), 1.21 (t, J = 7.2 Hz, 3H), 1.42−1.48 (m, 1H), 1.72−1.80 (m, 1H), 1.86−1.94 (m, 2H), 1.95−2.00 (m, 1H), 2.39 (dd, J = 15.2 and 6.0 Hz, 1H), 2.50 (dd, J = 15.2 and 8.0 Hz, 1H), 3.55−3.60 (m, 1H), 4.11 (q, J = 7.2 Hz, 2H), 4.47−4.52 (m, 1H), 5.58−5.62 (m, 1H), 5.77−5.81 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 22.5, 23.2, 24.6, 31.5, 40.9, 45.0, 60.5, 71.9, 72.5, 126.0, 129.0, 171.3. IR (KBr, neat): 2955, 2917, 1738, 1650, 1465, 1375, 1171, 1084, 1035, 685 cm^{-1}. HRMS (APCI) calcd for $C_{13}H_{22}O_3$ $(M + H)^+$, 227.1642; found, 227.1633.

*Ethyl 2-(6-Hexyl-5,6-dihydro-2H-pyran-2-yl)acetate (**2k**).* Colorless oil (200 mg, 79%). ^1H NMR (400 MHz, $CDCl_3$): δ 0.84 (d, J = 6.4 Hz, 3H), 1.20−1.30 (m, 9H), 1.34−1.42 (m, 2H), 1.48−1.53 (m, 2H), 1.88−1.94 (m, 2H), 2.39 (dd, J = 15.2 and 6.4 Hz, 1H), 2.52 (dd, J = 15.2 and 7.6 Hz, 1H), 3.37−3.52 (m, 1H), 4.12 (q, J = 7.2 Hz, 2H), 4.45−4.52 (m, 1H), 5.58−5.64 (m, 1H), 5.77−5.82 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 14.3, 22.6, 25.4, 29.3, 31.1, 31.9, 36.0, 40.8, 60.5, 71.8, 74.2, 125.8, 128.9, 171.3. IR (KBr, neat): 2956, 2928, 1738, 1653, 1466, 1395, 1164, 1081, 1031, 685 cm^{-1}. HRMS (APCI) calcd for $C_{15}H_{26}O_3$ $(M + H)^+$, 255.1955; found, 255.1943.

*Ethyl 2-(6-Cyclohexyl-5,6-dihydro-2H-pyran-2-yl)acetate (**2l**).* Colorless oil (166 mg, 66%). ^1H NMR (400 MHz, $CDCl_3$): δ 0.85−0.98 (m, 2H), 1.08−1.20 (m, 2H), 1.23 (t, J = 7.2 Hz, 3H), 1.28−1.38 (m, 2H), 1.58−1.70 (m, 4H), 1.91−2.98 (m, 3H), 2.39 (dd, J = 14.8 and 6.0 Hz, 1H), 2.50 (dd, J = 14.8 and 8.0 Hz, 1H), 3.18−3.24 (m, 1H), 4.11 (q, J = 7.2 Hz, 2H), 4.42−4.50 (m, 1H), 5.58−5.63 (m, 1H), 5.78−5.84 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.5, 26.1, 26.3, 26.8, 28.5, 28.6, 29.3, 41.1, 43.0, 60.6, 72.2, 78.6, 126.2, 129.1, 171.5. IR (KBr, neat): 2925, 2852, 1731, 1447, 1287, 1174, 1080, 1033, 853, 682 cm^{-1}. HRMS (APCI) calcd for $C_{15}H_{24}O_3$ $(M + H)^+$, 253.1797; found, 253.1795.

*Ethyl 2-(6-(p-Tolyl)-5,6-dihydro-2H-pyran-2-yl)acetate (**2m**).* Colorless oil (78 mg, 30%). ^1H NMR (600 MHz, $CDCl_3$): δ 1.27 (t, J = 7.2 Hz, 3H), 2.24−2.32 (m, 2H), 2.33 (s, 3H), 2.53 (dd, J = 15.6 and 6.6 Hz, 1H), 2.68 (dd, J = 15.6 and 7.2 Hz, 1H), 4.14−4.19 (m, 2H), 4.61 (dd, J = 10.0 and 3.6 Hz, 1H), 4.70−4.78 (m, 1H), 5.75−5.78 (m, 1H), 5.92−5.96 (m, 1H), 7.14 (d, J = 7.8 Hz, 2H), 7.25 (d, J = 7.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 21.3, 32.9, 40.9, 60.7, 72.5, 75.6, 125.8, 125.9, 129.0, 129.1, 137.2, 139.7, 171.3. IR (KBr, neat): 2924, 2857, 1733, 1591, 1455, 1280, 1172, 1074, 1030, 810, 678 cm^{-1}. HRMS (ESI) calcd for $C_{16}H_{20}NaO_3$ $(M + Na)^+$, 283.1305; found, 283.1301.

*Diethyl 2,2′-(3,6-Dihydro-2H-pyran-2,6-diyl)diacetate (**2m′**).* Colorless oil (84 mg, 33%). ^1H NMR (400 MHz, $CDCl_3$): δ 1.26 (t, J = 7.2 Hz, 3H), 1.27 (t, J = 7.2 Hz, 3H), 2.02−2.08 (m, 2H), 2.45−2.63 (m, 4H), 4.02−4.10 (m, 1H), 4.15 (q, J = 7.2 Hz, 4H), 4.60−4.64 (m, 1H), 5.64−5.69 (m, 1H), 5.58−5.88 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4 (2C), 30.5, 40.7, 41.2, 60.8 (2C), 70.8, 72.0, 125.3, 128.8, 171.5, 171.7. IR (KBr, neat): 2980, 2924, 1733, 1579, 1378, 1286, 1166, 1081, 1031, 810, 680 cm^{-1}. HRMS (ESI) calcd for $C_{13}H_{20}NaO_5$ $(M + Na)^+$, 279.1203; found, 279.1210.

*Ethyl 2-(6-(4-Chlorophenyl)-4-phenyltetrahydro-2H-pyran-2-yl)-acetate (**5**) and Ethyl-2-(6-(4-chlorophenyl)-5,6-dihydro-2H-pyran-2-yl)acetate (**2b**) (**5**/**2b** 1:1).* Colorless oil (250 mg, 76%). ^1H NMR (400 MHz, $CDCl_3$): δ 1.20−1.30 (m, 6H), 1.50−1.68 (m, 2H), 1.96−2.15 (m, 2H), 2.20−2.24 (m, 2H), 2.54 (dd, J = 15.2 and 7.5 Hz, 2H), 2.60−2.75 (m, 2H), 2.98−3.04 (m, 1H), 4.10−4.21 (m, 5H), 4.52−4.55 (m, 1H), 4.58−4.62 (m, 1H), 4.72−4.78 (m, 1H), 5.75−5.78 (m, 1H), 5.91−5.95 (m, 1H), 7.19−7.35 (m, 10H), 7.43−7.46 (m, 3H).

*(S,E)-Ethyl 3-(Pent-4-en-2-yloxy)acrylate (**17**).*[14c] Colorless oil (147 mg, 80%). ^1H NMR (400 MHz, $CDCl_3$): δ 1.15 (d, J = 6.0 Hz, 3H), 1.18 (t, J = 7.2 Hz, 3H), 2.18−2.24 (m, 1H), 2.28−2.36 (m, 1H), 3.98−4.10 (m, 3H), 5.00−5.10 (m, 2H), 5.15 (d, J = 12.4 Hz, 1H), 5.62−5.71 (m, 1H), 7.44 (d, J = 12.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 19.2, 40.2, 59.2, 78.4, 97.1, 117.9, 132.9, 161.4, 167.5. IR (KBr, neat): 2982, 2934, 1709, 1634, 1454, 1378, 1130, 1050, 832, 740 cm^{-1}. HRMS (APCI) calcd for $C_{10}H_{16}O_3$ $(M + H)^+$, 185.1172; found, 185.1179. $[\alpha]_D^{20}$ −8.2 (c 1.00, CH_2Cl_2).

*Ethyl 2-(2R,6S)-6-Methyl-5,6-dihydro-2H-pyran-2-yl)acetate (**18**).* Prepared as per the procedure mentioned for the synthesis of compound **2a**. Colorless oil (161 mg, 88%). ^1H NMR (400 MHz, $CDCl_3$): δ 1.19 (d, J = 6.0 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H), 1.90−1.95 (m, 2H), 2.40 (dd, J = 15.2 and 6.4 Hz, 1H), 2.55 (dd, J = 15.2 and 7.6 Hz, 1H), 3.64−3.73 (m, 1H), 4.13 (q, J = 7.2 Hz, 2H), 4.50−4.56 (m, 1H), 5.60−5.65 (m, 1H), 5.77−5.83 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 21.7, 32.8, 40.9, 60.7, 70.4, 71.8, 125.9, 128.9, 171.4. IR (KBr, neat): 2984, 1721, 1621, 1462, 1372, 1249, 1178, 1097, 1027, 858, 748 cm^{-1}. HRMS (APCI) calcd for $C_{10}H_{16}O_3$ $(M + H)^+$, 185.1172; found, 185.1181. $[\alpha]_D^{20}$ +3.7 (c 0.70, CH_2Cl_2).

*Ethyl 2-((2S,6S)-6-Methyltetrahydro-2H-pyran-2-yl)acetate (**19**).*[12] Colorless oil (184 mg, 99%) (reported[23] 86 mg, 92%). ^1H NMR (400 MHz, $CDCl_3$): δ 1.09 (d, J = 6.4 Hz, 3H), 1.11−1.17 (m, 1H), 1.24 (t, J = 7.2 Hz, 3H), 1.40−1.65 (m, 4H), 1.72−1.79 (m, 1H), 2.32 (dd, J = 15.2 and 5.6 Hz, 1H), 2.49 (dd, J = 15.2 and 7.6 Hz, 1H), 3.37−3.44 (m, 1H), 3.68−3.75 (m, 1H), 4.09 (q, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 7.4, 17.0, 17.9, 25.4, 27.4, 35.2, 53.8, 67.6, 67.8, 165.0. IR (KBr, neat): 2923, 1730, 1636, 1457, 1371, 1257, 1091, 802 cm^{-1}. HRMS (APCI) calcd for $C_{10}H_{18}O_3$ $(M + H)^+$, 187.1329; found, 187.1329. $[\alpha]_D^{20}$ +17.0 (c 0.50, $CHCl_3$), lit.[23] $[\alpha]_D^{20}$ +16.43 (c 0.30, $CHCl_3$).

*2-((2S,6S)-6-Methyltetrahydro-2H-pyran-2-yl)acetic Acid, (+)-Civet (**20**).*[14a] Colorless gum (134 mg, 85%) (reported[20c] 164 mg, 80%). ^1H NMR (400 MHz, $CDCl_3$): δ 1.15 (d, J = 6.0 Hz, 3H), 1.17−1.28 (m, 1H), 1.45−1.63 (m, 4H), 1.77−1.84 (m, 1H), 2.45 (dd, J = 15.6 and 5.2 Hz, 1H), 2.55 (dd, J = 15.6 and 7.6 Hz, 1H), 3.46−3.54 (m, 1H), 3.70−3.78 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 22.2, 23.3, 31.0, 33.0, 41.4, 74.2, 74.8, 174.5. IR (KBr, neat): 2929, 2855, 1717, 1449, 1206, 1076, 1097, 860, 799 cm^{-1}. HRMS (APCI) calcd for $C_8H_{14}O_3$ $(M + H)^+$, 159.1016; found, 159.1016. $[\alpha]_D^{20}$ +22.4 (c 0.25, $CHCl_3$), lit.[20a] $[\alpha]_D^{20}$ +22.0° (c 1.23, $CHCl_3$), lit.[20b] $[\alpha]_D^{20}$ +21.0° (c 0.3, $CHCl_3$), and lit.[20c] $[\alpha]_D^{20}$ +21.9° (c 1.108, $CHCl_3$).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H and ^{13}C NMR and HRMS spectra of all compounds, and NOE spectrum of **2j**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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