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Synthesis of 6-Substituted 2-Pyrones Starting from Renewable Resources: Total Synthesis of Sibirinone, (*E*)-6-(Pent-1-en-1-yl)-2*H*-pyran-2-one, and (*E*)-6-(Hept-1-en-1-yl)-2*H*-pyran-2-one

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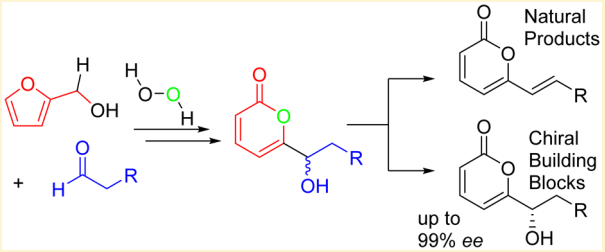
Supporting Information

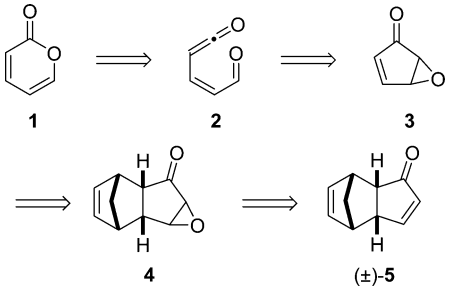
ABSTRACT: An atom-economic reaction sequence to 6-substituted 2-pyrones was developed starting from furfuryl alcohol, a renewable resource made from bran or bagasse, and aldehydes, utilizing a thermal rearrangement of cyclopentadienone epoxides as key step. Derivatives bearing a hydroxyalkyl side chain could be enzymatically resolved, providing access to enantiomerically pure 2-pyrones, or converted to alkenyl-substituted 2-pyrones such as naturally occurring sibirinone, (*E*)-6-(pent-1-en-1-yl)-2*H*-pyran-2-one, and (*E*)-6-(hept-1-en-1-yl)-2*H*-pyran-2-one.



INTRODUCTION

Furfural is a readily available, inexpensive commodity based on nonedible renewable resources such as bran and bagasse. Consequently, it is considered as a platform chemical, having found use in the production of biofuels or solvents.[1] Furfuryl alcohol, produced from furfural by catalytic reduction on ton scale, offers particularly attractive opportunities for the production of fine chemicals and drugs due to the versatile skeletal transformations it can undergo, e.g., by the Achmatowicz[2] or Piancatelli[3] rearrangement. Based on the latter, we report here the atom-economic conversion of furfuryl alcohol and aldehydes to 6-substituted 2-pyrones, a scaffold that is present in a number of natural products[4] and also a proven building block for the synthesis of complex molecules.[5] The synthesis of substituted 2-pyrones is therefore of broad interest, and a number of elegant methods to access this compound class have been developed.[6] Among those, the thermal rearrangement of cyclopentadienone epoxide (**3**) provides an atom-economical approach to 2-pyrone (**1**),[7] which proceeds by a 6π electrocyclic reaction via a vinyl ketene **2** (Scheme 1).[8]

Scheme 1. Synthetic Approach toward 2-Pyrone (1)



Although the mechanism of the reaction is well studied, this rearrangement did not attract much attention for the synthesis of 2-pyrone derivatives. This could be due to difficulties in accessing the required starting materials, often requiring harsh reaction conditions resulting in low yields.[8] In particular, cyclopentadienone epoxide (**3**) cannot be synthesized from cyclopentadienone due to the high tendency of the latter to dimerize. As a well-known surrogate for cyclopentadienone,[9] we therefore explored enone (±)-**5** and derivatives thereof being accessible by Baylis–Hillman reactions with aldehydes.[10]

RESULTS AND DISCUSSION

We recently reported that the Piancatelli rearrangement[3a] of furfuryl alcohol (**6**) to 4-hydroxy-2-cyclopentenone ((±)-**7**) can be conducted on large scale and high yield using a microreactor setup.[3c] Acylation of (±)-**7** to (±)-**8**[11] proceeds in good yields employing acetic anhydride and catalytic amounts of toluenesulfonic acid. The [4 + 2] cycloaddition of acetate (±)-**8** with cyclopentadiene in the presence of zinc(II) chloride following the protocol (toluene instead of benzene was used as solvent, upscale from 1.1 to 240 mmol) developed by Zwanenburg et al.[12] directly leads to (±)-**5**,[13] being accessible by this route on a multigram scale in a total yield of 61% starting from **6** (Scheme 2).

The Baylis–Hillman reaction of (±)-**5** and aldehydes (Table 1), precedented by Eddolls et al.,[10] smoothly gave rise to adducts (±)-**11** that were envisioned to be suitable precursors for the synthesis of 6-substituted 2-pyrones. Expanding the scope previously reported,[10] different aliphatic and aromatic aldehydes with both electron-withdrawing and -donating

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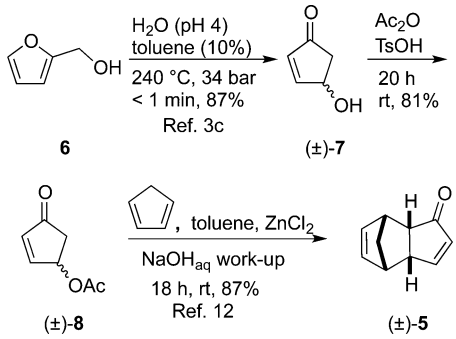
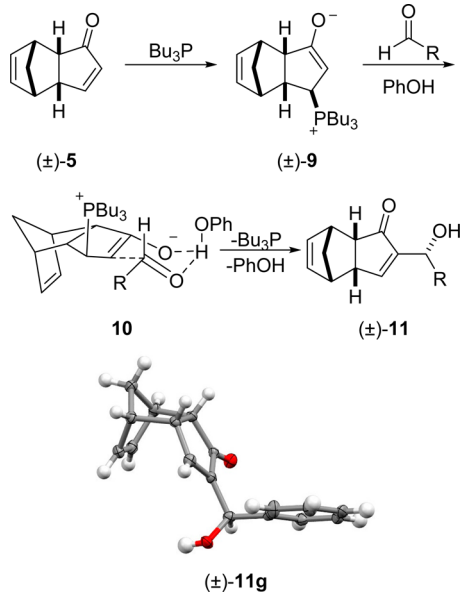
Scheme 2. Synthesis of Enone (±)-5 from Furfuryl Alcohol 6



Scheme 3. Diastereoselective Baylis–Hillman Reaction



groups yielded the target compounds in good yields. Sterically less hindered aliphatic and aromatic aldehydes with electron-withdrawing groups were more active, and therefore shorter reaction times were required. Notably, the Baylis–Hillman reaction to (±)-**11** takes place with complete diastereoselectivity, which can be rationalized by addition of the phosphine catalyst to enone (±)-**5** from its less hindered convex side followed by an aldol reaction of the resulting (±)-**9** via the Zimmerman–Traxler-type transition state **10** (Scheme 3). The relative stereochemistry could be unambiguously assigned by X-ray-crystallography of (±)-**11g**.

Epoxidation of (±)-**11** with hydrogen peroxide proceeded in excellent yield (Table 1) and chemo- and diastereoselectivity from the convex face of the enone, which was ascertained by X-ray-crystallography of (±)-**12g** (see the Supporting Information).

Finally, epoxides (±)-**12** were subjected to flash vacuum thermolysis (FVT[14]), triggering extrusion of cyclopentadiene by a retro-Diels–Alder reaction and the subsequent rearrangement to 2-pyrones (±)-**13**. A temperature of 650 °C at 0.02 mbar was found to be necessary, and lower temperatures resulted in the incomplete conversion of the starting materials. High yields (88–98%) and no byproducts or decomposition were generally observed. The only exception was the furyl-substituted derivative (±)-**13k**, which was formed in only 62% yield. In this case, significant quantities of polymeric material were formed during the FVT, indicating the thermal lability of 2-pyrone (±)-**13k**. The structure of 2-pyrone (±)-**13** was ascertained by X-ray-crystallography to be (±)-**13j** (see the Supporting Information).

Compounds (±)-**13b**, (±)-**13e**, and (±)-**13f** allowed the facile synthesis of sibrinone (**15a**) and related natural products **15b**,**c**, which have been found in cultures of fungi. Sibirinone **15a** was isolated from *Hypomyces semitranslucens*,[15] and **15b** and **15c** were reported as metabolite from strains of *Trichoderma viride* along with their elegant synthesis starting from propargyl bromide and propiolic acid.[16] Additionally, **15c** was found in the marine isolate of fungus *Botrytis* sp.,[17] while **15b** is also a component of the queen recognition pheromone of fire ants *Solenopsis invicta*.[18]

Table 1. Synthesis of 6-Substituted 2-Pyrones Starting from Enone (±)-5

entry	R	11–13	yield (%) 11	12	13
1	Me	**a**	84	91	98
2	Et	**b**	79	92	92
3	*i*-Pr	**c**	85 (87)[a]	97	96
4	*n*-Pr	**d**	83	95	92
5	*n*-Bu	**e**	80	92	91
6	*n*-Hex	**f**	82	96	90
7	Ph	**g**	83 (89)[a]	96	98
8	4-Cl-Ph	**h**	79	91	97
9	4-NO_2-Ph	**i**	86	89	88
10	4-MeO-Ph	**j**	85	92	98
11	2-Furyl	**k**	90	97	62

[a]Taken from ref 10.

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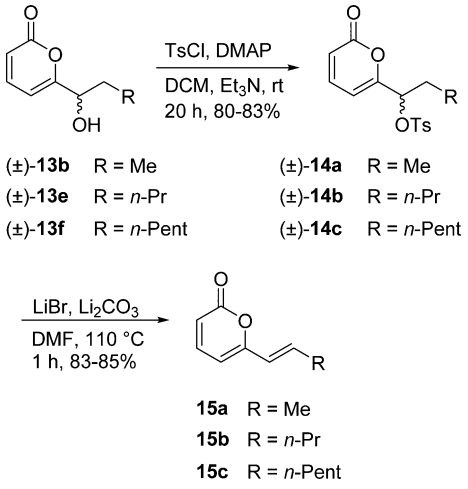
Attempting the direct elimination of water from (±)-**13** under acidic conditions failed; therefore, the α-hydroxy group was tosylated followed by elimination under basic conditions (Scheme 4). The desired compounds were exclusively obtained in the naturally occurring (*E*)-configuration.

Scheme 4. Synthesis of Sibirinone (15a) and Related Natural Products 15b−c



Since 2-pyrones are valuable building blocks in organic chemistry,[5] we furthermore investigated the enzymatic resolution of (±)-**13** to arrive at enantiomerically pure compounds. Using isopropenyl acetate as acylation agent and Novozym 435 for 2-pyrone (±)-**13a** gave (*S*)-**13a** with >99% ee in 38% yield. The stereochemistry was assigned by applying Kazlauskas' rule[19] and proven by X-ray-crystallography after derivatization of (*S*)-**13a** to (*S*)-**17** (Scheme 5).

However, these conditions were not suitable for 2-pyrone (±)-**13e**, containing a longer alkyl side chain. Therefore, we changed our strategy to an enzymatic hydrolysis of the racemic acetate (±)-**18**, which was prepared from (±)-**13e** with acetic anhydride in 95% yield. Hydrolysis of (±)-**18** with Amano lipase from *Burkholderica cepacia* (AL-PS) in a buffer/acetone mixture provided (*S*)-**18** with >99% ee in 39% yield (Scheme 6).

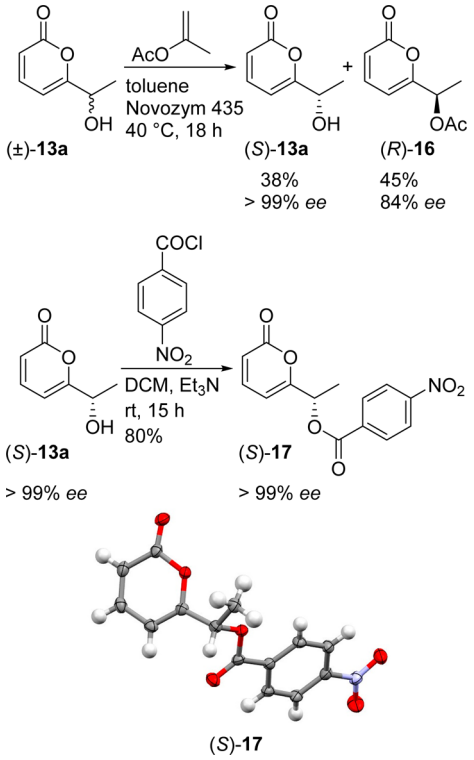
CONCLUSION

In conclusion, we developed an atom-economic and scalable synthesis of 6-substituted 2-pyrones (±)-**13** from furfuryl alcohol (**6**) which were readily available in large quantities at low cost. The title compounds could be converted into natural products **15** or enzymatically resolved to enantiomerically pure building blocks (*S*)-**13a** and (*S*)-**18**.

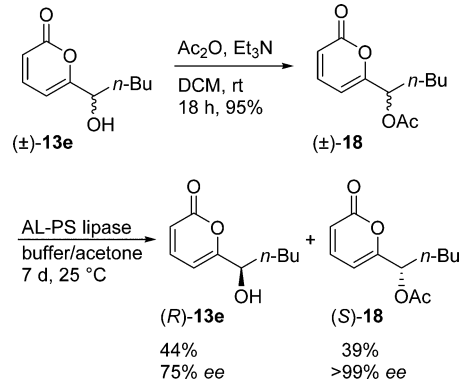
EXPERIMENTAL SECTION

General Information. Commercially available chemicals were purchased in high quality and used without any further purification. 4-Hydroxy-2-cyclopentenone ((±)-**7**)[3c] and 3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-**5**)[12] were synthesized according to published procedures. DCM, ethyl acetate, and hexanes (petroleum ether, PE (60/40)) were distilled prior to use. THF was received from a solvent purification system. All reactions were monitored by thin-layer chromatography (TLC). Visualization was performed with UV light (254 nm), and staining was done with vanillin or potassium permanganate solutions followed by heating. All NMR spectra were recorded in $CDCl_3$. Chemical shifts are reported as δ (ppm) relative to

Scheme 5. Enzymatic Kinetic Resolution and Derivatization



Scheme 6. Acetylation of (±)-13e and Enzymatic Hydrolysis of (±)-18



the signal of the solvent. Characterization of the signals: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, m = multiplet, bs = broad singlet, dd = doublet of a doublet, dt = doublet of a triplet, dq = doublet of a quartet, ddd = doublet of a doublet of a doublet. Integration is determined as the relative number of atoms, and the coupling constants (*J*) are given in Hertz (Hz). The multiplicity of the carbon atoms is given as (+) = CH_3 or CH (positive DEPT signal), (−) = CH_2 (negative DEPT signal) and (C_q) for quaternary carbon atoms (no DEPT signal). High-resolution mass spectra were recorded using atmospheric pressure chemical ionization (APCI) or electrospray ionization (ESI) with a quadrupole time-of-flight (Q-TOF) detector. The optical rotation of optical active compounds was determined at 589 nm (sodium D line) in a 1 dm measuring cell.

General Procedure A. *Baylis−Hillman Reaction of (±)-5 to (±)-11.*[10] Under nitrogen, enone (±)-**5** (1.0 equiv) and the aldehyde (1.5 equiv) were dissolved in dry, degassed THF (1 M) at room temperature, and phenol (0.2 equiv) and Bu_3P (0.4 equiv) were added. The progress of the reaction was monitored by TLC. After completion

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of the reaction, the solvent was evaporated, and the crude product was purified via flash chromatography by an appropriate PE/EA mixture.

General Procedure B. *Epoxidation of (±)-**11** to (±)-**12**.* To a solution of the Baylis–Hillman adduct (±)-**11** (1.0 equiv) in DCM/MeOH 1:1 (5 M) were added 2 M NaOH (1.2 equiv) and 30% H_2O_2 (5.4 equiv), and the reaction mixture was stirred for 30 min at room temperature. The reaction mixture was poured into DCM (30 mL) and washed once with brine. The organic layer was dried over $MgSO_4$ and concentrated under vacuum to yield the pure compound.

General Procedure C. *Flash Vacuum Thermolysis of (±)-**12** to (±)-**13**.* For flash vacuum thermolysis, a high-quality glass tube (length 90 cm, diameter 1 cm) open at both ends was fixed horizontally in a tube furnace connected to a cooling trap and a flask containing epoxide (±)-**12**. The tube furnace was heated to 650 °C and connected to a high-vacuum line at 2×10^{-2} mbar. The starting material was slowly distilled through the tube furnace, and the product was collected in a trap cooled with liquid nitrogen. The product was washed off the cooling trap with DCM, the solvent was removed and the product was dried under reduced pressure to yield the pure compound.

General Procedure D. *Tosylation of (±)-**13** to (±)-**14**.* To a solution of 2-pyrone (±)-**13** (1.0 mmol) in DCM (10 mL) were added DMAP (12 mg, 0.1 mmol), Et_3N (0.42 mL, 3.0 mmol), and 4-toluenesulfonyl chloride (229 mg, 1.2 mmol), and the reaction mixture was stirred at room temperature. After 20 h, saturated $KHSO_4$ solution (20 mL) was added, the water phase was extracted with DCM (3×), and the organic phase was dried over $MgSO_4$. The crude was purified via flash chromatography (silica, PE/EA = 3:1) to yield (±)-**14**.

General Procedure E. *Elimination of (±)-**14** to (±)-**15**.* To a solution of tosylated compound (±)-**14** (0.5 mmol) in DMF (5 mL) were added LiBr (261 mg, 3.0 mmol) and Li_2CO_3 (222 mg, 3.0 mmol), and the reaction mixture was heated for 1 h at 110 °C. After the solution was cooled to room temperature, H_2O (20 mL) was added, and the mixture was extracted with ethyl acetate (3×) and dried over $MgSO_4$. The crude was purified via flash chromatography (silica, PE/EA = 5:1) to yield **15**.

*4-Oxocyclopent-2-en-1-yl Acetate ((±)-**8**).*[11] A solution of 4-hydroxycyclopent-2-en-1-one ((±)-7) (50.3 g, 513 mmol) in Ac_2O (75 mL, 793 mmol) was cooled to 0 °C, and 4-toluenesulfonic acid (100 mg, 0.53 mmol) was added. The reaction mixture was stirred at room temperature for 18 h, and the product was purified by distillation under reduced pressure to give 58.5 g (417 mmol, 81%) of a colorless oil which solidified to white crystals: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H = (dd, J = 5.7, 2.4 Hz, 1H), 6.26 (dd, J = 5.7, 1.2 Hz, 1H), 5.78 (ddd, J = 6.1, 3.5, 2.2 Hz, 1H), 2.75 (dd, J = 18.7, 6.4 Hz, 1H), 2.25 (dd, J = 18.7, 2.2 Hz, 1H), 2.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 204.8 (C_q), 170.3 (C_q), 159.0 (+), 136.9 (+), 71.9 (+), 41.0 (−), 20.8 (+).

*2-(1-Hydroxyethyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one ((±)-**11a**).* According to general procedure A, enone (±)-**5** (4.386 g, 30.0 mmol), acetaldehyde (2.53 mL, 45.0 mmol), phenol (0.565 g, 6.0 mmol), and Bu_3P (2.96 mL, 12.0 mmol) were used, and the reaction was complete after 3 d. Purification via flash chromatography (PE/EA 3:1) yielded a colorless oil (4.803 g, 25.25 mmol, 84%): R_f = 0.17 (PE/EA 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.13–7.10 (m, 1H), 5.93 (dd, J = 5.6, 2.9 Hz, 1H), 5.79 (dd, J = 5.6, 2.9 Hz, 1H), 4.48 (q, J = 6.5 Hz, 1H), 3.34–3.28 (m, 1H), 3.25–3.20 (m, 1H), 2.99–2.93 (bs, 1H), 2.87 (t, J = 5.0 Hz, 1H), 1.75 (dt, J = 8.5, 1.7 Hz, 1H), 1.64–1.59 (m, 1H), 1.30 (d, J = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.6 (C_q), 157.1 (+), 151.6 (C_q), 132.5 (+), 132.3 (+), 63.9 (+), 52.7 (−), 51.6 (+), 45.4 (+), 45.2 (+), 44.1 (+), 22.0 (+); IR (ν/cm^{-1}) 3500–3200, 2971, 2933, 2870, 1742, 1679, 1627, 1453, 1365, 1338, 1118, 1068, 1019, 714; HRMS (ESI) m/z calcd for $C_{12}H_{15}O_2$ [MH$^+$] 191.1067, found 191.1067.

*2-(1-Hydroxypropyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one ((±)-**11b**).* According to general procedure A, enone (±)-**5** (4.386 g, 30.0 mmol), propionaldehyde (3.23 mL, 45.0 mmol), phenol (0.565 g, 6.0 mmol), and Bu_3P (2.96 mL, 12.0 mmol) were used, and the reaction was complete after 3 d. Purification via flash chromatography (PE/EA 3:1) yielded a white solid (4.814 g, 23.57 mmol, 79%): mp 58.7–61.5 °C; R_f = 0.30 (PE/EA 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.04 (d, J = 2.6 Hz, 1H), 5.85 (dd, J = 5.6, 2.9 Hz, 1H), 5.72 (dd, J = 5.6, 3.0 Hz, 1H), 4.13 (t, J = 6.5 Hz, 1H), 3.30–3.22 (m, 1H), 3.18–3.12 (m, 1H), 2.93–2.87 (m, 1H), 2.81 (t, J = 5.0 Hz, 1H), 1.69 (dt, J = 8.5, 1.7 Hz, 1H), 1.60–1.49 (m, 3H), 0.82 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.7 (C_q), 158.1 (+), 150.0 (C_q), 132.6 (+), 132.4 (+), 69.8 (+), 52.7 (−), 51.6 (+), 45.5 (+), 45.2 (+), 44.1 (+), 29.2 (−), 9.8 (+); IR (ν/cm^{-1}) 3500–3300, 2963, 2934, 2870, 1677, 1624, 1451, 1332, 1293, 1251, 1228, 1204, 1086, 1040, 975, 879, 837, 803, 771, 750, 724; HRMS (ESI) m/z calcd for $C_{13}H_{17}O_2$ [MH$^+$] 205.1223, found 205.1229.

*2-(1-Hydroxy-2-methylpropyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one ((±)-**11c**).*[10] According to general procedure A, enone (±)-**5** (438 mg, 3.0 mmol), isobutyraldehyde (0.41 mL, 4.5 mmol), phenol (56 mg, 0.6 mmol), and Bu_3P (0.30 mL, 1.2 mmol) were used, and the reaction was complete after 7 d. Purification via flash chromatography (PE/EA 3:1) yielded a white solid (553 mg, 2.53 mmol, 85%): mp 76.3–78.0 °C; R_f = 0.69 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.07 (d, J = 2.7 Hz, 1H), 5.92 (dd, J = 5.6, 2.9 Hz, 1H), 5.79 (dd, J = 5.6, 2.9 Hz, 1H), 3.98 (d, J = 6.5 Hz, 1H), 3.36–3.30 (m, 1H), 3.24–3.18 (m, 1H), 3.00–2.94 (m, 1H), 2.87 (t, J = 5.0 Hz, 1H), 1.90–1.78 (m, 1H), 1.75 (dt, J = 8.5, 1.7 Hz, 1H), 1.64–1.59 (m, 1H), 0.88 (d, J = 6.7 Hz, 3H), 0.81 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 211.0 (C_q), 159.3 (+), 148.8 (C_q), 132.9 (+), 132.6 (+), 74.5 (+), 52.8 (−), 51.6 (+), 45.8 (+), 45.1 (+), 44.2 (+), 33.2 (+), 18.9 (+), 17.6 (+).

*2-(1-Hydroxybutyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one ((±)-**11d**).* According to general procedure A enone (±)-**5** (438 mg, 3.0 mmol), butyraldehyde (0.41 mL, 4.5 mmol), phenol (56 mg, 0.6 mmol), and Bu_3P (0.30 mL, 1.2 mmol) were used, and the reaction was complete after 3 d. Purification via flash chromatography (PE/EA 3:1) yielded a colorless oil (541 mg, 2.48 mmol, 83%): R_f = 0.20 (PE/EA 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.04 (d, J = 2.6 Hz, 1H), 5.85 (dd, J = 5.6, 2.9 Hz, 1H), 5.72 (dd, J = 5.5, 2.9 Hz, 1H), 4.21 (t, J = 6.5 Hz, 1H), 3.28–3.22 (m, 1H), 3.18–3.12 (m, 1H), 2.92–2.87 (m, 1H), 2.80 (t, J = 5.0 Hz, 1H), 1.69 (dt, J = 8.5, 1.7 Hz, 1H), 1.59–1.44 (m, 3H), 1.38–1.19 (m, 2H), 0.84 (t, J = 7.3 Hz, 3H), ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.7 (C_q), 157.8 (+), 150.5 (C_q), 132.6 (+), 132.3 (+), 68.1 (+), 52.7 (−), 51.6 (+), 45.5 (+), 45.2 (+), 44.1 (+), 38.3 (−), 18.6 (−), 13.9 (+); IR (ν/cm^{-1}) 3500–3200, 2958, 2933, 2872, 1743, 1678, 1623, 1456, 1337, 1294, 1228, 1122, 1070, 1024, 957, 839, 805, 748, 714; HRMS (ESI) m/z calcd for $C_{14}H_{19}O_2$ [MH$^+$] 219.1380, found 219.1380.

*2-(1-Hydroxypentyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one ((±)-**11e**).* According to general procedure A, enone (±)-**5** (4.386 g, 30.0 mmol), valeraldehyde (4.79 mL, 45.0 mmol), phenol (0.565 g, 6.0 mmol), and Bu_3P (2.96 mL, 12.0 mmol) were used,and the reaction was complete after 3 d. Purification via flash chromatography (PE/EA 5:1) yielded a colorless oil (5.583 g, 24.03 mmol, 80%): R_f = 0.32 (PE/EA 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.09 (d, J = 2.6 Hz, 1H), 5.92 (dd, J = 5.6, 2.9 Hz, 1H), 5.78 (dd, J = 5.6, 2.9 Hz, 1H), 4.25 (t, J = 6.6 Hz, 1H), 3.35–3.28 (m, 1H), 3.25–3.18 (m, 1H), 2.99–2.93 (m, 1H), 2.87 (t, J = 5.0 Hz, 1H), 2.47–2.25 (bs, 1H), 1.75 (dt, J = 8.5, 1.7 Hz, 1H), 1.66–1.51 (m, 3H), 1.42–1.19 (m, 4H), 0.88 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.8 (C_q), 157.9 (+), 150.3 (C_q), 132.6 (+), 132.4 (+), 68.5 (+), 52.7 (−), 51.6 (+), 45.5 (+), 45.2 (+), 44.1 (+), 35.9 (−), 27.6 (−), 22.5 (−), 14.1 (+); IR (ν/cm^{-1}) 3500–3200, 2957, 2929, 2870, 1682, 1458, 1337, 1258, 1205, 1124, 1072, 1043, 1015, 795, 714; HRMS (ESI) m/z calcd for $C_{15}H_{21}O_2$ [MH$^+$] 233.1536, found 233.1540.

*2-(1-Hydroxyheptyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one ((±)-**11f**).* According to general procedure A, enone (±)-**5** (4.386 g, 30.0 mmol), *n*-heptanal (6.27 mL, 45.0 mmol), phenol (0.565 g, 6.0 mmol), and Bu_3P (2.96 mL, 12.0 mmol) were used, and the reaction was complete after 3 d. Purification via flash chromatography (PE/EA 5:1) yielded a colorless oil (6.436 g, 24.72 mmol, 82%): R_f = 0.53 (PE/EA 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.08 (d, J = 2.6 Hz, 1H), 5.89 (dd, J = 5.6, 2.9 Hz, 1H), 5.76 (dd, J = 5.6, 2.9 Hz, 1H), 4.23 (t, J = 6.6 Hz, 1H), 3.33–3.26 (m, 1H), 3.22–3.16 (m, 1H), 2.97–2.91 (m, 1H), 2.84 (t, J = 5.0 Hz, 1H), 2.81–2.75

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(bs, 1H), 1.73 (dt, J = 8.5, 1.7 Hz, 1H), 1.63−1.48 (m, 3H), 1.37−1.15 (m, 8H), 0.84 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.7 (C_q), 157.9 (+), 150.4 (C_q), 132.6 (+), 132.3 (+), 68.4 (+), 52.7 (−), 51.6 (+), 45.5 (+), 45.2 (+), 44.1 (−), 36.2 (−), 31.8 (−), 29.1 (−), 25.4 (−), 22.6 (−), 14.1 (+); IR (ν/cm^{-1}) 3600−3200, 3064, 2930, 2859, 1681, 1625, 1457, 1379, 1338, 1293, 1204, 1126, 1066, 1040, 913, 876, 805, 749, 716; HRMS (ESI) m/z calcd for $C_{17}H_{25}O_2$ [MH$^+$] 261.1849, found 261.1850.

*2-(Hydroxy(phenyl)methyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one ((±)-**11g**).*[10] According to general procedure A, enone (±)-**5** (4.386 g, 30.0 mmol), benzaldehyde (4.55 mL, 45.0 mmol), phenol (0.565 g, 6.0 mmol), and Bu_3P (2.96 mL, 12.0 mmol) were used, and the reaction was complete after 2 d. Purification via flash chromatography (PE/EA 3:1) yielded a white solid (6.284 g, 24.91 mmol, 83%): mp 108.7−110.0 °C; R_f = 0.25 (PE/EA 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.36−7.26 (m, 5H), 6.96−6.92 (m, 1H), 5.90 (dd, J = 5.5, 2.9 Hz, 1H), 5.76 (dd, J = 5.5, 2.9 Hz, 1H), 5.43−5.40 (m, 1H), 3.32−3.26 (m, 1H), 3.24−3.19 (m, 1H), 2.95−2.91 (m, 1H), 2.89 (t, J = 5.0 Hz, 1H), 1.74 (dt, J = 8.5, 1.7 Hz, 1H), 1.64−1.57 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.2 (C_q), 159.3 (+), 150.4 (C_q), 141.5 (C_q), 132.6 (+), 132.5 (+) 128.4 (+), 127.7 (+), 126.4 (+), 70.2 (+), 52.7 (−), 51.7 (+), 45.6 (+), 45.2 (+), 44.2 (+).

*2-((4-Chlorophenyl)(hydroxy)methyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one ((±)-**11h**).* The compound was prepared according to general procedure A. Enone (±)-**5** (438 mg, 3.0 mmol), 4-chlorobenzaldehyde (633 mg, 4.5 mmol), phenol (56 mg, 0.6 mmol), and Bu_3P (0.30 mL, 1.2 mmol) were used, and the reaction was complete after 1 d. Purification via flash chromatography (PE/EA 5:1) yielded a white solid (675 mg, 2.35 mmol, 79%): mp 114.6−116.3 °C; R_f = 0.29 (PE/EA 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.33−7.23 (m, 4H), 6.94 (d, J = 2.1 Hz, 1H), 5.89 (dd, J = 5.6, 2.9 Hz, 1H), 5.74 (dd, J = 5.6, 3.0 Hz, 1H), 5.39 (s, 1H), 3.59−3.35 (bs, 1H), 3.32−3.27 (m, 1H), 3.24−3.19 (m, 1H), 2.96−2.91 (m, 1H), 2.89 (t, J = 5.0 Hz, 1H), 1.75 (dt, J = 8.5, 1.7 Hz, 1H), 1.63−1.58 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.2 (C_q), 159.4 (+), 150.0 (C_q), 140.1 (C_q), 133.5 (C_q), 132.6 (+), 132.5 (+), 128.5 (+), 127.8 (+), 69.6 (+), 52.8 (−), 51.7 (+), 45.6 (+), 45.3 (+), 44.2 (+); IR (ν/cm^{-1}) 3500−3200, 3067, 2989, 2968, 2940, 2918, 2899, 2870, 1668, 1616, 1483, 1341, 1330, 1291, 1248, 1225, 1187, 1122, 1084, 1027, 1003, 847, 821, 800, 711; HRMS (ESI) m/z calcd for $C_{17}H_{15}ClNaO_2$ [MNa$^+$] 309.0653, found 309.0657.

*2-(Hydroxy(4-nitrophenyl)methyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one ((±)-**11i**).* According to general procedure A, enone (±)-**5** (438 mg, 3.0 mmol), 4-nitrobenzaldehyde (680 mg, 4.5 mmol), phenol (56 mg, 0.6 mmol), and Bu_3P (0.30 mL, 1.2 mmol) were used, and the reaction was complete after 1 d. Purification via flash chromatography (PE/EA 3:1) yielded a yellow solid (763 mg, 2.57 mmol, 86%): mp 138.6−140.5 °C; R_f = 0.38 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 8.23−8.16 (m, 2H), 7.55−7.48 (m, 2H), 6.99 (d, J = 2.3 Hz, 1H), 5.86 (dd, J = 5.6, 2.9 Hz, 1H), 5.74 (dd, J = 5.6, 2.9 Hz, 1H), 5.52 (s, 1H), 3.69−3.45 (bs, 1H), 3.37−3.31 (m, 1H), 3.26−3.20 (m, 1H), 2.99−2.94 (m, 1H), 2.92 (t, J = 5.0 Hz, 1H), 1.76 (dt, J = 8.6, 1.7 Hz, 1H), 1.65−1.59 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.0 (C_q), 160.0 (+), 149.2 (C_q), 148.9 (C_q), 147.3 (C_q), 132.6 (+) 132.5 (+), 127.1 (+), 123.6 (+), 69.2 (+), 52.8 (−), 51.6 (+), 45.8 (+), 45.3 (+), 44.2 (+); IR (ν/cm^{-1}) 3500−3300, 3065, 2985, 2941, 2913, 2875, 1666, 1619, 1606, 1515, 1345, 1293, 1250, 1226, 1187, 1124, 1109, 1079, 1029, 1005, 839, 803, 751, 718; HRMS (ESI) m/z calcd for $C_{17}H_{16}NO_4$ [MH$^+$] 298.1074, found 298.1069.

*2-(Hydroxy(4-methoxyphenyl)methyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one ((±)-**11j**).* According to general procedure A, enone (±)-**5** (438 mg, 3.0 mmol), 4-methoxybenzaldehyde (0.55 mL, 4.5 mmol), phenol (56 mg, 0.6 mmol), and Bu_3P (0.30 mL, 1.2 mmol) were used, and the reaction was complete after 7 d. Purification via flash chromatography (PE/EA 3:1) yielded a colorless oil (716 mg, 2.54 mmol, 85%): R_f = 0.24 (PE/EA 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.25−7.20 (m, 2H), 6.97−6.93 (m, 1H), 6.89−6.82 (m, 2H), 5.92 (dd, J = 5.6, 2.9 Hz, 1H), 5.77 (dd, J = 5.6, 2.9 Hz, 1H), 5.36 (s, 1H), 3.79 (s, 3H), 3.32−3.25 (m, 1H), 3.24−3.19 (m, 1H), 2.95−2.91 (m, 1H), 2.88 (t, J = 5.0 Hz, 1H), 1.74 (dt, J = 8.5, 1.7 Hz, 1H), 1.63−1.58 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.2 (C_q), 159.1 (C_q), 159.1 (+), 150.7 (C_q), 133.8 (C_q), 132.6 (+), 132.5 (+), 127.7 (+), 113.7 (+), 69.7 (+), 55.3 (+), 52.7 (−), 51.7 (+), 45.5 (+), 45.2 (+), 44.1 (+); IR (ν/cm^{-1}) 3500−3300, 3063, 2973, 2868, 2836, 1686, 1610, 1510, 1462, 1337, 1302, 1246, 1173, 1125, 1078, 1030, 1000, 830, 804, 749, 710; HRMS (ESI) m/z calcd for $C_{18}H_{19}O_3$ [MH$^+$] 283.1329, found 283.1329.

*2-(Furan-2-yl(hydroxy)methyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one ((±)-**11k**).* According to general procedure A, enone (±)-**5** (438 mg, 3.0 mmol), furfural (0.37 mL, 4.5 mmol), phenol (56 mg, 0.6 mmol), and Bu_3P (0.30 mL, 1.2 mmol) were used, and the reaction was complete after 3 d. Purification via flash chromatography (PE/EA 3:1) yielded a yellow solid (653 mg, 2.70 mmol, 90%): mp 89.8−91.4 °C; R_f = 0.34 (PE/EA 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.36 (dd, J = 1.8, 0.9 Hz, 1H), 7.22−7.19 (m, 1H), 6.31 (dd, J = 3.2, 1.8 Hz, 1H), 6.22 (dt, J = 3.3, 0.7 Hz, 1H), 5.94 (dd, J = 5.6, 2.9 Hz, 1H), 5.80 (dd, J = 5.6, 2.9 Hz, 1H), 5.43 (s, 1H), 3.40−3.33 (m, 1H), 3.27−3.21 (m, 1H), 3.01−2.96 (m, 1H), 2.92 (t, J = 4.9 Hz, 1H), 1.76 (dt, J = 8.5, 1.7 Hz, 1H), 1.66−1.60 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 209.8 (C_q), 159.9 (+), 154.0 (C_q), 147.2 (C_q), 142.3 (+), 132.6 (+), 132.5 (+), 110.3 (+), 107.1 (+), 64.2 (+), 52.7 (−), 51.5 (+), 45.8 (+), 45.2 (+), 44.2 (+); IR (ν/cm^{-1}) 3500−3200, 2977, 2937, 2870, 1685, 1626, 1501, 1338, 1293, 1228, 1201, 1145, 1081, 1011, 742; HRMS (ESI) m/z calcd for $C_{15}H_{15}O_3$ [MH$^+$] 243.1016, found 243.1011.

*6a-(1-Hydroxyethyl)-1a,1b,2,5,5a,6a-hexahydro-6H-2,5-methanoindeno[1,2-b]oxiren-6-one ((±)-**12a**).* According to general procedure B, (±)-**11a** (3.805 g, 20.0 mmol), 2 M NaOH (12.0 mL, 24.0 mmol), and 30% H_2O_2 (11.0 mL, 108.0 mmol) were used to afford a colorless oil (3.749 g, 18.18 mmol, 91%): R_f = 0.47 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 6.08 (dd, J = 5.5, 2.8 Hz, 1H), 6.04 (dd, J = 5.6, 2.8 Hz, 1H), 4.03−3.91 (m, 1H), 3.64 (d, J = 1.7 Hz, 1H), 3.29−3.22 (m, 1H), 3.12−3.07 (m, 1H), 3.05−2.99 (m, 1H), 2.90−2.84 (m, 1H), 2.09 (d, J = 8.0 Hz, 1H), 1.65−1.62 (dt, J = 8.6, 1.8 Hz, 1H), 1.49−1.43 (m, 1H), 1.26 (d, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.9 (C_q), 135.1 (+), 133.7 (+), 68.5 (C_q), 64.9 (+), 63.9 (+), 51.8 (−), 50.9 (+), 45.9 (+), 43.5 (+), 43.0 (+), 19.2 (+); IR (ν/cm^{-1}) 3600−3300, 2978, 2940, 2870, 1730, 1454, 1417, 1121, 1041, 724, 633; HRMS (ESI) m/z calcd for $C_{12}H_{15}O_3$ [MH$^+$] 207.1016, found 207.1017.

*6a-(1-Hydroxypropyl)-1a,1b,2,5,5a,6a-hexahydro-6H-2,5-methanoindeno[1,2-b]oxiren-6-one ((±)-**12b**).* According to general procedure B, (±)-**11b** (4.085 g, 20.0 mmol), 2 M NaOH (12.0 mL, 24.0 mmol), and 30% H_2O_2 (11.0 mL, 108.0 mmol) were used to afford a colorless oil (4.036 g, 18.32 mmol, 92%): R_f = 0.50 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 6.02 (dd, J = 5.6, 2.8 Hz, 1H), 5.97 (dd, J = 5.6, 2.8 Hz, 1H), 3.61 (dd, J = 9.8, 3.3 Hz, 1H), 3.56 (d, J = 1.6 Hz, 1H), 3.21−3.15 (m, 1H), 3.06−3.00 (m, 1H), 2.98−2.92 (m, 1H), 2.83−2.77 (m, 1H), 2.17−2.08 (bs, 1H), 1.65−1.52 (m, 2H), 1.43−1.33 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 211.0 (C_q), 135.1 (+), 133.8 (+), 69.3 (+), 68.0 (C_q), 64.7 (+), 51.9 (−), 50.9 (+), 45.9 (+), 43.5 (+), 43.1 (+), 26.1 (−), 10.2 (+); IR (ν/cm^{-1}) 3600−3300, 2970, 2937, 2876, 1730, 1457, 1336, 1235, 1122, 1038, 975, 766, 728, 633; HRMS (ESI) m/z calcd for $C_{13}H_{17}O_3$ [MH$^+$] 221.1172, found 221.1171.

*6a-(1-Hydroxy-2-methylpropyl)-1a,1b,2,5,5a,6a-hexahydro-6H-2,5-methanoindeno[1,2-b]oxiren-6-one ((±)-**12c**).* According to general procedure B, (±)-**11c** (218 mg, 1.0 mmol), 2 M NaOH (0.6 mL, 1.2 mmol), and 30% H_2O_2 (0.55 mL, 5.4 mmol) were used to afford a white solid (227 mg, 0.97 mmol, 97%): mp 54.1−56.8 °C; R_f = 0.82 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 6.05 (dd, J = 5.7, 2.9 Hz, 1H), 5.99 (dd, J = 5.7, 2.8 Hz, 1H), 3.59 (d, J = 1.7 Hz, 1H), 3.56 (d, J = 4.9 Hz, 1H), 3.22−3.16 (m, 1H), 3.07−3.02 (m, 1H), 2.98−2.92 (m, 1H), 2.86−2.79 (m, 1H), 2.20−2.03 (m, 1H), 1.98−1.82 (bs, 1H), 1.57 (dt, J = 8.6, 1.7 Hz, 1H), 1.45−1.37 (m, 1H), 0.90 (d, J = 6.9 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.6 (C_q), 135.1 (+), 134.0 (+), 71.6 (+), 67.7 (C_q), 64.3 (+), 51.9 (−), 50.9 (+), 45.8 (+), 43.5 (+), 43.0 (+), 29.9 (+), 20.0 (+), 16.5 (+); IR (ν/cm^{-1}) 3500−3200, 2981, 2961, 2933, 2863,

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1736, 1467, 1414, 1386, 1335, 1246, 1227, 1139, 1061, 1020, 928, 739, 719, 702; HRMS (ESI) m/z calcd for $C_{14}H_{19}O_3$ [MH^+] 235.1329, found 235.1326.

*6a-(1-Hydroxybutyl)-1a,1b,2,5,5a,6a-hexahydro-6H-2,5-methanoindeno[1,2-b]oxiren-6-one ((±)-**12d**).* According to general procedure B, (±)-**11d** (218 mg, 1.0 mmol), 2 M NaOH (0.6 mL, 1.2 mmol), and 30% H_2O_2 (0.55 mL, 5.4 mmol) were used to afford a colorless oil (222 mg, 0.95 mmol, 95%): R_f = 0.59 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 6.01 (dd, J = 5.7, 2.9 Hz, 1H), 5.97 (dd, J = 5.6, 2.8 Hz, 1H), 3.72 (d, J = 9.1 Hz, 1H), 3.56 (d, J = 1.6 Hz, 1H), 3.20−3.16 (m, 1H), 3.05−3.00 (m, 1H), 2.97−2.92 (m, 1H), 2.82−2.77 (m, 1H), 2.12−2.06 (bs, 1H), 1.55 (dt, J = 8.6, 1.8 Hz, 1H), 1.53−1.45 (m, 2H), 1.42−1.38 (m, 1H), 1.37−1.24 (m, 2H), 0.85 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 211.0 (C_q), 135.1 (+), 133.8 (+), 68.2 (C_q), 67.5 (+), 64.7 (+), 51.8 (−), 50.9 (+), 45.9 (+), 43.5 (+), 43.1 (+), 34.9 (−), 18.7 (−), 13.8 (+); IR (ν/cm^{-1}) 3600−3300, 2959, 2938, 2872, 1730, 1458, 1414, 133, 1123, 1075, 1033, 952, 911, 845, 776, 715; HRMS (ESI) m/z calcd for $C_{14}H_{19}O_3$ [MH^+] 235.1329, found 235.1328.

*6a-(1-Hydroxypentyl)-1a,1b,2,5,5a,6a-hexahydro-6H-2,5-methanoindeno[1,2-b]oxiren-6-one ((±)-**12e**).* According to general procedure B, (±)-**11e** (4.646 g, 20.0 mmol), 2 M NaOH (12.0 mL, 24.0 mmol), and 30% H_2O_2 (11.0 mL, 108.0 mmol) were used to afford a colorless oil (4.578 g, 18.44 mmol, 92%): R_f = 0.76 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 6.08 (dd, J = 5.5, 2.8 Hz, 1H), 6.04 (dd, J = 5.6, 2.7 Hz, 1H), 3.77 (dd, J = 9.4, 3.0 Hz, 1H), 3.63 (d, J = 1.5 Hz, 1H), 3.28−3.22 (m, 1H), 3.12−3.07 (m, 1H), 3.04−2.98 (m, 1H), 2.89−2.832 (m, 1H), 12.93−1.82 (bs, 1H), 1.63−1.25 (m, 8H), 0.89 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 211.1 (C_q), 135.1 (+), 133.8 (+), 68.1 (C_q), 67.9 (+), 64.8 (+), 51.9 (−), 50.9 (+), 45.9 (+), 43.5 (+), 43.1 (+), 32.6 (−), 27.7 (−), 22.5 (−), 14.0 (+); IR (ν/cm^{-1}) 3600−3300, 2934, 2871, 1731, 1457, 1336, 1125, 1039, 717; HRMS (ESI) m/z calcd for $C_{15}H_{21}O_3$ [MH^+] 249.1485, found 249.1488.

*6a-(1-Hydroxyheptyl)-1a,1b,2,5,5a,6a-hexahydro-6H-2,5-methanoindeno[1,2-b]oxiren-6-one ((±)-**12f**).* According to general procedure B, (±)-**11f** (5.208 g, 20.0 mmol), 2 M NaOH (12.0 mL, 24.0 mmol), and 30% H_2O_2 (11.0 mL, 108.0 mmol) were used to afford a colorless oil (5.328 g, 19.28 mmol, 96%): R_f = 0.79 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 6.07 (dd, J = 5.6, 2.8 Hz, 1H), 6.03 (dd, J = 5.6, 2.7 Hz, 1H), 3.76 (dd, J = 9.5, 2.9 Hz, 1H), 3.62 (d, J = 1.6 Hz, 1H), 3.27−3.21 (m, 1H), 3.12−3.06 (m, 1H), 3.04−2.97 (m, 1H), 2.90−2.82 (m, 1H), 2.10−1.97 (bs, 1H), 1.67−1.18 (m, 12H), 0.87 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 211.1 (C_q), 135.1 (+), 133.8 (+), 68.1 (C_q), 67.9 (+), 64.8 (+), 51.9 (−), 50.9 (+), 45.9 (+), 43.5 (+), 43.1 (+), 33.0 (−), 31.8 (−), 29.1 (−), 25.5 (−), 22.6 (−), 14.1 (+); IR (ν/cm^{-1}) 3600−3300, 2930, 2859, 1733, 1461, 1416, 1338, 1234, 1200, 1126, 1085, 1029, 913, 865, 775, 716; HRMS (EI) m/z calcd for $C_{17}H_{25}O_3$ [MH^+] 277.1798, found 277.1803.

*6a-(Hydroxy(phenyl)methyl)-1a,1b,2,5,5a,6a-hexahydro-6H-2,5-methanoindeno[1,2-b]oxiren-6-one ((±)-**12g**).* According to general procedure B, (±)-**11g** (5.046 g, 1.0 mmol), 2 M NaOH (12.0 mL, 24.0 mmol), and 30% H_2O_2 (11.0 mL, 108.0 mmol) were used to afford a white solid (5.142 g, 19.16 mmol, 96%): mp 121.5−123.0 °C; R_f = 0.63 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.36−7.26 (m, 5H), 5.74 (dd, J = 5.7, 2.8 Hz, 1H), 5.68 (dd, J = 5.7, 2.8 Hz, 1H), 4.94 (s, 1H), 3.39 (d, J = 1.6 Hz, 1H), 3.20−3.15 (m, 1H), 3.02−2.97 (m, 1H), 2.96−2.91 (m, 1H), 2.87−2.81 (m, 1H), 1.54 (dt, J = 8.6, 1.7 Hz, 1H), 1.41−1.36 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 211.2 (C_q), 138.5 (C_q), 134.6 (+), 133.5 (+), 128.2 (+), 128.1 (+) 126.9 (+), 70.7 (+), 67.7 (C_q), 64.9 (+), 51.7 (−), 50.9 (+), 45.9 (+), 43.4 (+), 43.0 (+); IR (ν/cm^{-1}): 3600−3400, 2979, 2941, 2868, 1739, 1495, 1451, 1407, 1339, 1307, 1197, 1036, 912, 866, 843, 757, 725, 704; HRMS (ESI) m/z calcd for $C_{17}H_{17}O_3$ [MH^+]: 269.1172, found 269.1175.

*6a-((4-Chlorophenyl)(hydroxy)methyl)-1a,1b,2,5,5a,6a-hexahydro-6H-2,5-methanoindeno[1,2-b]oxiren-6-one ((±)-**12h**).* According to general procedure B, (±)-**11h** (287 mg, 1.0 mmol), 2 M NaOH (0.6 mL, 1.2 mmol), and 30% H_2O_2 (0.55 mL, 5.4 mmol) were used to afford a white solid (274 mg, 0.91 mmol, 91%): mp 128.8−130.9 °C; R_f = 0.32 (PE/EA 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.34−7.28 (m, 2H), 7.26−7.21 (m, 2H), 5.82 (dd, J = 5.6, 2.8 Hz, 1H), 5.77 (dd, J = 5.6, 2.8 Hz, 1H), 4.97 (s, 1H), 3.35 (d, J = 1.6 Hz, 1H), 3.23−3.18 (m, 1H), 3.05−2.99 (m, 1H), 2.98−2.93 (m, 1H), 2.89−2.83 (m, 1H), 1.57 (dt, J = 8.6, 1.7 Hz, 1H), 1.44−1.38 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 211.1 (C_q), 136.9 (C_q), 134.8 (+), 133.9 (C_q), 133.6 (+), 128.3 (+), 128.2 (+), 69.6 (+), 67.6 (C_q), 64.8 (+), 51.8 (−), 50.9 (+), 45.9 (+), 43.4 (+), 42.9 (+); IR (ν/cm^{-1}) 3600−3400, 2984, 2929, 2872, 1723, 1489, 1404, 1334, 1275, 1258, 1213, 1198, 1089, 1060, 1033, 1016, 939, 898, 850, 820, 745, 723; HRMS (ESI) m/z calcd for $C_{17}H_{16}ClO_3$ [MH^+] 303.0782, found 303.0791.

*6a-(Hydroxy(4-nitrophenyl)methyl)-1a,1b,2,5,5a,6a-hexahydro-6H-2,5-methanoindeno[1,2-b]oxiren-6-one ((±)-**12i**).* According to general procedure B, (±)-**11i** (297 mg, 1.0 mmol), 2 M NaOH (0.6 mL, 1.2 mmol), and 30% H_2O_2 (0.55 mL, 5.4 mmol) were used to afford a yellow solid (279 mg, 0.89 mmol, 89%): mp 141.6−143.4 °C; R_f = 0.56 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 8.23−8.17 (m, 2H), 7.54−7.47 (m, 2H), 5.88 (dd, J = 5.6, 2.8 Hz, 1H), 5.82 (dd, J = 5.7, 2.8 Hz, 1H), 5.16 (s, 1H), 3.33 (d, J = 1.6 Hz, 1H), 3.25−3.20 (m, 1H), 3.06−3.01 (m, 1H), 3.00−2.95 (m, 1H), 2.91−2.85 (m, 1H), 1.60 (dt, J = 8.7, 1.7 Hz, 1H), 1.46−1.40 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.7 (C_q), 147.7 (C_q), 145.4 (C_q), 135.0 (+), 133.6 (+), 127.8 (+), 123.3 (+), 68.9 (+), 67.4 (C_q), 64.7 (+), 51.8 (−), 50.8 (+), 45.9 (+), 43.4 (+), 42.8 (+); IR (ν/cm^{-1}) 3600−3400, 2962, 2937, 2872, 1725, 1602, 1509, 1397, 1346, 1260, 1235, 1193, 1106, 1064, 1034, 899, 834, 806, 754, 718; HRMS (ESI) m/z calcd for $C_{17}H_{16}NO_5$ [MH^+] 314.1023, found 314.1026.

*6a-(Hydroxy(4-methoxyphenyl)methyl)-1a,1b,2,5,5a,6a-hexahydro-6H-2,5-methanoindeno[1,2-b]oxiren-6-one ((±)-**12j**).* According to general procedure B, (±)-**11j** (282 mg, 1.0 mmol), 2 M NaOH (0.6 mL, 1.2 mmol), and 30% H_2O_2 (0.55 mL, 5.4 mmol) were used to afford a colorless oil (273 mg, 0.92 mmol, 92%): R_f = 0.64 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.25−7.19 (m, 2H), 6.90−6.83 (m, 2H), 5.80 (dd, J = 5.6, 2.8 Hz, 1H), 5.75 (dd, J = 5.6, 2.8 Hz, 1H), 4.91 (s, 1H), 3.80 (s, 3H), 3.39 (d, J = 1.6 Hz, 1H), 3.22−3.16 (m, 1H), 3.04−2.99 (m, 1H), 2.98−2.92 (m, 1H), 2.88−2.82 (m, 1H), 1.55 (dt, J = 8.6, 1.7 Hz, 1H), 1.43−1.37 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 211.25 (C_q), 159.4 (C_q), 134.7 (+), 133.5 (+), 130.7 (C_q), 128.1 (+), 113.6 (+), 70.1 (+), 67.9 (C_q), 64.9 (+), 55.3 (+), 51.7 (−), 50.9 (+), 45.9 (+), 43.4 (+), 42.9 (+); IR (ν/cm^{-1}) 3600−3400, 2984, 2938, 2867, 1720, 1613, 1587, 1511, 1462, 1416, 1335, 1306, 1245, 1200, 1170, 1126, 1062, 1034, 939, 898, 866, 827, 712; HRMS (ESI) m/z calcd for $C_{18}H_{18}NaO_4$ [MNa^+] 321.1097, found 321.1093.

*6a-(Furan-2-yl(hydroxy)methyl)-1a,1b,2,5,5a,6a-hexahydro-6H-2,5-methanoindeno[1,2-b]oxiren-6-one ((±)-**12k**).* According to general procedure B, (±)-**11k** (242 mg, 1.0 mmol), 2 M NaOH (0.6 mL, 1.2 mmol), and 30% H_2O_2 (0.55 mL, 5.4 mmol) were used to afford a yellowish oil (251 mg, 0.97 mmol, 97%): R_f = 0.50 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.38 (dd, J = 1.8, 0.8 Hz, 1H), 6.36 (dd, J = 3.3, 1.8 Hz, 1H), 6.34−6.31 (m, 1H), 5.85 (dd, J = 5.7, 2.8 Hz, 1H), 5.74 (dd, J = 5.7, 2.8 Hz, 1H), 4.83 (s, 1H), 3.68 (d, J = 1.6 Hz, 1H), 3.22−3.17 (m, 1H), 3.09−3.04 (m, 1H), 3.04−2.99 (m, 1H), 2.89−2.83 (m, 1H), 1.57 (dt, J = 8.6, 1.7 Hz, 1H), 1.45−1.40 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 210.5 (C_q), 151.9 (C_q), 142.1 (+), 134.5 (+), 133.2 (+), 110.6 (+), 108.0 (+), 66.5 (C_q), 65.7 (+), 64.9 (+), 51.7 (−), 50.9 (+), 45.8 (+), 43.5 (+), 43.3 (+); IR (ν/cm^{-1}) 3600−3300, 2970, 2937, 2870, 1734, 1502, 1421, 1374, 1338, 1230, 1145, 1126, 1011, 912, 831, 729, 715; HRMS (ESI) m/z calcd for $C_{15}H_{15}O_4$ [MH^+] 259.0965, found 259.0962.

*6-(1-Hydroxyethyl)-2H-pyran-2-one ((±)-**13a**).* Following general procedure C, (±)-**12a** (1.650 g, 8.0 mmol) was used to give rise to a brownish oil (1.098 g, 7.84 mmol, 98%): R_f = 0.29 (PE/EA 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.34 (dd, J = 9.4, 6.6 Hz, 1H), 6.29 (dt, J = 6.6, 0.9 Hz, 1H), 6.21 (d, J = 9.4 Hz, 1H), 4.60 (q, J = 6.6 Hz, 1H), 2.46−2.29 (bs, 1H), 1.51 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 167.7 (C_q), 162.3 (C_q), 144.0 (+), 114.2 (+), 100.6 (+), 66.7 (+), 21.4 (+); IR (ν/cm^{-1}) 3500−3200, 2982, 2932, 1698, 1630, 1558, 1453, 1409, 1366, 1309, 1214, 1093, 1015, 976, 906,

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858, 804; HRMS (EI) m/z calcd for $C_7H_9O_3$ [MH^+] 141.0546, found 141.0547.

*6-(1-Hydroxypropyl)-2H-pyran-2-one ((±)-**13b**).* Following general procedure C, (±)-**12b** (1.762 g, 8.0 mmol) was used to give rise to a brownish oil (1.134 g, 7.36 mmol, 92%): R_f = 0.39 (PE/EA 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.34 (dd, J = 9.4, 6.6 Hz, 1H), 6.28 (d, J = 6.6 Hz, 1H), 6.21 (d, J = 9.4 Hz, 1H), 4.37 (dd, J = 7.3, 5.1 Hz, 1H), 2.29−2.15 (bs, 1H), 1.98−1.69 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 166.8 (C_q), 162.4 (C_q), 143.9 (+), 114.1 (+), 101.6 (+), 71.9 (+), 28.3 (−), 9.4 (+); IR (ν/cm^{-1}) 3500−3200, 2968, 2934, 2878, 1707, 1631, 1557, 1462, 1412, 1313, 1210, 1094, 1050, 995, 808, 633; HRMS (EI) m/z calcd for $C_8H_{11}O_3$ [MH^+] 155.0703, found 155.0704.

*6-(1-Hydroxy-2-methylpropyl)-2H-pyran-2-one ((±)-**13c**).* Following general procedure C, (±)-**14c** (117 mg, 0.5 mmol) was used to give rise to a brownish oil (81 mg, 0.48 mmol, 96%): R_f = 0.44 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.33 (dd, J = 9.4, 6.6 Hz, 1H), 6.27 (dt, J = 6.6, 0.8 Hz, 1H), 6.19 (dd, J = 9.4, 0.5 Hz, 1H), 4.18 (d, J = 5.4 Hz, 1H), 2.54−2.38 (bs, 1H), 2.22−2.06 (m, 1H), 0.97 (d, J = 6.9 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 166.3 (C_q), 162.1 (C_q), 143.6 (+), 114.1 (+), 102.3 (+), 75.8 (+), 32.3 (+), 19.0 (+), 16.6 (+); IR (ν/cm^{-1}) 3500−3200, 2963, 2930, 2875, 1708, 1629, 1557, 1467, 1410, 1386, 1368, 1259, 1212, 1177, 1095, 1027, 937, 900, 869, 804; HRMS (ESI) m/z calcd for $C_9H_{13}O_3$ [MH^+] 169.0859, found 169.0859.

*6-(1-Hydroxybutyl)-2H-pyran-2-one ((±)-**13d**).* Following general procedure C, (±)-**12d** (117 mg, 0.5 mmol) was used to give rise to a brownish oil (77 mg, 0.49 mmol, 92%): R_f = 0.27 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.33 (dd, J = 9.4, 6.6 Hz, 1H), 6.28 (d, J = 6.6 Hz, 1H), 6.19 (d, J = 9.3 Hz, 1H), 4.41 (dd, J = 8.0, 4.8 Hz, 1H), 2.83−2.50 (bs, 1H), 1.86−1.65 (m, 2H), 1.53−1.34 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 167.1 (C_q), 162.2 (C_q), 143.7 (+), 114.2 (+), 101.3 (+), 70.7 (+), 37.4 (−), 18.4 (−), 13.8 (+); IR (ν/cm^{-1}) 3500−3200, 2961, 2935, 2873, 1704, 1630, 1556, 1465, 1413, 1380, 1315, 1259, 1209, 1094, 1035, 864, 806; HRMS (EI) m/z calcd for $C_9H_{13}O_3$ [MH^+] 169.0859, found 169.0858.

*6-(1-Hydroxypentyl)-2H-pyran-2-one ((±)-**13e**).* Following general procedure C, (±)-**12e** (1.986 g, 8.0 mmol) was used to give rise to a brownish oil (1.327 g, 7.28 mmol, 91%): R_f = 0.35 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.34 (dd, J = 9.4, 6.6 Hz, 1H), 6.27 (d, J = 6.6 Hz, 1H), 6.21 (d, J = 9.3 Hz, 1H), 4.41 (dd, J = 7.9, 4.8 Hz, 1H), 2.19−2.06 (bs, 1H), 1.93−1.66 (m, 2H), 1.47−1.30 (m, 4H), 0.91 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 167.0 (C_q), 162.2 (C_q), 143.8 (+), 114.2 (+), 101.3 (+), 70.9 (+), 35.0 (−), 27.3 (−), 22.4 (−), 14.0 (+); IR (ν/cm^{-1}) 3500−3200, 2960, 2936, 2863, 1703, 1633, 1558, 1461, 1409, 1316, 1264, 1208, 1092, 1044, 865, 805; HRMS (EI) m/z calcd for $C_{10}H_{15}O_3$ [MH^+] 183.1016, found 183.1019.

*6-(1-Hydroxyheptyl)-2H-pyran-2-one ((±)-**13f**).* Following general procedure C, (±)-**12f** (2.211 g, 8.0 mmol) was used to give rise to a brownish oil (1.511 g, 7.19 mmol, 90%): R_f = 0.47 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.33 (dd, J = 9.4, 6.6 Hz, 1H), 6.27 (d, J = 6.6 Hz, 1H), 6.19 (d, J = 9.4, 1H), 4.40 (dd, J = 7.9, 4.8 Hz, 1H), 2.94−2.72 (s, 1H), 1.91−1.63 (m, 2H), 1.42−1.21 (m, 8H), 0.86 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 167.0 (C_q), 162.2 (C_q), 143.8 (+), 114.2 (+), 101.3 (+), 70.9 (+), 35.3 (−), 31.7 (−), 29.0 (−), 25.1 (−), 22.6 (−), 14.1 (+); IR (ν/cm^{-1}) 3500−3200, 2926, 2859, 1703, 1633, 1558, 1461, 1409, 1316, 1211, 1092, 1047, 913, 865, 805; HRMS (ESI) m/z calcd for $C_{12}H_{19}O_3$ [MH^+] 211.1329, found 211.1334.

*6-(Hydroxy(phenyl)methyl)-2H-pyran-2-one ((±)-**13g**).* Following general procedure C, (±)-**12g** (2.147 g, 8.0 mmol) was used to give an orange solid (1.588 g, 7.85 mmol, 98%): mp 78.4−79.8 °C; R_f = 0.19 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.47−7.30 (m, 6H), 6.33 (dt, J = 6.6, 1.0 Hz, 1H), 6.23−6.15 (m, 1H), 5.50 (s, 1H), 2.65−2.45 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 165.5 (C_q), 161.8 (C_q), 143.5 (+), 139.1 (C_q), 128.9 (+), 126.9 (+), 114.5 (+), 101.7 (+), 73.0 (+); IR (ν/cm^{-1}) 3400−3200, 1687, 1630, 1557, 1491, 1454, 1423, 1329, 1258, 1213, 1099, 1033, 903, 796, 750, 707; HRMS (EI) m/z calcd for $C_{12}H_{11}O_3$ [MH^+] 203.0703, found 203.0700.

*6-((4-Chlorophenyl) (hydroxy)methyl)-2H-pyran-2-one ((±)-**13h**).* Following general procedure C, (±)-**12h** (151 mg, 0.5 mmol) was used to give an orange solid (114 mg, 0.48 mmol, 97%): mp 98.6−101.7 °C; R_f = 0.39 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.33−7.24 (m, 5H), 6.26 (dt, J = 6.6, 0.9 Hz, 1H), 6.18−6.12 (m, 1H), 5.43 (s, 1H), 3.24−2.54 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 165.0 (C_q), 161.7 (C_q), 143.6 (+), 137.5 (C_q), 134.7 (C_q), 129.0 (+), 128.2 (+), 114.7 (+), 101.8 (+), 72.2 (+); IR (ν/cm^{-1}) 3400−3200, 2865, 1695, 1625, 1554, 1483, 1408, 1271, 1237, 1191, 1086, 1013, 885, 868, 846, 798, 782; HRMS (ESI) m/z calcd for $C_{12}H_{10}ClO_3$ [MH^+] 237.0313, found 237.0313.

*6-(Hydroxy(4-nitrophenyl)methyl)-2H-pyran-2-one ((±)-**13i**).* Following general procedure C, (±)-**12i** (157 mg, 0.5 mmol) was used to give an orange solid (109 mg, 0.43 mmol, 88%): mp 118.4−120.7 °C; R_f = 0.33 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 8.27−8.21 (m, 2H), 7.69−7.62 (m, 2H), 7.34 (dd, J = 9.4, 6.6 Hz, 1H), 6.33 (dt, J = 6.6, 0.8 Hz, 1H), 6.22 (d, J = 9.4 Hz, 1H), 5.62 (s, 1H), 3.22−2.72 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 163.9 (C_q), 161.3 (C_q), 148.1 (C_q), 145.8 (C_q), 143.4 (+), 127.7 (+), 124.0 (+), 115.3 (+), 102.0 (+), 72.0 (+); IR (ν/cm^{-1}) 3500−3300, 3107, 3076, 1716, 1632, 1600, 1556, 1515, 1409, 1344, 1289, 1232, 1213, 1197, 1097, 1064, 1037, 986, 907, 856, 821, 801, 740; HRMS (ESI) m/z calcd for $C_{12}H_{10}NO_5$ [MH^+] 248.0553, found 248.0556.

*6-(Hydroxy(4-methoxyphenyl)methyl)-2H-pyran-2-one ((±)-**13j**).* Following general procedure C, (±)-**12j** (149 mg, 0.5 mmol) was used to give an orange solid (114 mg, 0.49 mmol, 98%): mp 109.6−111.4 °C; R_f = 0.31 (PE/EA 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.37−7.30 (m, 3H), 6.94−6.87 (m, 2H), 6.33 (dt, J = 6.6, 0.9 Hz, 1H), 6.19 (d, J = 9.3 Hz, 1H), 5.45 (s, 1H), 3.81 (s, 3H), 2.05−1.69 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 165.7 (C_q), 161.8 (C_q), 160.0 (C_q), 143.5 (+), 131.3 (C_q), 128.3 (+), 114.4 (+), 114.3 (+), 101.4 (+), 72.6 (+), 55.4 (+); IR (ν/cm^{-1}) 3500−3300, 3080, 2963, 1690, 1626, 1553, 1509, 1410, 1306, 1287, 1249, 1228, 1173, 1098, 1066, 1022, 876, 839, 792; HRMS (ESI) m/z calcd for $C_{13}H_{13}O_4$ [MH^+] 233.0808, found 233.0808.

*6-(Furan-2-yl(hydroxy)methyl)-2H-pyran-2-one ((±)-**13k**).* Following general procedure C, (±)-**12k** (129 mg, 0.5 mmol) was used to give rise to a yellow oil (59 mg, 0.31 mmol, 62%) after purification via flash chromatography (silica, PE/EA = 2:1): R_f = 0.21 (PE/EA 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 7.42 (dd, J = 1.7, 0.7 Hz, 1H), 7.36 (dd, J = 9.4, 6.6 Hz, 1H), 6.43−6.37 (m, 3H), 6.25 (d, J = 9.4 Hz, 1H), 5.53 (s, 1H), 2.03−1.64 (bs, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 162.6 (C_q), 161.4 (C_q), 151.2 (C_q), 143.4 (+), 143.3 (+), 115.2 (+), 110.8 (+), 109.1 (+), 102.3 (+), 67.0 (+); IR (ν/cm^{-1}) 3500−3200, 1700, 1633, 1558, 1521, 1409, 1208, 1148, 1092, 1062, 883, 809, 738; HRMS (ESI) m/z calcd for $C_{10}H_9O_4$ [MH^+] 193.0495, found 193.0496.

*1-(2-Oxo-2H-pyran-6-yl)propyl 4-Methylbenzenesulfonate ((±)-**14a**).* Following general procedure D, (±)-**13b** (154 mg, 1.0 mmol) was used to give rise to a white solid (249 mg, 0.81 mmol, 81%): mp 69.7−71.1 °C; R_f = 0.43 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.77−7.69 (m, 2H), 7.34−7.27 (m, 2H), 7.21 (dd, J = 9.3, 6.7 Hz, 1H), 6.23−6.11 (m, 2H), 5.00 (t, J = 6.5 Hz, 1H), 2.41 (s, 3H), 1.90 (qui, J = 7.3 Hz, 2H), 0.84 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 160.93 (C_q), 160.0 (C_q), 145.3 (C_q), 142.8 (+), 133.3 (C_q), 129.9 (+), 127.9 (+), 115.6 (+), 104.0 (+), 79.9 (+), 26.3 (−), 21.7 (+), 9.0 (+); IR (ν/cm^{-1}) 3097, 2974, 2937, 2881, 1730, 1640, 1595, 1562, 1461, 1409, 1361, 1215, 1174, 1096, 890, 850; HRMS (ESI) m/z calcd for $C_{15}H_{17}O_5S$ [MH^+] 309.0791, found 309.0792.

*1-(2-Oxo-2H-pyran-6-yl)pentyl 4-Methylbenzenesulfonate ((±)-**14b**).* Following general procedure D, (±)-**13e** (182 mg, 1.0 mmol) was used to give rise to a white solid (278 mg, 0.83 mmol, 83%): mp 63.4−65.1 °C; R_f = 0.48 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.77−7.71 (m, 2H), 7.34−7.27 (m, 2H), 7.20 (dd, J = 9.2, 6.8 Hz, 1H), 6.17−6.13 (m, 2H), 5.05 (t, J = 6.2 Hz, 1H), 2.43 (s, 3H), 1.92−1.80 (m, 2H), 1.31−1.12 (m, 4H), 0.82 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 160.8 (C_q), 160.3 (C_q), 145.2 (C_q), 142.7 (+), 133.4 (C_q), 129.8 (+), 127.9 (+), 115.6 (+), 103.7 (+), 78.8 (+), 32.8 (−), 26.6 (−), 22.0 (−), 21.7 (+), 13.8 (+); IR (ν/cm^{-1})

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2960, 2933, 2870, 1737, 1640, 1599, 1558, 1461, 1405, 1364, 1174, 1092, 1036, 992, 805; HRMS (ESI) m/z calcd for $C_{17}H_{21}O_5S$ [MH^+] 337.1104, found 337.1106.

*1-(2-Oxo-2H-pyran-6-yl)heptyl 4-methylbenzenesulfonate ((±)-**14c**).* Following general procedure D, (±)-**13f** (210 mg, 1.0 mmol) was used to give rise to a colorless oil (291 mg, 0.80 mmol, 80%): R_f = 0.46 (PE/EA 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.77−7.71 (m, 2H), 7.34−7.28 (m, 2H), 7.21 (dd, J = 9.3, 6.6 Hz, 1H), 6.20−6.13 (m, 2H), 5.04 (t, J = 7.2 Hz, 1H), 2.42 (s, 3H), 1.93−1.78 (m, 2H), 1.33−1.06 (m, 8H), 0.84 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 161.0 (C_q), 160.4 (C_q), 145.3 (C_q), 142.9 (+), 133.3 (C_q), 129.8 (+), 127.9 (+), 115.6 (+), 103.8 (+), 78.8 (+), 33.1 (−), 31.5 (−), 28.5 (−), 24.5 (−), 22.4 (−), 21.7 (+), 14.0 (+); IR (ν/cm^{-1}) 2930, 2859, 1737, 1640, 1599, 1558, 1461, 1364, 1174, 1096, 1006, 887, 805; HRMS (ESI) m/z calcd for $C_{19}H_{25}O_5S$ [MH^+] 365.1417, found 365.1411.

*(E)-6-(Prop-1-en-1-yl)-2H-pyran-2-one (**15a**).*[6e] Following general procedure E, (±)-**14a** (154 mg, 0.5 mmol) was used to give rise to a white solid (58 mg, 0.43 mmol, 85%): ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.22 (dd, J = 9.3, 6.7 Hz, 1H), 6.62 (dq, J = 14.0, 7.0 Hz, 1H), 6.08 (d, J = 9.3 Hz, 1H), 5.98−5.91 (m, 1H), 5.89 (d, J = 6.7 Hz, 1H), 1.83 (dd, J = 7.0, 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 162.1 (C_q), 159.7 (C_q), 143.9 (+), 134.7 (+), 122.9 (+), 113.7 (+), 102.9 (+), 18.5 (+).

*(E)-6-(Pent-1-en-1-yl)-2H-pyran-2-one (**15b**).*[16a] Following general procedure E, (±)-**14b** (168 mg, 0.5 mmol) was used to give rise to a colorless oil (68 mg, 0.41 mmol, 83%): ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.23 (dd, J = 9.3, 6.7 Hz, 1H), 6.63 (dt, J = 15.6, 7.2 Hz, 1H), 6.09 (d, J = 9.2 Hz, 1H), 5.96−5.88 (m, 2H), 2.13 (dq, J = 7.3, 1.5 Hz, 2H), 1.42 (sext, J = 7.4 Hz, 2H), 0.87 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 162.1 (C_q), 159.7 (C_q), 143.9 (+), 139.7 (+), 121.7 (+), 113.7 (+), 103.1 (+), 34.9 (−), 21.9 (−), 13.7 (+).

*(E)-6-(Hept-1-en-1-yl)-2H-pyran-2-one (**15c**).*[16a] Following general procedure E, (±)-**14c** (182 mg, 0.5 mmol) was used to give rise to a colorless oil (81 mg, 0.42 mmol, 84%): ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.22 (dd, J = 9.3, 6.7 Hz, 1H), 6.63 (dt, J = 15.6, 7.2 Hz, 1H), 6.09 (d, J = 9.2 Hz, 1H), 5.96−5.87 (m, 2H), 2.14 (dq, J = 7.3, 1.4 Hz, 2H), 1.44−1.33 (m, 2H), 1.31−1.15 (m, 4H), 0.82 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 162.1 (C_q), 159.7 (C_q), 143.9 (+), 139.9 (+), 121.5 (+), 113.6 (+), 103.1 (+), 32.8 (−), 31.3 (−), 28.3 (−), 22.5 (−), 14.0 (+).

Enzymatic Resolution. To a solution of (±)-**13a** (140 mg, 1.0 mmol) in absolute toluene (8 mL) were added Novozyme 435 (200 mg, immobilized on acrylic resin), molecular sieves 4 Å (1.0 g), and isopropenyl acetate (0.44 mL, 4.0 mmol). The reaction mixture was stirred at 40 °C for 18 h. After filtration and evaporation of the solvent, the products were separated via flash chromatography (silica, PE/EA = 1:1) to yield (*R*)-**16** (81 mg, 0.45 mmol, 45%) as a colorless oil and (*S*)-**13a** (53 mg, 0.38 mmol, 38%) as a brownish oil.

*(R)-1-(2-Oxo-2H-pyran-6-yl)ethyl acetate (**16**):* R_f (PE/EA 1:1) = 0.5; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.29 (dd, J = 9.4, 6.6 Hz, 1H), 6.23 (d, J = 9.0 Hz, 1H), 6.20−6.16 (m, 1H), 5.55 (q, J = 6.7 Hz, 1H), 2.09 (s, 3H), 1.52 (d, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 169.8 (C_q), 162.7 (C_q)), 161.5 (C_q)), 143.2 (+), 115.4 (+), 102.2 (+), 68.2 (+), 21.0 (+), 18.3 (+); IR (ν/cm^{-1}) 3092, 2993, 2940, 1727, 1640, 1561, 1370, 1321, 1227, 1085, 1066, 1043, 943, 868, 801, 726, 610, 542, 442; HRMS (APCI) m/z calcd for $C_9H_{11}O_4$ [MH^+] 183.0652, found 183.0656; Chiral HPLC 84% ee (t_R major, minor = 42.1, 69.5 min, Chiralpak AS-H 4.6 × 250 mm 10 μm, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min); $[\alpha]_D^{25}$ = −142.1 (c = 1.0, $CHCl_3$).

*(S)-6-(1-Hydroxyethyl)-2H-pyran-2-one (**13a**).* Chiral HPLC >99% ee (t_R major, minor = 46.9, 52.0 min, Chiralpak AS-H 4.6 × 250 mm 10 μm, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min); $[\alpha]_D^{25}$ = +52.6 (c = 1.0, $CHCl_3$).

*(S)-1-(2-Oxo-2H-pyran-6-yl)ethyl 4-nitrobenzoate (**17**).* To a solution of (*S*)-**13a** > 99% ee (70 mg, 0.5 mmol) and Et_3N (0.1 mL, 0.7 mmol) in DCM (2 mL) was added a solution of 4-nitrobenzoyl chloride (111 mg, 0.6 mmol) in DCM (2 mL). The reaction mixture was stirred at room temperature for 15 h, and the product was purified via flash chromatography (silica, PE/EA = 2:1) to yield (*S*)-**17** (116 mg, 0.40 mmol, 80%) as a white solid: mp 162.3−164.1 °C; R_f (PE/EA 2:1) = 0.40; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 8.34−8.28 (m, 2H), 8.28−8.19 (m, 2H), 7.33 (dd, J = 9.4, 6.6 Hz, 1H), 6.33−6.30 (m, 1H), 6.30−6.26 (m, 1H), 5.86 (q, J = 6.7 Hz, 1H), 1.72 (d, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 163.6 (C_q), 161.6 (C_q), 161.3 (C_q), 150.8 (C_q), 143.0 (+), 134.8 (C_q), 131.0 (+), 123.7 (+), 116.0 (+), 102.9 (+), 69.8 (+), 18.2 (+); IR (ν/cm^{-1}) 3116, 2986, 2941, 2863, 1715, 1636, 1607, 1558, 1525, 1346, 1312, 1267, 1103, 1015, 891, 839, 805, 716; HRMS (CI) m/z calcd for $C_{14}H_{12}NO_6$ [MH^+] 290.06591, found 290.06596; Chiral HPLC >99% ee (t_R major, minor = 29.0, 36.4 min, Chiralpak AS-H 4.6 × 250 mm 10 μm, *n*-heptane/-PrOH 50:50, 0.5 mL/min); $[\alpha]_D^{25}$ = −65.9 (c = 1.0, $CHCl_3$).

*1-(2-Oxo-2H-pyran-6-yl)pentyl Acetate ((±)-**18**).* To a solution of (±)-**13e** (1.093 g, 6.0 mmol) in DCM (40 mL) were added Et_3N (4.2 mL, 30.0 mmol) and Ac_2O (2.8 mL, 30.0 mmol). The reaction mixture was stirred at room temperature for 18 h. The solvent was evaporated. and the product was purified via flash chromatography (silica, PE/EA = 3:1) to yield (±)-**18** (1.279 g, 5.70 mmol, 95%) as a yellowish oil: R_f (PE/EA 2:1) = 0.62; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.24 (dd, J = 9.4, 6.5 Hz, 1H), 6.17 (dd, J = 9.4, 0.9 Hz, 1H), 6.11 (d, J = 6.5 Hz, 1H), 5.41−5.34 (m, 1H), 2.05 (s, 3H), 1.89−1.74 (m, 2H), 1.35−1.15 (m, 4H), 0.83 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 170.0 (C_q), 162.1 (C_q), 161.6 (C_q), 143.1 (+), 115.3 (+), 102.9 (+), 71.9 (+), 31.9 (−), 27.1 (−), 22.3 (−), 20.9 (+), 13.9 (+); IR (ν/cm^{-1}) 2958, 2934, 2873, 1730, 1639, 1561, 1371, 1221, 1092, 1022, 803; HRMS (ESI) m/z calcd for $C_{12}H_{17}O_4$ [MH^+] 225.1121, found 225.1116.

Enzymatic Hydrolysis. To a solution of (±)-**18** (224 mg, 1.0 mmol) in acetone (5 mL) were added phosphate buffer (25 mL, 50 mM, pH 8) and Amano lipase from *B. cepacia* (200 mg), and the reaction mixture was stirred at 25 °C for 7 d. After filtration, the mixture was extracted with DCM (3×) and dried over $MgSO_4$. The products were separated via flash chromatography (silica, PE/EA = 2:1) to yield (*S*)-**18** (87 mg, 0.39 mmol, 39%) as a yellowish oil and (*R*)-**13e** (80 mg, 0.44 mmol, 44%) as a brownish oil.

*(S)-1-(2-Oxo-2H-pyran-6-yl)pentyl acetate (**18**):* chiral HPLC >99% ee (t_R major, minor = 28.9, 37.1 min, Chiralpak AS-H 4.6 × 250 mm 10 μm, *n*-heptane/-PrOH 90:10, 0.5 mL/min); $[\alpha]_D^{25}$ +127.3 (c = 1.0, $CHCl_3$).

*(R)-6-(1-Hydroxypentyl)-2H-pyran-2-one (**13e**):* Chiral HPLC 75% ee (t_R major, minor = 33.4, 40.2 min, Chiralpak AS-H 4.6 × 250 mm 10 μm, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min); $[\alpha]_D^{25}$ −62.2 (c = 1.0, $CHCl_3$).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01339.

X-ray data; NMR and HPLC spectra (PDF)
X-ray data for compound **11g** (CIF)
X-ray data for compound **12g** (CIF)
X-ray data for compound **13j** (CIF)
X-ray data for compound (*S*)-**17** (CIF)

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Notes

The authors declare no competing financial interest.
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