Electronic supporting information

Carbon chain shape selectivity by the mouse olfactory receptor OR-I7

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1. General Information

Unless otherwise stated, chemical reagents and solvents were purchased from VWR International, Fisher Scientific, or Sigma Aldrich and used without further purification. Tetrahydrofuran (THF) was either dried and distilled from Na/benzophenone or purified by passing through two packed columns of neutral alumina under argon prior to use. Octanal (I) and pentanal (3) were freshly distilled under nitrogen. Freshly prepared, argon-flushed aldehyde stock solutions (1.0 M in DMSO) were stored at 4°C in flame-sealed, evacuated ampoules while awaiting testing. Analytical TLC was performed on silica gel 60 F_{254} plates. Flash chromatography\(^1\) was performed on Teledyne Isco CombiFlash Rf-200 flash chromatography system. Melting points were measured on a Laboratory Devices Mel-Temp apparatus. \(^1\)H and \(^{13}\)C NMR spectra were recorded on a Varian Mercury 300 spectrometer or a Bruker Ultrashield 500 spectrometer. HRMS was performed on a Waters LCT XE (TOF) mass spectrometer using electrospray ionization (ESI). Infrared (IR) spectra were recorded using Thermo Nicolet 6700 FT-IR spectrometer. GC/MS analysis was performed on Shimadzu GCMS QP-2010 with GC-2010 Plus Gas Chromatograph using electron ionization (EI): Injection temperature: 250°C; held at 65°C for 1 min, heated from 65 to 80°C at 5°C/min, heated from 80 to 120°C at 15°C/min, heated from 120 to 200°C at 40°C/min, and held at 200°C for 3 min.

2. Experimental Procedures

2.1. General Procedure for Lithium Aluminum Hydride (LAH) Reduction\(^2\)

The acid or ester (1 mol equiv.) in diethyl ether was added slowly to lithium aluminum hydride (1.1 mol equiv.) suspended in diethyl ether at 0°C. The suspension was stirred at room temperature for 2-3 h and then cooled to 0°C. Water (1 mL per g of LAH) was added, followed by 15% sodium hydroxide (1 mL per g of LAH) and water (3 mL per g of LAH). The solution
was stirred for a few minutes at room temperature, filtered through a celite pad, washed with diethyl ether, dried, and concentrated to give the alcohol. Flash chromatography was used to purify the product.

2.2. General Procedure for Pyridinium Chlorochromate (PCC) Oxidation

The alcohol (1 equiv.) was added to pyridinium chlorochromate (1.1 equiv.) and silica gel (1 g/g of PCC) in dry dichloromethane under inert atmosphere. The suspension was stirred for 2 h and then passed through a silica gel pad. The solution was concentrated to give the aldehyde. Flash chromatography or distillation was used to purify the product.

2.3. General Procedure for Hydrogenation Reaction

The alkene was hydrogenated in ethyl acetate with a catalytic amount of Pd/C for 3 h using a balloon filled with hydrogen gas. The solution was filtered through celite and concentrated to give the alkane.

2.4. Synthesis of 2, 5, and 12

\[
\begin{align*}
\text{Scheme 1: Synthetic of 2, 5, and 12.}
\end{align*}
\]

The target compounds were synthesized from commercially available starting materials. Compound 2 was synthesized in two steps from the ester through LAH reduction followed by PCC oxidation, and compounds 5 and 12 were synthesized in one step from the alcohols through PCC oxidation (Scheme 1).

2-Cyclohexylethanol (2a). Ethyl cyclohexylacetate (2 g, 11.7 mmol) was LAH reduced according to the general procedure to obtain the alcohol 2a (1.5 g, 11.7 mmol) as a clear liquid in 99% yield. \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 3.68 (t, \(J = 6.7\) Hz, 2H), 1.78 - 1.59 (m, 5H), 1.51 - 1.11 (m, 7H), 1.02 - 0.84 (m, 2H). \(^13\)C NMR (CDCl\(_3\)) \(\delta\): 60.89, 40.39,
34.22, 33.38, 26.57, 26.29. IR (thin film, KBr plates) $\nu$ (cm$^{-1}$): 3332 (broad), 2922, 2852, 1448, 1051, 1011, 978. Spectral data match those reported previously.$^2$

**Cyclohexylethanal (2).** Compound 2a (200 mg, 1.56 mmol) was PCC oxidized according to the general procedure to obtain the aldehyde 2 (140 mg, 1.11 mmol) as a clear liquid in 71% yield. $^1$H NMR (CDCl$_3$) $\delta$: 9.75 (s, 1H), 2.29 (dd, $J = 1.9$, 6.9 Hz, 2H), 1.97 - 1.57 (m, 6H), 1.40 - 0.84 (m, 5H). $^{13}$C NMR (CDCl$_3$) $\delta$: 203.00, 51.38, 33.22, 32.68, 26.04, 25.97. IR (thin film, KBr plates) $\nu$ (cm$^{-1}$): 2925, 2853, 2712, 1725, 1449, 1408, 1297, 1193, 1020, 900. Spectral data match those reported previously.$^2$

**3-Methylpentanal (5).** 3-Methyl-1-pentanol (2 g, 19.6 mmol) was PCC oxidized according to the general procedure. The product was purified by distillation to give 5 (450 mg, 4.5 mmol) as a clear liquid in 23% yield as a racemic mixture. $^1$H NMR (CDCl$_3$) $\delta$: 9.80 - 9.72 (m, 1H), 2.46 - 2.31 (m, 1H), 2.21 (ddd, $J = 2.5$, 7.8, 16.1 Hz, 1H), 1.97 (qd, $J = 6.8$, 13.3 Hz, 1H), 1.45 - 1.17 (m, 2H), 1.02 - 0.78 (m, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$: 203.19, 50.69, 29.74, 29.51, 19.52, 11.30. IR (thin film, KBr plates), $\nu$ (cm$^{-1}$): 2964, 2932, 2878, 2822, 2717, 1728, 1463, 1381, 1209, 1141, 1021, 946, 875, 776. Spectral data match those reported previously.$^3$-$^5$

**2-(1-Adamantyl)ethanal (12).** 2-(1-Adamantyl)ethanol (200 mg, 1.1 mmol) was PCC oxidized according to the general procedure to the aldehyde 12 (140 mg, 0.79 mmol) in 71% yield. This compound was noticed to have a camphor odor. $^1$H NMR (CDCl$_3$) $\delta$: 9.87 (t, $J = 3.2$ Hz, 1H), 2.13 (d, $J = 3.0$ Hz, 2H), 1.99 (br. s., 3H), 1.78 - 1.59 (m, 12H). $^{13}$C NMR (CDCl$_3$) $\delta$: 203.59, 57.25, 42.73, 36.65, 33.34, 28.49. IR (thin film, KBr plates), $\nu$ (cm$^{-1}$): 2903, 2848, 2728, 1721, 1450, 1406, 1362, 1346. GC retention time: 10.68 min. MS (EI) [M]$^+$: 178. Spectral data match those previously reported.$^6$-$^7$


![Scheme 2: Synthesis of 6.](image)

Compound 6 was synthesized in four steps from 3-pentanone (Scheme 2). 3-Pentanone was subjected to a Horner-Wadsworth-Emmons reaction to afford the α,β-unsaturated ester 6a, which was then hydrogenated to give the saturated ester 6b. The ester was reduced to the alcohol 6c and oxidized into the aldehyde 6.

*Ethyl 3-ethylded-2-enoate (6a).* Compound 6a was synthesized according to a literature procedure.\(^8\) Triethyl phosphonoacetate (7.8 g, 34 mmol) in THF (12.5 mL) was slowly added to 57-63% sodium hydride, in oil, (1.4 g, 34 mmol) in dry THF (10 mL) at 0°C. The suspension was stirred for 1 h and then 3-pentanone (3 g, 34 mmol) in THF (12.5 mL) was slowly added. The solution was stirred for an hour and quenched with water. The solution was extracted with diethyl ether, and the organic layer was dried and concentrated. The crude was purified by flash chromatography eluting with hexanes/diethyl ether (99:1) to give 6a (1.58 g, 10.1 mmol) as a yellowish liquid in 29% yield. \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 5.59 (s, 1H), 4.14 (q, \(J = 6.7\) Hz, 2H), 2.61 (q, \(J = 7.4\) Hz, 2H), 2.18 (q, \(J = 7.4\) Hz, 2H), 1.27 (t, \(J = 6.6\) Hz, 3H), 1.06 (t, \(J = 7.4\) Hz, 6H). \(^13\)C NMR (CDCl\(_3\)) \(\delta\): 167.30, 166.65, 113.71, 59.44, 30.74, 25.44, 14.33, 13.04, 12.02. IR (thin film, KBr plates) \(\nu\) (cm\(^{-1}\)): 2972, 2936, 2877, 1717, 1645, 1463, 1380, 1307, 1273, 1205, 1148, 1105, 1040, 868. Spectral data match those previously reported.\(^9\)

*Ethyl 3-ethylpentanoate (6b).* Compound 6a (1.48 g, 9.47 mmol) was hydrogenated according to the general procedure to give 6b (1.35 g, 8.53
mmol) as a clear liquid in 90% yield. $^1$H NMR (CDCl$_3$) $\delta$: 4.12 (q, $J = 7.1$ Hz, 2H), 2.22 (d, $J = 6.9$ Hz, 2H), 1.74 (p, $J = 6.4$ Hz, 1H), 1.42 - 1.18 (m, 7H), 0.87 (t, $J = 7.4$ Hz, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$: 173.76, 60.08, 38.56, 37.93, 25.85, 14.28, 10.82. IR (thin film, KBr plates) $\nu$ (cm$^{-1}$): 2962, 2926, 2857, 1738, 1461, 1374, 1178, 1097, 1034. Spectral data match those previously reported.$^{10}$

**3-Ethylpentan-1-ol (6c).** This and the following compound were previously synthesized,$^{8}$ but no spectral data was reported. Compound 6b (1.25 g, 7.9 mmol) was LAH reduced according to the general procedure and purified by flash chromatography eluting with hexanes/ethyl acetate (49:1) to give 6c (480 mg, 4.13 mmol) as a clear liquid in 52% yield. $^1$H NMR (CDCl$_3$) $\delta$: 3.64 (t, $J = 7.2$ Hz, 2H), 1.93 - 1.63 (br. s., 1H), 1.63 - 1.40 (m, 2H), 1.29 (d, $J = 5.5$ Hz, 5H), 0.84 (t, $J = 6.9$ Hz, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$: 61.37, 37.08, 36.11, 25.50, 10.78. IR (thin film, KBr plates), $\nu$ (cm$^{-1}$): 3331 (broad), 2961, 2925, 2874, 1461, 1379, 1062.

**3-Ethylpentanal (6).** Compound 6c (100 mg, 0.875 mmol) was PCC oxidized according to the general procedure to obtain 6 (32 mg, 0.280 mmol) as a clear liquid in 33% yield. $^1$H NMR (CDCl$_3$) $\delta$: 9.77 (t, $J = 2.3$ Hz, 1H), 2.33 (dd, $J = 2.5$, 6.6 Hz, 2H), 1.84 (td, $J = 6.5$, 12.8 Hz, 1H), 1.46 - 1.25 (m, 4H), 0.88 (t, $J = 7.4$ Hz, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$: 203.43, 47.84, 35.88, 26.15, 10.92. IR (thin film, KBr plates), $\nu$ (cm$^{-1}$): 2964, 2935, 2878, 2714, 1727, 1461, 1412, 1382, 1337, 1246, 1136, 1096, 1021. GC retention time: 2.82 min. MS (EI) [M-CH$_2$CH$_3$]$^+$: 85.
2.6. Synthetic route to compounds 7, 8, 10, and 11.

![Scheme 3: Synthetic route of compounds 7, 8, 10, and 11.](image)

Compound 7 was synthesized starting from 3-pentanone. 3-Pentanone reacted with ethyl cyanoacetate to form the α,β-unsaturated cyanoester 7a, which served as the Michael acceptor in the following 1,4 addition reaction with a Grignard reagent, formed from magnesium and iodomethane, as the Michael donor, to obtain 7b. The ester 7b was hydrolyzed and decarboxylated to form the nitrile 7d, which was then hydrolyzed and reduced to the alcohol 7f. The alcohol 7f was oxidized to form the aldehyde 7. Compound 8 was synthesized in a similar manner but using bromoethane instead of iodomethane to form the Grignard reagent. Compounds 10 and 11 were also synthesized through the same route but starting with cyclohexanone instead of pentanone (Scheme 2.3).

**Ethyl 2-cyano-3-ethylpent-2-enoate (7a).** Compound 7a was synthesized based on a literature procedure. Ethyl cyanoacetate (56.5 g, 0.5 mol), 3-pentanone (51.7 g, 0.6 mol), ammonium acetate (3.85 g, 0.05 mol), and acetic acid (6 g, 0.1 mol) were added to benzene (50 mL) in a round bottom flask connected to a Dean-Stark apparatus. The solution was refluxed for 6 h and then washed three times with water. The organic layer was dried and concentrated. The product was purified by distillation to give 7a (58.5 g, 0.32 mol) as a clear liquid in 64.6% yield. $^1$H NMR (CDCl$_3$) $\delta$: 4.26 (q, $J = 7.2$ Hz, 2H), 2.78 (q, $J = 7.4$ Hz, 2H), 2.57 (q, $J = 7.4$ Hz, 2H), 1.34 (t, $J = 7.2$ Hz, 3H), 1.13 (t, $J = 7.4$ Hz,
3H), 1.19 (t, \( J = 7.7 \) Hz, 3H). \(^{13}\)C NMR (CDCl\(_3\)) \( \delta \): 184.19, 161.70, 115.62, 104.01, 61.68, 31.40, 26.51, 14.08, 12.65, 12.38. IR (thin film, KBr plates), \( \nu \) (cm\(^{-1}\)): 2981, 2941, 2879, 2223, 1731, 1602, 1465, 1368, 1245, 1270, 1211, 1099, 1022, 912, 857, 817.

*Ethyl 2-cyano-3-ethyl-3-methylpentanoate (7b).* Compound 7b was synthesized based on literature procedures.\(^{12}\) \(^{13}\) Iodomethane (11.3 g, 80 mmol) in diethyl ether (10 mL) was slowly added to magnesium turnings (1.83 g, 76 mmol) in diethyl ether (10 mL) at 0°C and the solution was stirred for 30 minutes. Copper chloride (100 mg, 1 mmol) was added, and 7a (9.06 g, 50 mmol) in diethyl ether (10 mL) was slowly added. The solution was stirred for 30 minutes and then added to 10% sulfuric acid (40 mL) in ice (50 g). The aqueous phase was extracted three times with diethyl ether. The combined organic layer was dried and concentrated. The resulting residue was purified by flash chromatography eluting with hexanes/ethyl acetate (9:1) to give 7b (4.3 g, 21.8 mmol) as a clear liquid in 43.6% yield. \(^1\)H NMR (CDCl\(_3\)) \( \delta \): 4.32 - 4.20 (m, 2H), 3.45 (s, 1H), 1.64 - 1.39 (m, 4H), 1.39 - 1.22 (m, 3H), 1.08 (s, 3H), 0.98 - 0.82 (m, 6H). \(^{13}\)C NMR (CDCl\(_3\)) \( \delta \): 165.57, 116.22, 62.32, 46.26, 40.47, 29.60, 28.91, 21.79, 14.06, 7.90, 7.75. IR (thin film, KBr plates), \( \nu \) (cm\(^{-1}\)): 2972, 2884, 2247, 1742, 1465, 1389, 1369, 1328, 1244, 1192.

*3-Ethyl-3-methylpentanenitrile (7d).* Compound 7d was synthesized based on a literature procedure.\(^{13}\) Compound 7b (4 g, 20 mmol) was added to a solution containing 85% potassium hydroxide (5.8 mL), water (25.4 mL), and ethanol (5 mL). The solution was refluxed for 6 h and then concentrated. The resulting residue was refluxed for 4 h in 20% sulfuric acid (31 mL). The solution was cooled to room temperature and extracted with diethyl ether. The organic layer was dried and concentrated. A catalytic amount of copper powder (70 mg) was added to the resulting residue (7c) and the suspension was slowly heated to
170°C. The suspension was then allowed to cool back to room temperature and was purified by flash chromatography, eluting with hexanes/ethyl acetate (19:1) to give 7d (1.26 g, 10.1 mmol) as a yellowish liquid in 50% yield. \[^1\]H NMR (CDCl\textsubscript{3}) \(\delta\): 2.20 (s, 2H), 1.40 (q, \(J = 7.2\) Hz, 4H), 0.98 (s, 3H), 0.84 (t, \(J = 7.6\) Hz, 6H). \[^{13}\]C NMR (CDCl\textsubscript{3}) \(\delta\): 118.57, 35.68, 30.88, 27.65, 23.65, 7.95. IR (thin film, KBr plates), \(\nu\) (cm\textsuperscript{-1}): 2969, 2941, 2883, 2243, 1463, 1425, 1385.

**3-Ethyl-3-methylpentan-1-ol (7f).** Compound 7d was hydrolyzed based on a literature procedure.\[^{14}\] Compound 7d (1.1 g, 8.8 mmol) was refluxed in a solution with sulfuric acid (8.1 mL) and water (9.8 mL) for 6 h. The solution was cooled to room temperature, diluted with water, and extracted with diethyl ether. The organic layer was dried and concentrated. The resulting residue 7e was LAH reduced according to the general procedure and purified by flash chromatography eluting with hexanes/ethyl acetate (9:1) to give 7f (650 mg, 5 mmol) as a clear liquid in 56.8% yield. \[^1\]H NMR (CDCl\textsubscript{3}) \(\delta\): 3.77 - 3.57 (m, 2H), 1.90 (s, 1H), 1.75 - 1.38 (m, 2H), 1.38 - 1.02 (m, 4H), 1.02 - 0.66 (m, 9H). \[^{13}\]C NMR (CDCl\textsubscript{3}) \(\delta\): 59.50, 41.12, 34.46, 31.36, 24.23, 7.89. IR (thin film, KBr plates) \(\nu\) (cm\textsuperscript{-1}): 3333 (broad), 2963, 2938, 2880, 1463, 1380.

**3-Ethyl-3-methylpentanal (7).** Compound 7f (100 mg, 0.77 mmol) was PCC oxidized according to the general procedure to give 7 (58 mg, 0.45 mmol) in 59% yield. \[^1\]H NMR (CDCl\textsubscript{3}) \(\delta\): 9.84 (t, \(J = 3.3\) Hz, 1H), 2.24 (d, \(J = 3.3\) Hz, 2H), 1.38 (q, \(J = 7.4\) Hz, 4H), 1.00 (s, 3H), 0.85 (t, \(J = 7.4\) Hz, 6H). \[^{13}\]C NMR (CDCl\textsubscript{3}) \(\delta\): 204.05, 52.00, 36.33, 31.81, 24.33, 7.91. IR (thin film, KBr plates), \(\nu\) (cm\textsuperscript{-1}): 2967, 2882, 2732, 1721, 1463, 1382. GC retention time: 3.93 min. MS (EI) [M-CH\textsubscript{2}CH\textsubscript{3}]\(^+\): 99. HRMS (ESI) [M+H]\(^+\): Calcd for C\textsubscript{8}H\textsubscript{16}O \(m/z = 129.1274\), found \(m/z = 129.1266\).
**Ethyl 2-cyano-3,3-diethylpentanoate (8b).** Compound 8b was synthesized based on literature procedures.\textsuperscript{12,13} Bromoethane (8.7 g, 80 mmol) in diethyl ether (10 mL) was slowly added to magnesium turnings (1.83 g, 76 mmol) in diethyl ether (10 mL) at 0°C and the solution was stirred for 30 minutes. Copper chloride (100 mg, 1 mmol) was added, and 7a (9.06 g, 50 mmol) in diethyl ether (10 mL) was slowly added. The solution was stirred for 30 minutes and then added to 10% sulfuric acid (40 mL) in ice (50 g). The aqueous phase was extracted three times with diethyl ether. The combined organic layer was dried and concentrated. The resulting residue was purified by flash chromatography eluting with hexanes/ethyl acetate (9:1) to give 8b (4.45 g, 21.1 mmol) as a clear liquid in 42% yield.\textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\): 4.31 - 4.20 (m, 2H), 3.49 - 3.43 (m, 1H), 1.65 - 1.41 (m, 6H), 1.38 - 1.25 (m, 3H), 0.99 - 0.84 (m, 9H).\textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\): 165.74, 116.67, 62.32, 44.43, 43.12, 27.59, 13.98, 7.90. IR (thin film, KBr plates), \(\nu\) (cm\textsuperscript{-1}): 2972, 2944, 2885, 2246, 1741, 1602, 1459.

**3,3-Diethylpentanenitrile (8d).** Compound 8d was synthesized according to a literature procedure.\textsuperscript{13} Compound 8b (4.2 g, 20 mmol) was added to a solution containing 85% potassium hydroxide (6.1 mL), water (26.7 mL), and ethanol (5.25 mL). The solution was refluxed for 6 hours and then concentrated. The resulting residue was refluxed for 4 h in 20% sulfuric acid (32.6 mL). The solution was cooled to room temperature and extracted with diethyl ether. The organic layer was dried and concentrated. A catalytic amount of copper powder (80 mg) was added to the resulting residue (8c) and the suspension was slowly heated to 170°C. The suspension was then allowed to cool back to room temperature and was purified by flash chromatography, eluting with hexanes/ethyl acetate (19:1) to give 8d (1.32 g, 9.5 mmol) as a yellowish liquid in 47% yield.\textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\): 2.19 (s, 2H), 1.44 -
1.31 (m, 6H), 0.82 (t, $J = 7.4$ Hz, 9H). $^{13}$C NMR (CDCl$_3$) $\delta$: 118.49, 38.10, 27.87, 24.80, 7.54. IR (thin film, KBr plates), $\nu$ (cm$^{-1}$): 2968, 2943, 2882, 2245, 1735, 1461, 1425, 1383.

3,3-Diethylpentan-1-ol (8f). Compound 8d (1.1 g, 7.9 mmol) was refluxed in a solution of sulfuric acid (8.1 mL) and water (9.8 mL) for 6 h. The solution was cooled to room temperature, diluted with water, and extracted with diethyl ether. The organic layer was dried and concentrated. The resulting residue 8e was LAH reduced according to the general procedure and purified by flash chromatography eluting with hexanes/ethyl acetate (9:1) to give 8f (350 mg, 2.4 mmol) as a clear liquid in 31% yield. $^1$H NMR (CDCl$_3$) $\delta$: 3.70 - 3.57 (m, 2H), 1.56 - 1.40 (m, 3H), 1.29 - 1.13 (m, 6H), 0.83 - 0.71 (m, 9H). $^{13}$C NMR (CDCl$_3$) $\delta$: 59.28, 38.08, 36.79, 27.99, 7.46. IR (thin film, KBr plates) $\nu$ (cm$^{-1}$): 3323 (broad), 2964, 2939, 2880, 1464, 1378, 1036.

3,3-Diethylpentanal (8). Compound 8f (100 mg, 0.69 mmol) was PCC oxidized according to the general procedure to give 8 (44 mg, 0.31 mmol) in 45% yield. $^1$H NMR (CDCl$_3$) $\delta$: 9.83 (t, $J = 3.3$ Hz, 1H), 2.24 (d, $J = 3.0$ Hz, 2H), 1.45 - 1.32 (m, 6H), 0.92 - 0.76 (m, 9H). $^{13}$C NMR (CDCl$_3$) $\delta$: 204.03, 49.23, 40.98, 28.55, 7.52. IR (thin film, KBr plates), $\nu$ (cm$^{-1}$): 2967, 2882, 2733, 1721, 1462, 1381, 1300, 1155, 1093, 1028. GC retention time: 6.03 min. MS (EI) [M-$\text{CH}_2\text{CH}_3$]$^+$: 113.

Ethyl cyano(cyclohexylidene)acetate (10a). Ethyl cyanoacetate (56.5 g, 0.5 mol), cyclohexanone (58.9 g, 0.6 mol), ammonium acetate (3.85 g, 0.05 mol), and acetic acid (6 g, 0.1 mol) were added to benzene (50 mL) in a round bottom flask connected to a Dean and Stark apparatus. The solution was refluxed for 6 h and then washed three times with water. The organic layer was dried and concentrated. The product was purified by distillation to give 10a (60.6 g, 0.31 mol) as a clear liquid in 63% yield.
\[^{1}\text{H NMR (CDCl}_3\) δ: 4.26 (q, J = 7.0 Hz, 2H), 2.97 (t, J = 5.8 Hz, 2H), 2.70 - 2.60 (m, 2H), 1.85 - 1.57 (m, 6H), 1.34 (t, J = 7.2 Hz, 3H). \[^{13}\text{C NMR (CDCl}_3\) δ: 180.03, 162.03, 115.63, 102.06, 61.72, 36.91, 31.59, 28.59, 28.26, 25.65, 14.09. IR (thin film, KBr plates) ν (cm\(^{-1}\)): 2939, 2861, 2224, 1729, 1601, 1447, 1367, 1201. Spectral data agree with those previously reported.\(^{15}\)

\[\text{Ethyl cyano(1-methylcyclohexyl)acetate (10b).} \]

Compound 10b was synthesized based on literature procedures.\(^{12}\)\(^{13}\) Iodomethane (11 g, 77 mmol) in diethyl ether (10 mL) was slowly added to magnesium turnings (1.83 g, 76 mmol) in diethyl ether (10 mL) at 0°C and the solution was stirred for 30 minutes. Copper chloride (100 mg, 1 mmol) was added, and 10a (9.66 g, 50 mmol) in diethyl ether (10 mL) was slowly added. The solution was stirred for 30 minutes and then added to 10% sulfuric acid (40 mL) in ice (50 g). The aqueous phase was extracted three times with diethyl ether. The combined organic layer was dried and concentrated. The resulting residue was purified by flash chromatography eluting with hexanes/ethyl acetate (9:1) to give 10b (10.4 g, 49.7 mmol) as a yellowish liquid in 99% yield. \[^{1}\text{H NMR (CDCl}_3\) δ: 4.32 - 4.19 (m, 2H), 3.45 (s, 1H), 1.62 - 1.37 (m, 10H), 1.31 (t, J = 7.0 Hz, 3H), 1.14 (s, 3H). \[^{13}\text{C NMR (CDCl}_3\) δ: 165.26, 115.88, 62.20, 48.21, 37.62, 36.25, 35.36, 25.45, 21.93, 21.60, 21.55, 14.04. IR (thin film, KBr plates), ν (cm\(^{-1}\)): 2933, 2861, 2247, 1742, 1601, 1448, 1388, 1370, 1325. Spectral data match those previously reported.\(^{12}\)

\[\text{(1-Methylcyclohexyl)acetonitrile (10d).} \]

Compound 10d was synthesized based on a literature procedure.\(^{13}\) Compound 10b (5.2 g, 25 mmol) was added to a solution containing 85% potassium hydroxide (7.5 mL), water (33 mL), and ethanol (6.5 mL). The solution was refluxed for 6 hours and then concentrated. The resulting residue was refluxed for 4 h in 20% sulfuric acid (40.3 mL). The solution was cooled to room temperature
and extracted with diethyl ether. The organic layer was dried and concentrated. A catalytic amount of copper powder (70 mg) was added to the resulting residue (10c) and the suspension was slowly heated to 170°C. The suspension was then allowed to cool back to room temperature and was purified by flash chromatography, eluting with hexanes/ethyl acetate (19:1) to give 10d (2.2 g, 16 mmol) as a yellowish liquid in 64% yield. ¹H NMR (CDCl₃) δ: 2.25 (s, 2H), 1.63 - 1.31 (m, 10H), 1.07 (s, 3H). ¹³C NMR (CDCl₃) δ: 118.44, 36.95, 33.01, 30.33, 25.75, 25.24, 21.88. IR (thin film, KBr plates) ν (cm⁻¹): 2929, 2855, 2242, 1742, 1453, 1422, 1384.

2-(1-Methylcyclohexyl)ethanol (10f). Compound 10d (1.89 g, 13.8 mmol) was refluxed in a solution with sulfuric acid (14 mL) and water (16.8 mL) for 6 h. The solution was cooled to room temperature, diluted with water, and extracted with diethyl ether. The organic layer was dried and concentrated. The resulting residue 10e was LAH reduced according to the general procedure and purified by flash chromatography eluting with hexanes/ethyl acetate (9:1) to give 10f (710 mg, 5 mmol) as a yellowish liquid in 36% yield. ¹H NMR (CDCl₃) δ: 3.75 - 3.65 (m, 2H), 1.61 - 1.48 (m, 2H), 1.48 - 1.17 (m, 11H), 0.90 (s, 3H). ¹³C NMR (CDCl₃) δ: 59.45, 44.49, 38.15, 32.16, 26.40, 25.39, 21.97. IR (thin film, KBr plates) ν (cm⁻¹): 3330 (broad), 2925, 2851, 1453, 1043, 1019.

(1-Methylcyclohexyl)acetaldehyde (10). Compound 10d (100 mg, 0.70 mmol) was PCC oxidized according to the general procedure to give 10 (62 mg, 0.44 mmol) in 63% yield. ¹H NMR (CDCl₃) δ: 9.86 (t, J = 3.3 Hz, 1H), 2.29 (d, J = 3.0 Hz, 2H), 1.55 - 1.31 (m, 10H), 1.08 (s, 3H). ¹³C NMR (CDCl₃) δ: 203.96, 54.53, 38.18, 33.69, 26.01, 25.77, 21.78. IR (thin film, KBr plates), ν (cm⁻¹): 2928, 2853, 2729, 1721, 1453, 1380. GC retention time: 6.79 min. MS (EI) [M]⁺: 140. Spectral data match those previously reported.¹⁶
**Ethyl cyano(1-ethylcyclohexyl)acetate** (**11b**). Compound **11b** was synthesized based on literature procedures.\(^{12, 13}\) Bromoethane (8.7 g, 80 mmol) in diethyl ether (10 mL) was slowly added to magnesium turnings (1.83 g, 76 mmol) in diethyl ether (10 mL) at 0°C and the solution was stirred for 30 minutes. Copper chloride (50 mg, 0.5 mmol) was added, followed by **10a** (9.06 g, 50 mmol) in diethyl ether (10 mL) was slowly added. The solution was stirred for 30 minutes and then added to 10% sulfuric acid (40 mL) in ice (50 g). The aqueous phase was extracted three times with diethyl ether. The combined organic layer was dried and concentrated. The resulting residue was purified by flash chromatography eluting with hexanes/ethyl acetate (9:1) to give **11b** (3.6 g, 16.2 mmol) as a clear liquid in 32% yield. \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 4.25 (q, \(J = 7.2\) Hz, 2H), 3.61 (s, 1H), 1.76 - 1.40 (m, 12H), 1.32 (t, \(J = 7.0\) Hz, 3H), 0.89 (t, \(J = 7.4\) Hz, 3H). \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\): 165.56, 116.26, 62.29, 45.57, 40.50, 32.54, 32.37, 26.66, 25.39, 21.31, 21.28, 14.08, 7.42. IR (thin film, KBr plates) \(\nu\) (cm\(^{-1}\)): 2935, 2865, 2246, 1741, 1456, 1387, 1369, 1323. HRMS (ESI) \([\text{M+Na}]^+\): Calcd for C\(_{13}\)H\(_{21}\)NO\(_2\) \(m/z = 246.1464\), found \(m/z = 246.1471\).

**\((1\text{-Ethylcyclohexyl})\text{acetonitrile}** (**11d**). Compound **11d** was synthesized based on a literature procedure.\(^{13}\) Compound **11b** (3.5 g, 15.7 mmol) was added to a solution containing 85% potassium hydroxide (5.1 mL), water (22.2 mL), and ethanol (4.38 mL). The solution was refluxed for 6 h and then concentrated. The resulting residue was refluxed for 4 h in 20% sulfuric acid (27.1 mL). The solution was cooled to room temperature and extracted with diethyl ether. The organic layer was dried and concentrated. A catalytic amount of copper powder (60 mg) was added to the resulting residue (**11c**) and the suspension was slowly heated to 170°C. The suspension was then allowed to cool to room temperature and was purified by flash chromatography, eluting with hexanes/ethyl acetate (19:1) to give **11d** (1.4 g, 9.3 mmol).
as a clear liquid in 59% yield. $^1$H NMR (CDCl$_3$) $\delta$: 2.28 (s, 2H), 1.58 - 1.36 (m, 12H), 0.92 - 0.81 (m, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$: 118.49, 35.38, 34.65, 30.00, 26.07, 25.80, 21.52, 7.36. IR (thin film, KBr plates) $\nu$ (cm$^{-1}$): 2966, 2929, 2857, 2243. HRMS (ESI) [M+Na]$^+$: Calcd for C$_{10}$H$_{17}$N $m/z = 174.1253$, found $m/z = 174.1266$.

2-(1-Ethylcyclohexyl)ethanol (11f). Compound 11d (1.26 g, 8.3 mmol) was refluxed in a solution of sulfuric acid (9.3 mL) and water (11.2 mL) for 6 hours. The solution was cooled to room temperature, diluted with water, and extracted with diethyl ether. The organic layer was dried and concentrated. The resulting residue 11e was LAH reduced according to the general procedure and purified by flash chromatography eluting with hexanes/ethyl acetate (9:1) to give 11f (690 mg, 4.4 mmol) as a yellowish liquid in 53% yield. $^1$H NMR (CDCl$_3$) $\delta$: 3.71 - 3.60 (m, 2H), 1.61 - 1.47 (m, 2H), 1.47 - 1.20 (m, 13H), 0.79 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$: 59.15, 39.20, 35.79, 34.37, 29.67, 26.47, 21.60, 7.42. IR (thin film, KBr plates) $\nu$ (cm$^{-1}$): 3329 (broad), 2925, 2859, 1460, 1379.

(1-Ethylcyclohexyl)acetaldehyde (11). Compound 11d (100 mg, 0.64 mmol) was PCC oxidized according to the general procedure to give 11 (70 mg, 0.45 mmol) in 71% yield. $^1$H NMR (CDCl$_3$) $\delta$: 9.84 (t, $J = 3.3$ Hz, 1H), 2.31 (d, $J = 3.3$ Hz, 2H), 1.53 - 1.35 (m, 12H), 0.90 - 0.80 (m, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$: 204.15, 49.99, 36.47, 35.80, 30.58, 26.10, 21.48, 7.48. IR (thin film, KBr plates), $\nu$ (cm$^{-1}$): 2928, 2856, 2726, 1720, 1456, 1381. GC retention time: 8.60 min. MS (EI) [M-CH$_2$CH$_3$]$^+$: 125. HRMS (ESI) [M+Na]$^+$: Calcd for C$_{10}$H$_{18}$O $m/z = 177.1255$, found $m/z = 177.1275$. 

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2.7. Synthesis of 9.

Scheme 4: Synthesis of 9.

Compound 9 was synthesized (Scheme 2.4) starting from crotonaldehyde. The bicyclic ring of 9 was obtained through two Diels-Alder reaction. First, crotonaldehyde was subjected to a nucleophilic addition reaction to form 9a, which was used as the diene in the following Diels-Alder reaction with ethyl acrylate as the dienophile to form 9b. Compound 9b was subjected to an elimination reaction to form the ester 9c, which would serve as the diene in another Diels-Alder reaction with maleic anhydride as the dienophile to form 9d. The alkene 9d was hydrogenated to the alkane 9e, which was then hydrolyzed to cleave the anhydride into carboxylates 9f. The carboxylate groups were decarboxylated to form 9g. The alkene 9g was hydrogenated to reduce the double bond on the ring to form 9h. The ester 9h was LAH reduced to the alcohol 9i. The alcohol 9i was homologated by an extra carbon via a PCC oxidation.
reaction, followed by a Wittig reaction and a hydroboration-oxidation reaction to form the aldehyde 9j, the alkene 9k, and the alcohol 9l, respectively. The alcohol 9l was then oxidized to the aldehyde 9.

\[
(1E)-N,N\text{-diethylbuta-1,3-dien-1-amine} \quad (9a).
\]

Compound 9a was synthesized according to a literature procedure.\(^{17}\) Crotonaldehyde (8 g, 0.114 mol) in toluene (15 mL) was added to a solution of diethylamine and potassium carbonate at 4°C. The solution was allowed to come to room temperature and was stirred for 4 h. The product was purified by distillation to give 9a as a yellow liquid (6.5 g, 52 mmol) in 45% yield. \(^{1}H\) NMR (CDCl\(_3\)) \(\delta\): 6.35 - 6.17 (m, 2H), 5.03 (dd, \(J = 10.7, 13.2\) Hz, 1H), 4.76 - 4.64 (m, 1H), 4.50 - 4.40 (m, 1H), 3.05 (q, \(J = 7.2\) Hz, 4H), 1.19 - 0.90 (m, 6H). Spectral data match those previously reported.\(^{17}\)

\[
Ethyl \ 2\text{-}(diethylamino)cyclohex-3-ene-1-carboxylate \quad (9b).
\]

Compound 9b was synthesized according to a literature procedure.\(^{17}\) To 9a (6.5 g, 52 mmol) in toluene (11.2 mL) was added ethyl acrylate (5.66 g, 56.5 mmol). The solution was stirred for 5 days in the dark under argon. The solution was diluted with diethyl ether and extracted three times with 2 M HCl. The combined aqueous layer was extracted twice with diethyl ether. The pH of the aqueous solution was raised to 10 by adding 6 M NaOH. The aqueous phase was extracted with diethyl ether three times. The combined ether layer was dried and concentrated to give 9b (9.8 g, 43 mmol) as a yellowish liquid in 84% yield. 9b was used for the next step without further purification. \(^{1}H\) NMR (CDCl\(_3\)) \(\delta\): 5.90 (br. s., 1H), 5.83 - 5.55 (m, 1H), 4.13 (dd, \(J = 6.9, 12.4\) Hz, 2H), 3.77 - 3.51 (m, 1H), 2.75 - 2.36 (m, 5H), 2.30 - 2.10 (m, 1H), 2.05 (br. s., 1H), 1.99 - 1.83 (m, 1H), 1.80 (br. s., 1H), 1.42 - 1.11 (m, 3H), 1.10 - 0.77 (m, 6H). Spectral data match those previously reported.\(^{17}\)
**Ethyl cyclohexa-1,3-diene-1-carboxylate (9c).** Compound 9c was synthesized according to a literature procedure. Compound 9b (9.8 g, 43 mmol) was added to acetic acid (48 mL) and refluxed for 2 h. The reaction was quenched with ice water and extracted three times with diethyl ether. The combined organic layer was washed with water, saturated sodium bicarbonate, and brine, dried, and concentrated. The resulting residue was purified by flash chromatography, eluting with hexanes/ethyl acetate (49:1) to give 9c (5 g, 33 mmol) as a yellowish liquid in 75.5% yield. $^1$H NMR (CDCl$_3$) δ: 6.95 (br. s., 1H), 6.16 - 5.94 (m, 2H), 4.26 - 4.09 (m, 2H), 2.50 - 2.31 (m, 2H), 2.31 - 2.13 (m, 2H), 1.35 - 1.18 (m, 3H). Spectral data match those previously reported.

**Ethyl 3,5-dioxo-4-oxatricyclo[5.2.2.0$^{2,6}$]undec-8-ene-1-carboxylate (9d).** Compound 9d was synthesized according to a literature procedure. Compound 9c (5 g, 33 mmol) was mixed with maleic anhydride (3.3 g, 33 mmol) and stirred for 30 minutes at 100°C and 30 minutes at 170°C. The product was purified by flash chromatography eluting with dichloromethane to give 9d (7.78 g, 31 mmol) as a white solid (m.p. 85-86°C) in 94.6% yield. $^1$H NMR (CDCl$_3$) δ: 6.73 (d, $J = 8.5$ Hz, 1H), 6.38 - 6.30 (m, 1H), 4.40 - 4.28 (m, 2H), 3.68 (d, $J = 8.5$ Hz, 1H), 3.29 (br. s., 1H), 3.20 (d, $J = 9.4$ Hz, 1H), 1.98 - 1.70 (m, 2H), 1.48 (br. s., 2H), 1.35 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (CDCl$_3$) δ: 171.92, 171.89, 170.67, 132.23, 132.08, 61.84, 46.99, 45.84, 44.69, 32.34, 28.18, 23.76, 14.13. Analytical data match those previously reported.

**Ethyl 3,5-dioxo-4-oxatricyclo[5.2.2.0$^{2,6}$]undecane-1-carboxylate (9e).** Compound 9d (7.78 g, 31 mmol) was hydrogenated according to the general procedure to give 9e (7.4 g, 29 mmol) as a white solid (m.p. 81-83°C) in 94% yield. Compound 9e was used for the next step without further purification. $^1$H
NMR (CDCl$_3$) $\delta$: 4.22 (q, $J = 6.3$ Hz, 2H), 3.69 (d, $J = 10.2$ Hz, 1H), 3.19 (d, $J = 10.5$ Hz, 1H), 2.30 (br. s., 1H), 1.96 - 1.71 (m, 6H), 1.71 - 1.45 (m, 2H), 1.28 (t, $J = 7.0$ Hz, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$: 173.85, 173.03, 171.66, 61.42, 45.53, 44.42, 40.36, 29.09, 26.70, 24.16, 22.65, 21.23, 14.09. Analytical data match those previously reported.$^{18}$

**Ethyl bicyclo[2.2.2]oct-2-ene-1-carboxylate (9g).** Compound 9g was synthesized according to a literature procedure.$^{18}$ Compound 9e (7.4 g, 29 mmol) and potassium carbonate (11.67 g, 65 mmol) were refluxed in water for 2 h. The solution was acidified to pH 1 with 10% HCl. The solution was extracted with ethyl acetate. The organic layer was dried and concentrated to give 9f (7 g, 26 mmol) as a white solid (m.p. 135-138°C), which was used for the next step without further purification. Compound 9f (7 g, 26 mmol) was added to acetonitrile (233 mL). Pyridine (2.8 g, 36 mmol) was added followed by lead acetate (11.66 g, 26 mmol). The solution was refluxed for 3 h and then filtered through a silica pad. The product was purified by flash chromatography eluting with hexanes/ethyl acetate (19:1) to give 9g (1.41 g, 7.8 mmol) as a clear liquid in 27% yield (in 2 steps from 9e). $^1$H NMR (CDCl$_3$) $\delta$: 6.47 - 6.39 (m, 1H), 6.36 - 6.27 (m, 1H), 4.18 (q, $J = 7.2$ Hz, 2H), 2.57 (br. s., 1H), 1.88 - 1.76 (m, 2H), 1.66 - 1.50 (m, 2H), 1.50 - 1.22 (m, 7H). $^{13}$C NMR (CDCl$_3$) $\delta$: 176.72, 134.27, 132.41, 60.44, 43.95, 29.71, 29.34, 25.56, 14.26. IR (thin film, KBr plates) $\nu$ (cm$^{-1}$): 2945, 2910, 2868, 1731, 1455, 1390, 1366, 1317, 1288, 1249.

**Ethyl bicyclo[2.2.2]octane-1-carboxylate (9h).** Compound 9g (1.41 g, 7.8 mmol) was hydrogenated according to the general procedure to give 9h (1.37 g, 7.5 mmol) as a clear liquid in 96% yield. Compound 9h was used for the next reaction without further purification. $^1$H NMR (CDCl$_3$) $\delta$: 4.07 (q, $J = 7.2$ Hz, 2H), 1.78 - 1.65 (m, 6H), 1.58 (d, $J = 7.4$ Hz, 7H), 1.22 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$: 178.25, 60.02, 38.19, 28.04, 25.41,
23.79, 14.21. IR (thin film, KBr plates) ν (cm⁻¹): 2945, 2921, 2866, 1726, 1457, 1365, 1336, 1243.

*Bicyclo[2.2.2]oct-1-ylmethanol* (9i). Compound 9h (1.37 g, 7.5 mmol) was LAH reduced according to the general procedure to give the alcohol 9i (1 g, 7.13 mmol) in 95% yield as a white solid (m.p. 60-61°C). Compound 9i was used for the next reaction without further purification. ¹H NMR (CDCl₃) δ: 3.21 (s, 2H), 1.68 - 1.46 (m, 7H), 1.46 - 1.08 (m, 7H). ¹³C NMR (CDCl₃) δ: 72.04, 32.44, 27.72, 25.71, 24.60.

*Bicyclo[2.2.2]octane-1-carbaldehyde* (9j). Compound 9i (1 g, 7.13 mmol) was PCC oxidized according to the general procedure to give aldehyde 9j, which was used for the next step without further purification. ¹H NMR (CDCl₃) δ: 9.40 (s, 1H), 1.79 - 1.51 (m, 13H). Spectral data match those reported previously.¹⁹

*1-Ethenylbicyclo[2.2.2]octane* (9k). Compound 9j was subjected to a Wittig reaction to form compound 9k. To methyltriphenylphosphonium bromide (5.4 g, 15 mmol) in THF (30 mL) at 0°C was added potassium butoxide (1.7 g, 15 mmol). The suspension was stirred for 1 h and then aldehyde 9j in THF (7 mL) was slowly added. The reaction was stirred for 2 h at room temperature and then water was added. The layers were separated and the aqueous phase was extracted with diethyl ether. The combined organic layer was dried, concentrated and purified by flash chromatography eluting with hexanes to give the alkene 9k. ¹H NMR (CDCl₃) δ: 5.72 - 5.64 (m, 1H), 4.85 - 4.77 (m, 2H), 1.63 - 1.51 (m, 7H), 1.51 - 1.40 (m, 6H). Spectral data agree with those reported previously.¹⁹

*2-(Bicyclo[2.2.2]oct-1-yl)ethanol* (9l). Compound 9k was subjected to a hydroboration-oxidation reaction to form compound 9l. Compound 9k was dissolved in THF and cooled to 0°C. 1 M Borane-tetrahydrofuran complex solution
in THF (2.4 mL, 2.4 mmol) was slowly added and the solution was stirred for 1 h at room temperature. The solution was cooled to 0°C and water (500 µL) was added followed by 3 M NaOH (750 µL) and 30% hydrogen peroxide (750 µL). The solution was stirred at room temperature for 2 h. The reaction was quenched with water and the layers were separated. The aqueous layer was extracted with diethyl ether and the combined organic layer was dried and concentrated. The product was purified by flash chromatography eluting with hexanes/ethyl acetate (9:1) to give the alcohol 9l (330 mg, 2.17 mmol) in 30% yield (over 3 steps from 9i). \[ ^{1}H \text{NMR (CDCl}_3 \delta: 3.83 - 3.63 (m, 2H), 1.64 - 1.32 (m, 15H), 1.28 (br. s., 1H). \] \[ ^{13}C \text{NMR (CDCl}_3 \delta: 59.49, 44.86, 31.15, 29.24, 26.17, 24.17. \] IR (thin film, KBr plates) \( \nu \) (cm\(^{-1}\)): 3331 (broad), 2930, 2859, 1455, 1352, 1265.

**Bicyclo[2.2.2]oct-1-ylacetaldehyde (9).** Compound 9l (100 mg, 0.65 mmol) was PCC oxidized according to the general procedure to the aldehyde 9 (70 mg, 0.46 mmol) as a clear liquid in 71% yield. \[ ^{1}H \text{NMR (CDCl}_3 \delta: 9.84 - 9.79 (m, 1H), 2.12 (d, } J = 3.0 \text{ Hz, 2H), 1.65 - 1.47 (m, 13H). \] \[ ^{13}C \text{NMR (CDCl}_3 \delta: 203.78, 55.19, 31.31, 30.70, 25.98, 24.11. \] IR (thin film, KBr plates), \( \nu \) (cm\(^{-1}\)): 2937, 2862, 2728, 1721, 1456, 1409, 1268. GC retention time: 9.03 min. MS (EI) [M]^+: 152. HRMS (ESI) [M+Na]^+: Calcd for C\(_{10}H\text{O}_{16}O m/z = 175.1099\), found m/z = 175.1098.
2.8. Time Course Plots

**Figure S1**: Time Course Plot of individually applied octanal, DMSO, and analogues 3, 5, 6, 7, 8, and 9. Hana3A cells transfected with the mouse OR-17 receptor were exposed to varying concentrations of each compound individually, as labeled on each plot. The luminescence readings were recorded for 24 minutes.
Figure S2: Time Course Plots of octanal (1) co-applied with octanal (1), DMSO, and analogues 3, 5, 6, 7, 8, and 9. Hana3A cells transfected with the mouse OR-I7 receptor were exposed to varying concentrations of each compound individually, as labeled on each plot. Octanal control was used to judge percent saturation.
Figure S3: Time Course Plot of octanal (1), DMSO, and analogues 2, 9, 10, 11, and 12. Hana3A cells transfected with the mouse OR-I7 receptor were exposed to varying concentrations of each compound: A) Octanal (1), B) DMSO, C) Cpd 2, D) Cpd 9, E) Cpd 10, F) Cpd 11, and G) Cpd 12. The luminescence readings were recorded for 24 minutes.
Figure S4: Time Course Plot of octanal (1) co-applied with octanal (1), DMSO, and analogues 2, 9, 10, 11, and 12. Hana3A cells transfected with the mouse OR-I7 receptor were exposed to binary mixtures containing 5 µM of octanal (1) and varying concentrations of each compound: A) Octanal (1), B) DMSO, C) Cpd 2, D) Cpd 9, E) Cpd 10, F) Cpd 11, and G) Cpd 12. The luminescence readings were recorded for 24 minutes.
2.9. Homology Model Comparisons

Figure S5 shows a comparison of the rat\textsuperscript{22} and mouse OR-I7 (this work) homology models, along with the starting rhodopsin/retinal X-ray crystal structure.

![Figure S5](image)

Figure S5: Left panel: Structural model of the rat OR-I7 (cyan) with octanal bound (blue), superimposed on the rhodopsin structure (PDB entry 1U19, in red) with retinal forming a protonated Schiff's base with K296 in TM7 (red spheres). Right panel: Structural model of the mOR-I7 with octanal bound (blue) superimposed on the rhodopsin structure (red) with retinal bound (red).

3. References

4. Appendix

4.1. Proton NMR spectra of 2, 5, 6, 7, 8, 9, 10, 11b, 11d, 11, and 12 in CDCl₃
4.2. Carbon NMR spectra of 2, 5, 6, 7, 8, 9, 10, 11b, 11d, 11, and 12