Supporting Information

Sphingosine kinases promote Ebola virus infection and can be targeted to inhibit filoviruses, coronaviruses, and arenaviruses using late endocytic trafficking to enter cells

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**Supplementary Figure 1. PF-543 blocks viral entry mediated by both full-length and delta mucin EBOV GP.**

HT1080 cells pre-treated with PF-543 (10µM) or vehicle (DMSO, 0.1%) for 1 hour and incubated with βlam VLPs harbouring EBOV GP full length or ΔM (delta muc) for 3 hours in the presence of the drug. Cells were stained with the βlam substrate, CCF2-AM, and relative entry % was determined by measuring the percentage of inhibitor-treated cells with cleaved CCF2 compared to vehicle-treated cells. Results are expressed as mean ± s.d. of triplicates and are representative of three experiments.
Supplementary Figure 2. SK1/2 inhibitory activity in relation to the relative entry of MLV pseudotypes harbouring EBOV GPΔM

SK1 (A) and SK2 (B) activity were measured in vitro by measuring fluorescence after incubation of PF-543 derivatives (1 µM) or vehicle (DMSO, 0.1%) with SK reaction buffers containing baculovirus-derived recombinant SK1 or SK2 and light-sensitive NBD-sphingosine. Percent SK activity was calculated in comparison to vehicle, which represents 100% activity. In parallel, relative entry was determined by treating HT1080 cells with the PF-543 derivatives (10 µM) or vehicle (0.1%) and transducing them with MLV pseudotypes encoding LacZ and harbouring EBOV GPΔM. Relative entry (%) was determined by quantifying LacZ positive inhibitor-treated cells compared to vehicle-treated cells.
Supplementary Figure 3. SK inhibitors block trafficking of EBOV VLPs to NPC1 (further enlarged pictures from Figure 7).

(A) HT1080 cells were pre-treated with vehicle (DMSO, 0.1%), AktiVIII (10 µM), PF-543 (10 µM), SK1-I (2.5 µM), or FTY720 (2.5 µM) for 1h, followed by incubation with GFP-labeled EBOV VLPs containing the fusion deficient GP^{F535RΔM} (Green) for 3h. CMAC cytoplasmic dye (Blue) was added to the media for the last 30 minutes of the incubation. Cells were then fixed, permeabilized, and immunostained with anti-NPC1 and DY-650 conjugated antiserum (Magenta). Cells were imaged on a LSM800 confocal microscope (Zeiss). Displayed images are maximum intensity Z-projections, yellow arrows indicate colocalization of VLPs and NPC1, red arrows point to dilated intracellular vesicles, bar = 10 µm.
**Supplementary Figure 4. Sphingosine kinase inhibitors do not block entry by H5N1 and H7N1 pseudotypes in HT1080 and A549 cells.**

(A) HT1080 and (B) A549 cells treated with vehicle (DMSO, 0.1%), PF-543 (10 µM), FTY720 (2.5 µM), or SK1-I (2.5 µM) for 1h were transduced with MLV pseudotypes encoding lacZ and harbouring the influenza A H5N1 or H7N1 glycoproteins in the presence of the drug for 6 hours. Media was then changed, and cells fixed and stained with X-Gal 72 hours post-infection. Relative transduction % was determined by quantifying LacZ positive inhibitor-treated cells compared to vehicle treated cells. Results are expressed as mean ± s.d. of triplicates and are representative of three experiments. Variance was analyzed by one-way ANOVA, followed by Dunnett’s multiple comparisons test to determine significance, and no significant differences were observed.
Synthesis of PF-543 derivatives

Overall synthesis

The overall synthetic scheme is shown below:

1. AcCl, pyridine 0°C-RT
2. NBS, AIBN, 1,2-DCE, Δ
3. Na$_2$CO$_3$, MeOH/H$_2$O
4. K$_2$CO$_3$, ACN, 60°C
5. (refer to experiment code)

X=Me, a
X=H, b

(DIBAL-H, toluene, 0°C)
Synthesis

The majority of the synthesis is adapted from Bioorg. Med. Chem. 2014 Vogt, unless indicated otherwise.

\[
\begin{align*}
\text{Br} & \rightarrow \text{CN} \\
\text{Br} & \rightarrow \text{toluene, 0°C} \\
\text{DIBAL-H} & \\
\end{align*}
\]

To a solution of \(\alpha\)-bromo-\(p\)-tolunitrile (1.0 eq) in toluene (0.5 M), cooled to 0°C and placed under argon, was added DIBAL-H (1.0 in toluene, 1.4 eq) prior to stirring at 0°C for one hour. The reaction was quenched by the addition of chloroform and 10% aqueous hydrochloric acid and stirring was maintained at 0°C for a second hour. The organic phase was isolated and washed with water prior to being dried over anhydrous magnesium sulfate, filtered and evaporated to dryness to obtain a white powder in an average yield of 80%. \(R_f\) (9:1 hex:EtOAc) ~0.28. \(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)) \(\delta\) 10.03 (s, 1H), 7.88 (d, \(J=8.2\) Hz, 2H), 7.57 (d, \(J=8.1\) Hz, 2H), 4.53 (s, 2H). \(^{13}\text{C NMR}\) (100 MHz, CDCl\(_3\)) \(\delta\) 191.5, 144.2, 136.1, 130.2, 129.7, 31.9. \(\text{HRMS (EI)}\) calc. for [C\(_8\)H\(_7\)OBr] 197.9680 Da, obt. 197.9687 Da.

\((\text{Mol. Pharmaceutics 2013 Zhang})\)

\[
\begin{align*}
\text{AcCl} & \rightarrow \text{ether} \\
\text{pyridine} & \rightarrow \text{0°C-RT} \\
\end{align*}
\]

To a solution of the phenol (1.0 eq) in pyridine (1.67 M), cooled to 0°C, was added dropwise the acid chloride (1.2 eq), resulting in the formation of a pale precipitate. The resulting heterogeneous mixture was stirred for 18 hours as it gradually warmed to room temperature and formed a dark orange solution. This solution was poured onto water prior to extracting the product with ethyl acetate. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure prior to being purified by flash column chromatography (100:0 to 9:1 hexanes:ethyl acetate). The average yield was 90% as a clear colourless oil. \(R_f\) (9:1) ~0.39. \(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)) \(\delta\) 6.88 (s, 1H), 6.71 (s, 2H), 2.32 (s, 6H), 2.29 (s, 3H). \(^{13}\text{C NMR}\) (100 MHz, CDCl\(_3\)) \(\delta\) 169.7, 150.6, 139.3, 127.6, 119.1, 21.2, 21.1.
Compound 1b was prepared in the same manner as 1a above, and purified by flash column chromatography (9:1 hexanes:ethyl acetate). The yield was 89% as a clear colourless oil. \( R_f (9:1) \sim 0.43. \)  \( ^1H \text{ NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 7.29-7.25 (m, 1H), 7.07-7.04 (m, 1H), 6.92-6.88 (m, 2H), 2.37 (s, 3H), 2.30 (s, 3H).  \( ^{13}C \text{ NMR} \) (100 MHz, CDCl\(_3\)) \( \delta \) 169.6, 150.6, 139.6, 129.1, 126.6, 122.1, 118.5, 21.3, 21.1.

To a solution of the phenyl acetate (1.0 eq) in 1,2-dichloroethane (1.0 M) were added N-bromosuccinimide (0.8 eq) and azobisisobutyronitrile (17.6 meq) prior to heating to reflux (83°C) and stirring for one hour. Upon cooling to room temperature, a white precipitate crashed out; it was removed by filtration and rinsed with diethyl ether. The filtrate and rinses were combined and evaporated under reduced pressure prior to being purified by flash column chromatography (190:10 to 9:1 hexanes:ethyl acetate). The average yield was 71% as a clear colourless oil. \( R_f (9:1) \sim 0.39. \)  \( ^1H \text{ NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 7.08 (s, 1H), 6.95 (s, 1H), 6.86 (s, 1H), 4.44 (s, 2H), 2.36 (s, 3H), 2.30 (s, 3H).  \( ^{13}C \text{ NMR} \) (100 MHz, CDCl\(_3\)) \( \delta \) 169.4, 150.7, 140.1, 138.9, 127.3, 122.3, 119.3, 32.7, 21.2, 21.1.

(Vogt and J. Org. Chem. 1977 Newman)

Compound 2b was prepared in the same manner as 2a above, and purified by flash column chromatography (95:5 hexanes:ethyl acetate). The yield was 43% as a pale yellow oil. \( R_f (95:5) \)
\[ \text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.36 (dd, J=7.9 Hz, J=7.8 Hz, 1H), 7.28-7.26 (m, 1H), 7.15 (dd, J=2.0 Hz, J=1.9 Hz, 1H), 7.06-7.03 (m, 1H), 4.48 (s, 2H), 2.31 (s, 3H). \]

\[ \text{C NMR (100 MHz, CDCl}_3\text{)} \delta 169.3, 150.7, 139.3, 129.8, 126.4, 122.2, 121.6, 32.5, 21.1. \]

A slurry of the benzyl bromide (1.0 eq), benzenesulfinic acid sodium salt (1.1 eq) and Aliquat 336 (20 meq) was heated to 85°C and stirred for 28 hours. Upon cooling to room temperature, the product was resuspended in ethyl acetate, using sonication, and filtered over Celite. This solution was evaporated under reduced pressure prior to being purified by flash column chromatography (0-7% ethyl acetate in DCM). The average yield was 72% as a clear colourless oil. 

\[ \text{Rf (95:5 DCM:ethyl acetate) ~0.55. H NMR (400 MHz, CDCl}_3\text{)} \delta 7.69-7.66 (m, 2H), 7.64-7.60 (m, 1), 7.50-7.46 (m, 2H), 6.87 (s, 1H), 6.76 (s, 1H), 6.66 (s, 1H), 4.26 (s, 2H), 2.27 (s, 3H), 2.25 (s, 3H). \]

\[ \text{C NMR (100 MHz, CDCl}_3\text{)} \delta 169.2, 150.5, 139.8, 137.7, 133.7, 129.2, 129.1, 128.9, 128.6, 122.7, 121.0, 62.4, 21.1, 21.0. \]

(Vogt and Biochem. J. 2012 Schnute)

Compound 3b was prepared in the same manner as 3a above, and purified by flash column chromatography (100% DCM to 9:1 DCM:ethyl acetate). The yield was 63% as a white powder. 

\[ \text{Rf (100% DCM) ~0.26. H NMR (400 MHz, CDCl}_3\text{)} \delta 7.67-7.60 (m, 3H), 7.49-7.46 (m, 2H), 7.27 (t, overlaps CHCl}_3\text{, 1H), 7.08-7.05 (m, 1H), 6.94-6.90 (m, 2H), 4.31 (s, 2H), 2.28 (s, 3H). \]

\[ \text{C NMR (100 MHz, CDCl}_3\text{)} \delta 169.1, 150.7, 137.7, 133.8, 129.7, 129.5, 129.0, 128.6, 128.2, 124.0, 122.1, 62.4, 21.0. \]
To a solution of the phenyl acetate (1.0 eq) in methanol (0.5 M) and water (0.25 M) was added saturated aqueous sodium bicarbonate (0.25 M) prior to stirring at room temperature for 21 hours, at which point TLC analysis showed complete reactant consumption. The organic solvent was removed by evaporation under reduced pressure and the aqueous phase was acidified to pH 1 using 6N HCl. The product was extracted with ethyl acetate and the combined organic extracts were washed with water and brine prior to being dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The average yield was 86% as an off-white powder. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.70-7.68 (m, 2H), 7.63-7.60 (m, 1H), 7.50-7.46 (m, 2H), 6.63 (s, 1H), 6.48 (s, 1H), 6.38 (s, 1H), 4.23 (s, 2H), 2.18 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 155.8, 139.9, 137.8, 133.8, 128.9, 128.6, 124.0, 116.7, 114.8, 62.7, 14.1.

Compound 4b was prepared in the same manner as 4a above, and obtained in 92% yield as a white powder. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.67 (dd, not fully resolved, 2H), 7.62 (dd, $J$=7.4 Hz, $J$=7.4 Hz, 1H), 7.48 (dd, $J$=8.0 Hz, $J$=7.5 Hz, 2H), 7.11 (dd, $J$=7.8 Hz, $J$=7.8 Hz, 1H), 6.81 (dd, $J$=8.0 Hz, $J$=2.4 Hz, 1H), 6.68 (dd, $J$=2.0 Hz, $J$=1.9 Hz, 1H), 6.58 (d, $J$=7.6 Hz, 1H), 4.27 (s, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 155.7, 137.8, 133.8, 129.8, 129.5, 128.9, 128.6, 123.2, 117.6, 116.0, 62.7.
To a solution of the phenol (1.0 eq) and benzyl bromide (1.0 eq) in acetonitrile (0.2 M) was added potassium carbonate (5.0 eq) prior to heating the reaction mixture to 60°C and stirring for 2 hours. Following cooling to room temperature, the reaction mixture was diluted with ethyl acetate and 50% aqueous brine. The organic phase was additionally washed with brine prior to being dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure. The product was purified by flash column chromatography (100% DCM to 9:1 DCM:ethyl acetate). The average yield was 56% as an off-white powder. \(R_f\) (95:5 DCM:ethyl acetate) ~0.73. \(^1H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 10.04 (s, 1H), 7.92 (d, \(J=8.0\) Hz, 2H), 7.68 (d, \(J=7.9\) Hz, 2H), 7.62 (dd, \(J=7.5\) Hz, \(J=7.4\) Hz, 1H), 7.57 (d, \(J=7.9\) Hz, 2H), 7.48 (dd, \(J=7.8\) Hz, \(J=7.8\) Hz, 2H), 6.76 (s, 1H), 6.56 (s, 1H), 6.50 (s, 1H), 5.05 (s, 2H), 4.24 (s, 2H), 2.24 (s, 3H). \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 191.8, 158.3, 143.7, 139.9, 138.1, 136.0, 133.7, 130.0, 129.2, 128.9, 128.7, 127.4, 124.8, 116.4, 113.9, 69.1, 62.8, 21.3.

Compound \(5b\) was prepared in the same manner as \(5a\) above, and purified by flash column chromatography (100% DCM to 9:1 DCM:ethyl acetate). The product was obtained in 66% yield as a white powder. \(R_f\) (100% DCM) ~0.14. \(^1H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 10.04 (s, 1H), 7.92 (d, \(J=8.2\) Hz, 2H), 7.67-7.57 (m, 5H), 7.49-7.45 (m, 2H), 7.17 (dd, \(J=7.9\) Hz, \(J=7.9\) Hz, 1H), 6.93
(ddd, $J$=8.3 Hz, $J$=2.5 Hz, $J$=0.78 Hz, 1H), 6.80 (dd, $J$=2.2 Hz, $J$=1.8 Hz, 1H), 6.66 (d, $J$=7.6 Hz, 1H), 5.08 (s, 2H), 4.29 (s, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 191.8, 158.3, 143.6, 137.9, 136.0, 133.7, 130.0, 129.7, 129.6, 128.9, 128.6, 127.5, 123.8, 116.9, 115.6, 69.2, 62.8.

Final compounds

![Chemical structure](image)

General procedure: To a solution of the pyrrolidine (1.1 eq) in 1,2-dichoroethane (0.2 M) was added the aldehyde (5a or 5b, 1.0 eq) prior to stirring at room temperature for one hour, after which sodium cyanoborohydride (1.5 eq) was added and stirring was continued at room temperature for 16 hours. The reaction mixture was diluted with DCM and washed with saturated aqueous sodium bicarbonate. The organic phase was collected and evaporated under a constant stream of compressed air prior to purifying the product by flash column chromatography. Some reactions were catalysed using a drop of glacial acetic acid; these will be indicated individually.

Compound KA-016 (PF-543) was prepared from 5a and (R)-(−)-2-prolinol, purified using a 0-10% gradient of methanol in DCM, and obtained in 17% yield as a yellow oil. R$_f$ (9:1 DCM:MeOH) ~0.27. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.67 (dd, $J$=8.5 Hz, $J$=1.4 Hz, 2H), 7.65-7.61 (m, 1H), 7.50-7.44 (m, 4H), 7.40 (d, $J$=8.0 Hz, 2H), 6.76 (s, 1H), 6.52 (s, 1H), 6.48 (s, 1H), 4.94 (s, 2H), 4.23 (s, 2H), 4.18 (d, $J$=13.2 Hz, 1H), 3.77-3.71 (m, 2H), 3.63 (dd, $J$=12.0 Hz, $J$=4.3 Hz, 1H), 3.23 (br s, 1H), 3.10 (br s, 1H), 2.58 (q, $J$=8.1 Hz, 1H), 2.23 (s, 3H), 2.03-1.80 (m, 4H). $^{13}$C NMR (100 MHz,
CDCl$_3$ δ 158.6, 139.8, 138.0, 133.7, 130.0, 129.0, 128.9, 128.7, 127.7, 124.6, 116.5, 113.8, 69.5, 66.3, 62.9, 61.4, 58.6, 54.1, 27.1, 23.5, 21.3. HRMS (ESI$^+$) calc. for [C$_{27}$H$_{31}$NO$_4$S+H]$^+$ 466.2052, obt. 466.2044.

Compound **KA-018 (Compound 18)** was prepared from 5a and (S)-pyrrolidin-2-ylmethanol, purified using a 0-10% gradient of methanol in DCM, and obtained in 12% **yield** as a clear oil. R$_f$ (9:1 DCM:MeOH) ~0.47. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.67-7.61 (m, 1H), 7.50-7.46 (m, 2H), 7.43-7.37 (m, 4H), 6.75 (s, 1H), 6.52 (s, 1H), 6.48 (s, 1H), 4.93 (s, 2H), 4.24 (s, 2H), 4.13 (d, $J$=13.0 Hz, 1H), 3.74-3.56 (m, 3H), 3.18-3.14 (m, 1H), 3.00 (br s, 1H), 2.50 (q, $J$=12.9 Hz, 1H), 2.23 (s, 3H), 2.00-1.77 (m, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 158.6, 139.8, 138.0, 136.5, 133.6, 129.7, 129.0, 128.8, 128.7, 127.7, 124.5, 116.5, 113.8, 69.6, 65.6, 62.9, 61.5, 58.4, 54.2, 27.3, 23.4, 21.3. HRMS (ESI$^+$) calc. for [C$_{27}$H$_{31}$NO$_4$S+H]$^+$ 466.2052, obt. 466.2066.

Compound **KA-019 (Compound 19)** was prepared from 5b and (R)-(−)-2-prolinol, purified using a 0-10% gradient of methanol in DCM and obtained in 19% **yield** as a yellow oil. R$_f$ (9:1 DCM:MeOH) ~0.44. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.67-7.60 (m, 3H), 7.47 (dd, $J$=8.0 Hz, $J$=7.6 Hz, 2H), 7.40 (q, $J$=8.2 Hz, $J$=7.4Hz, 4H), 7.16 (dd, $J$=8.0 Hz, $J$=7.8 Hz, 1H), 6.94-6.91 (m, 1H), 6.75 (dd, $J$=2.2 Hz, $J$=1.8 Hz, 1H), 6.64 (br d, $J$=7.6 Hz, 1H), 4.96 (s, 2H), 4.28 (s, 2H), 4.14 (d, $J$=13.1 Hz, 1H), 3.72 (dd, $J$=11.6 Hz, $J$=3.3 Hz, 1H), 3.63 (d, $J$=13.1 Hz, 1H), 3.58 (dd, $J$=11.6 Hz, $J$=13.1 Hz, 1H).
Hz, J=3.8 Hz, 1H), 3.17-3.13 (m, 1H), 2.53-2.47 (m, 1H), 2.01-1.77 (m, 4H). 13C NMR (100 MHz, CDCl3) δ 158.6, 137.9, 136.4, 133.7, 129.7, 129.6, 129.4, 128.9, 128.6, 127.7, 123.5, 116.9, 115.7, 69.6, 65.6, 62.8, 61.5, 58.4, 54.2, 27.3, 23.4. HRMS (ESI+) calc. for [C26H29NO4S+H]+ 452.1896, obt. 452.1896.

Compound KA-020 (Compound 20) was prepared from 5b and (S)-pyrrolidin-2-ylmethanol, purified using a 0-10% gradient of methanol in DCM, and obtained in 17% yield as a yellow oil. Rr (9:1 DCM:MeOH) ~0.35. 1H NMR (400 MHz, CDCl3) δ 7.65 (dd, ill-defined, 2H), 7.63-7.60 (m, 1H), 7.48 (d, J=8.0 Hz, 2H), 7.46-7.44 (m, 2H), 7.40 (d, J=8.1 Hz, 2H), 7.16 (dd, J=8.0 Hz, J=7.8 Hz, 1H), 6.92 (dd, J=8.3 Hz, J=1.8 Hz, 1H), 6.75 (dd, J=2.2 Hz, J=1.9 Hz, 1H), 6.64 (d, J=7.5 Hz, 1H), 4.94 (s, 2H), 4.28 (s, 2H), 4.15 (d, J=13.0 Hz, 1H), 3.73 (dd, J=11.7 Hz, J=3.2 Hz, 1H), 3.67 (d, J=11.8 Hz, 1H), 3.60 (dd, J=11.6 Hz, J=3.6 Hz, 1H), 3.19 (br s, 1H), 3.04 (br s, 1H), 2.56-2.48 (m, 1H), 2.02-1.78 (m, 4H). 13C NMR (100 MHz, CDCl3) δ 158.6, 137.9, 133.7, 129.8, 129.6, 129.4, 128.9, 128.6, 127.7, 123.5, 116.9, 115.7, 69.6, 62.8, 61.4, 58.5, 54.2, 27.2, 23.5. HRMS (ESI+) calc. for [C26H29NO4S+H]+ 452.1896, obt. 452.1899.

Compound KA-035 (Compound 35) was prepared from 5a and pyrrolidine, purified using a 0-10% gradient of methanol in DCM, and obtained in 12% yield. Rr (9:1 DCM:MeOH) ~0.62. 1H NMR (400 MHz, CDCl3) δ 7.68-7.62 (m, 3H), 7.51-7.42 (m, 6H), 6.76 (s, 1H), 6.53 (s, 1H), 6.47 (s, 1H), 4.96 (s, 2H), 4.22 (s, 2H), 4.03 (s, 2H), 3.02 (br s, 4H), 2.23 (s, 3H), 2.05-1.98 (m, 4H).
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 158.5, 139.8, 138.0, 137.9, 133.7, 130.1, 129.0, 128.9, 128.6, 127.9, 124.6, 116.5, 113.9, 69.3, 62.9, 58.9, 53.5, 50.8, 45.9, 23.1, 21.3. HRMS (ESI\(^+\)) calc. for [C\(_{26}\)H\(_{29}\)NO\(_3\)S+H]\(^+\) 436.1941, obt. 436.1950.

Compound KA-036 (Compound 36) was prepared from 5a and ethanolamine, purified using a 2-8% gradient of methanol in DCM, and obtained in 6% yield as a yellow oil. \(R_t\) (9:1 DCM:MeOH) \(~0.59. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.67\) (dd, ill-defined, 2H), \(7.65-760\) (m, 1H), \(7.56\) (d, \(J=8.2\) Hz, 2H), \(7.50-7.43\) (m, 4H), \(6.75\) (s, 1H), \(6.54\) (s, 1H), \(6.48\) (s, 1H), \(4.97\) (s, 2H), \(4.24\) (s, 2H), \(3.81-3.71\) (m, 2H), \(3.06-3.01\) (m, 1H), \(2.96-2.91\) (m, 1H), \(2.23\) (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 158.5, 139.8, 138.0, 134.3, 133.7, 129.1, 128.9, 128.7, 127.9, 127.6, 124.7, 116.6, 113.9, 69.3, 62.9, 61.3, 54.1, 48.8, 21.3. MS (ESI\(^+\)) was unsuccessful.

Compound KA-037 (Compound 37) was prepared from 5a and (R)-pyrrolidin-3-ylmethanol with acetic acid as a catalyst, purified using a methanol in DCM gradient over three columns, and obtained in 0.8% yield. \(R_t\) (9:1 DCM:MeOH) \(~0.56. \(^1\)H NMR (400 MHz, CDCl\(_3\)): compound was too dilute for quantification from the observed peaks, and too dilute for a \(^{13}\)C NMR spectrum. MS (ESI\(^+\)) was unsuccessful.
Compound KA-038 (Compound 38) was prepared from 5a and (S)-pyrrolidin-3-ylmethanol with acetic acid as a catalyst, purified using a 99:1 DCM:methanol eluent system, and obtained in 4% yield. Rf (9:1 DCM:MeOH) ~0.42. 1H NMR (400 MHz, CDCl3): compound was too dilute for quantification from the observed peaks, and too dilute for a 13C NMR spectrum. MS (ESI+) was unsuccessful.

Compound KA-039 (Compound 39) was prepared from O-methyl-D-prolinol with acetic acid as a catalyst, purified using a 99:1 DCM:methanol eluent system, and obtained in 21% yield. Rf (9:1 DCM:MeOH) ~0.79. 1H NMR (400 MHz, CDCl3) δ 7.67 (dd, J=8.3 Hz, J=1.2 Hz, 2H), 7.62 (dd, J=7.4 Hz, J=7.4 Hz, 1H), 7.55 (d, J=8.0 Hz, 2H), 7.48 (dd, J=7.9 Hz, J=7.7 Hz, 2H), 7.40 (d, J=8.2 Hz, 2H), 6.75 (s, 1H), 6.52 (s, 1H), 6.49 (s, 1H), 5.60 (s, 1H), 4.95 (s, 2H), 4.24 (s, 2H), 3.55-3.47 (m, 2H), 3.41 (s, 2H), 3.23-3.15 (m, 1H), 2.70-2.65 (m, 1H), 2.58-2.51 (m, 1H), 2.23 (s, 3H), 2.04-1.95 (m, 1H), 1.81-1.67 (m, 2H), 1.57-1.48 (m, 1H). 13C NMR (100 MHz, CDCl3) δ 158.6, 139.8, 138.0, 137.1, 134.6, 129.1, 128.8, 128.7, 127.8, 127.8, 127.6, 127.4, 124.5, 116.7, 113.8, 69.4, 62.9, 60.5, 59.2, 58.7, 49.3, 27.8, 22.8, 21.3. MS (ESI+) was unsuccessful.