Supporting Information

Enantiomeric atropisomers inhibit HCV polymerase and/or HIV matrix: Characterizing hindered bond rotations and target selectivity

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Table of Contents:

Appendix 1: Information are provided for the assay and NMR of HIV matrix.

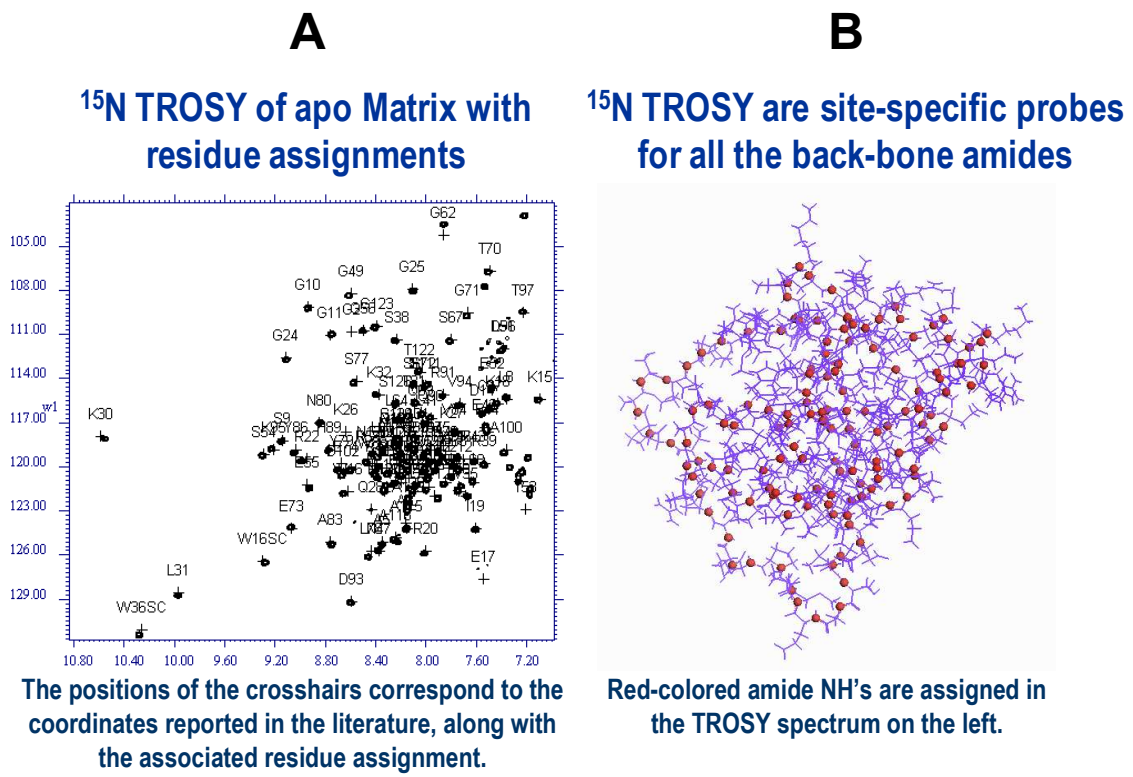


Figure S1. (A) ^{15}N TROSY spectrum of apo matrix along with the resonance assignments. (B) This data can be regarded as structural probes as displayed on the X-ray structure.

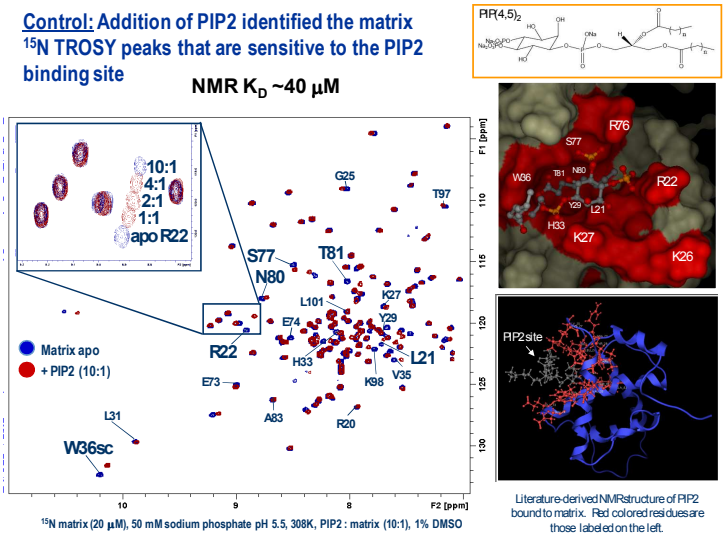


Figure S2. Addition PIP2 substrate shows the peaks that change positions due to binding. K_D determinations for PIP2 binding employed the ratios of ligand to matrix shown in Figure S2. The shift changes (Hz) versus compound concentration were fit using Graphpad (one-site binding), and a K_D of ~40 µM was determined.

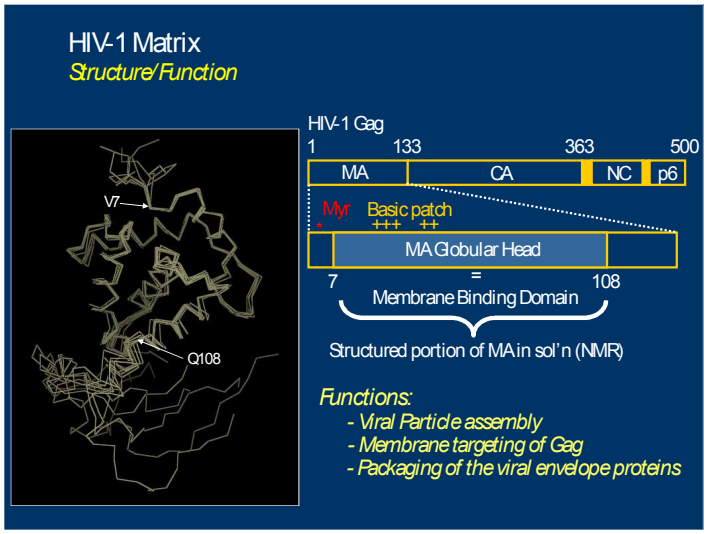


Figure S3. Shown are information regarding the constructs and functions.

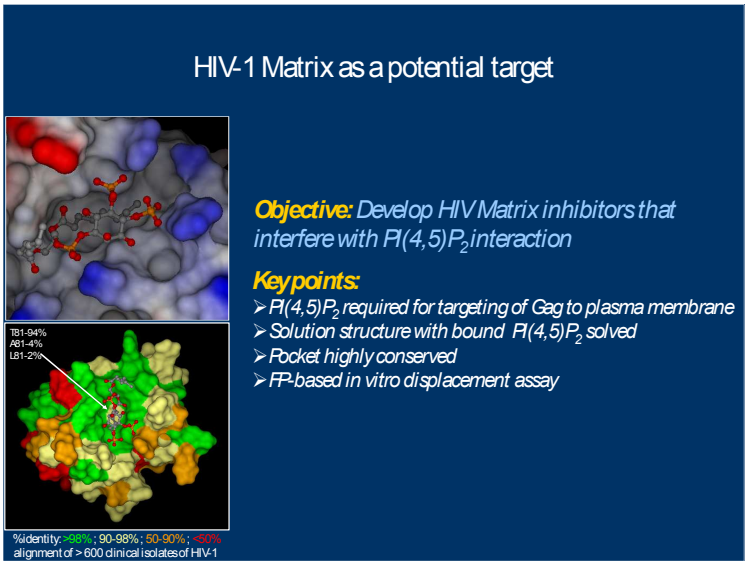


Figure S4. Information regarding matrix as a potential target.

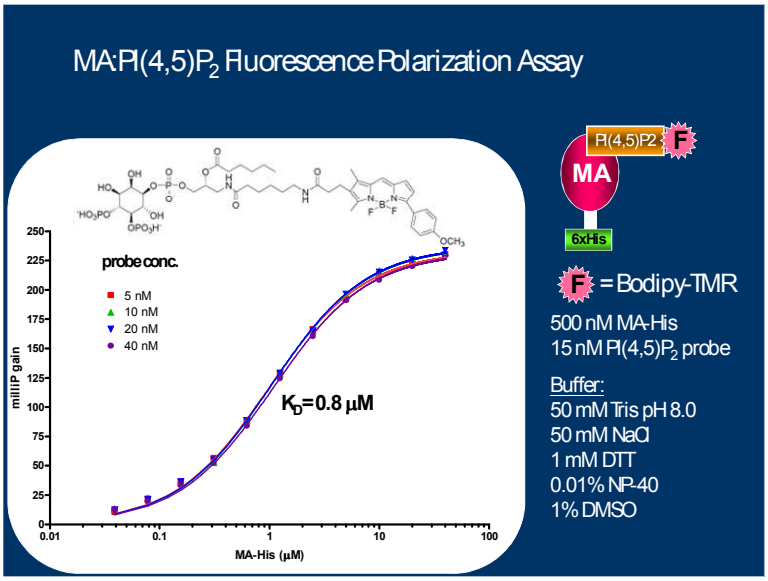
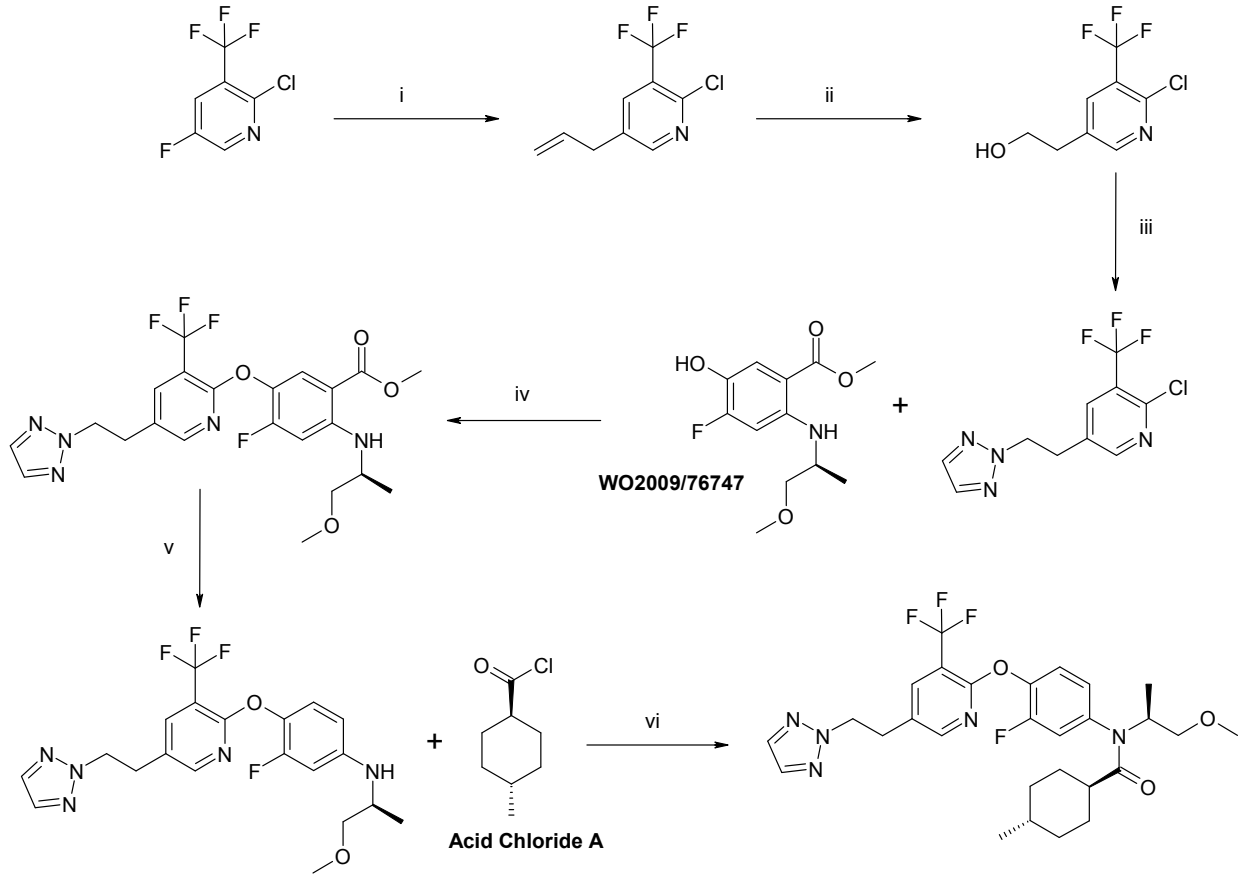


Figure S5. Flourescence polarization assay.

Appendix 2: Compound Characterization (continuation from Materials and Methods)

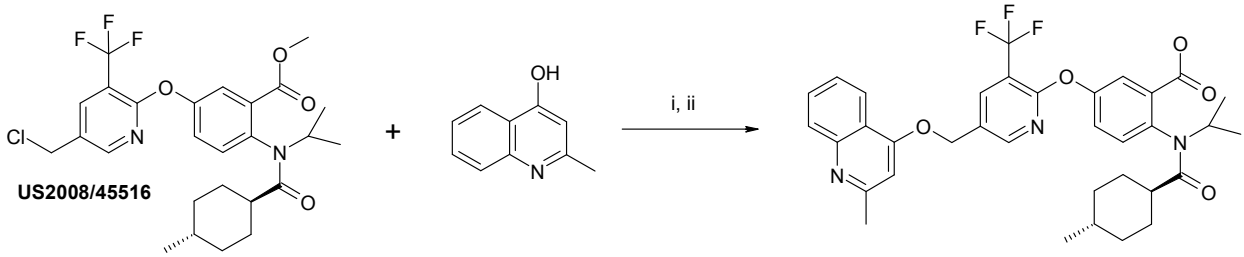
Compound syntheses. Synthesis of compounds **1** and **2** are described in **WO2009/018656.**

The synthesis of Compound **3** is described below.



Reagents and conditions: i) iPrMgCl / THF / allyl bromide /-40°C to RT ii) OsO_4 / $NaIO_4$ / water / THF / $NaBH_4$ / RT iii) 1H-1,2,3-triazole / PPh_3 / DEAD / THF / 0°C iv) DMSO / Cs_2CO_3 / 65°C v) **Acid Chloride A** / pyridine / 165°C / vi) DCM / pyridine / **Acid Chloride A**

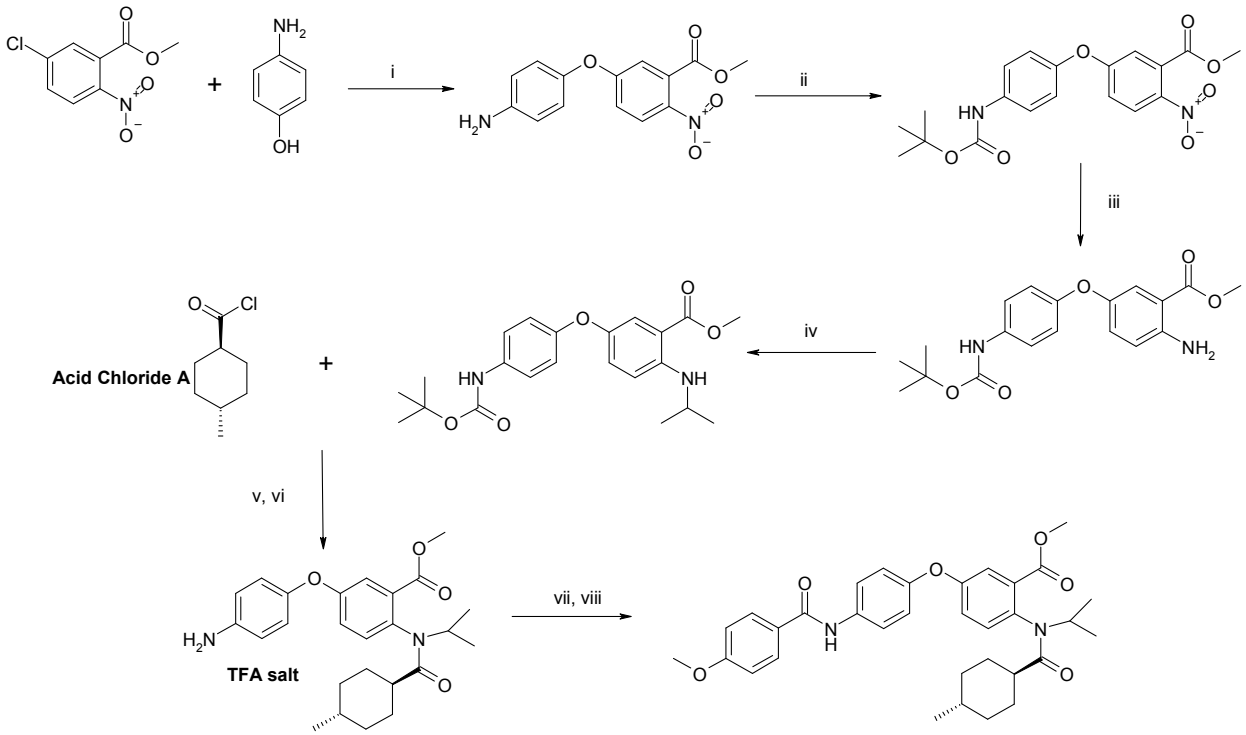
The synthesis of Compound **4** is described below.



Reagents and conditions: i) NaH / DMF / RT ii) LiOH / water / MeOH / RT

The synthesis of compounds **5** to **8** are described in **WO2007/87717.**

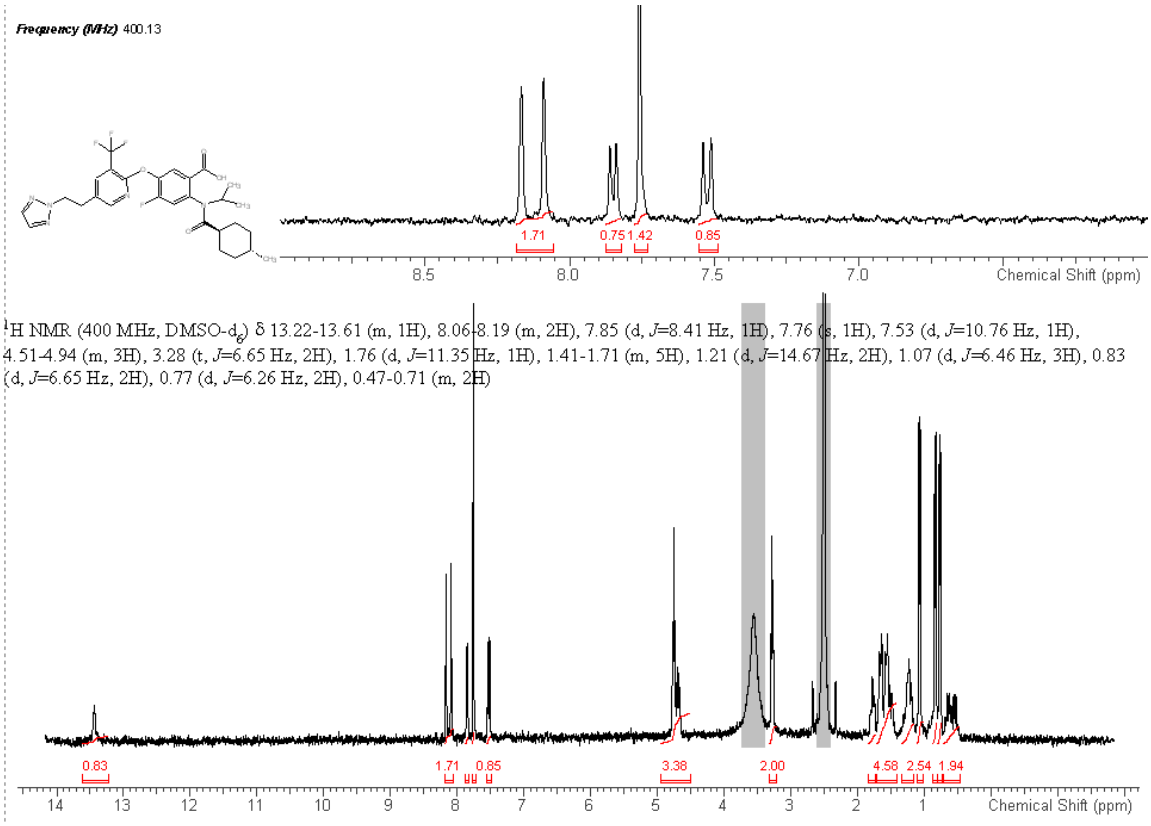
The synthesis of Compound **9** is described below.



Reagents and conditions: i) DMSO / K_2CO_3 / 75^oC ii) $NHCO_3$ / Boc_2O / THF / RT iii) 10% Pd/C / MeOH / EtOAc / RT iv) 2-methoxypropene / HOAc / DCM / $NaBH(OAc)_3$ / RT v) **Acid Chloride A** / pyridine / DMAP / 60^oC vi) DCM / TFA / RT vii) *p*-methoxybenzoic acid / TEA / DMSO / TBTU / RT viii) NaOH / water / 50$_o$C.

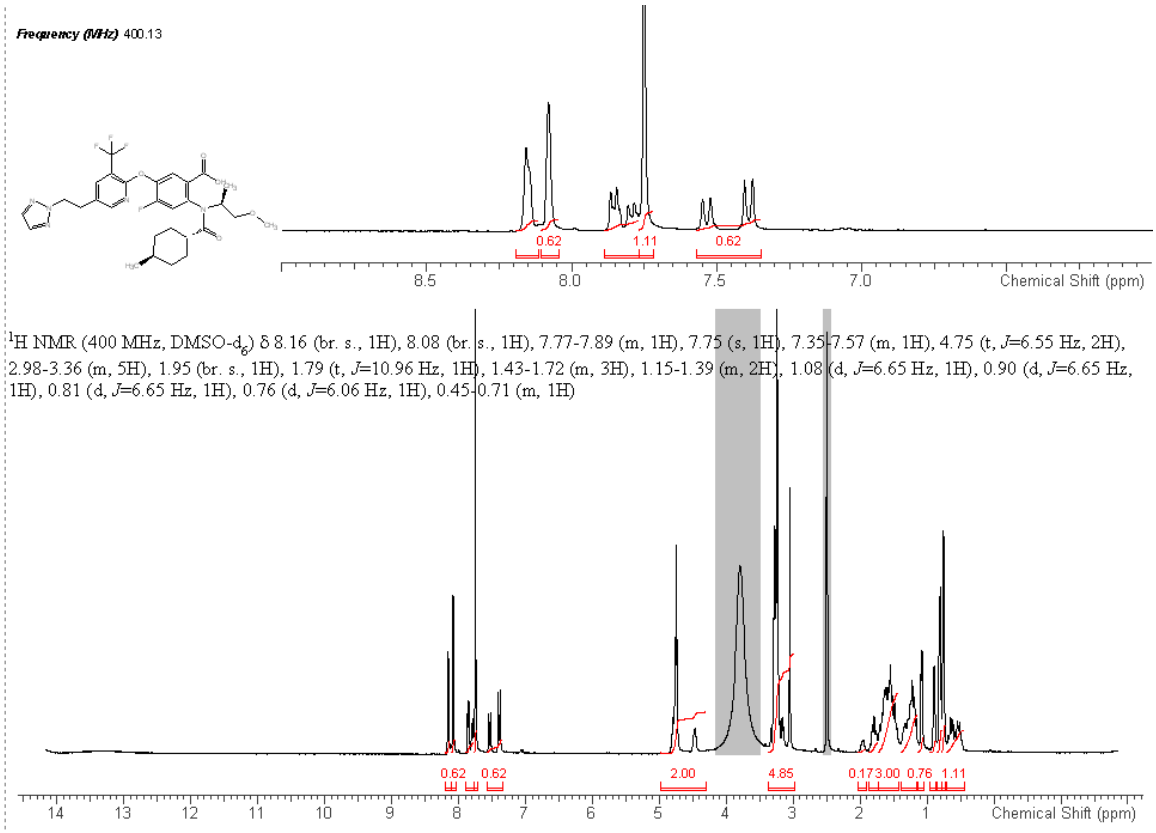
Compound 1

White lyophilized solid. Purity by HPLC > 99%. MS found MH+ 578.2 Da. HRMS calculated 578.2385, found 578.2388.



Compound 2

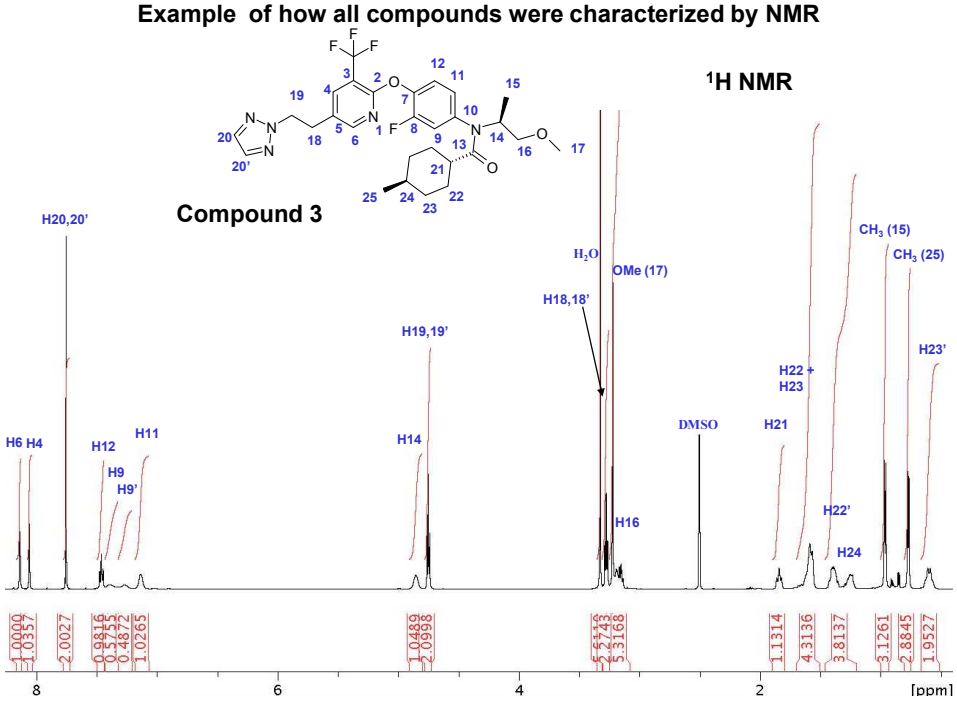
White lyophilized solid. Purity by HPLC 100%. MS found MH+ 608.3 Da. HRMS calculated 5608.2491, found 608.2516.



Compound 3

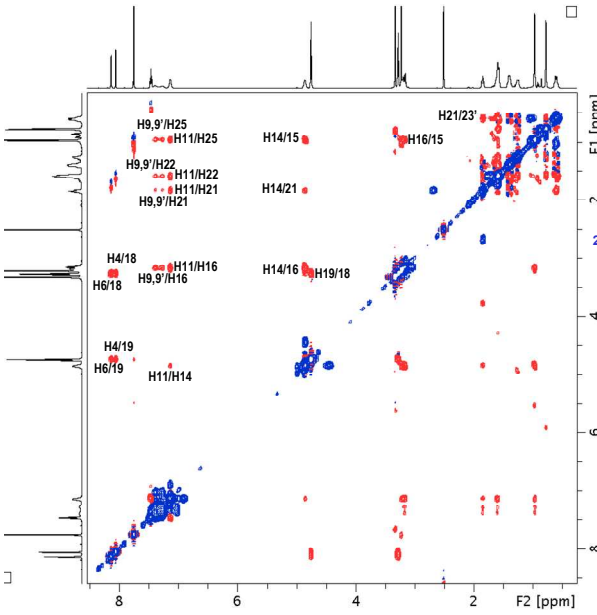
Off-white solid. Purity by HPLC >95%. HRMS calculated 564.2592, found 564.2590.

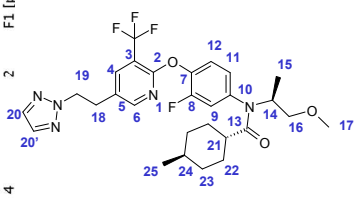
Example of how all compounds were characterized by NMR



Example of how all compounds were characterized by NMR

ROESY

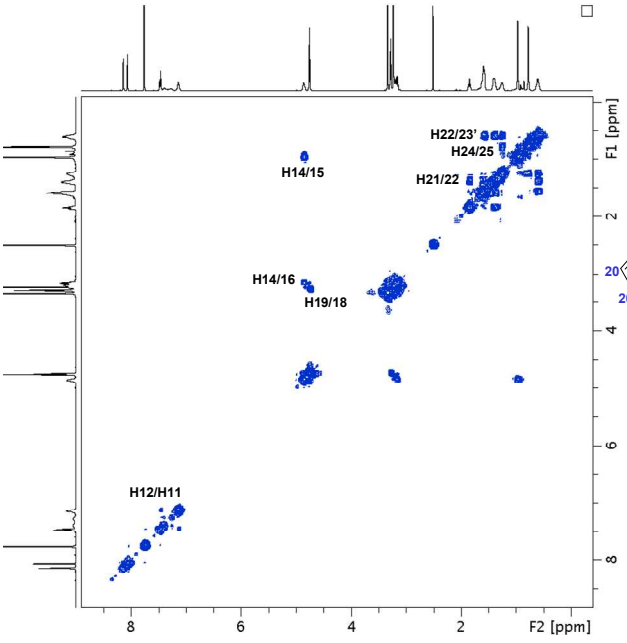


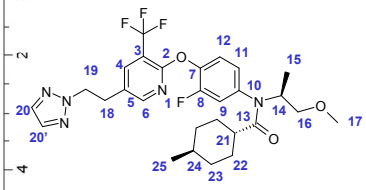


Compound 3

Example of how all compounds were characterized by NMR

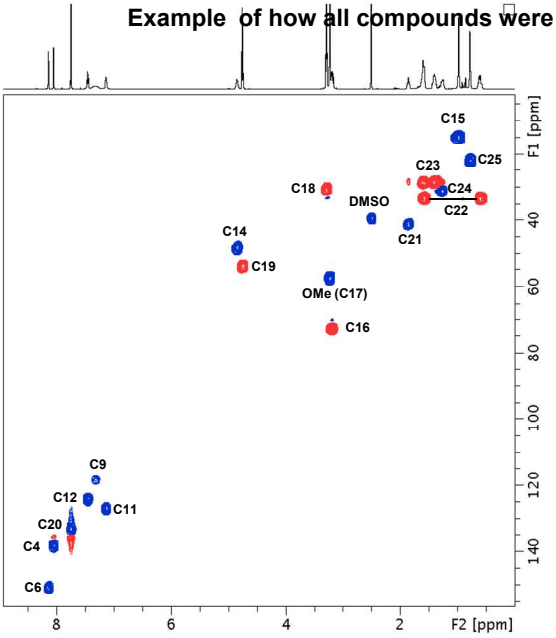
COSY



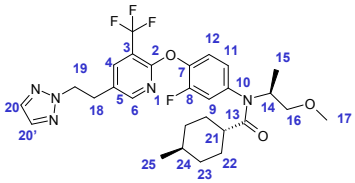


Compound 3

Example of how all compounds were characterized by NMR



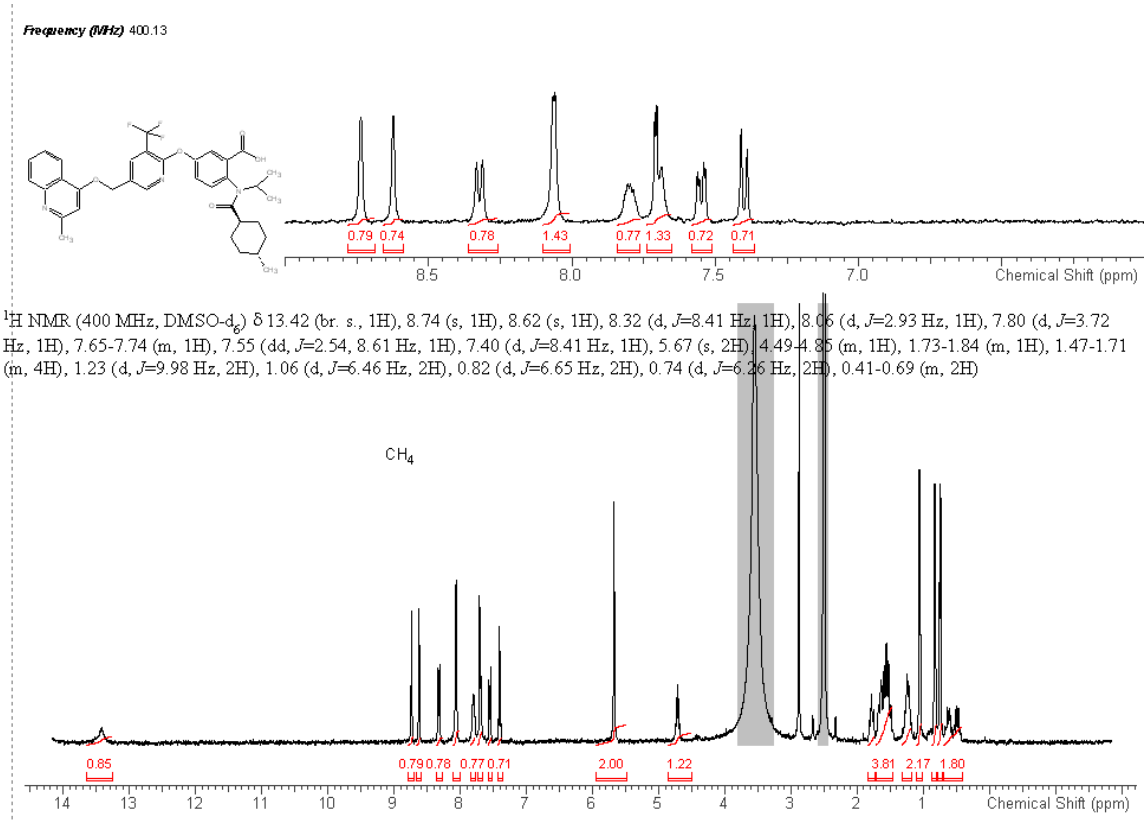
^{1}H-^{13}C HSQC



Compound 3

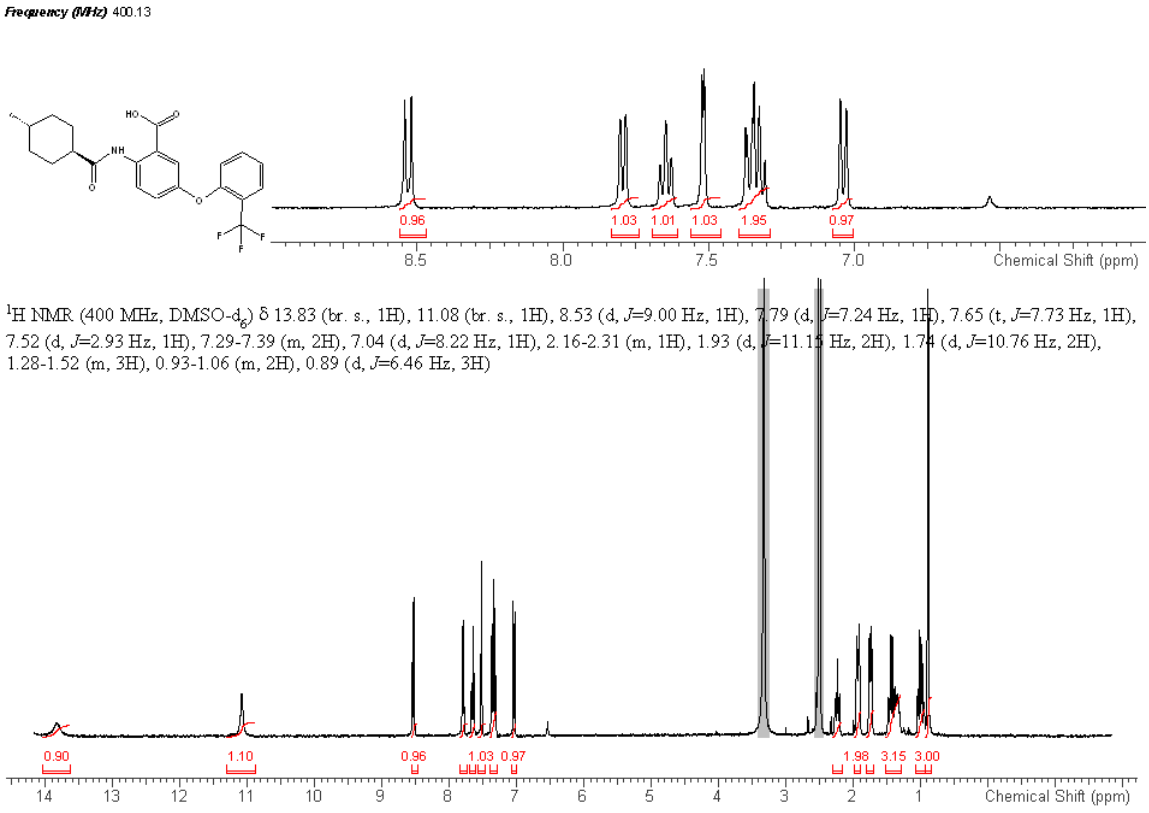
Compound 4

White lyophilized solid. Purity by HPLC 100%. MS found MH+ 636.3 Da. HRMS calculated 636.2680, found 636.2677.



Compound 5

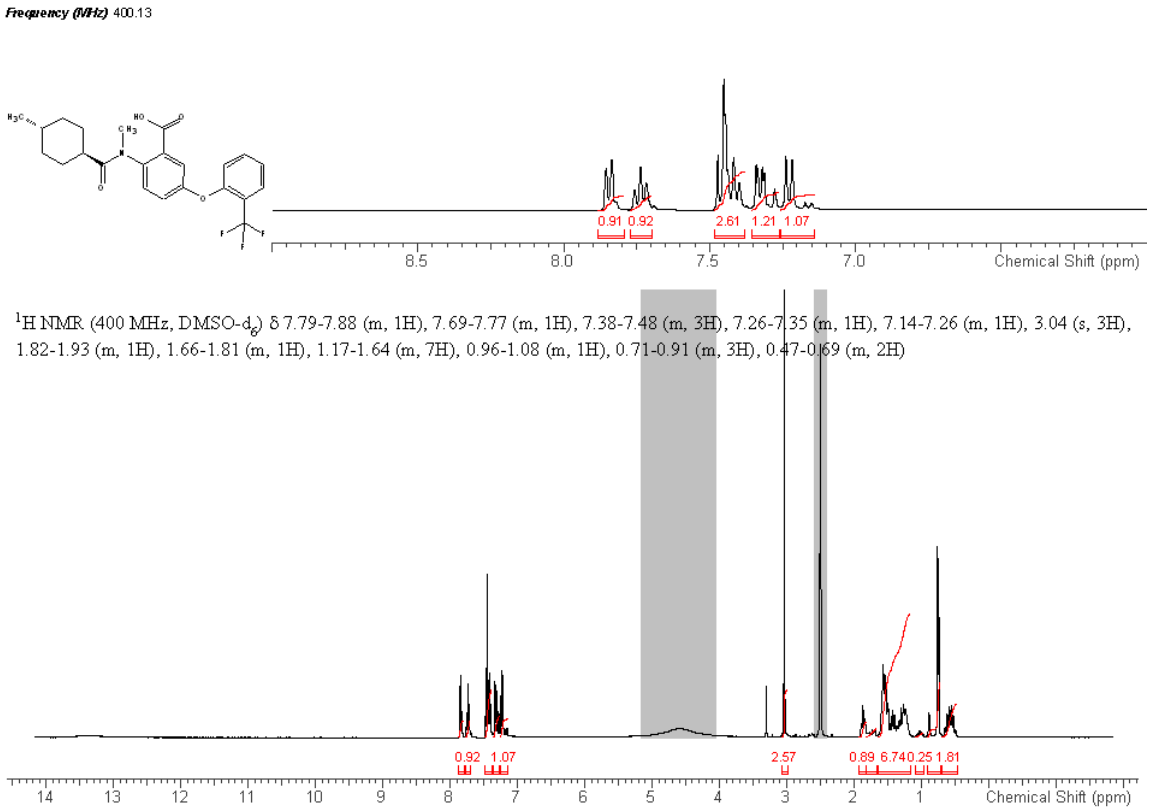
Beige solid. Purity by HPLC >99.9%. MS found MH+ 422.1 Da. HRMS calculated 422.1574, found 422.1592.



^{1}H NMR (400 MHz, DMSO-d_6) δ 13.83 (br. s., 1H), 11.08 (br. s., 1H), 8.53 (d, *J*=9.00 Hz, 1H), 7.79 (d, *J*=7.24 Hz, 1H), 7.65 (t, *J*=7.73 Hz, 1H), 7.52 (d, *J*=2.93 Hz, 1H), 7.29-7.39 (m, 2H), 7.04 (d, *J*=8.22 Hz, 1H), 2.16-2.31 (m, 1H), 1.93 (d, *J*=11.15 Hz, 2H), 1.74 (d, *J*=10.76 Hz, 2H), 1.28-1.52 (m, 3H), 0.93-1.06 (m, 2H), 0.89 (d, *J*=6.46 Hz, 3H)

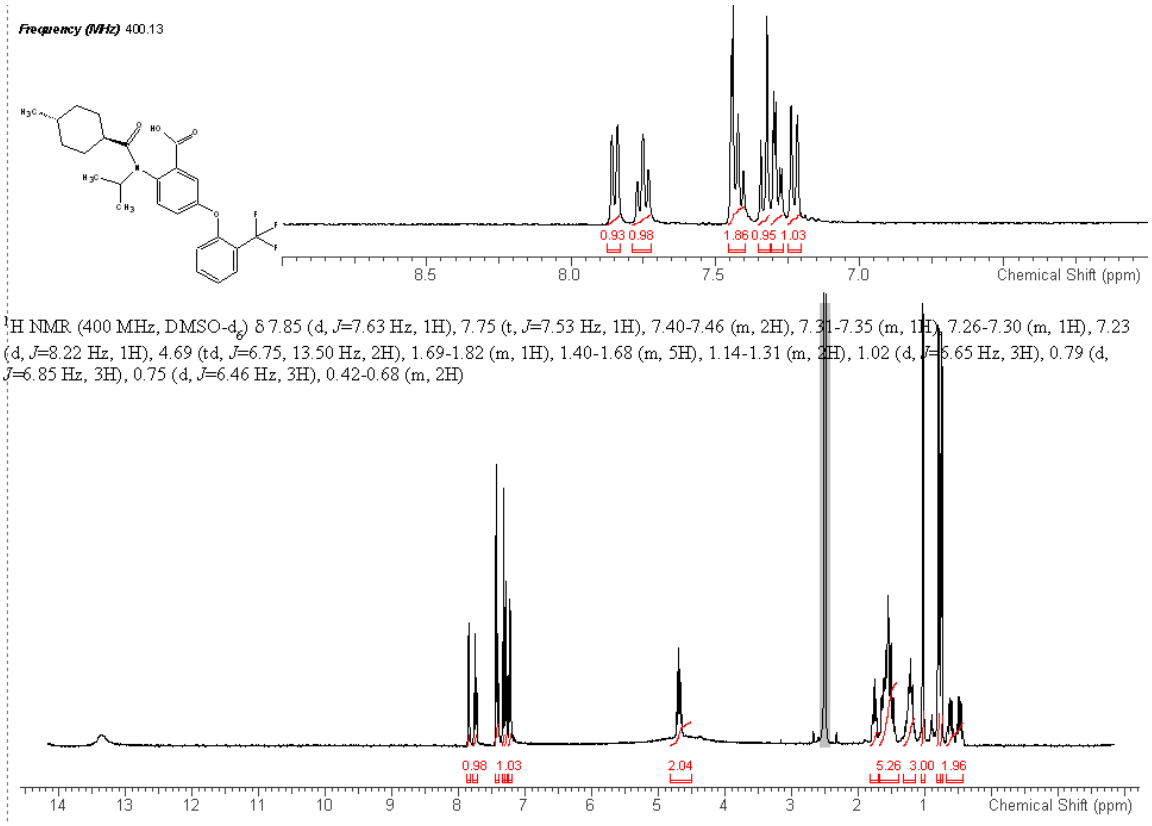
Compound 6

Off-white lyophilized powder. Purity by HPLC >99.9%. MS found MH+ 436.1 Da. HRMS calculated 436.1730, found 436.1746.



Compound 7

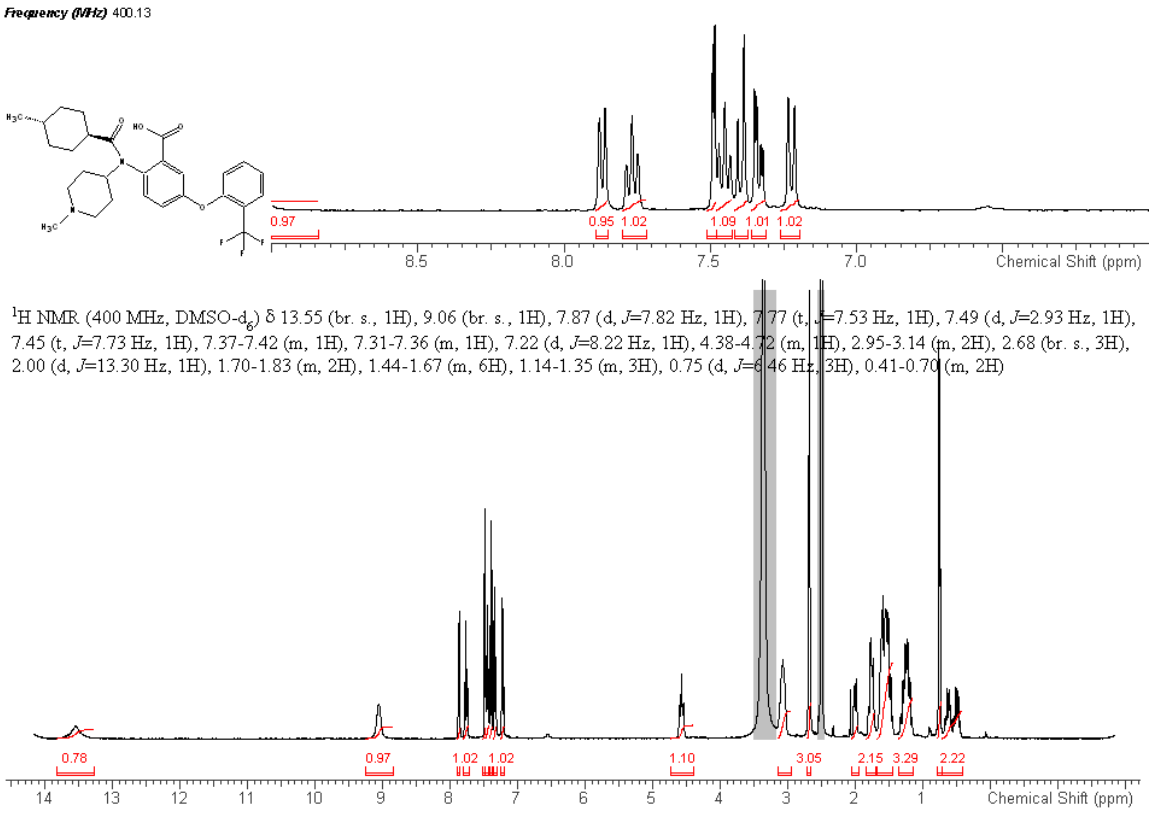
Off-white lyopholized powder. Purity by HPLC >99.9%. MS found MH+ 464.1 Da. HRMS calculated 464.2043, found 464.2058.



^{1}H NMR (400 MHz, DMSO-d_6) δ 7.85 (d, *J*=7.63 Hz, 1H), 7.75 (t, *J*=7.53 Hz, 1H), 7.40-7.46 (m, 2H), 7.31-7.35 (m, 1H), 7.26-7.30 (m, 1H), 7.23 (d, *J*=8.22 Hz, 1H), 4.69 (td, *J*=6.75, 13.50 Hz, 2H), 1.69-1.82 (m, 1H), 1.40-1.68 (m, 5H), 1.14-1.31 (m, 2H), 1.02 (d, *J*=6.65 Hz, 3H), 0.79 (d, *J*=6.85 Hz, 3H), 0.75 (d, *J*=6.46 Hz, 3H), 0.42-0.68 (m, 2H)

Compound 8

Off-white lyophilized powder. Purity by HPLC >99.9%. MS found MH+ 519.2 Da. HRMS calculated 519.2465, found 519.2477.



^{1}H NMR (400 MHz, DMSO-d_6) δ 13.55 (br. s., 1H), 9.06 (br. s., 1H), 7.87 (d, *J*=7.82 Hz, 1H), 7.77 (t, *J*=7.53 Hz, 1H), 7.49 (d, *J*=2.93 Hz, 1H), 7.45 (t, *J*=7.73 Hz, 1H), 7.37-7.42 (m, 1H), 7.31-7.36 (m, 1H), 7.22 (d, *J*=8.22 Hz, 1H), 4.38-4.72 (m, 1H), 2.95-3.14 (m, 2H), 2.68 (br. s., 3H), 2.00 (d, *J*=13.30 Hz, 1H), 1.70-1.83 (m, 2H), 1.44-1.67 (m, 6H), 1.14-1.35 (m, 3H), 0.75 (d, *J*=6.46 Hz, 3H), 0.41-0.70 (m, 2H)

Compound 9

White solid. Purity by HPLC 99%. MS found M+H = 545.2 Da. HRMS calculated 545.2646, found 545.2670.