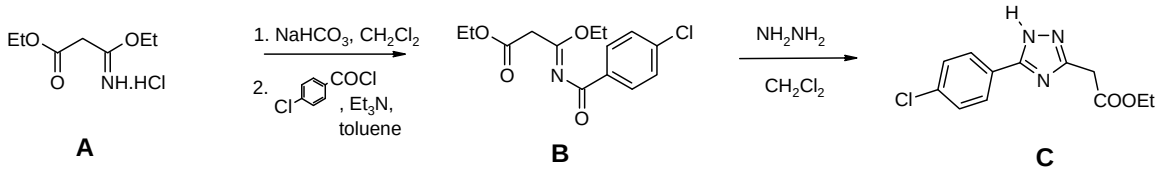
Supplemental Methods S1

Preparation of DAS734 ***[5-(4-chlorophenyl)-1-isopropyl-1H-[1,2,4]triazol-3-yl]-acetic acid***

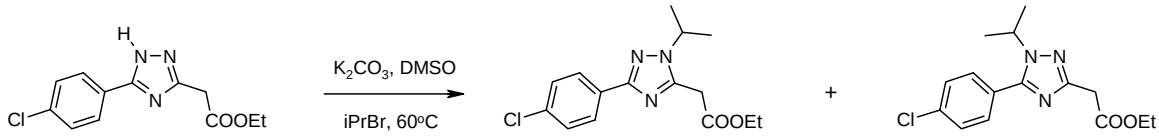
[5-(4-chlorophenyl)-1H-[1,2,4]triazol-3-yl]-acetic acid ethyl ester **C**:



A **B** **C**

Ethyl 3-ethoxy-3-iminopropionate hydrochloride **A** (3.38 g, 21.2 mmmol) was added to a mixture of chloroform (30 mL) and saturated $NaHCO_3$ solution (30 mL). The mixture was vigorously stirred at room temperature for 10 minutes. The organic layer was then separated and washed with brine, dried (Na_2SO_4), filtered, and the solvent removed *in vacuo* to provide the crude free imine. Immediately, the imine was taken up into toluene (65 mL) and cooled to 0^oC under nitrogen. Et_3N (3.55 mL, 25.5 mmol) was added followed by 4-chlorobenzoyl chloride (2.97 mL, 23.4 mmol) and the mixture was stirred at room temperature over night. The mixture was then filtered to remove the unwanted precipitate and the organic solution was concentrated to provide the crude imine **B** (6.51 g) which was used without further purification. Imine **B** was taken up into $CHCl_3$ at room temperature and anhydrous hydrazine (0.82 mL, 26.20 mmoL) was added. After stirring for 2 hrs the mixture was washed with brine, dried (Na_2SO_4), filtered, and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (hexane, ethyl acetate, 1:1) to provide triazole **C** (1.86 g, 34% from **A**); ^1H NMR ($CDCl_3$): δ 8.01 (d, *J* = 8.6 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 4.31 (q, 2H), 4.04 (s, 2H), 1.35 (t, 3H).

[5-(4-chlorophenyl)-2-isopropyl-2H-[1,2,4]triazol-3-yl]-acetic acid ethyl ester **D** and *[5-(4-chlorophenyl)-1-isopropyl-1H-[1,2,4]triazol-3-yl]-acetic acid ethyl ester* **E**:

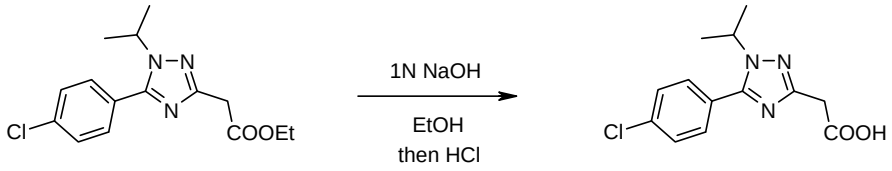


C **D** **E**

Triazole **C** (1.74 g, 65.3 mmol) was dissolved in anhydrous DMSO (20 mL) at room temperature under nitrogen followed by the addition of K_2CO_3 (2.71 g, 0.196 mol). After stirring for 10 mins, isopropyl bromide (1.23 mL, 0.131 mol) was added and the mixture heated at 60^oC for 2 hrs. Ice cold water was then added and the mixture extracted with ethyl ether (3 x 10 mL). The organic layers were combined, washed with water, brine,

dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2 to 10% acetone in CH_2Cl_2) to provide triazole **D** (1.57 g, 78% yield); ^{1}H NMR ($CDCl_3$): δ 8.04 (d, *J* = 8.6 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 4.50 (m, 1H), 4.22 (q, 2H), 3.93 (s, 2H), 1.56 (d, *J* = 6.6 Hz, 6H), 1.30 (t, 3H) and then triazole **E** (0.27 g, 13% yield)); ^{1}H NMR ($CDCl_3$): δ 7.55 (d, *J* = 8.6 Hz, 2H), 7.50 (d, *J* = 8.6 Hz, 2H), 4.62 (m, 1H), 4.23 (q, 2H), 3.84 (s, 2H), 1.53 (d, *J* = 6.6 Hz, 6H), 1.35 (t, 3H).

[5-(4-chlorophenyl)-1-isopropyl-1H-[1,2,4]triazol-3-yl]-acetic acid **F**:



E **F**

1N NaOH (2 mL) was added to a solution of the ester **E** (250 mg, 0.81 mmol) in EtOH (4 mL) and the mixture stirred at room temperature for 2 hr. After diluting with water (10 mL) the solution was acidified to pH 4 with 1N HCl and extracted with EtOAc (3 x 5 mL). The solvent was washed with water, brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. to provide acid **F** (0.198 g, 87% yield) as a white solid; ^{1}H NMR (DMSO-D^6): δ 7.64 (m, 4H), 4.62 (m, 1H), 3.67 (s, 2H), 1.41 (d, *J* = 6.6 Hz, 6H).