Supplementary Material

Auxiliary-controlled diastereoselective synthesis of a syn C-6-epimer of the ADAM 10 inhibitor GI254023X

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(R)-4-Benzyl oxazolidin-2-one (1)

1. $^1$H NMR in CDCl$_3$

- E (s) 6.24
- D (m) 4.32
- C (m) 4.05
- B (m) 2.84
- A (m) 2.76

2. $^{13}$C NMR in CDCl$_3$

- $\delta$ 155.4
- $\delta$ 124.2
- $\delta$ 21.2
- $\delta$ 114.8
- $\delta$ 31.8
- $\delta$ 16.7
- $\delta$ 15.3
- $\delta$ 15.2
(R)-4-Benzyl-3-(5-phenylpentanoyl)oxazolidin-2-one (3)

3 - $^1$H NMR in CDCl$_3$

3 - $^{13}$C NMR in CDCl$_3$
(R)-4-Benzyl-3-((R)-2-((S)-1-hydroxyethyl)-5-phenylpentanoyl)oxazolidin-2-one (4)

4 - $^1$H NMR in CDCl$_3$

4 - $^{13}$C NMR in CDCl$_3$
(R)-2-((S)-1-Hydroxyethyl)-5-phenylpentanoic acid (5)
(R)-N-(Benzyloxy)-2-((S)-1-hydroxyethyl)-5-phenylpentanamide (6)

$\text{6} - ^1\text{H NMR in CD}_3\text{OD}$

$\text{6} - ^{13}\text{C NMR in CD}_3\text{OD}$
(3R,4R)-1-(Benzyloxy)-4-methyl-3-(3-phenylpropyl)azetidin-2-one (7)

Expansion of the 3.17-3.25 ppm signal for H-4 of 7 is shown above, revealing a dq with $J = 2.0, 6.1$ Hz vicinal couplings. This confirms the trans-relative stereochemistry between H-3 and H-4 based on a near 90 ° dihedral angle and, hence, a low vicinal $J$ value (2.0 Hz). In the Hoettecke paper (reference 7 in the text) for the cis-isomer (14 in the text of their paper), their $J$ value was recorded as close to 6 Hz. The cis-stereochemistry of 14 was confirmed by X-ray. The absolute stereochemistry in our case was taken to be in accordance with the Evans’ model.
$^1$H NMR in CDCl$_3$
(R)-2-((R)-1-((Benzyloxy)amino)ethyl)-5-phenylpentanoic acid (8)
(R)-2-((R)-1-(N-(Benzyloxy)formamido)ethyl)-5-phenylpentanoic acid (9)
(S)-2-Amino-N,3,3-trimethylbutanamide (10)
(R)-2-((R)-1-(N-(Benzyloxy)formamido)ethyl)-N-((R)-3,3-dimethyl-1-(methylamino)-1-oxobutan-2-yl)-5-phenylpentanamide (11)

**1H NMR in CD$_3$OD**

**13C NMR in CD$_3$OD**
(R)-N-((R)-3,3-Dimethyl-1-(methylamino)-1-oxobutan-2-yl)-2-((R)-1-(N-hydroxyformamido)ethyl)-5-phenylpentanamide (12)
Chiral HPLC analysis of 12 on a Chiracel OD column with the eluent composed of Hex (60%): i-PrOH (40%), for 20 min with a flow rate of 1 mL/min at λ = 254 nm