Supplementary Material

An efficient and scalable synthesis of thiazolo ring fused 2-pyridones using flow chemistry

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Table of Contents

C10 from flow synthesis..............................................................................................................................................S2
Chiral HPLC traces ......................................................................................................................................................S3
C10 from flow synthesis:

**1H NMR:**

![1H NMR spectrum](image)

Current Data Parameters

NAME AL_C10_largehetero
SERIES
PROCEDURE 1
F1 - Acquisition Parameters
Data: 10020012
Time: 4.46 h
INSTRUM spect
FREQMOD EN099_0090
POLARIZATION applpD
TD 125.77MHz
SOLVENT CDCl3
BS 1.00
SNR 217511.9 Hz
FIDRES 0.0025 Hz
AQ 1.0102146 sec
AB 16.850 s
DE 13.00 sec
TE 198.0 s
D1 2.060000 sec
D2 0.000000 sec
ADC 125.77MHz
SOLV 150
F1 13.00 sec
SLR1 96.3269027 N
SP2 500.1325025 MHz
SPUD 1.00
DGEM12 waltis12
B0 1.00 Hz
SLR2 8.4809999 N
SLR3 0.1717737 N
SLR4 0.0678737 N

F2 - Processing parameters

SI 32768
SP 125.77MHz
MCR 2 AD
B0 0
AM 0
FAC 1.0 Hz
BC 1.40

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**13C NMR:**

![13C NMR spectrum](image)

Current Data Parameters

NAME AL_C10_largehetero
SERIES
PROCEDURE 1
F2 - Acquisition Parameters
Data: 10020012
Time: 4.46 h
INSTRUM spect
FREQMOD EN099_0090
POLARIZATION applpD
TD 125.77MHz
SOLVENT CDCl3
BS 1.00
SNR 217511.9 Hz
FIDRES 0.0025 Hz
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SLR3 0.1717737 N
SLR4 0.0678737 N

F2 - Processing parameters

SI 32768
SP 125.77MHz
MCR 2 AD
B0 0
AM 0
FAC 1.0 Hz
BC 1.40
Chiral HPLC traces:

Chiral HPLC of cyclopropyl thiazoline 11 was carried out using a Diacel Chiracel OD-H (250 x 4.6 mm) column and eluting isocratically (Hexane:iPrOH 90:10) at ambient temperature, then detected by UV at 254 nm. Injection was 10 μL at 1 mg/mL in CHCl₃. Chiral HPLC of pyridone 13 was carried out using a Lux 5 μm i-amylose-1 (250 x 4.6 mm) column and eluting on a gradient (iPrOH 30:70 to 100% hexane) at ambient temperature, then detected by UV at 254 nm. Injection was 10 μL at 1 mg/mL in MeOH.

**Thiazoline (pure):**

![Chiral HPLC trace of thiazoline 12](image)

**Supporting Figure 1.** Chiral HPLC trace of thiazoline 12, as used for MWI and flow syntheses. ee of the mixture = 100%, [α]₀ +83° (c 0.5, CHCl₃)
Thiazoline (epimerized):

**Supporting Figure 2.** Thiazoline 12 post-epimerization, demonstrating that $R$ and $S$ forms can be distinguished. $ee$ of the mixture = 52%, $[\alpha]_D +44^\circ$ (c 0.5, CHCl$_3$).
Thiazoline (mixture of enantiopure and epimerized thiazoline):

**Supporting Figure 3.** Mixture of pure and epimerised thiazoline 12 confirms the identity of the peaks. ee of the mixture = 74% (c 0.5, CHCl₃).
2-Pyridone 13 (Prepared using MWI conditions):

**Supporting Figure 4.** Enantiopurity of pyridone 13, as synthesised by MWI. ee of the mixture = 82%, $[\alpha]_D$ -188º (c 0.5, CHCl$_3$).
2-Pyridone 13 (Prepared under flow conditions):

Supporting Figure 5. Enantiopurity of pyridone 13, as synthesised by flow. ee of the mixture = 73%, [α]D -146° (c 0.5, CHCl₃).
MeOH blank injection (baseline control)

Supporting Figure 6. Blank Injection of MeOH to account for the HPLC baseline.