Supplementary Material

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

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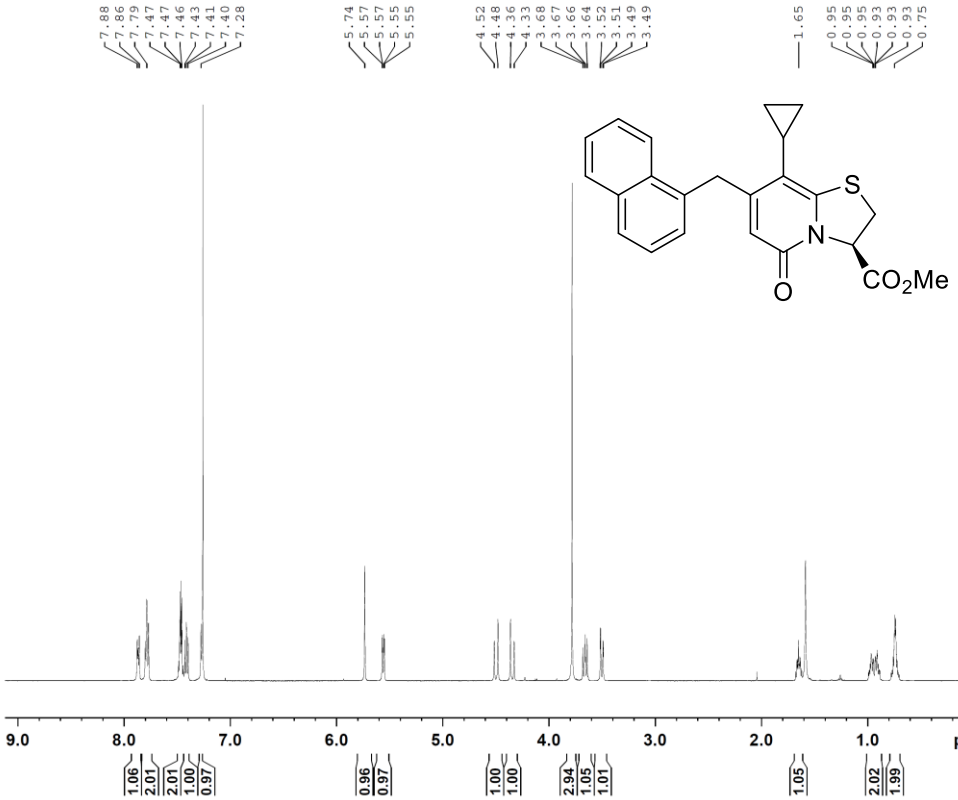
Table of Contents

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

C10 from flow synthesis:

^{1}H NMR:

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TD0                       1
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NUC1                      1H
P1                       12.00 usec
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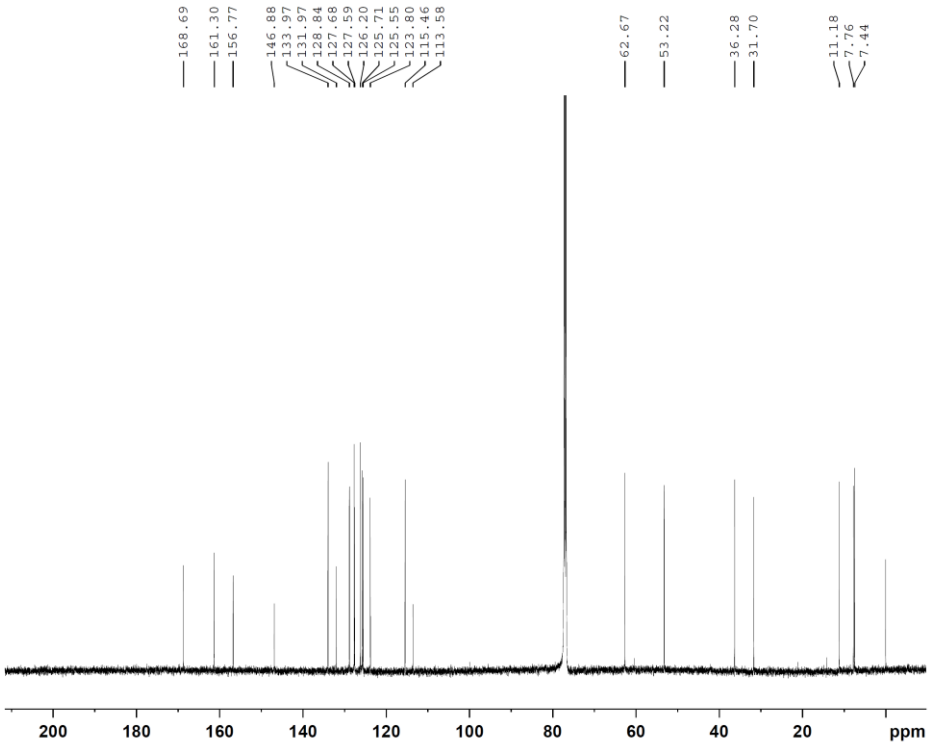
^{13}C NMR:

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NUC2                      1H
CPDPRG[2             waltz16
PCPD2                    80.00 usec
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PLW13              0.08678737 W

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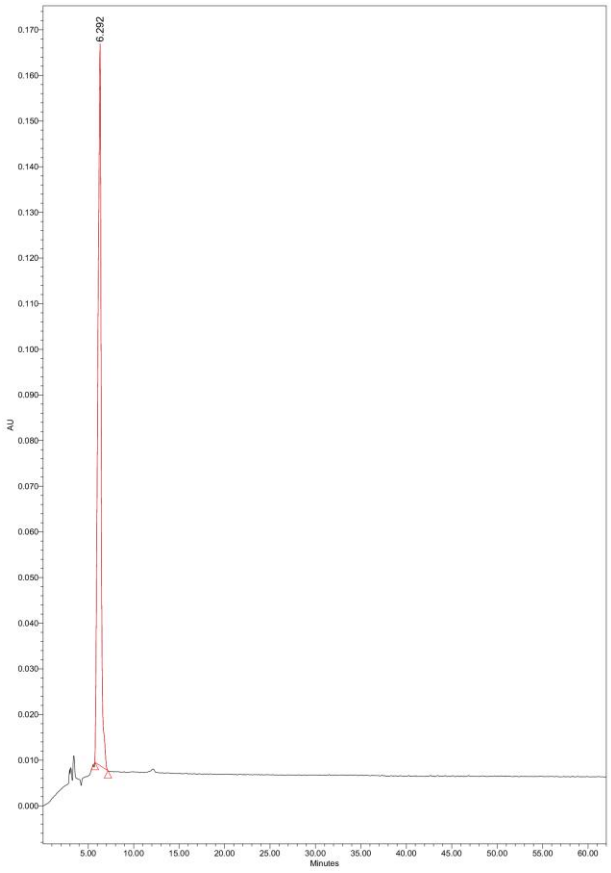
Chiral HPLC traces:

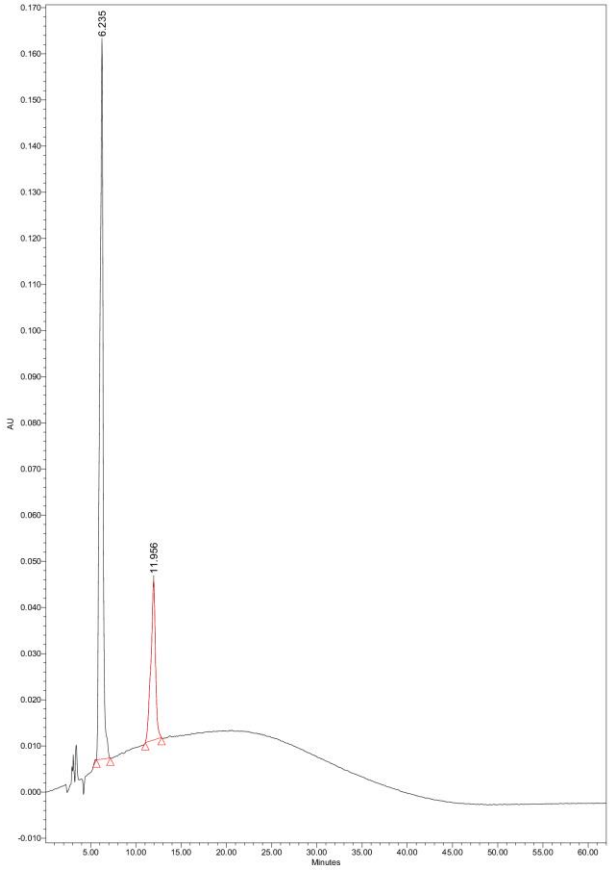
Chiral HPLC of cyclopropyl thiazoline **11** was carried out using a Diacel Chiracel OD-H (250 x 4.6 mm) column and eluting isocratically (Hexane:^{i}PrOH 90:10) at ambient temperature, then detected by UV at 254 nm. Injection was 10 µL at 1 mg/mL in $CHCl_3$. Chiral HPLC of pyridone **13** was carried out using a Lux 5 µm i-amylose-1 (250 x 4.6 mm) column and eluting on a gradient (^{i}PrOH 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):



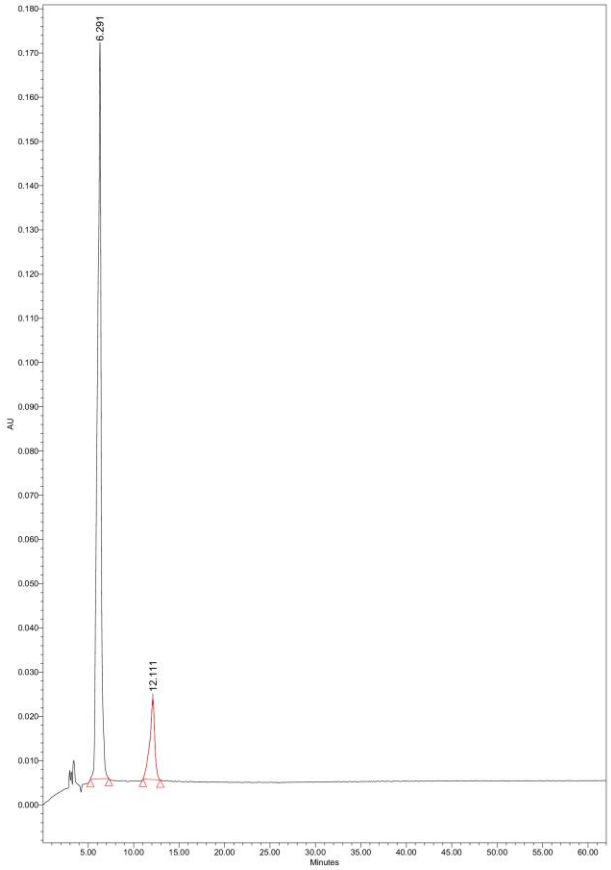
Supporting Figure 1. Chiral HPLC trace of thiazoline **12**, as used for MWI and flow syntheses. *ee* of the mixture = 100%, $[\alpha]_D$ +83° (c 0.5, $CHCl_3$)

Thiazoline (epimerized):



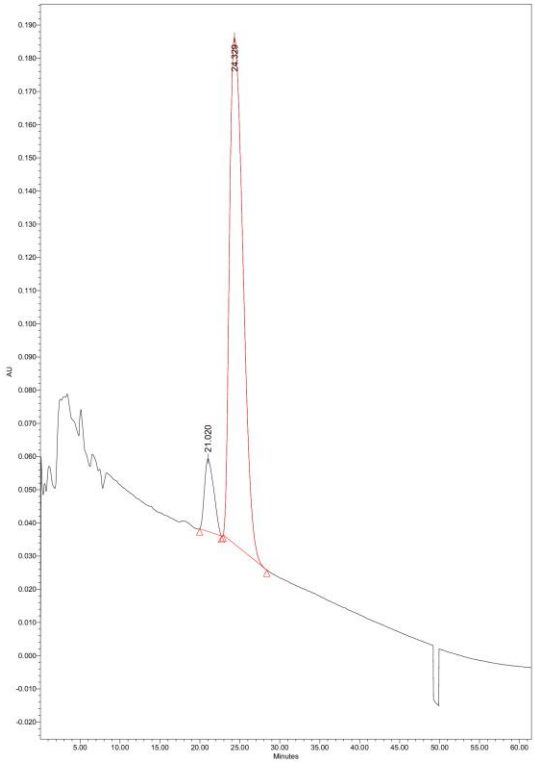
Supporting Figure 2. Thiazoline **12** post-epimerization, demonstrating that *R* and *S* forms can be distinguished. *ee* of the mixture = 52%, $[\alpha]_D$ +44° (c 0.5, $CHCl_3$).

Thiazoline (mixture of enantiopure and epimerized thiazoline):



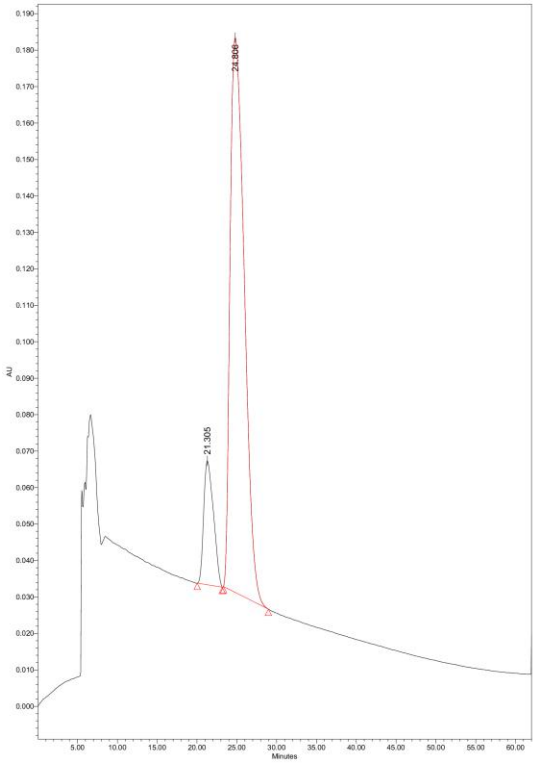
Supporting Figure 3. Mixture of pure and epimerised thiazoline **12** confirms the identity of the peaks. *ee* of the mixture = 74% (c 0.5, $CHCl_3$).

2-Pyridone 13 (Prepared using MWI conditions):



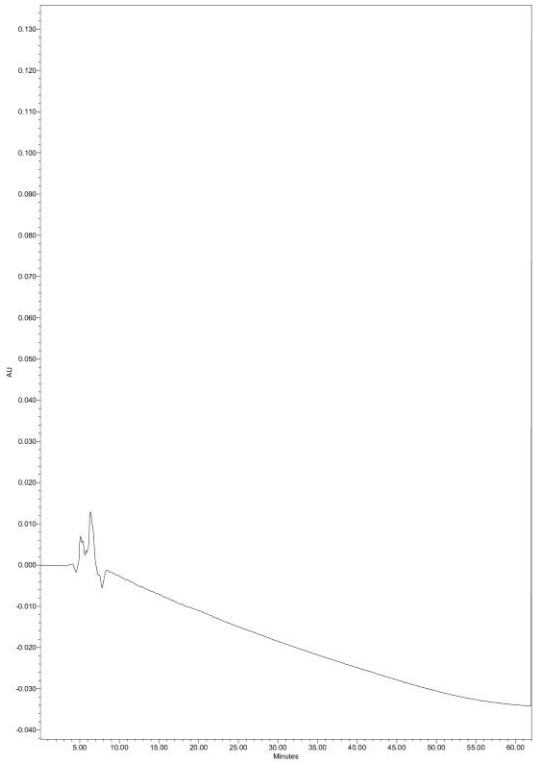
Supporting Figure 4. Enantiopurity of pyridone **13**, as synthesised by MWI. *ee* of the mixture = 82%, $[\alpha]_D$ -188° (c 0.5, $CHCl_3$).

2-Pyridone 13 (Prepared under flow conditions):



Supporting Figure 5. Enantiopurity of pyridone **13**, as synthesised by flow. *ee* of the mixture = 73%, $[\alpha]_D$ -146° (c 0.5, $CHCl_3$).

MeOH blank injection (baseline control)



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