

Representative student results

Base	Solvent	Step 1 Temp (°C)	Step 2 Temp (°C)	Step 1 Time (h)	Step 2 Time (h)	Pyrimetazole peak area (%)	R-Enantiomer peak area (%) ²	Esomeprazole peak area (%)
TEA ¹	EtOAc	50	30	1	0.25	13.0	5.7	79.2
TEA	EtOAc	30	30	1	1	7.1	10.5	71.9
DIPEA	EtOAc	50	30	1	1	0.7	5.4	82.5
DIPA	EtOAc	50	30	1	1	30.9	12.8	56.3
DIPEA	EtOAc	50	30	1	1	3.9	19.0	77.1
TEA	EtOAc	50	0	1	1	97.2	2.8	0
TEA	2-methyl THF	50	30	1	1	78.1	10.8	10.6
DIPEA	2-methylTHF	50	30	0.25	0.25	3.1	25.4	54.3
DIPEA	2-methylTHF	50	30	0.25	1	34.4	34.1	31.6
DIPEA	2-methyl THF	50	30	0.25	1	40.6	27.6	31.8
DIPEA	2-methylTHF	30	30	0.25	0.25	19.3	26.9	47.3
DIPEA	2-methylTHF	50	30	1	1	2.2	20	77.8
DIPEA	2-methylTHF	50	30	1	1	0.0	3.7	81.3

¹ Medicinal group conditions (i.e. the starting point)

² Often overlaps with a much smaller peak for the sulfone (the sulfone is typically below 30% of the peak area for the *R*-enantiomer)

HPLC conditions

Agilent 1100 series HPLC system
Chiralpak AD column, 250 x 4.6 mm
All samples run in 1:1 propan-2-ol:hexane
Flow rate: 1.0 mL/min
Sample concentration: 1 mg/mL
Injection volume: 20 µL
Detection at 302.8 nm

Racemic sample: Peaks at ~6.0 (*R*) and ~7.0 (*S*) mins for the two enantiomers

Sulfone: Peak ~6.5 min

Starting material (pyrimetazole): Peak at ~4.7 min

CAS numbers for all chemicals

Compound	CAS
Pyrmethyl alcohol (2-(hydroxymethyl)-4-methoxy-3,5-dimethylpyridine)	86604-78-6
Metmercazole (5-methoxy-2,3-dihydro-1H-1,3-benzodiazole-2-thione)	37052-78-1
Pyrmetazone (5-Methoxy-2-(((3,5-dimethyl-4-methoxy-2-pyridinyl)methyl)thio)-1H-benzimidazole)	73590-85-9
Esomeprazole	161796-78-7
Thionyl chloride	7719-09-7
Cumene hydroperoxide	80-15-9
Titanium(IV) isopropoxide	546-68-9
(S,S)-Diethyl L-tartrate	87-91-2
Triethylamine	121-44-8
<i>N,N</i> -Diisopropylethylamine	7087-68-5
Ethyl acetate	141-78-6
2-Methyltetrahydrofuran	96-47-9