**Representative student results**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Base** | **Solvent** | **Step 1 Temp (°C)** | **Step 2 Temp (°C)** | **Step 1 Time (h)** | **Step 2 Time (h)** | **Pyrmetazole peak area (%)** | ***R*-Enantiomer**  **peak area (%)**2 | **Esomeprazole peak area**  **(%)** |
| TEA1 | 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 (pyrmetazole): 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 |
| Pyrmetazole  (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 |
| *N*,*N*-Diisopropylethylamine | 7087-68-5 |
| Ethyl acetate | 141-78-6 |
| 2-Methyltetrahydrofuran | 96-47-9 |