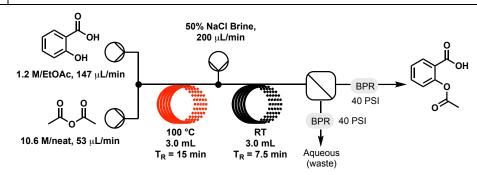
Aspirin

| Date: | |
|------------|--|
| Reference: | |
| | |



| Stream | Conc (mol/L) | Equiv | Flow (uL/min) |
|------------------|--------------|------------|---------------|
| Salicylic Acid | 1.2000 | 1 | 146.6 |
| H2SO4 | 0.1200 | 0.1 | |
| Acetic Anhydride | 10.6000 | 3.21157344 | 53.3 |
| Brine (50%) | N/A | | 200 |

| | Stream 1 | | | | | | | | |
|--------------------|------------------|--------|-------|---------|------------------|--|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | | |
| Salicylic Acid (g) | 8.29 | 138.12 | 0.06 | | | | | | |
| H2SO4 (mL) | 0.30 | 98.08 | 0.006 | 1.84 | | | | | |
| EtOAc (mL) | up to 50 mL | | | | Sigma HPLC grade | | | | |
| Total Volume | 50 | | | | | | | | |

| Stream 2 | | | | | | | | |
|-----------------------|-------------|--------|------|---------|-------|--|--|--|
| Reagent | Amount (mL) | MW | mmol | Density | Notes | | | |
| Acetic Anhydride (mL) | 20.0399 | 102.09 | 212 | | Neat | | | |
| Total Volume | 20 | | | | | | | |

| Stream 3 | | | | | | | |
|------------------|------------------|----|------|---------|------------------------------|--|--|
| Reagent | Amount (g or mL) | MW | mmol | Density | Notes | | |
| Brine (50%) (mL) | | | | | 1:1 Distilled water to brine | | |
| Total Volume | 100 | | | | | | |

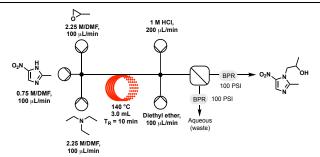
| Reactor 1 | | | | |
|----------------|--------|--|--|--|
| Volume | 3 ml | | | |
| Tubing Inner D | 0.03" | | | |
| Tubing L | 658 cm | | | |
| Res Time | 15 min | | | |
| Temp. | 100 °C | | | |

| Reactor 2 | | | | | | |
|----------------|---------|--|--|--|--|--|
| Volume | 3 ml | | | | | |
| Tubing Inner D | 0.03" | | | | | |
| Tubing L | 658 cm | | | | | |
| Res Time | 7.5 min | | | | | |
| Temp. | RT | | | | | |

| BPR | |
|----------|--------|
| Pressure | 40 psi |

Secnidazole

| Date: | |
|------------|--|
| Reference: | |
| | |



| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL) |
|--------------------------|--------------|-------|---------------|-------------|------------------------------|
| Propylene oxide | 2.25 | 3.00 | 100.0 | 1.67 | 36 |
| 2-methyl-5nitroimidazole | 0.75 | 1.00 | 100.0 | 1.67 | 36 |
| Triethylamine | 2.25 | 3.00 | 100 | 1.67 | 36 |
| HCI | 1.00 | 2.67 | 200 | 3.33 | 72 |
| Diethyl Ether | 9.62 | 12.83 | 100 | 1.67 | 36 |

| Stream 1 | | | | | | | | |
|----------------------|------------------|-------|---------|---------|---------------------------------|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | |
| Propylene oxide (mL) | 7.8723 | 58.08 | 0.11250 | 0.83 | | | | |
| DMF (mL) | up to 50 mL | 73.09 | | 0.944 | | | | |
| Total Volume | 50 | | | | up to 50 mL in volumetric flask | | | |

| Stream 2 | | | | | | | | |
|------------------------------|-------------|--------|---------|---------|---------------------------------|--|--|--|
| Reagent | Amount (g) | MW | mol | Density | Notes | | | |
| 2-methyl-5nitroimidazole (g) | 4.7663 | 127.10 | 0.03750 | | | | | |
| DMF (mL) | up to 50 mL | 73.09 | | 0.944 | | | | |
| Total Volume | 50 | | | | up to 50 mL in volumetric flask | | | |

| Stream 3 | | | | | | | | | |
|--------------------|------------------|--------|--------|---------|---------------------------------|--|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | | |
| Triethylamine (mL) | 15.6803 | 101.19 | 0.1125 | 0.726 | | | | | |
| DMF (mL) | up to 50 mL | 73.09 | | 0.944 | | | | | |
| Total Volume | 50 | | | | up to 50 mL in volumetric flask | | | | |

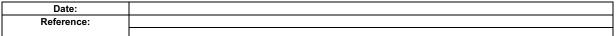
| Stream 4 | | | | | | | | |
|--------------|---|-------|------|-----|----------------------------------|--|--|--|
| Reagent | Amount (g or mL) Conc mol Density Notes | | | | | | | |
| HCI (mL) | 8.2102 | 12.18 | 0.10 | 1.2 | ACS reagent grade, 37% | | | |
| water (mL) | up to 100 mL | | | | | | | |
| Total Volume | 100 | | | | up to 100 mL in volumetric flask | | | |

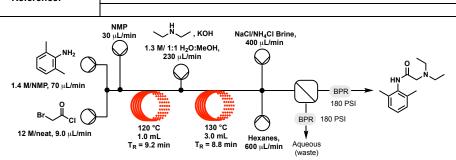
| Stream 5 | | | | | | | | |
|--------------------|------------------|------|-------|---------|-------|--|--|--|
| Reagent | Amount (g or mL) | Conc | mol | Density | Notes | | | |
| Diethyl Ether (mL) | 50.0000 | 9.62 | 0.481 | 0.713 | | | | |
| Total Volume | 50 | | | | | | | |

| Reactor 1 | |
|-----------|--------|
| Volume | 3 ml |
| Res Time | 10 min |
| Temp. | 140 °C |

| BPR | |
|----------|----------|
| Pressure | 100 psig |

Lidocaine





| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL |
|------------------------|--------------|-------|---------------|-------------|-----------------------------|
| Xylidine | 1.40 | 1.00 | 70.0 | 1.17 | 33.6 |
| Bromoroacetyl chloride | 12.01 | 1.10 | 9.0 | 0.15 | 4.32 |
| NMP | 10.37 | 3.17 | 30 | 0.50 | 14.4 |
| Diehtylamine | 1.28 | 3.00 | 230 | 3.83 | 110.4 |
| Hexanes | 7.80 | 47.74 | 600 | 10.00 | 288 |
| NaCI/NH4CI | 3.42 | 13.96 | 400 | 6.67 | 192 |

| Stream 1 | | | | | | | | |
|--------------|------------------|--------|------|---------|--|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | |
| xylidene (g) | 8.48 | 121.18 | 0.07 | | | | | |
| NMP (mL) | up to 50 mL | | | | SPS but not rigorous anhydrous technique | | | |
| Total Volume | 50 | | | | up to 50 mL in volumetric flask | | | |

| Stream 2 | | | | | | | | |
|---------------------------|-------------|--------|--------|---------|--------------|--|--|--|
| Reagent | Amount (mL) | MW | mol | Density | Notes | | | |
| Bromoacetyl chloride (mL) | 10.0013 | 157.39 | 0.1201 | 1.89 | Sigma (neat) | | | |
| Total Volume | 10 | | | | | | | |

| Stream 3 | | | | | | | |
|--------------|------------------|-------|--------|---------|---|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | |
| NMP (mL) | 19.9996 | 99.13 | 0.2074 | 1.028 | SPS but not rigoursly anhydrous in handling | | |
| Total Volume | 20 | | | | | | |

| Stream 4 | | | | | | | | |
|-------------------|------------------|-------|------|---------|--|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | |
| Diethylamine (mL) | 18.5385 | 73.14 | 0.18 | 0.707 | dissolve amine in MeOH | | | |
| Methanol (mL) | 60.68 | 32.04 | | 0.791 | Reagent grade nothing special | | | |
| KOH (g) | 3.35 | 56.11 | 0.06 | | dissolve KOH in DI water | | | |
| DI water (mL) | 60.68 | 18.02 | | 1 | | | | |
| Total Volume | 140 | | | | mix the two components together slowly (divide into 3 vials) | | | |

| Stream 5 | | | | | | | | |
|--------------|------------------|-------|---------|---------|-------------------------------|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | |
| Hexanes (mL) | 368.0795 | 88.11 | 2.80728 | 0.672 | Reagent grade nothing special | | | |
| Total Volume | 360 | | | | Need 6 full vials | | | |

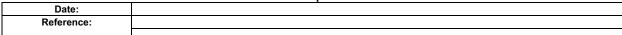
| Stream 6 | | | | | | | | |
|---------------|------------------|-------|-------|---------|-------------------|--|--|--|
| Reagent | Amount (g or mL) | MW | mmol | Density | Notes | | | |
| NaCl (g) | 50.0000 | 58.44 | #REF! | | | | | |
| NH4Cl (g) | 50.0000 | 53.49 | | | | | | |
| DI Water (mL) | 500.0000 | 18.02 | | | | | | |
| Total Volume | 500 | | | | Need 4 full vials | | | |

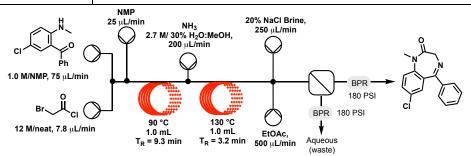
| Reactor 1 | | | | |
|-----------|---------|--|--|--|
| Volume | 1 ml | | | |
| Res Time | 9.2 min | | | |
| Temp. | 120 °C | | | |

| Reactor 2 | | | | |
|-----------|---------|--|--|--|
| Volume | 3 ml | | | |
| Res Time | 8.8 min | | | |
| Temp. | 130 °C | | | |

| BPR | |
|----------|----------|
| Pressure | 180 psig |

Diazepam





| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL |
|------------------------|--------------|-------|---------------|-------------|-----------------------------|
| Benzophenone | 1.00 | 1.00 | 75.0 | 1.25 | 36 |
| Bromoroacetyl chloride | 12.01 | 1.25 | 7.8 | 0.13 | 3.744 |
| NMP | 10.37 | 3.46 | 25 | 0.42 | 12 |
| Ammonia | 2.70 | 7.20 | 200 | 3.33 | 96 |
| Ethylacetate | 10.24 | 68.27 | 500 | 8.33 | 240 |
| NaCl | 4.62 | 15.40 | 250 | 4.17 | 120 |

| | Stream 1 | | | | | | | | |
|---|-------------|--------|------|--|--|--|--|--|--|
| Reagent Amount (g or mL) MW mol Density Notes | | | | | | | | | |
| Benzophenone (g) | 12.29 | 245.70 | 0.05 | | | | | | |
| NMP (mL) | up to 50 mL | | | | SPS but not rigorous anhydrous technique | | | | |
| Total Volume | 50 | | | | up to 50 mL in volumetric flask | | | | |

| Stream 2 | | | | | | | |
|--|---------|--------|--------|------|---|--|--|
| Reagent Amount (mL) MW mol Density Notes | | | | | | | |
| Bromoacetyl chloride (mL) | 10.0013 | 157.39 | 0.1201 | 1.89 | Sigma (neat) | | |
| Total Volume | 10 | | | | Unnecessary if we are doing back to back with lidocaine | | |

| Stream 3 | | | | | | | |
|--------------|------------------|-------|--------|---------|---|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | |
| NMP (mL) | 19.9996 | 99.13 | 0.2074 | 1.028 | SPS but not rigoursly anhydrous in handling | | |
| Total Volume | 20 | | | | | | |

| Stream 4 | | | | | | | | |
|-------------------------|------------------|-------|------|---------|--|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | |
| Ammonium Hydroxide (mL) | 22.00 | 73.14 | 0.33 | 0.707 | 28-30% ACS grade from BDH, add to water | | | |
| DI water (mL) | 22.00 | 18.02 | | 1 | | | | |
| Methanol (mL) | 77.00 | 32.04 | | 0.791 | add to diluted ammonium hydroxide solution | | | |
| Total Volume | 121 | | | | divide into 2 vials | | | |

| Stream 5 | | | | | | | |
|-------------------|---|-------|-------|-------|-------------------------------|--|--|
| Reagent | ent Amount (g or mL) MW mol Density Notes | | | | | | |
| Ethylacetate (mL) | 300.0000 | 88.11 | 3.072 | 0.902 | Reagent grade nothing special | | |
| Total Volume | 300 | | | | Need 5 full vials | | |

| Stream 6 | | | | | | | |
|---------------|------------------|-------|-------|---------|---------------------|--|--|
| Reagent | Amount (g or mL) | MW | mmol | Density | Notes | | |
| NaCl (g) | 40.5000 | 58.44 | #REF! | | | | |
| DI Water (mL) | 150.0000 | 18.02 | | | | | |
| Total Volume | 150 | | | | Divide into 3 vials | | |

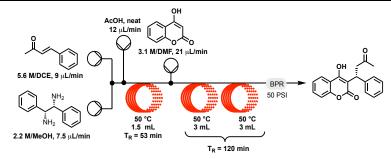
| Reactor 1 | | | | | |
|-----------|---------|--|--|--|--|
| Volume | 1 ml | | | | |
| Res Time | 9.3 min | | | | |
| Temp. | 90 °C | | | | |

| Reactor 2 | | | | |
|-----------|---------|--|--|--|
| Volume | 1 ml | | | |
| Res Time | 3.2 min | | | |
| Temp. | 130 °C | | | |

| BPR | |
|----------|----------|
| Pressure | 180 psig |

Warfarin

| Date: | |
|------------|--|
| Reference: | |
| | |



| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL) |
|-------------------|--------------|-------|---------------|-------------|------------------------------|
| Benzylacetone | 5.60 | 1.00 | 9.0 | 0.15 | 12.96 |
| (S,S)-DPEN | 2.20 | 0.33 | 7.5 | 0.13 | 10.8 |
| Acetic Acid | 17.50 | 4.17 | 12 | 0.20 | 17.28 |
| 4-Hydroxycoumarin | 3.10 | 1.29 | 21 | 0.35 | 30.24 |

| | Stream 1 | | | | | | |
|---|-------------|--------|---------|------|---------------------------------|--|--|
| Reagent Amount (g or mL) MW mol Density Notes | | | | | | | |
| Benzylacetone (g) | 20.4666 | 146.19 | 0.14000 | | | | |
| DCE | up to 25 mL | 98.96 | | 1.25 | | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | |

| Stream 2 | | | | | | |
|----------------|-------------|--------|---------|---------|---------------------------------|--|
| Reagent | Amount (g) | MW | mol | Density | Notes | |
| (S,S)-DPEN (g) | 11.6760 | 212.29 | 0.05500 | | | |
| MeOH (mL) | up to 25 mL | 32.04 | | 0.792 | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | |

| Stream 3 | | | | | |
|------------------|------------------|-------|--------|---------|-------|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes |
| Acetic Acid (mL) | 25.0447 | 60.05 | 0.4375 | 1.049 | |
| Total Volume | 25 | | | | |

| Stream 4 | | | | | | |
|---|-------------|--------|------|-------|---------------------------------|--|
| Reagent Amount (g or mL) MW mol Density Notes | | | | | | |
| 4-Hydroxycoumarin (g) | 25.1317 | 162.14 | 0.16 | | | |
| DMF (mL) | up to 50 mL | 73.09 | | 0.944 | | |
| Total Volume | 50 | | | | up to 50 mL in volumetric flask | |

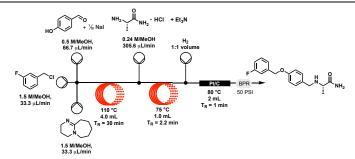
| Reactor 1 + 2 | | | | |
|---------------|----------------|--|--|--|
| Volume | 0.5 mL+ 1.0 mL | | | |
| Res Time | 53 min | | | |
| Temp. | 50 °C | | | |

| 222 | |
|----------|---------|
| Pressure | 50 psig |

| Reactor 3 + 4 | | | | | |
|--------------------|---------|--|--|--|--|
| Volume 3 ml + 3 mL | | | | | |
| Res Time | 120 min | | | | |
| Temp. | 50 °C | | | | |

Safinamide

| Date: | |
|------------|--|
| Reference: | |
| | |



| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Volume |
|-------------------------|--------------|------------|---------------|--------|
| 4-hydoxybenzaldehyde | 0.5000 | 1 | 66.7 | 40.0 |
| Sodium iodide | 0.0500 | 0.1 | 00.7 | |
| 3-Fluorobenyzl chloride | 1.5000 | 1.49775112 | 33.3 | 40.0 |
| DBU | 1.5000 | 1.49775112 | 33.3 | 19.98 |
| Alaninamide | 0.2400 | 2.2 | 305.6 | 183.36 |

Time 10

| Stream 1 | | | | | | | | | | |
|---------------------------|----------------|--------|--------|-------|--|--|--|--|--|--|
| Reagent | Amount (g /mL) | MW | mmol | Notes | | | | | | |
| 4-hydroxybenzaldehyde (g) | 3.053 | 122.12 | 0.025 | 1 | | | | | | |
| Sodium iodide (g) | 0.374725 | 149.89 | 0.0025 | 1 | | | | | | |
| MeOH (mL) | up to 50 mL | 1 | / | 1 | | | | | | |
| Total Volume | 50 | / | 1 | 1 | | | | | | |

| Stream 2 | | | | | | | | | |
|------------------------------|-------------|--------|-------|---------|-------|--|--|--|--|
| Reagent | Amount (mL) | MW | mmol | Density | Notes | | | | |
| 3-Fluorobenzyl chloride (mL) | 9.081030151 | 144.57 | 0.075 | 1.194 | | | | | |
| MeOH (mL) | up to 50 mL | | | | | | | | |
| Total Volume | 50 | | | | | | | | |

| Stream 3 | | | | | | | | | |
|--------------|-------------|--------|-------|---------|-------|--|--|--|--|
| Reagent | Amount (mL) | MW | mmol | Density | Notes | | | | |
| DBU (mL) | 11.19411765 | 152.24 | 0.075 | 1.02 | | | | | |
| MeOH (mL) | up to 50 mL | | | | | | | | |
| Total Volume | 50 | | | | | | | | |

| Stream 4 | | | | | | | | | |
|-----------------|---------------|--------|------|---------|-------|--|--|--|--|
| Reagent | Amount (g/mL) | MW | mmol | Density | Notes | | | | |
| Alaninamide (g) | 7.4742 | 124.57 | 0.06 | 1 | | | | | |
| NEt3 (mL) | 8.362809917 | 101.19 | 0.06 | 0.726 | | | | | |
| MeOH (mL) | up to 250 mL | | | | | | | | |
| Total Volume | 250 | | | | | | | | |

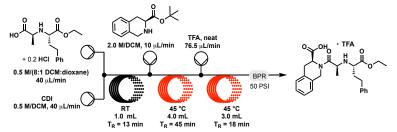
| Reactor 1 | | | | | | | |
|----------------|--------|--|--|--|--|--|--|
| Volume | 4 ml | | | | | | |
| Tubing Inner D | 0.03" | | | | | | |
| Tubing L | 880 cm | | | | | | |
| Res Time | 30 min | | | | | | |
| Temp. | 110 °C | | | | | | |

| Reactor 2 | | | | | | |
|----------------|---------|--|--|--|--|--|
| Volume | 1 ml | | | | | |
| Tubing Inner D | 0.03" | | | | | |
| Tubing L | 220 | | | | | |
| Res Time | 2.3 min | | | | | |
| Temp. | 75 | | | | | |

| BPR | |
|----------|---------|
| Pressure | 150 psi |

Quinapril

| | a a map m |
|------------|-----------|
| Date: | |
| Reference: | |
| | |



| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL) |
|---|--------------|-------|---------------|-------------|------------------------------|
| N-[(S)-1-Ethoxycarbonyl-3-phenylpropyl]-L-alanine | 0.50 | 1.00 | 40.0 | 0.67 | 28.8 |
| CDI | 0.50 | 1.00 | 40.0 | 0.67 | 28.8 |
| tert-butyl (S)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate | 2.00 | 1.00 | 10 | 0.17 | 7.2 |
| TFA | 13.06 | 49.95 | 76.5 | 1.28 | 55.08 |

| Stream 1 | | | | | | | | |
|---|-------------|--------|---------|--|--|--|--|--|
| Reagent Amount (g or mL) MW mol Density Notes | | | | | | | | |
| N-[(S)-1-Ethoxycarbonyl-3-phenylpropyl]-L-alanine (g) | 3.4918 | 279.34 | 0.01250 | | | | | |
| HCI (mL) | 0.63 | 36.46 | 0.00250 | | 4 M in 1,4-dioxane | | | |
| DCM (mL) | up to 25 mL | | | | SPS but not rigorous anhydrous technique | | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | | |

| Stream 2 | | | | | | | | |
|--------------|-------------|--------|--------|---------|--|--|--|--|
| Reagent | Amount (g) | MW | mol | Density | Notes | | | |
| CDI (g) | 2.0269 | 162.15 | 0.0125 | | | | | |
| DCM (mL) | up to 25 mL | | | | SPS but not rigorous anhydrous technique | | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | | |

| Stream 3 | | | | | | | | |
|--------------|------------------|-----|-------|---------|-------|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | |
| TFA (mL) | 49.9698 | 114 | 0.653 | 1.49 | Neat | | | |
| Total Volume | 50 | | | | | | | |

| Stream 4 | | | | | | | | |
|---|------------------|--------|------|---------|--|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | |
| tert-butyl (S)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate (g) | 4.6662 | 233.31 | 0.02 | | | | | |
| DCM (mL) | up to 10 mL | | | | SPS but not rigorous anhydrous technique | | | |
| Total Volume | 10 | | | | up to 10 mL in volumetric flask | | | |

| Reactor 1 | | | | |
|-----------|--------|--|--|--|
| Volume | 1 ml | | | |
| Res Time | 13 min | | | |
| Temp. | rt | | | |

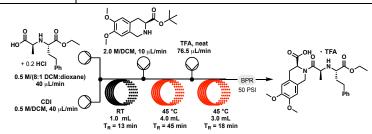
| Reac | Reactor 2 | | | | | | |
|----------|-----------|--|--|--|--|--|--|
| Volume | 1 ml | | | | | | |
| Res Time | 11 min | | | | | | |
| Temp. | 45 °C | | | | | | |

| Reactor 3 | | | | | | |
|-----------|--------|--|--|--|--|--|
| Volume | 3 ml | | | | | |
| Res Time | 18 min | | | | | |
| Temp. | 45 °C | | | | | |

| Proceure | 50 peig |
|----------|---------|
| BPR | |
| | |

Moexipril

| Date: | |
|------------|--|
| Reference: | |
| | |



| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL) |
|---|--------------|-------|---------------|-------------|------------------------------|
| N-[(S)-1-Ethoxycarbonyl-3-phenylpropyl]-L-alanine | 0.50 | 1.00 | 40.0 | 0.67 | 28.8 |
| CDI | 0.50 | 1.00 | 40.0 | 0.67 | 28.8 |
| tert-butyl (S)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylate | 2.00 | 1.00 | 10 | 0.17 | 7.2 |
| TFA | 13.06 | 49.95 | 76.5 | 1.28 | 55.08 |

| Stream 1 | | | | | | | | |
|---|------------------|--------|---------|---------|--|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | |
| N-[(S)-1-Ethoxycarbonyl-3-phenylpropyl]-L-alanine (g) | 3.4918 | 279.34 | 0.01250 | | | | | |
| HCI (mL) | 0.63 | 36.46 | 0.00250 | | 4 M in 1,4-dioxane | | | |
| DCM (mL) | up to 25 mL | | | | SPS but not rigorous anhydrous technique | | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | | |

| Stream 2 | | | | | | | | |
|--------------|-------------|--------|--------|---------|--|--|--|--|
| Reagent | Amount (g) | MW | mol | Density | Notes | | | |
| CDI (g) | 2.0269 | 162.15 | 0.0125 | | | | | |
| DCM (mL) | up to 25 mL | | | | SPS but not rigorous anhydrous technique | | | |
| Total Volume | 25 | _ | | | up to 25 mL in volumetric flask | | | |

| Stream 3 | | | | | | | |
|--------------|------------------|-----|-------|---------|-------|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | |
| TFA (mL) | 49.9698 | 114 | 0.653 | 1.49 | Neat | | |
| Total Volume | 50 | | | | | | |

| Stream 4 | | | | | | | | |
|---|------------------|--------|------|---------|--|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | |
| tert-butyl (S)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylate (g) | 5.8672 | 293.36 | 0.02 | | | | | |
| DCM (mL) | up to 10 mL | | | | SPS but not rigorous anhydrous technique | | | |
| Total Volume | 10 | | | | up to 10 mL in volumetric flask | | | |

| Reactor 1 | | | | | |
|-----------|--------|--|--|--|--|
| Volume | 1 ml | | | | |
| Res Time | 13 min | | | | |
| Temp. | rt | | | | |

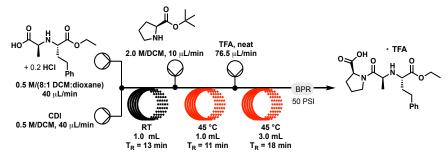
| Reactor 2 | | | | |
|-----------------|-------|--|--|--|
| Volume 1 ml | | | | |
| Res Time 11 min | | | | |
| Temp. | 45 °C | | | |

| Reactor 3 | | | | |
|-------------|--------|--|--|--|
| Volume 3 ml | | | | |
| Res Time | 18 min | | | |
| Temp. | 45 °C | | | |

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| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL) |
|------------------------|--------------|-------|---------------|-------------|------------------------------|
| N-Substituted Alanine | 0.50 | 1.00 | 40.0 | 0.67 | 28.8 |
| CDI | 0.50 | 1.00 | 40.0 | 0.67 | 28.8 |
| tert-Butyl L-Prolinate | 2.00 | 1.00 | 10 | 0.17 | 7.2 |
| TFA | 13.06 | 49.95 | 76.5 | 1.28 | 55.08 |

Run Time (h) 12

| | Stream 1 | | | | | |
|---|---|--------|---------|--|--|--|
| Reagent Amount (g or mL) MW mol Density Notes | | | | | | |
| N-Substituted Alanine (g) | 3.4918 | 279.34 | 0.01250 | | | |
| HCI (mL) | 0.63 | 36.46 | 0.00250 | | 4 M in 1,4-dioxane | |
| DCM (mL) | up to 25 mL | | | | SPS but not rigorous anhydrous technique | |
| Total Volume | Total Volume 25 up to 25 mL in volumetric flask | | | | | |

| Stream 2 | | | | | | |
|--------------|---|--|--|--|--|--|
| Reagent | Reagent Amount (g) MW mol Density Notes | | | | | |
| CDI (g) | 2.0269 162.15 0.0125 | | | | | |
| DCM (mL) | up to 25 mL | | | | SPS but not rigorous anhydrous technique | |
| Total Volume | Total Volume 25 up to 25 mL in volumetric flask | | | | | |

| Stream 3 | | | | | |
|--------------|------------------|--------|-------|---------|-------|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes |
| TFA (mL) | 49.9698 | 114.02 | 0.653 | 1.49 | Neat |
| Total Volume | 50 | | | | |

| Stream 4 | | | | | |
|---|---|--------|------|--|---------------------------------|
| Reagent Amount (g or mL) MW mol Density Notes | | | | | |
| tert-Butyl L-Prolinate (g) | 3.4248 | 171.24 | 0.02 | | |
| DCM (mL) | DCM (mL) up to 10 mL SPS but not rigorous anhydrous technique | | | | |
| Total Volume | 10 | | | | up to 10 mL in volumetric flask |

Reactor 2

| Reactor 1 | | | | |
|-----------|--------|--|--|--|
| Volume | 1 ml | | | |
| Res Time | 13 min | | | |
| Temp. | rt | | | |

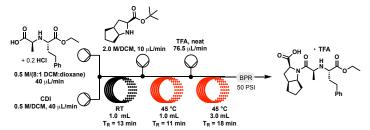
| 1 ml | | Volume | 1 ml |
|--------|---|----------|--------|
| 13 min | | Res Time | 11 min |
| rt | | Temp. | 45 °C |
| | • | | |

| Reactor 3 | | | | |
|-------------|--------|--|--|--|
| Volume 3 ml | | | | |
| Res Time | 18 min | | | |
| Temp. | 45 °C | | | |

| BPR | | |
|----------|---------|--|
| Pressure | 50 psig | |

Ramipril

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| Date: | |
| Reference: | |
| | |



| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL) |
|---|--------------|-------|---------------|-------------|------------------------------|
| N-[(S)-1-Ethoxycarbonyl-3-phenylpropyl]-L-alanine | 0.50 | 1.00 | 40.0 | 0.67 | 28.8 |
| CDI | 0.50 | 1.00 | 40.0 | 0.67 | 28.8 |
| tert-butyl (2S,3aS,6aS)-octahydrocyclopenta[b]pyrrole-2-carboxylate | 2.00 | 1.00 | 10 | 0.17 | 7.2 |
| TFA | 13.06 | 49.95 | 76.5 | 1.28 | 55.08 |

| Stream 1 | | | | | |
|---|------------------|--------|---------|---------|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes |
| N-[(S)-1-Ethoxycarbonyl-3-phenylpropyl]-L-alanine (g) | 3.4918 | 279.34 | 0.01250 | | |
| HCI (mL) | 0.63 | 36.46 | 0.00250 | | 4 M in 1,4-dioxane |
| DCM (mL) | up to 25 mL | | | | SPS but not rigorous anhydrous technique |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask |

| Stream 2 | | | | | |
|--------------|-------------|--------|--------|---------|--|
| Reagent | Amount (g) | MW | mol | Density | Notes |
| CDI (g) | 2.0269 | 162.15 | 0.0125 | | |
| DCM (mL) | up to 25 mL | | | | SPS but not rigorous anhydrous technique |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask |

| Stream 3 | | | | | |
|--------------|------------------|-----|-------|---------|-------|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes |
| TFA (mL) | 49.9698 | 114 | 0.653 | 1.49 | Neat |
| Total Volume | 50 | | | | |

| Stream 4 | | | | | |
|--|------------------|--------|------|---------|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes |
| tert-butyl (2S,3aS,6aS)-octahydrocyclopenta[b]pyrrole-2-carboxylate (g | 4.2262 | 211.31 | 0.02 | | |
| DCM (mL) | up to 10 mL | | | | SPS but not rigorous anhydrous technique |
| Total Volume | 10 | | | | up to 10 mL in volumetric flask |

| Reactor 1 | | |
|-----------|--------|--|
| Volume | 1 ml | |
| Res Time | 13 min | |
| Temp. | rt | |

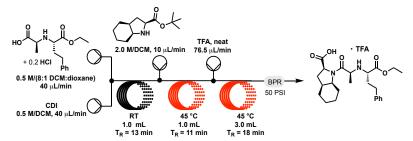
| Reactor 2 | | |
|-----------|--------|--|
| Volume | 1 ml | |
| Res Time | 11 min | |
| Temp. | 45 °C | |

| Reactor 3 | | | |
|-----------|--------|--|--|
| Volume | 3 ml | | |
| Res Time | 18 min | | |
| Temp. | 45 °C | | |

| BPR | |
|----------|---------|
| Pressure | 50 psig |

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| Date: | |
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| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL) |
|---|--------------|-------|---------------|-------------|------------------------------|
| N-[(S)-1-Ethoxycarbonyl-3-phenylpropyl]-L-alanine | 0.50 | 1.00 | 40.0 | 0.67 | 28.8 |
| CDI | 0.50 | 1.00 | 40.0 | 0.67 | 28.8 |
| tert-butyl (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylate | 2.00 | 1.00 | 10 | 0.17 | 7.2 |
| TFA | 13.06 | 49.95 | 76.5 | 1.28 | 55.08 |

| Stream 1 | | | | | | | |
|---|-------------|--------|---------|--|--|--|--|
| Reagent Amount (g or mL) MW mol Density Notes | | | | | | | |
| N-[(S)-1-Ethoxycarbonyl-3-phenylpropyl]-L-alanine (g) | 3.4918 | 279.34 | 0.01250 | | | | |
| HCI (mL) | 0.63 | 36.46 | 0.00250 | | 4 M in 1,4-dioxane | | |
| DCM (mL) | up to 25 mL | | | | SPS but not rigorous anhydrous technique | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | |

| Stream 2 | | | | | | | |
|---|--------|--------|--------|--|---------------------------------|--|--|
| Reagent Amount (g) MW mol Density Notes | | | | | | | |
| CDI (g) | 2.0269 | 162.15 | 0.0125 | | | | |
| DCM (mL) up to 25 mL SPS but not rigorous anhydrous technique | | | | | | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | |

| Stream 3 | | | | | | | |
|---|---------|-----|-------|------|------|--|--|
| Reagent Amount (g or mL) MW mol Density Notes | | | | | | | |
| TFA (mL) | 49.9698 | 114 | 0.653 | 1.49 | Neat | | |
| Total Volume | 50 | | | | _ | | |

| Stream 4 | | | | | | | | |
|---|--|--------|------|--|---------------------------------|--|--|--|
| Reagent Amount (g or mL) MW mol Density Notes | | | | | | | | |
| tert-butyl (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylate (g) | 4.2262 | 211.31 | 0.02 | | | | | |
| DCM (mL) | SPS but not rigorous anhydrous technique | | | | | | | |
| Total Volume | 10 | | | | up to 10 mL in volumetric flask | | | |

| Reactor 1 | | | | |
|-------------|--------|--|--|--|
| Volume 1 ml | | | | |
| Res Time | 13 min | | | |
| Temp. | rt | | | |

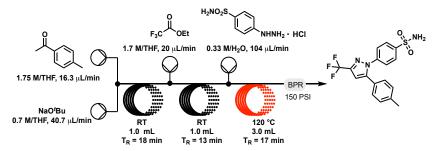
| Reac | Reactor 2 | | | | | |
|----------|-----------|--|--|--|--|--|
| Volume | 1 ml | | | | | |
| Res Time | 11 min | | | | | |
| Temp. | 45 °C | | | | | |

| Reactor 3 | | | | | |
|-------------|--------|--|--|--|--|
| Volume 3 ml | | | | | |
| Res Time | 18 min | | | | |
| Temp. | 45 °C | | | | |

| BPR | Proceuro | 50 peig |
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| Date: | |
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| Reference: | |
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| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL) |
|------------------------------|--------------|-------|---------------|-------------|------------------------------|
| 4'-Methylacetophenone | 1.75 | 1.00 | 16.3 | 0.27 | 11.736 |
| Sodium tert-butoxide | 0.70 | 1.00 | 40.7 | 0.68 | 29.304 |
| Ethyl trifluoroacetate | 1.70 | 1.19 | 20 | 0.33 | 14.4 |
| 4-sulfonamidophenylhydrazine | 0.33 | 1.20 | 104 | 1.73 | 74.88 |

Run Time (h) 12

| Stream 1 | | | | | | | | |
|---|--------|--------|---------|-------|---------------------------------|--|--|--|
| Reagent Amount (g or mL) MW mol Density Notes | | | | | | | | |
| 4'-Methylacetophenone (mL) | 5.8412 | 134.18 | 0.04375 | 1.005 | | | | |
| THF (mL) up to 25 mL 72.11 0.889 | | | | | | | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | | |

| Stream 2 | | | | | | | | |
|--------------------------|------------|-------|---------|---------|-------------------------------------|--|--|--|
| Reagent | Amount (g) | MW | mol | Density | Notes | | | |
| Sodium tert-butoxide (g) | 4.0362 | 96.10 | 0.04200 | | | | | |
| THF (mL) | 60 mL | 72.11 | | 0.889 | SPS, prepared in glovebox, filtered | | | |
| Total Volume | 60 | | | | | | | |

| Stream 3 | | | | | | | | | |
|----------------------------|------------------|--------|--------|---------|---------------------------------|--|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | | |
| Ethyl trifluoroacetate (g) | 6.0384 | 142.08 | 0.0425 | | | | | | |
| THF (mL) | up to 25 mL | 72.11 | | 0.889 | | | | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | | | |

| Stream 4 | | | | | | | | | |
|---------------------------------|------------------|--------|------|---------|----------------------------------|--|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | | |
| 4-sulfonamidophenylhydrazine (g | 7.3814 | 223.68 | 0.03 | | | | | | |
| Water (mL) | up to 100 mL | 18.02 | | 1 | | | | | |
| Total Volume | 100 | | | | up to 100 mL in volumetric flask | | | | |

Reactor 2

| Reactor 1 | | | | | |
|-----------|--------|--|--|--|--|
| Volume | 1 ml | | | | |
| Res Time | 18 min | | | | |
| Temp. | rt | | | | |

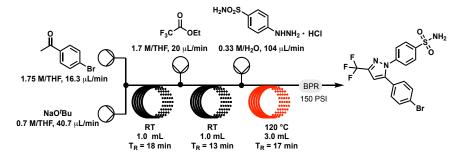
| volume | 1 1111 | | volume | 1 111 |
|----------|--------|---|----------|--------|
| Res Time | 18 min | | Res Time | 13 mir |
| Temp. | rt | | Temp. | rt |
| | | _ | | |

| Reactor 3 | | | | | | |
|-----------|--------|--|--|--|--|--|
| Volume | 3 ml | | | | | |
| Res Time | 17 min | | | | | |
| Temp. | 120 °C | | | | | |

| BPR | |
|----------|----------|
| Pressure | 150 psig |

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| Date: | |
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| Reference: | |
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| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL) |
|------------------------------|--------------|-------|---------------|-------------|------------------------------|
| 4'-Bromoacetophenone | 1.75 | 1.00 | 16.3 | 0.27 | 11.736 |
| Sodium tert-butoxide | 0.70 | 1.00 | 40.7 | 0.68 | 29.304 |
| Ethyl trifluoroacetate | 1.70 | 1.19 | 20 | 0.33 | 14.4 |
| 4-sulfonamidophenylhydrazine | 0.33 | 1.20 | 104 | 1.73 | 74.88 |

| Stream 1 | | | | | | | | | |
|--------------------------|---|--------|---------|-------|---------------------------------|--|--|--|--|
| Reagent | Reagent Amount (g or mL) MW mol Density Notes | | | | | | | | |
| 4'-Bromoacetophenone (g) | 8.7080 | 199.04 | 0.04375 | | | | | | |
| THF (mL) | up to 25 mL | 72.11 | | 0.889 | | | | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | | | |

| Stream 2 | | | | | | | | |
|--------------------------|------------|-------|---------|---------|-------------------------------------|--|--|--|
| Reagent | Amount (g) | MW | mol | Density | Notes | | | |
| Sodium tert-butoxide (g) | 4.0362 | 96.10 | 0.04200 | | | | | |
| THF (mL) | 60 mL | 72.11 | | 0.889 | SPS, prepared in glovebox, filtered | | | |
| Total Volume | 60 | | | | | | | |

| Stream 3 | | | | | | | | |
|----------------------------|------------------|--------|--------|---------|---------------------------------|--|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | | |
| Ethyl trifluoroacetate (g) | 6.0384 | 142.08 | 0.0425 | | | | | |
| THF (mL) | up to 25 mL | 72.11 | | 0.889 | | | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | | |

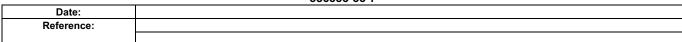
| Stream 4 | | | | | | | |
|---------------------------------|------------------|--------|------|---------|----------------------------------|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | |
| 4-sulfonamidophenylhydrazine (g | 7.3814 | 223.68 | 0.03 | | | | |
| Water (mL) | up to 100 mL | 18.02 | | 1 | | | |
| Total Volume | 100 | | | | up to 100 mL in volumetric flask | | |

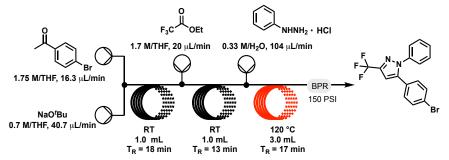
| Reactor 1 | | | | | |
|-----------|--------|--|--|--|--|
| Volume | 1 ml | | | | |
| Res Time | 18 min | | | | |
| Temp. | rt | | | | |

| Reactor 2 | | | | | |
|-----------|--------|--|--|--|--|
| Volume | 1 ml | | | | |
| Res Time | 13 min | | | | |
| Temp. | rt | | | | |

| Reactor 3 | | | | | |
|-----------|--------|--|--|--|--|
| Volume | 3 ml | | | | |
| Res Time | 17 min | | | | |
| Temp. | 120 °C | | | | |

| BPR | |
|----------|----------|
| Pressure | 150 psig |





| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL) |
|------------------------------|--------------|-------|---------------|-------------|------------------------------|
| 4'-Bromoacetophenone | 1.75 | 1.00 | 16.3 | 0.27 | 11.736 |
| Sodium tert-butoxide | 0.70 | 1.00 | 40.7 | 0.68 | 29.304 |
| Ethyl trifluoroacetate | 1.70 | 1.19 | 20 | 0.33 | 14.4 |
| 4-sulfonamidophenylhydrazine | 0.33 | 1.20 | 104 | 1.73 | 74.88 |

| Stream 1 | | | | | | | |
|--------------------------|------------------|--------|---------|---------|---------------------------------|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | |
| 4'-Bromoacetophenone (g) | 8.7080 | 199.04 | 0.04375 | | | | |
| THF (mL) | up to 25 mL | 72.11 | | 0.889 | | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | |

| Stream 2 | | | | | | | |
|--------------------------|------------|-------|---------|---------|-------------------------------------|--|--|
| Reagent | Amount (g) | MW | mol | Density | Notes | | |
| Sodium tert-butoxide (g) | 4.0362 | 96.10 | 0.04200 | | | | |
| THF (mL) | 60 mL | 72.11 | | 0.889 | SPS, prepared in glovebox, filtered | | |
| Total Volume | 60 | | | | | | |

| Stream 3 | | | | | | | |
|----------------------------|------------------|--------|--------|---------|---------------------------------|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | |
| Ethyl trifluoroacetate (g) | 6.0384 | 142.08 | 0.0425 | | | | |
| THF (mL) | up to 25 mL | 72.11 | | 0.889 | | | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask | | |

| Stream 4 | | | | | | | |
|-------------------------|------------------|--------|------|---------|----------------------------------|--|--|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes | | |
| Phenylhydrazine•HCI (g) | 4.7718 | 144.60 | 0.03 | | | | |
| Water (mL) | up to 100 mL | 18.02 | | 1 | | | |
| Total Volume | 100 | | | | up to 100 mL in volumetric flask | | |

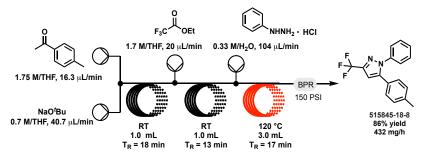
| Reactor 1 | | | | | |
|-----------|--------|--|--|--|--|
| Volume | 1 ml | | | | |
| Res Time | 18 min | | | | |
| Temp. | rt | | | | |

| Reactor 2 | | | | | |
|-----------|--------|--|--|--|--|
| Volume | 1 ml | | | | |
| Res Time | 13 min | | | | |
| Temp. | rt | | | | |

| Reactor 3 | | | |
|-----------|--------|--|--|
| Volume | 3 ml | | |
| Res Time | 17 min | | |
| Temp. | 120 °C | | |

| BPR | |
|----------|----------|
| Pressure | 150 psig |

| Date: | |
|------------|--|
| Reference: | |
| | |



| Stream | Conc (mol/L) | Equiv | Flow (uL/min) | Flow (uL/s) | Volume Required For Run (mL) |
|------------------------|--------------|-------|---------------|-------------|------------------------------|
| 4'-Methylacetophenone | 1.75 | 1.00 | 16.3 | 0.27 | 11.736 |
| Sodium tert-butoxide | 0.70 | 1.00 | 40.7 | 0.68 | 29.304 |
| Ethyl trifluoroacetate | 1.70 | 1.19 | 20 | 0.33 | 14.4 |
| Phenylhydrazine•HCl | 0.33 | 1.20 | 104 | 1.73 | 74.88 |

| Stream 1 | | | | | |
|----------------------------|------------------|--------|---------|---------|---------------------------------|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes |
| 4'-Methylacetophenone (mL) | 5.8412 | 134.18 | 0.04375 | 1.005 | |
| THF (mL) | up to 25 mL | 72.11 | | 0.889 | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask |

| Stream 2 | | | | | | |
|--------------------------|------------|-------|---------|---------|-------------------------------------|--|
| Reagent | Amount (g) | MW | mol | Density | Notes | |
| Sodium tert-butoxide (g) | 4.0362 | 96.10 | 0.04200 | | | |
| THF (mL) | 60 mL | 72.11 | | 0.889 | SPS, prepared in glovebox, filtered | |
| Total Volume | 60 | | | | | |

| Stream 3 | | | | | |
|----------------------------|------------------|--------|--------|---------|---------------------------------|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes |
| Ethyl trifluoroacetate (g) | 6.0384 | 142.08 | 0.0425 | | |
| THF (mL) | up to 25 mL | 72.11 | | 0.889 | |
| Total Volume | 25 | | | | up to 25 mL in volumetric flask |

| Stream 4 | | | | | |
|-------------------------|------------------|--------|------|---------|----------------------------------|
| Reagent | Amount (g or mL) | MW | mol | Density | Notes |
| Phenylhydrazine•HCI (g) | 4.7718 | 144.60 | 0.03 | | |
| Water (mL) | up to 100 mL | 18.02 | | 1 | |
| Total Volume | 100 | | | | up to 100 mL in volumetric flask |

| Reactor 1 | | | |
|-----------|--------|--|--|
| Volume | 1 ml | | |
| Res Time | 18 min | | |
| Temp. | rt | | |

| | Reactor 2 | | |
|----|-----------|--------|--|
| ٧ | olume | 1 ml | |
| Re | es Time | 13 min | |
| - | Гетр. | rt | |

| Reactor 3 | | | | |
|-------------|--------|--|--|--|
| Volume 3 ml | | | | |
| Res Time | 17 min | | | |
| Temp. | 120 °C | | | |

| BPR | |
|----------|----------|
| Pressure | 150 psig |