Tools for Innovation in Chemistry
from the
ACS Green Chemistry Institute Pharmaceutical Roundtable

Paul Richardson, Ph.D.
Director of Analytical and Synthetic Technologies, Pfizer
Co-Chair of the ACS GCI Pharmaceutical Roundtable
About Us

Natalie O’Neil, Ph.D.
Program Manager
Higher Education
Beyond Benign
@natjoneil

- Massachusetts-based 501-c3 non-profit
- Dedicated to green chemistry education
  - K-12 & Higher Ed.
- Develop curriculum resources centered around the principles and practices of green chemistry
- Green Chemistry Commitment

ACS Green Chemistry Institute: Washington, DC, 501-c3 non-profit
  - Advancing Science
  - Advocating for Education
  - Accelerating Industry

ACS GCI Pharmaceutical Roundtable:
  - Catalyzes the integration of green chemistry and engineering in the pharmaceutical industry.
Welcome to the Green Chemistry Commitment
Green Chemistry Education Webinar Series

Submit questions at any time during the webinar in the Control/Chat box on the Control Panel

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Manager of Scientific Alliances
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Business Engagement
ACS Green Chemistry Institute

Recording and supporting documents will be available:
https://www.beyondbenign.org/he-webinars/
Join the conversation!

@beyondbenign
#greenchemistry
#GCCwebinars

https://www.facebook.com/beyondbenign/
What is the GCC?

The **Green Chemistry Commitment** (GCC) is a consortium program that unites the green chemistry community around shared goals and a common vision to:

- expand the community of **green chemists**
- **grow** departmental resources
- share **best practices** in green chemistry education
- affect systemic and lasting **change** in chemistry education

[https://www.beyondbenign.org/he-green-chemistry-commitment/](https://www.beyondbenign.org/he-green-chemistry-commitment/)
Green Chemistry Swag
Tools for Innovation in Chemistry from the ACS Green Chemistry Institute Pharmaceutical Roundtable

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ACS GCIPR “Tools for Innovation in Chemistry”

20th November 2019
Why Green Chemistry?

• Provide the **best efficiency** for a **chemical process**.

• **New frontier of exploration**

• **Great opportunity for innovation**

• **The achievement of superior synthetic efficiency** will **ultimately deliver a competitive advantage**.

*US EPA & OPRD., 2006, 10, 315.*
Principles encompass both the process and the product

“...the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products.”

Where we stand today!!

“Green chemistry can deliver for people, planet and profit. Those who embrace it will reap the benefits in future. Those who fail to evolve may cease to be relevant”.

Drug companies must adopt green chemistry

Nature, 2016, 534, 27
**ACS GCI Pharma Roundtable**

**Strategic Priorities**

- Inform and Influence the Research Agenda
- Define and Deliver Tools for Innovation
- Promote Education and Training
- Enable Global Collaboration

**Mission of the ACS**

“To catalyze the implementation of green chemistry and engineering in the pharmaceutical industry globally”

**GCIPR created in 2005 with 3 members, now > 30 members**

- **Pharma and generics produce > 100 million kg of API per year**
- **Estimated 150 kg waste per kg API (> 99.3%). > 15 billion kg of waste/year**
- **Estimated cost of waste disposal ca. $30 billion**

American Chemical Society
Development/Evolution of Tools
Accessing the Tools!!

About the Roundtable

The ACS GCI Pharmaceutical Roundtable is the leading organization dedicated to catalyzing the integration of green chemistry and engineering in the pharmaceutical industry. Established in 2005 by the American Chemical Society’s Green Chemistry Institute, the Roundtable’s activities are driven by the shared belief that green chemistry and engineering is imperative for business and environmental sustainability. By exploring this site, you can learn how to bring more sustainable approaches into your lab and see if membership in the Roundtable could benefit your company.

Tools for Innovation in Chemistry
- Solvent Selection
- Reagent Guides
- PMI-LCA & PMI Prediction
- MedChem Tips & Tricks

Advancing Research
- Key Research Areas
- Research Grants
- Journal Publications
- Impact

Educating Leaders
- Chem21
- Training Workshops
- Presentations
- Awards

Global Collaboration
- India
- China
- PSCI & IQ
- Benchmarking

Become a Member
- Membership FAQs
- Mission & Strategic Priorities
- Request more information

Current Members
- AbbVie
- Amgen
- Astrazeneca
- Bayer
- Biogen
- Boehringer Ingelheim
- Bristol-Myers Squibb
- Eli Lilly and Company
- F. Hoffmann-La Roche Ltd.
- GlaxoSmithKline
- Ipsen
- Johnson & Johnson
- Merck & Co., Inc.
- Neurocrine
- Novartis
- Novo Nordisk
- Pfizer, Inc.
- Sanofi

www.acsgcipr.org
Accessing the Tools!!

https://www.acsgcipr.org/tools-for-innovation-in-chemistry/

Tools for Innovation in Chemistry

The ACS GCI Pharmaceutical Roundtable is dedicated to the implementation of green chemistry and engineering and member companies have collaboratively developed a variety of high-quality tools and metrics to help scientists and engineers make better decisions about chemical selection and route and process design. All tools have been thoroughly vetted by Roundtable companies prior to their public release.

The impetus for tool development can be traced to the late 1990’s when early adopters in the Pharmaceutical Industry began asking how green chemistry and engineering could be more broadly implemented in the industry. On the basis of early life cycle inventory/assessment of an active pharmaceutical ingredient, it became clear that chemical selection (i.e., solvents, reagents, etc.) played an enormous role in determining synthetic process cost and environmental, safety and health impacts across the life cycle. This insight led to the development of scientifically valid and industrially relevant bench level tools that could be used by scientists and engineers on a daily basis.

American Chemical Society
Tools We Will Discuss Today!!

Metrics (PMI)  Solvents  Reagents
Why Metrics ??

“You can’t manage what you don’t measure.”

• We measure what we care about ↔ we care about what we measure

• Standardize measurement of chemical process greenness when possible

• Proper choice of metrics is critical for ‘behavior of system

• Green metrics correlate to process economics !!!
Initial Metrics…….

**Yield**
- Pharma Average ~ 86%/step.
- Does not capture all materials used.

**Atom Economy**
- Mass Product/Mass Reagents * 100.

**E-Factor**
- Total kg waste/kg product.
  - *Green Chem.*, 2017, 19, 18

<table>
<thead>
<tr>
<th>Industry segment</th>
<th>Tonnes per annum</th>
<th>E factor (kg waste per kg product)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oil refining</td>
<td>$10^6$ – $10^8$</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Bulk chemicals</td>
<td>$10^4$ – $10^6$</td>
<td>&lt;1–5</td>
</tr>
<tr>
<td>Fine chemicals</td>
<td>$10^2$ – $10^4$</td>
<td>5–50</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td>$10$ – 10$^4$</td>
<td>25 – &gt;100</td>
</tr>
</tbody>
</table>
“Metrics……But which one do you use?”

<table>
<thead>
<tr>
<th>Metric</th>
<th>Waste</th>
<th>Yield</th>
<th>Stoich.</th>
<th>Solvents</th>
<th>Water</th>
<th>Optimal</th>
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<tbody>
<tr>
<td>Chemical Yield</td>
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<td></td>
<td></td>
<td></td>
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<td>100%</td>
</tr>
<tr>
<td>Atom Economy</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>E-Factor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
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<tr>
<td>Mass Intensity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Process Mass Intensity (PMI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Process Mass Efficiency (PME)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>Mass Productivity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>Reaction Mass Efficiency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>Effective Mass Yield</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>Reaction Mass Intensity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Carbon Efficiency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>Solvent Intensity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Wastewater Intensity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
</tbody>
</table>
Solvent Impact in Pharma Manufacturing

- **Solvents & water** contribute significant waste to process mass intensity
  - **PMI** = kg inputs / kg product
  - If PMI = 100, 1 kg of API needs 100 kg of input materials
- **Solvents and water** represent > 85% of total input and waste
- **Clear need** for process intensification to reduce solvent waste
- **Opportunity to minimize waste hazards** (through better choices)

Source: 2008 ACS GCIPR benchmarking exercise of 10 member companies
**Process Mass Intensity (PMI) Metric**

Process mass intensity = \( \frac{\text{quantity of raw materials input (kg)}}{\text{quantity of bulk API out (kg)}} \)

Where:

*Process* is all steps of a synthetic path from *commonly available materials* to the final bulk active pharmaceutical ingredient (“API”).

*Raw Materials* are all materials including water that are used directly in the process of synthesizing, isolating, and purifying the API final form.

*Bulk API out* is the final form of the active ingredient that was produced in the synthesis, dried to the expected specification.
Why Measure PMI?

• Drive change towards more sustainable manufacturing processes
  – Track environmental manufacturing footprint.
  – Measurement of process efficiency.

• Quantify improvements throughout process development life-cycle

• To be more transparent; basis for objective comparison
  – Increasing expectations from internal and external audiences to describe progress, demonstrate improvement.

• Benchmark
  – Allows a simple comparison to the on-going green efforts throughout the industry in the pursuit of mass efficient pharmaceutical processes.

• Insight in sustainability of overall manufacturing process, from bulk chemicals to API, is required
**PMI Calculator Tool**

<table>
<thead>
<tr>
<th>Step Name/Number</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>Units</td>
</tr>
<tr>
<td>Physical Batch Size</td>
<td></td>
</tr>
<tr>
<td>Assay Purity</td>
<td></td>
</tr>
<tr>
<td>Assay Batch Size</td>
<td></td>
</tr>
<tr>
<td>Yield</td>
<td></td>
</tr>
<tr>
<td>Assay Kg Product</td>
<td></td>
</tr>
<tr>
<td>Product Purity</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Raw Materials</th>
<th>Physical Charge (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substrates</td>
<td></td>
</tr>
<tr>
<td>Reagents</td>
<td></td>
</tr>
<tr>
<td>Solvents</td>
<td></td>
</tr>
<tr>
<td>Aqueous</td>
<td></td>
</tr>
</tbody>
</table>

**PMI Excel Spreadsheet**

- Spreadsheet with embedded Calculations.
- Only need to fill in amounts of reagents, solvents, and aqueous.
- Spreadsheet calculates step and overall PMI for linear sequences.
- Calculates overall PMI as well as separate PMI for solvents, water, and reagents.
PMI by Development Phase – Median Values

Sildenafil Citrate

Initial Medicinal Chemistry 17675
Optimized Med Chem (through phase 3) 116
Commercial Route 60

Green Chem., 2004, 6, 43; Green Chem., 2015, 17, 3390
Convergent PMI Calculator

Goal to maintain simplicity and the calculations behind the original PMI calculation tool whilst allowing convergent syntheses with a range of complexities to be accommodated.
Convergent PMI Tool

- Up to 11 step linear sequence.
- Up to 3 branches for convergent synthesis (11 steps per branch).
- Multiple branch points possible in a single step.
- Up to 44 step linear sequence if treating additional steps as branches.
PMI Prediction Tool - App

• PMI and various reported metrics provide assessment on Greenness after synthesis.

• Goal: To provide a quantitative method to predict potential efficiency.

• Increased molecular complexity leads to increased synthetic complexity and consequently the potential number of approaches to access a target molecule (how to evaluate?).

• Predicts a range of probable process efficiencies of proposed synthetic routes at various phases of drug development.

• Uses historical PMI (and yield) data from pharma companies and predictive analytics (Monte Carlo simulations) to estimate the probable PMI ranges.

• Assess and compare potential route changes!!
15 examples

**PMI Predictor - Benchmarking**

Accuracy of the prediction shown to be dependent on development status of the compound.

<table>
<thead>
<tr>
<th>Entry</th>
<th>API Examples</th>
<th>Actual cPMI</th>
<th>Predicted cPMI, [95% CI]&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Company/Drug/Stage&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.18</td>
<td><img src="image1.png" alt="Image" /></td>
<td>905</td>
<td>930, [683,1222]</td>
<td>Astella 5HT Candidate Early</td>
</tr>
<tr>
<td>3.19</td>
<td><img src="image2.png" alt="Image" /></td>
<td>656</td>
<td>632, [507,782]</td>
<td>Pfizer UK 432097 Mid-Late</td>
</tr>
<tr>
<td>4.20</td>
<td><img src="image3.png" alt="Image" /></td>
<td>198</td>
<td>240, [186,298]</td>
<td>AstraZeneca AZD7545 Mid-Late</td>
</tr>
</tbody>
</table>
PMI Tracks With Environmental Impacts

Global Warming Potential

Aqueous Mass Intensity

- Global Warming Potential
  \[ y = 0.1835x + 31.237 \]
  \[ R^2 = 0.878 \]

- Aqueous Mass Intensity
  \[ y = 1.5241x - 36.568 \]
  \[ R^2 = 0.9458 \]
Tangible Value of Greener Processes

Cost and PMI – Green Drivers

Late stage development compounds and marketed products
Importance of Solvent Selection

- Solvents are critical parameters in chemical processing.
  - Promoting chemistry
  - Control of reaction temperature
  - Dissolving reactants
  - Modifying solute properties
    - pKa
    - Redox potential
    - H-Bonding
  - Removing impurities/by-products (partitioning)
  - Isolating products (crystallization)

Judicious solvent selection for a chemical reaction can often be the difference between a straightforward outcome and a host of problems.
Solvent Guide Considerations

- **Worker Safety** – including carcinogenicity, mutagenicity, reprotoxicity, skin absorption/sensitization and toxicity.

- **Process Safety** – including flammability, potential for high emissions through high vapour pressure, static charge, potential for peroxide formation and odour issues.

- **Environmental and Regulatory considerations** – including ecotoxicity and ground water contamination, potential EHS regulatory restrictions, ozone depletion potential, photoreactive potential. Compliance with regulations and company guidelines.
## Examples of Solvent Selection Guides

### Use of Internal Tools – Med. Chem. Solvent Selection Guide

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Usable</th>
<th>Undesirable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>Cyclohexane</td>
<td>Pentane</td>
</tr>
<tr>
<td>Acetone</td>
<td>Heptane</td>
<td>Hexane(s)</td>
</tr>
<tr>
<td>Ethanol</td>
<td>Toluene</td>
<td>Di-isopropyl ether</td>
</tr>
<tr>
<td>2-Propanol</td>
<td>Methylcyclohexane</td>
<td>Diethyl ether</td>
</tr>
<tr>
<td>1-Propanol</td>
<td>TBME</td>
<td>Dichloromethane</td>
</tr>
<tr>
<td>Ethyl Acetate</td>
<td>Isoctane</td>
<td>Dichloroethane</td>
</tr>
<tr>
<td>Isopropyl acetate</td>
<td>Acetonitrile</td>
<td>Chloroform</td>
</tr>
<tr>
<td>Methanol</td>
<td>2-MeTHF*</td>
<td>NMP</td>
</tr>
<tr>
<td>MEK</td>
<td>THF</td>
<td>DMF</td>
</tr>
<tr>
<td>1-Butanol</td>
<td>Xylenes</td>
<td>Pyridine</td>
</tr>
<tr>
<td>t-Butanol</td>
<td>DMSO</td>
<td>DMAc</td>
</tr>
<tr>
<td>Acetic Acid</td>
<td>Ethylene Glycol</td>
<td>Dioxane</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dimethoxyethane</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Benzene</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carbon tetrachloride</td>
</tr>
</tbody>
</table>

### GSK Solvent Sustainability Guide

*The scoring assessment for this solvent includes 4 or more data gaps, therefore there is a lower level of confidence in the solvent's placement on this guide.*

*The composite colour represents an overall categorization of the holistic sustainability of a solvent, taking all category scores into consideration.*

AZ, GSK, Pfizer, ACS GCIPR, Sanofi
Green Chem., 2014, 16, 4546

American Chemical Society
Select from 77 solvents, ranking based on:

- Health, Safety, Environment criteria
- physical data and GHS (Global Harmonized System)
- Recommended, Problematic or Hazardous rating

**Table 1: CHEM21 solvent guide: ethers, hydrocarbons, halogenated**

<table>
<thead>
<tr>
<th>Family</th>
<th>Solvent</th>
<th>CAS</th>
<th>EP (°C)</th>
<th>FP (°C)</th>
<th>Worst H3xx*</th>
<th>HAxoviel</th>
<th>Safety score</th>
<th>Health score</th>
<th>Env. score</th>
<th>Ranking by default</th>
<th>Ranking after discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>Water</td>
<td>100</td>
<td>na</td>
<td>none</td>
<td>none</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>Recommended</td>
<td>Recommended</td>
</tr>
<tr>
<td></td>
<td>MeOH</td>
<td>67- 56-1</td>
<td>65</td>
<td>11</td>
<td>H301</td>
<td>4</td>
<td>7</td>
<td>5</td>
<td>Problematic</td>
<td>Recommended</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETOH</td>
<td>64- 17-5</td>
<td>78</td>
<td>13</td>
<td>H319</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>Recommended</td>
<td>Recommended</td>
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<td>n-PrOH</td>
<td>71- 23-8</td>
<td>97</td>
<td>15</td>
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<td>i-PrOH</td>
<td>87- 03-0</td>
<td>82</td>
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<td>3</td>
<td>Recommended</td>
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<td></td>
<td>n-BuOH</td>
<td>71- 36-3</td>
<td>118</td>
<td>29</td>
<td>H318</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>Recommended</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>/-Butanol</td>
<td>78- 83-1</td>
<td>107</td>
<td>28</td>
<td>H318</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>Recommended</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>t-BuOH</td>
<td>75- 65-0</td>
<td>82</td>
<td>11</td>
<td>H319</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>Recommended</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>/-Amyl alcohol</td>
<td>123- 51-3</td>
<td>131</td>
<td>43</td>
<td>H315</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>Recommended</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Solvent Selection Guides

• Guides offer assistance in identifying solvents
• Most support post-selection comparison between solvent options
• **Objective selection decisions for comparison can sometimes be compromised in such situations:**
  – What is in the lab solvent cupboard?
  – What did I use last time, or what does the literature say?
  – What other similar solvents are commercially available?
• **The choice of solvent is often restricted to simple consideration of the chemistry**
  – Polarity, incompatible functional groups, temperature window

“Solvent Selection Tool reverses this philosophy, and provides a proactive approach to solvent selection”
Solvent Selection Tool for Pharma

- Selection variables based on:
  - molecular & physical properties
  - EH&S criteria
  - ICH guidelines
  - Over 100 properties !!!
- 272 solvents in the dataset
- Properties refined through PCA (5 PCs)
- Interactive, adjustable visualization

OPRD, 2016, 20, 760
Optimization/Screening of Solvents

• Applying an appropriate set of filters provides a shortlist of potential solvents for initial evaluation in a specific transformation.

• With an initial hit, it is reasonable to expect that proximal solvents will display some degree of similar behavior.
Development of a Reagent Guide

Three Ideal Characteristics……

1) To provide a balanced assessment of chemical methods.
   – Ability to work in good yield in a wide variety of “drug-like” molecules.
   – Ability to be utilized for “scale-up” purposes.
   – To be as “green as possible”. (worker safety, atom economy etc).

2) To provide easy access to the chemical literature.

3) To raise awareness of newer emerging “greener” methodologies.

Green Chem., 2008, 10, 31
Reagent Guides

**Boc deprotection**

**Amide reduction**

**Bromination**

**Reductive amination**

**Metals removal**

**Buchwald-Hartwig**

**Iodination**

**Chlorination**

**Chiral Hydrogenation**

**Suzuki-Miyaura**

**In Progress**

**Biocatalysis**

**Fluorination**

**Amide bond formation**

**Borylation**

**Thioether Formation**

**Achiral Hydrogenation**

**Cyclopropanation**

Oxidation to aldehyde and ketones

Nitro reduction

N-Alkylation

O-dealkylation

Ester Deprotection

Epoxidation
Alcohol Oxidation - Visual Depiction of a Reagent’s Utility

Details include i) mechanism, ii) comments, iii) references, iv) scale-up examples, and v) a “Green” review.
Synthesis of Maraviroc

First generation synthesis:

\[
\begin{align*}
\text{F} & \quad \text{F} \\
\text{O} & \quad \text{NH} \\
\text{C} & \quad \text{H} \\
\text{C} & \quad \text{H} \\
\text{O} & \quad \text{OH}
\end{align*}
\]

SO\textsubscript{3}•Py (3 equiv)
Hunig’s (3 equiv)
DMSO/CH\textsubscript{2}Cl\textsubscript{2}
0–10 °C
(95% crude yield)

\[
\begin{align*}
\text{F} & \quad \text{F} \\
\text{O} & \quad \text{NH} \\
\text{C} & \quad \text{C} \\
\text{C} & \quad \text{H}
\end{align*}
\]

\[
\begin{align*}
\text{F} & \quad \text{F} \\
\text{O} & \quad \text{NH}
\end{align*}
\]

Maraviroc (Selzentry\textsuperscript{TM})
HIV treatment

Second generation synthesis:

\[
\begin{align*}
\text{F} & \quad \text{F} \\
\text{O} & \quad \text{NH} \\
\text{C} & \quad \text{H} \\
\text{C} & \quad \text{H}
\end{align*}
\]

TEMPO (0.01 equiv)
NaOCl, NaBr
CH\textsubscript{2}Cl\textsubscript{2}/H\textsubscript{2}O
10 °C
88% yield

\[
\begin{align*}
\text{F} & \quad \text{F} \\
\text{O} & \quad \text{NH}
\end{align*}
\]

+ H\textsubscript{2}O + NaCl

TEMPO radical

CH\textsubscript{2}Cl\textsubscript{2} can be Replaced with EtOAc

Green Review

i) Atom Efficiency
ii) Safety
iii) Toxicity/environmental impact
iv) Cost, availability and sustainable feedstocks
v) Sustainable implications

(Pfizer)
Catalyzing the integration of green chemistry and engineering in the pharmaceutical industry since 2005.

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Questions

Submit questions at any time during the webinar in the Control/Chat box on the Control Panel.

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