

Sustainable Oxidants for the Photooxidation of Organic Molecules in Flow

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The contents of this thesis are previously published. The original, peer-reviewed works are listed below.

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Plutschack, M. B.; Correia, C. A.; Seeberger, P. H.; Gilmore, K. Organic Photoredox Chemistry in Flow In *Organometallic Flow Chemistry*; Noël, T., Ed.; Springer International Publishing: Cham, 2016; pp 43-76. (Chapter 3.)

Plutschack, M. B.; Seeberger, P. H.; Gilmore, K. Visible-Light-Mediated Achmatowicz Rearrangement. *Org. Lett.* **2017**, *19*, 30-33. (Chapter 4.)

Table of Contents

Summary	v
Zusammenfassung	vii
Chapter 1.	1
The Hitchhiker's Guide to Flow Chemistry	1
1. Introduction	1
2. Why Run a Reaction in Flow?	2
2.1. Multiphasic Systems	2
2.2. Mixing	6
2.3. Temperature	8
2.4. Photo- and Electrochemistry	11
2.5. Batch Versus Flow Analysis	13
2.6. Automation	16
3. Anatomy of a Flow Reaction	17
3.1. Connecting Flow Zones	18
3.2. Fluid and Reagent Delivery	19
3.3. Mixer	21
3.4. Reactor Unit	24
3.5. Quenching Unit	29
3.6. Pressure Regulating Unit	30
3.7. Collection Unit	30
3.8. Optional Zones	31
4. Considerations for Flow Experiments	32
4.1. Key Parameters	32
4.2. Common Problems	34
5. Multiphasic Reactions	35
5.1. Gas–Liquid Reactions	36
5.2. Solid–Liquid Reactions	53
5.3. Gas–Liquid–Solid Reactions	72
5.4. Liquid–Liquid Reactions	75
5.5. Liquid–Liquid–Solid Reactions	79
6. Mixing	80
6.1. Outpacing Intermediate Decomposition	81
6.2. Outpacing Intramolecular Reactions.	84
6.3. Nucleophilic Reactions with Multiple Electrophiles	86

6.4. Selective Carbonyl Syntheses	90
6.5. Reductions with DIBAL-H	93
6.6. Electrophilic Trapping for Subsequent Cross-Coupling Reactions	95
6.7. Miscellaneous Fast Reactions	98
7. Temperature	103
7.1. Heated Reactions below 100 °C	104
7.2. Heated Reactions between 100 and 200 °C	106
7.3. Reactions above 200 °C	115
8. Traceless Reagents in Flow – Photo- and Electrochemistry	122
8.1. Photochemistry	122
8.2. Electrochemistry	137
9. Feedback Optimization	144
10. Conclusions	148
Notes	148
Diagram Legened	149
References	149
Chapter 2.	167
Oxidation of Secondary Amines Using Singlet Oxygen	167
2.1. Factors Influencing the Regioselectivity of the Oxidation of Asymmetric Secondary Amines with Singlet Oxygen	167
References	176
2.2. Experimental	179
General information.	179
General procedure for the preparation of secondary amines.	179
Spectroscopic data for secondary amines with decoupled ¹³ C NMR data for the relevant C-H bonds	179
General procedure for the photooxidation of amines.	191
Selective Imine Synthesis	196
NMR Spectra of previously unreported secondary amines	198
Chapter 3.	223
Organic Photoredox Chemistry in Flow	223
Photoredox Catalysis	223
Photochemistry in Flow	225
Oxidative Quenching	227
Reductive Quenching	234
Conclusions	246
References	246

Chapter 4.	249
Oxidation of Furfuryl Alcohols Using Sodium Persulfate.	249
3.1. Visible-Light-Mediated Achmatowicz Rearrangement	249
References	253
3.2. Experimental	255
General:	255
Hair Bleach Titration	255
Batch Photoreactor Setup	256
Sunlight Photoreactor Setup	257
Control Studies	257
Reaction Robustness and Sustainability	258
Stern-Volmer Experiments	260
Synthesis and Characterization of Products	262
Formal synthesis of (\pm)-Monanchorin: Synthesis of tert-butyl (5-oxo-6-pentyl-5,6-dihydro-2 <i>H</i> -pyran-2-yl) carbonate	279
NMR Spectra	281
Postface	313
Discussion of individual works.	313
The Hitchhiker's Guide to Flow Chemistry – Why Flow Popularity Elicited a New Review Structure	313
Specific Contributions	314
Factors Influencing the Regioselectivity of the Oxidation of Asymmetric Secondary Amines with Singlet Oxygen – Background of the Mechanistic Discovery	314
Specific Contributions	316
Organic Photoredox Chemistry in Flow – Why Flow Chemists Should Use Reaction Productivities for Batch versus Flow Comparisons	317
Specific Contributions	317
Visible-Light-Mediated Achmatowicz Rearrangement – From a Proposed Process to a New Reaction	318
Specific Contributions	319
References	319
List of Publications	321
Research Presentations	321
Curriculum Vitae	323

Summary

Flow chemistry uses channels or tubing to conduct a reaction in a continuous stream rather than in a flask. This method provides chemists with unique control over reaction parameters, enhancing reactivity or in some cases enabling new reactions. Flow chemistry has received a remarkable amount of attention in the past decade with many reports on what can be done in flow. While this approach to publishing papers has led to the development of elegantly conceived processes, it has neglected to properly differentiate the examples which have benefits over conventional batch methods. This poor distinction between what **can** be done and what **should** be done in flow has shrouded useful contributions to synthetic organic chemistry and created flow chemistry skeptics. For this reason, flow techniques are still not integrated into synthetic laboratories and probably will not be for years to come. In order to make flow equipment part of the every-day-toolbox, reactions need to be classified and applied on the basis of the benefits that flow offers. In this thesis, how flow enhances these classes of reactions is explained and various examples of these different methods are highlighted.

Biphasic reactions and photochemistry are two classes of reactions that benefit flow fluidic conditions. The small dimensions of microreactors increase mass transfer and accelerate the rate of biphasic reactions involving gases. Pressurizing the system is also more convenient in flow and is done by simply incorporating a backpressure regulator into the setup. Photochemistry benefits greatly from fluidic conditions because of the attenuation of light. According to the Beer-Lambert-Bouguer law, common reaction mixture concentrations can result in less than 0.5 mm of light penetration. For a batch reaction, this is detrimental to the rate of the reaction since the reactor dimensions are usually on the order of centimeters. On the other hand, the inner diameter of common tubing for photoflow reactors is usually between 0.25-0.8 mm, resulting in the irradiation of a much higher percentage of the reaction mixture. Singlet oxygen generation in flow is one example which exploits both of the enhancements of biphasic reactions and photochemistry and is applied here for studying the oxidation of secondary amines.

Aerobic amine oxidation is an attractive process for the α -functionalization of amines because of its sustainability. However, there were still several mechanistic uncertainties; for instance, the factors governing the regioselectivity of the oxidation of asymmetric secondary amines. In the present work, flow conditions were used to generate singlet oxygen and perform mechanistic studies on the factors influencing the regioselectivity for the oxidation of asymmetric secondary amines. A predictive model was constructed with the use of a substrate scope of 20 secondary amines. The strength of the α -CH bonds and the functional groups' steric bulk influenced the selectivity the most. This model estimated oxidation selectivity on the basis of the relative bond dissociation energy which was determined by natural bond order analysis or NMR spectroscopy.

Similar to aerobic oxidations, photoredox chemistry is another example of the recent movement toward greener, more sustainable chemistry. This field of photocatalysis has led to the emergence of a wide berth of new visible-light-mediated transformations and flow chemistry has been utilized to enhance the productivity of these photoredox processes. The increased productivity is particularly interesting for the development of a wide variety of practical,

preparative methods for synthesis. Organometallic polypyridyl structures offer versatility in terms of reactivity providing access to a multitude of oxidative and reductive transformations.

The Achmatowicz rearrangement involves the oxidative ring expansion of furfuryl alcohols into dihydropyranones. It is utilized in natural product synthesis since it is a versatile method for constructing highly functionalized pyran moieties. Here, photoredox-catalysis was used to perform the Achmatowicz reaction with $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$ and sodium persulfate. Sodium persulfate is an attractive oxidant because it is cheap, shelf-stable, and produces water soluble byproducts which facilitate column-free synthesis. This was exemplified with the direct Boc-protection of the resulting Achmatowicz product without column purification of the intermediate. Also, the reaction was very robust and permitted the use of various aqueous solutions and light sources including sunlight. Investigations into other oxidation reactions with this catalyst/oxidant combination are currently underway.

Zusammenfassung

Im Gegensatz zu konventionellen Batchverfahren werden in der Durchfluschemie Reaktionsmischungen durch dünne Schläuche oder Kapillaren gepumpt. Durch die Charakteristika dieser Technologie ergibt sich eine verbesserte Kontrolle der Reaktionsbedingungen was zu einer Beschleunigung von chemischen Prozessen oder vollkommen neuen Reaktionen führen kann. Daraus resultierte eine Fülle an Publikationen in denen gezeigt wurde, dass der Großteil aller bekannten Reaktionen in Durchflussreaktoren durchgeführt werden kann. Obwohl die meisten dieser Arbeiten interessante, kontinuierliche Prozesse beschreiben, wurde nur selten kritisch darüber diskutiert, ob diese Technologie eine signifikante Verbesserung zu konventionellen Batchverfahren für die jeweilige chemische Reaktion darstellt. Die daraus entstandene Skepsis hatte zur Folge, dass durchfluschemische Verfahren nach wie vor selten in Syntheselaboren angewandt werden. Um dies langfristig zu ändern müssen Reaktionen, welche von der Durchfluschemie profitieren, identifiziert und klassifiziert werden. In dieser Dissertation wird anhand von theoretischen Aspekten und Literaturbeispielen erklärt warum gewisse Reaktionsklassen in Durchflussreaktoren durchgeführt werden sollten.

Zweiphasigen Systeme und photochemische Prozesse sind zwei Reaktionsklassen die von durchfluschemischen Verfahren profitieren. Aufgrund der kleinen Dimensionen in Durchflussreaktoren wird ein äußerst effizienter Stofftransport in zweiphasigen (gas-flüssig) Systemen erzielt. Zusätzlich kann der Systemdruck mittels Gegendruckregulatoren relativ einfach variiert werden, wodurch solche Verfahren zusätzlich beschleunigt werden können. Photochemische Prozesse in Batch sind durch die Abschwächung der Lichtintensität beim Durchgang durch das Reaktionsmedium meist ineffizient (Beer-Lambert-Boguer Gesetz), da die Eindringtiefe oftmals bei nur 0.5 mm liegt. Da die Kapillaren, die in der Durchfluschemie Anwendung finden meist lediglich einen Durchmesser von 0.25-0.8 mm haben, erlauben solche Reaktoren eine extreme Verbesserung der Bestrahlung der Reaktionsmischung was eine erhöhte Reaktionsgeschwindigkeit zur Folge hat. Ein klassisches Beispiel, das diese Vorteile der Durchfluschemie nutzt, ist die Herstellung von Singulett-Sauerstoff, welcher im Zuge dieser Arbeit für die Oxidation von sekundären Aminen verwendet wurde.

Die aerobe Oxidation von Aminen ist eine elegante und nachhaltige Möglichkeit diese in α -Position zu funktionalisieren. Der Mechanismus dieser Reaktion ist jedoch noch nicht vollständig aufgeklärt und speziell die Faktoren, welche die Regioselektivität bei der Oxidation von asymmetrischen sekundären Aminen beeinflussen ist unklar. Um diese zu erforschen wurden eben diese Parameter mittels durchfluschemischer Verfahren für die aerobe Oxidation mittels Singulett Sauerstoff untersucht, um Rückschlüsse auf den Reaktionsmechanismus zu erhalten. Es konnte gezeigt werden, dass die Stärke der α -CH Bindung, sowie der sterische Anspruch der funktionellen Gruppen den größten Einfluss haben. Basierend auf den experimentellen Ergebnissen der Oxidation von 20 unterschiedlichen Aminen wurde ein Modell erstellt, welches anhand der Bindungsenergie Voraussagen über die Regioselektivität erlaubt.

Die Photoredoxkatalyse ist, ähnlich der aeroben Oxidation, ein Zweig der modernen Synthesechemie, der eine Verbesserung der Nachhaltigkeit von Reaktionen mit sich bringt. Das Studium dieser Methode der Katalyse hat in jüngster Zeit zu einer Vielzahl an Reaktionen geführt, welche sichtbares Licht als Energiequelle nutzen. Die

Durchflusschemie konnte in weiterer Folge genutzt werden, um die Produktivität dieser Prozesse erheblich zu steigern und somit präparative Anwendungen zu ermöglichen.

Die Achmatowicz Umlagerung beschreibt die oxidative Ringerweiterung von Furfurylalkoholen zu α,β -ungesättigtem Pyranonen und wird in der Naturstoffsynthese angewandt. Im Zuge dieser Arbeit wurde eine photokatalytische Variante dieser Umlagerungsreaktion mittels $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$ als Katalysator und Natriumpersulfat entwickelt. Dieses Oxidationsmittel ist billig, stabil und produziert ausschließlich wasserlösliche Nebenprodukte. Dadurch kann das resultierende Hemiacetal direkt durch eine Boc-Gruppen geschützt werden und benötigt keinerlei Aufreinigung des Zwischenprodukts durch chromatographische Methoden. Die entwickelte photoredoxkatalytische Umsetzung ist äußerst robust und kann in verschiedensten wässrigen Medien und mittels Sonnenlicht durchgeführt werden.

Chapter 1. The Hitchhiker's Guide to Flow Chemistry

Plutschack, M. B.; Pieber, B., Gilmore, K., Seeberger, P. H.; The Hitchhiker's Guide to Flow Chemistry. *Chem. Rev.* **2017**, *117*, 11796–11893. <http://dx.doi.org/10.1021/acs.chemrev.7b00183>

Chapter 2.

Oxidation of Secondary Amines Using Singlet Oxygen

Ushakov, D. B.; **Plutschack, M. B.**; Gilmore, K.; Seeberger, P. H. Factors Influencing the Regioselectivity of the Oxidation of Asymmetric Secondary Amines with Singlet Oxygen. *Chem. Eur. J.* **2015**, *21*, 6528-6534.
<http://dx.doi.org/10.1002/chem.201500121>

Chapter 3.

Organic Photoredox Chemistry in Flow

Plutschack, M. B.; Correia, C. A.; Seeberger, P. H.; Gilmore, K. Organic Photoredox Chemistry in Flow In *Organometallic Flow Chemistry*; Noël, T., Ed.; Springer International Publishing: Cham, 2016; pp 43-76.
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Chapter 4.

Oxidation of Furfuryl Alcohols Using Sodium Persulfate.

Plutschack, M. B.; Seeberger, P. H.; Gilmore, K. Visible-Light-Mediated Achmatowicz Rearrangement. *Org. Lett.* **2017**, *19*, 30-33. <http://dx.doi.org/10.1021/acs.orglett.6b03237>

Postface

Discussion of individual works.

Each of the previous chapters contains reformatted versions of peer-reviewed articles in which I was a primary contributor to the conception, execution, and preparation of the publications. This section discusses the content of each chapter and explains my contributions in detail. Particular emphasis is made for the conception of the research and/or writing, putting them into the context of my Ph.D. work, which focused on the use of fluidic devices as tools for synthesis.

The Hitchhiker's Guide to Flow Chemistry – Why Flow Popularity Elicited a New Review Structure

Chapter 1 consists of “The Hitchhiker's Guide to Flow Chemistry” published in *Chemical Reviews*. This work introduces the fundamentals of flow chemistry and highlights reports which exploit fluidic devices to enhance reactivity. I suggested the title and the overall structure for this review, with the goal of introducing microfluidic principles and flow equipment, as well as providing a critical review of the current flow chemistry literature. This was necessary for several reasons.

Flow chemistry is not in the curriculum of most universities and it is also not a common topic of discussion for most research groups. Therefore, nearly all students and postdocs joining a flow group have little to no knowledge about flow chemistry. I wanted to introduce not only how and why flow reactors differ from batch reactors but also include sections discussing the equipment and some general considerations for running a flow experiment. Flow equipment and operation are largely unfamiliar to chemists, and with the exception of a few reports,¹ these topics are sparsely discussed. This scarcity of fundamental knowledge has contributed to why flow chemistry is such a closed community and I thought that it would be prudent to include sections 2, 3, and 4 for the general scientific audience. We hope that these sections will be read and discussed by flow-chemistry newcomers for years to come.

While collecting literature for the main sections, we quickly recognized a problem; there are so many articles, which examples should we include in our review? After the end of the cold war, DARPA started to develop systems for detecting chemical and biological threats.² Microfluidic devices were well suited for this goal because their small size made them field-deployable. This government incentive was a major reason for the rapid proliferation of microfluidics in academia throughout the 1990s. Even though the spread of microfluidics to synthetic organic chemistry laboratories lagged behind, this field has followed a similar trend with a rapid increase in publications in the past decade due to an increased pharmaceutical interest.³ Unfortunately, flow chemistry's popularity has actually curbed its impact in synthetic laboratories. Some researchers have used flow chemistry to produce publications or improve the impact factor of their journal articles. This misuse of flow chemistry has left outsiders skeptical of the actual usefulness of

flow methods. To alleviate current prejudices, we sought to emphasize that we do not believe that every reaction **should** be run in flow.

The flow chemistry craze of the past decade also has produced such a large volume of publications that reading, let alone writing an all-inclusive review would be downright exhausting. I thought that the introductory sections could serve not only an educational purpose but also serve to organize and put the main sections (5,6,7, and 8) into perspective. Previous flow chemistry reviews have focused on the types of chemical transformations, however, I felt that categorizing the flow literature by the type of chemistry was not only a large task but also diminished the appeal to the general community since each individual field has reviews of their own. For this reason, the main sections were structured to highlight literature that exemplifies the topics in the introductory sections (multiphase, mixing, temperature, photo- and electrochemistry). This structure allowed us to define our selection criteria (what **should** be done in flow?) and design a decision tree for whether or not to run a reaction in flow. The main selection of literature examples comes from the past five years of literature and focuses on examples which fit the criteria we established.

Specific Contributions

For the preparation of the review, Dr. Bartholomäus Pieber and I shared the majority of the work. I was responsible for sections 1, 2, 6, 7, 9, and 10. For these sections, I collected, evaluated, and selected relevant literature, as well as wrote, and created the tables, figures, and schemes for these sections. I undertook most of the editorial responsibility for all sections; combining section drafts, unifying text and figures, numbering schemes and compounds, and making corrections from the other co-authors, the reviewers, and the editors.

Factors Influencing the Regioselectivity of the Oxidation of Asymmetric Secondary Amines with Singlet Oxygen – Background of the Mechanistic Discovery

Dr. Dmitry B. Ushakov's work toward the synthesis of amino nitriles⁴ and cyanoepoxides⁵ via the oxidation of amines led to our interest in the mechanism of amine oxidation by singlet oxygen. Chapter 2 includes my work with D.B. Ushakov, "Factors Influencing the Regioselectivity of the Oxidation of Asymmetric Secondary Amines with Singlet Oxygen," published in *Chemistry – A European Journal*. I became involved with this project as a result of my interest in reaction mechanisms and my knowledge of Density Functional Theory (DFT) calculations. Our work intended to identify the mechanistic step in which selectivity is determined, and leverage that knowledge for highly selective imine synthesis. While we were not able to identify conditions that altered selectivity, we filled a gap in the mechanistic understanding for the oxidation of amines with singlet oxygen.

At the time, little work had been done on the oxidation of asymmetric secondary amines, and two prevailing mechanisms were possible: a deprotonation or an H-atom abstraction (Figure 1). Zhao and co-workers proposed a deprotonation mechanism,⁶ however they measured a ρ value close to zero and concluded that *para*-substitution has no effect on the rate of oxidation. Others provided evidence for a singlet oxygen mediated oxidation, however, reported a similar lack of selectivity for *para*-substituted compounds leaving the mechanism open to debate.⁷

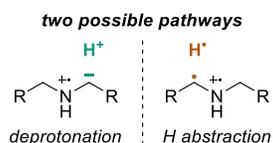


Figure 1. Deprotonation and H-atom abstraction mechanisms were previously proposed.

D.B. Ushakov's initial substrate scope did not reveal an obvious trend either (Table 1, entries 1-4). Regardless of differences in catalyst and solvent, the oxidation selectivity was nearly identical to that reported by Zhao and co-workers. However, unlike the other authors, we looked into the selectivity of an *ortho*-substituted compound and observed a noticeable and reproducible difference in selectivity (entry 5). This significant difference in selectivity prompted me to calculate the relative energies of the B3LYP optimized structures of the corresponding amines, benzylic radicals, and anions. The stabilities did not reveal a discernable trend that agreed with our experimental data. However, Natural Bond Orbital (NBO) analysis showed a correlation between the oxidation selectivity and the %s-character of the benzylic C-H bonds in the starting material. Owing to the small substrate scope, I remained skeptical about this relationship between %s-character and the oxidation selectivity and wanted an experimental method to validate my computational values. I measured the one-bond C-H coupling constants ($^1J_{\text{CH}}$) of the starting material since there is a direct correlation between the coupling constant and the bond hybridization ($^1J_{\text{CH}}/5 = \%s\text{-character}$). The computed %s-character and the measured values showed the same general trend (Figure 2). This validation prompted us to study other *ortho*-substituted compounds and helped us to determine a strong relationship between the oxidation selectivity and the calculated/measured C-H bond hybridization.

Table 1. Our initial substrate scope does not reveal an obvious trend for selectivity.

entry	R ¹ , R ²	oxidation R ¹ :R ²
1	Ph, 4-OMePh	1.1:1 (1.1:1) ^a
3	Ph, 4-MePh	1.1:1 (1:1.1) ^a
4	Ph, 3,4,5-OMePh	1.3:1
5	Ph, 2-OMePh	2.4:1

^aratios reported by Zhao and co-workers.^{6a}

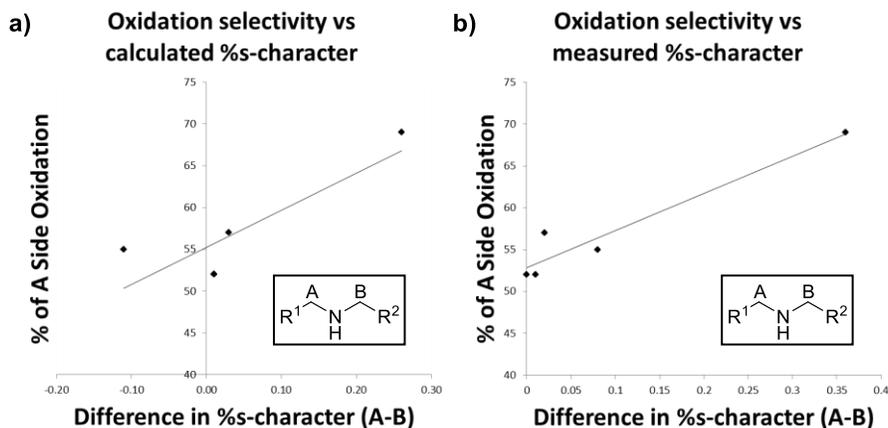


Figure 2. Substrates from Table 1. The trend between oxidation selectivity and a) calculated %s-character and b) measured %s-character.

The strong correlation between the oxidation selectivity and %s-character helped us determine that the oxidation selectivity was governed by an H-atom abstraction (homolytic C-H bond cleavage) since the deprotonation pathway would have shown an inverse relationship with %s-character (Figure 3). With my selectivity plots, we were able to identify a steric component for selectivity as well. I showed that deviations from the hybridization trend correlated with the relative A-values for each functional group.

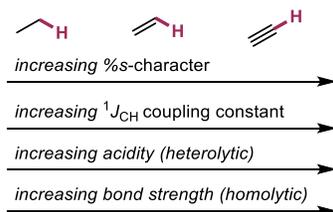


Figure 3. General trends for %s-character, $^1J_{\text{CH}}$ constants, acidity, and bond strength for sp^3 , sp^2 and sp hybridized C-H bonds.

Specific Contributions

The initial substrate scope was synthesized and oxidized by D.B. Ushakov. I conducted all DFT calculations and NBO analysis and identified the trend between %s-character and the oxidation selectivity. I also realized we could corroborate our calculated %s-character values by measuring the $^1J_{\text{CH}}$ constants with the use of NMR spectroscopy. I created all the correlation plots and contributed to selecting the substrates which would prove or disprove our proposed trend. I synthesized and oxidized approximately half of the remaining substrates. For the sterically bulky substrates, I decided to plot the deviation from the fitted line for selectivity versus the functional groups' A-values. I had mostly an editorial role in preparing the manuscript but contributed equally to putting together the supporting information.

Organic Photoredox Chemistry in Flow – Why Flow Chemists Should Use Reaction Productivities for Batch versus Flow Comparisons

Chapter 3 contains the book chapter “Organic Photoredox Chemistry in Flow” which I wrote for *Organometallic Flow Chemistry*. This chapter introduces photoredox catalysis and photochemistry in flow and then summarizes recent

photoredox reactions that have been reported in flow. I structured the chapter to categorize reactions by oxidative or reductive quenching. I aimed to show that these processes were more productive in flow since a higher productivity would warrant the use of flow conditions for synthesis. The problem I observed in flow literature was the direct comparison between reaction time and residence time. This comparison is very misleading for a number of reasons.

The first and most frustrating reason is that flow and batch processes are fundamentally different in regard to the preparation of a compound. For instance, a researcher reacts 10 mmol of a substrate in 100 mL of solvent and it takes 1 hour for full conversion in a flask. The same researcher then makes the comparison to a flow reaction which has a 10 minute residence time and says it is faster. The problem is that with a 5 mL reactor, the flow rate is 0.5 mL min⁻¹ and the time it would take to pump a reaction of the same scale (10 mmol, 100 mL) is actually over three hours. Clearly, this is not faster and yet these reaction time/residence time comparisons continue to be made. To make a more accurate comparison, I calculated and reported reaction productivities (mmol h⁻¹) even when the authors of the original works did not. While reaction productivity is better for comparison, admittedly, they can be misleading as well.

Both batch and flow conditions are rarely optimized separately by the same researcher. A paper focused on flow chemistry usually varies the reaction parameters to give the optimal results for the flow process. Subsequent comparisons are made with a reaction in batch under identical conditions. Optimal batch conditions are not necessarily the same as the optimal flow conditions, making a comparison with the use of the optimal flow conditions for both flow and batch potentially misleading. A similar problem exists for the comparison of the optimized flow conditions with previously reported conditions. In flow, the residence time is a commonly optimized reaction parameter. In contrast, often, batch reactions are optimized according to the time it takes to have a coffee, eat lunch, or get a night's rest and the reaction time is hardly a reflection of the batch reactor's performance. For this reason, the use of previously reported conditions for comparison is also flawed. For an accurate comparison of productivity, both the batch conditions and the flow conditions need to be optimized independent of each other. Having said that, I still used the productivities for comparison and hoped that reactions, where the flow productivity was orders of magnitude higher, were suggestive enough that flow processes are more efficient.

Specific Contributions

For the preparation of the book chapter, Dr. Camille A. Correia did the initial literature collection before passing on the sole responsibility to me. I collected and organized the remaining photoredox flow literature and decided the structure for the book chapter. I created all figures, tables, and schemes and wrote all sections of the chapter.

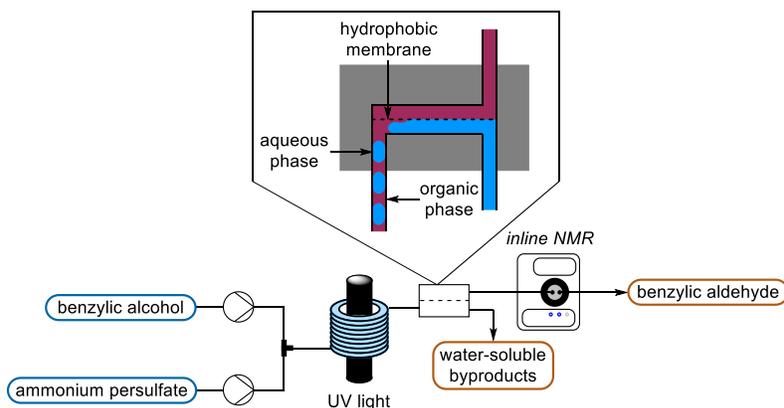
Visible-Light-Mediated Achmatowicz Rearrangement – From a Proposed Process to a New Reaction

Chapter 4 consists of my article on the “Visible-Light-Mediated Achmatowicz Rearrangement” published in *Organic Letters*. This paper presents the organic synthesis application of a catalyst/oxidant combination which is well-known to the field of water oxidation. The discovery of this reaction was somewhat serendipitous and stemmed from another project of my own conception.

Originally, I sought to oxidize benzylic alcohols in flow (Scheme 1). The process combined an aqueous solution of ammonium persulfate with an organic solution of benzyl alcohol and used ultraviolet (UV) light to activate the

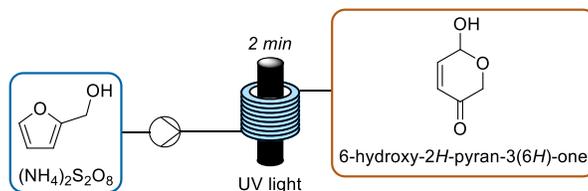
persulfate ion. This mixture was going to be separated inline with the use of a hydrophobic membrane, facilitating easy analysis of the organic phase with the use of inline NMR spectroscopy. While the oxidation of alcohols is simplistic, I thought the novelty of inline separation, analysis, and potential real-time optimization warranted investigation.

Scheme 1. Original project plan for the biphasic oxidation of benzylic alcohols with the use of sodium persulfate and ultraviolet light with inline separation and NMR analysis.



Unfortunately, biphasic conditions were quickly abandoned because conversion was low for all organic solvents and overoxidation was more prevalent with extended residence times. Phase transfer catalysts and cosolvents failed to improve the conversion. Therefore, I investigated a homogeneous reaction mixture (DMSO: water) and obtained acceptable results (85% conversion with 50% yield). I began to develop a method to quantify the yield by inline NMR, however, water complicated the analysis of the unreacted alcohol, and the lack of an inert and water soluble internal standard made the real-time quantification of the product problematic. I was concurrently investigating the substrate scope when interestingly, the oxidation of furfuryl alcohol gave very clean conversion (50%) to 6-hydroxy-2*H*-pyran-3(6*H*)-one with only a 2 minute residence time (Scheme 2). I realized that the homolytic cleavage of the persulfate ion closely resembled the cleavage of bromine, the oxidant used by Achmatowicz et al. for the oxidative rearrangement of furfuryl alcohols, and I thought a similar mechanism for the Achmatowicz rearrangement was feasible with sulfate radicals. I began optimization of this reaction but increasing the residence time only increased the conversion slightly. I hypothesized that the newly formed α,β -unsaturated ketone was absorbing UV light in the same region as ammonium persulfate and decelerating conversion. To combat this deceleration, I added a photocatalyst $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$, switched to visible light (450 nm), and obtained full conversion with a 2 minute residence time.

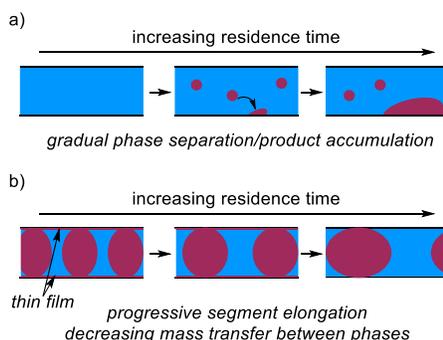
Scheme 2. The serendipitous Achmatowicz rearrangement of furfuryl alcohol.



I began to investigate the substrate scope in flow and struggled greatly with the solubility of the organic substrates in the mostly aqueous mixture. Biphasic mixtures with DCM, ethyl acetate, and 2-butanone appeared to solve solubility issues but failed to reach full conversion. Other photoredox catalysts also proved fruitless. I believed the main issue

was mixing related. The organic substrate accumulated on the walls of the reactor in homogeneous aqueous/organic solvent mixtures (Scheme 3a) and for biphasic mixtures, efficient phase mixing was not maintained leading to catalyst decomposition and poor conversion (Scheme 3b). On the other hand, batch conditions maintained efficient phase mixing with rapid stirring and as such, all subsequent reactions were run in batch.

Scheme 3. Poor residence time distributions and reproducibility issues caused by a) a gradual phase separation for reaction mixtures which were initially homogeneous or b) a progressive elongation of the phase segments leading to poorer phase transfer with increasing residence time.



Specific Contributions

I was solely responsible for the conception and implementation of this project. I planned and executed all of the experiments and wrote the manuscript. I chose the formal synthesis of (\pm)-monanchorin as a demonstration of the usefulness of this procedure.

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Research Presentations

Presentation at the JungChemikerForum - Berliner Chemie Symposium, *Visible-Light-Mediated Achmatowicz Rearrangement*, **2017** (awarded the best presentation)

Poster Talk at the JungChemikerForum - Frühjahrssymposium, *Visible-Light-Mediated Achmatowicz Rearrangement*, **2017** (awarded the best poster)

Poster at the 1st Biomolecular Systems Conference, *Visible-Light-Mediated Achmatowicz Rearrangement*, **2016**

Poster at the 129th BASF International Summer Course, *Factors Influencing the Regioselectivity of the Oxidation of Asymmetric Secondary Amines*, **2015**

Poster at the JungChemikerForum - Berliner Chemie Symposium, *Factors Influencing the Regioselectivity of the Oxidation of Asymmetric Secondary Amines with Singlet Oxygen*, **2015**

Poster at the JungChemikerForum - Frühjahrssymposium, *Factors Influencing the Regioselectivity of the Oxidation of Asymmetric Secondary Amines with Singlet Oxygen*, **2015**

Presentation at the Ringberg Conference, *Oxidation of Asymmetric Secondary Amines*, **2014**

Presentation at Florida State University, *Understanding Carbohydrate Uptake via Glucose Transporters*, **2012**

Curriculum Vitae

Education

2013-present **Ph.D. candidate**, Max Planck Institute of Colloids and Interfaces (MPIKG)
 2013 **M.S.**, Florida State University
 2011 **B.S.**, University of Wisconsin – Madison

Research Experience

Max Planck Institute of Colloids and Interfaces

2013-present **Biomolecular Systems, Prof. Dr. Peter H. Seeberger**
Ph.D. candidate
 Photoredox chemistry which substitutes powerful oxidants/reductants with the photoactivation of less reactive and shelf-stable reagents; Utilization of fluidic devices to enhance synthetic methods
Skills: microfluidic devices, DFT calculations

Florida State University

2011-2013 **Prof. Dr. D. Tyler McQuade**
Research Assistant
 Synthesis of fluorescent carbohydrate mimics for determining the structural specificity of carbohydrate uptake mediated by facilitative glucose transporters
Skills: general cell culture techniques and fluorescence measurement methods (fluorescent plate reader, fluorescence-activated cell sorting, confocal microscopy),

University of Wisconsin – Madison

2008-2010 **Prof. Dr. Howard E. Zimmerman**
Research Assistant
 Synthesis and photochemical rearrangement of a diphenylpyrimidine-dione
Skills: general organic chemistry knowledge and lab techniques; NMR spectroscopy; photochemistry; physical organic chemistry

Awards/Nominations

2017 Best Presentation, JCF-BCS
 2017 Best Poster, JCF - Frühjahrssymposium
 2015-2016 Ph.D. student representative for Biomolecular Systems (MPIKG)
 2015 129th BASF international summer course participant
 2015 65th Lindau Nobel laureate meeting participant
 2014-2017 DAAD Fellow
 2013 Fulbright Fellow alternate
 2011-2012 Hoffman Fellow

Teaching Experience

Research/Thesis Mentor

- 2015 **Bachelor thesis mentor**, N. Okuniek
2013 **Erasmus student mentor/thesis co-signer**, G. Valenti
2012 **Honor student mentor**, N. Vijapura, C. Caldwell, A. Pitt

Teaching Assistant

- 2012 2nd semester organic chemistry
2012 1st semester general chemistry
2011 1st semester general chemistry lab

Tutoring/grading

- 2011 organic chemistry tutor
2011 2nd semester organic chemistry exam grader

Related Training Experience

- 2007 & 2008 **Brigg & Stratton Corp. - Information Technology**, Training and Documentation