CORNING
Advanced-Flow™ Reactors

AFR-related publications

Complete list of published scientific papers that utilize Corning® Advanced-Flow™ Reactor Technology

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This list compiles all scientific papers published that utilize Corning® Advanced-Flow™ Reactor (AFR) Technology. We express our thanks to all authors who used our technology in their experiments. If you would like to include your published paper using AFR Technology, please contact us at reactors@corning.com and we will be pleased to review your submission for inclusion in this document.

1. Reactors: Goal, Design & Characterization

As an on-going effort toward process intensification, Corning developed Flow Reactors to support the synthetic industry.[1] For this, switching the synthetic paradigm[2] from traditional batch to flow chemistry, was pursued.[3] Corning mindset being focused on industrialization, the reactors were designed towards high scale production,[4–10] with plethora of applications.[11]

2. Reactors Engineering & Characterization

Using Corning's expertise, reactors were designed either in resistant glass[12] or Silicon Carbide (no chemical limitation found yet).[13]. The mass transfer properties,[14] the heat exchange,[15] pressure drop,[16] residence time distribution[17] were fully characterized for single[18,19] or dual phase systems.[20–22] The hydrodynamic properties of liquid and gas liquid[23] flow were published.[24,25] The same work was also carried out for the Low-Flow Reactor.[26]

To help with industrialization, the design of reactors ensured a scalable system such as liquid/liquid systems from Low-Flow to G1[27] and up to production.[28,29] The whole concept behind flow reactor and scale-up has been summarized.[30]

3. Published applications in Corning AFR

3.1. Photochemistry

Photochemistry is possible due to an LED system, used from laboratory to industrial scale.[31–33] The multiphase system with photochemistry was also characterized.[34]

3.1.1. Gas photochemistry: Oxygen oxidation.

For alpha-terpinene oxidation, optimizing photochemistry guidelines was published.[35] β-dicarbonyl compounds were enantioselectively oxidated.[36] Sulfured Methionine amino acid was oxidisized[37] and the protocol was extended so that mustard gas can be neutralized by air.[38]

3.1.2. Materials

Gold nanoparticles can be synthesized, showing the multi-purpose possibility of the reactor.[39]
On top of it, daily use of *aqua regia* showed the chemical tolerance of the reactor.

3.1.3. Halogen Photo-Chemistry

Iodoperlfuoroalkylation of alkenes were carried out.[40] Benzylic bromination reaction was also successfully performed[41]. Another example on G1 scale using NBS was successful.[42]

3.1.4. Dangerous species "in situ"

Dangerous species can be generated and used *in situ*, maximizing safety. Amongst them, Bromine can be generated and reacted *in situ* at Laboratory[43] and industrial scale.[44,45] Similarly nitrosyl chloride can perform photonitrisation.[46]

3.1.5. Cycloaddition

Selective photoredox transformation can be performed.[47] [2+2] Cycloaddition reaction, supported *in silico*, were performed in G1 reactors .[48] Cerium also catalyzed Cycloalkanols Cycloaddition[49] or also functionalize alkanes.[50]

Using renewable source chemicals, γ-butyrolactone were synthesized.[51]

3.1.6. Organometallics

Using Nickel catalyst, arylhydrazines were synthesized.[52] Using inline NMR monitoring, Nickel Negishi coupling reactions was also carried out.[53]

3.1.7. Green Chemistry

Direct metal free organocatalytic arylation coupling to Aryl bromide was performed.[54]

3.2. Thermal Chemistry

3.2.1. Classical Chemistry/Batch to Flow

Plant design and economic study of Ibuprofen and artemisinin was evaluated in flow.[55]The use of the appropriate analytical tools (such as Raman spectroscopy) is an asset to ensure a full optimization of process in flow.[56]

Collecting internal data, a Moffat-Swern oxidation was translated from Batch to Flow Chemistry.[57] This showcase highlights the number of possible reactions which can be used in flow. The exothermic chlorination of a compound with thionyl Chloride was performed from Laboratory to industrial scale both in simulation and experimentally.[58]

Benzoic acid alkylation reaction was performed in flow.[59] Tetrazole reaction was done.[60]

3.2.2. Synthesis of dangerous chemicals

Using flow reactors, dangerous species can be synthesized, minimizing risks.

3.2.2.1. Nitric acid use.

Alcohol esterification with nitrous acid, while being a very exothermic process, could be carried safely in G1 Reactors to be turned into synthetically useful alkyl nitrites.[61] Similar nitration reactions can be performed effectively.[62]

3.2.2.2. Azide compounds,

While dangerous but synthetically interesting, have been successfully implemented in AFR. Monomethylhydrazine was synthesised.[63] Minimizing the danger with hydrazoic acid, there is a synthesis of Diphenylphosphoryl azide.[64]

Using dangerous azides, Ritalin was synthesized.[65] Similarly, *in situ* generated diazomethane was used in a synthetic way.[66] Cyclopropanation was successfully implemented through DoE experiment.[67]

3.2.2.3. Use of Gas.

Using oxygen, benzylic oxidation was carried out in metal free and reagent recyclable conditions.[68] Oxygen was also helped with the hydroxylation of ketones and ketamine synthesis.[69]

Ozonolysis, very dangerous with deadly gas even at trace level, was performed in a Low Flow Reactor.[70] Successful case was published at kilo lab scale.[71]

On the other hand, reduction via hydrogenation could be performed too.[72,73] For hydrogenation reaction, a system with Pd allowed a temporary Pd deposit in situ.[74]

Challenging Bunsen reaction (Gas SO_2/liquid) using was industrially implemented. [75,76]

Synthesis of anti-bacterial agent performic peracid (peracid) was successfully carried out.[77]

The electrophilic α-aminohydroxylation of ketones was carried out by preparing *in situ* the 1-chloro-1-nitrosocyclopentane reagent.[78]

3.2.3. Green Process

Using flow chemistry, a strong emphasis on Green Chemistry is pushed.[79,80]

3.2.3.1. Greener conditions

First, existing application are optimized in a more ecofriendly way. Tertiary Ketone were hydroxylated without need for metal.[81]

Cyclic organic carbonates were synthesized[82] and solvent-free options were also developed.[83] Solvent free biphasic alcohol oxidation was carried out and scaled up in a LF .[84] Using bleach, alcohol were oxidized and scale up in a biphasic mixture in a metal free process.[85] LAH reduction of esters into aldehyde was performed in mild conditions.[86]

3.2.3.2. Sustainable Material

Synthesis from green glycerol towards oxiranes were performed. Biodiesel could be synthesized from cooking oil.[87] Similarly, biodiesel additive STBE was synthesized from bio-sourced glycerol.[88,89]

3.2.3.3. Biosynthesis

The bioprocess of lipase β-catalyzed isoamyl acetate synthesis was carried out in flow.[90]

3.2.4. Material Chemistry/Nanoparticles

Iron oxide nanoparticles were synthesized.[91] Further characterization of the equipment and synthesis of Iron nanoparticles was successfully carried out.

Working on asteroids, valuable metals were extracted.[92]

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