**Most prevalent reaction classes.1**

**Amide Coupling**

Yield data:

* “Evaluation of alternative solvents in common amide coupling reactions: replacement of dichloromethane and N,N-dimethylformamide”2
* “Study of 1,3,5-Triazine-Based Catalytic Amide-Forming Reactions: Effect of Solvents and Basicity of Reactants” 3

Properties of solvent important to reaction class:

* “Scope and Limitations of γ-Valerolactone (GVL) as a Green Solvent to be Used with Base for Fmoc Removal in Solid Phase Peptide Synthesis”3
* “Green Solid-Phase Peptide Synthesis (GSPPS) 3. Green Solvents for Fmoc Removal in Peptide Chemistry”4
* *“N*-Butylpyrrolidinone as Alternative Solvent for Solid-Phase Peptide Synthesis”5

Other useful papers:

* “Cyrene as a bio-based solvent for HATU mediated amide coupling”6
* “Peptide synthesis beyond DMF: THF and ACN as excellent and friendlier alternatives”7
* “Replacement of Less-Preferred Dipolar Aprotic and Ethereal Solvents in Synthetic Organic Chemistry with More Sustainable Alternatives”8
* “Green solvents for the formation of amide linkages” 9

**Grignard**

Yield data:

* “Comparative performance evaluation and systematic screening of solvents in a range of Grignard reactions”10

Properties important to reaction class:

* “Solvent effects in palladium catalysed cross-coupling reactions”11
* “Solvent effects in the Grignard reaction with alkynes”12
* “Solvent effects in the Grignard reaction”13
* “Solvent effects in the Grignard reaction. Ethylmagnesium Bromide with Benzonitrile”14

Other useful papers:

* “Replacement of Less-Preferred Dipolar Aprotic and Ethereal Solvents in Synthetic Organic Chemistry with More Sustainable Alternatives”8
* “Efficient chemoselective addition of Grignard reagents to carbonyl compounds in 2-methyltetrahydrofuran”15
* “Solvent applications of 2-Methyltetrahydrofuran in organometallic and biphasic reactions”16
* “Grignard Reactions in Cyclopentyl Methyl Ether”17
* “2-Methyltetrahydrofuran (2-MeTHF): A Biomass-Derived Solvent with Broad Application in Organic Chemistry”18
* “Polymerization of methyl methacrylate under ultrasonic irradiation. Part IV. Effect of ultrasonic irradiation on Grignard catalyst and stereoregularity of the polymers produced in dioxane–tetrahydrofuran mixed solvent”19

**Alkene Metathesis**

Yield:

* “An attempt to provide an environmentally friendly solvent selection guide for olefin metathesis”20
* “Olefin Metathesis in Homogeneous Aqueous Media Catalyzed by Conventional Ruthenium Catalysts”21

Properties important to reaction class:

* “DFT Investigation into the Role of Conventional and Ionic Liquids as Solvents in Olefin Metathesis”22
* “How the Nature of an Alpha-Nucleophile Determines a Brønsted Type-Plot and Its Reaction Pathways. An Experimental Study”23

Other useful papers:

* “Ring-Opening Metathesis Polymerization and Related Olefin Metathesis Reactions in Benzotrifluoride as an Environmentally Advantageous Medium”24
* “Benzotrifluoride:  A Useful Alternative Solvent for Organic Reactions Currently Conducted in Dichloromethane and Related Solvents”25

**Suzuki-Miyaura**

Yield:

* “Green Solvent Selection for Suzuki-Miyaura Coupling of Amides”26
* “Replacement of Less-Preferred Dipolar Aprotic and Ethereal Solvents in Synthetic Organic Chemistry with More Sustainable Alternatives”8
* “Nickel-Catalyzed Suzuki–Miyaura Couplings in Green Solvents”27

Properties important to reaction class:

* “Solvent effects in palladium catalysed cross-coupling reactions”11
* “Suzuki–Miyaura cross coupling is not an informative reaction to demonstrate the performance of new solvents”28

# “Green Suzuki–Miyaura coupling reaction catalyzed by palladium nanoparticles supported on graphitic carbon nitride”29

# “Mechanistic and kinetic studies of palladium catalytic systems”30

# “Solvent effects in catalysis: rational improvements of catalysts *via* manipulation of solvent interactions”31

* “Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds”32

Other useful papers:

* Section 3 of “Solvent effects in palladium catalysed cross-coupling reactions”11 gives solvent substitutions for more specific Suzuki reactions with reagents.
* “Efficient Ligandless Palladium-Catalyzed Suzuki Reactions of Potassium Aryltrifluoroborates”15

**SN2/SNAr**

Yield:

* “Towards cleaner PolarClean: efficient synthesis and extended applications of the polar aprotic solvent methyl 5-(dimethylamino)-2-methyl-5-oxopentanoate”33
* “Dihydrolevoglucosenone (Cyrene) as a bio-based alternative for dipolar aprotic solvents”34

Properties important to reaction class:

* “Solvation of Ions. Part II. Dipolar Aprotic Solvents as Media for Nucleophilic Substitution Reactions at a Saturated Carbon Atom.”35
* “Protic-dipolar aprotic solvent effects on rates of bimolecular reactions”36
* “Dipolar Aprotic Solvents in Bimolecular Aromatic Nucleophilic Substitution Reactions”37
* “Solvent Effects and Mechanism for a Nucleophilic Aromatic Substitution from QM/MM Simulations”38
* “Solvents and Solvent effects in Organic Chemistry”39
* “Kinetics and solvent effects in the synthesis of ionic liquids: imidazolium”40

**Alcohol Oxidation**

Yield:

* “Towards greener solvents for the bleach oxidation of alcohols catalysed by stable *N*-oxy radicals”41: this paper reports no correlation between any solvent property and good performance, and instead looks at solvent screening.

Difficult reaction class as very dependent on type of oxidation.

**Heck C-C**

Yield:

* “Direct comparison of safer or sustainable alternative dipolar aprotic solvents for use in carbon–carbon bond formation”42

Properties important to reaction class:

# “Solvent effects in palladium catalysed cross-coupling reactions”11

# “Cyclic Carbonates as Green Alternative Solvents for the Heck Reaction”43

* “Optimal Heck Cross-Coupling Catalysis: A Pseudo-Pharmaceutical Approach”44
* “A biomass-derived safe medium to replace toxic dipolar solvents and access cleaner Heck coupling reactions”45
* “Mechanism, Reactivity, and Selectivity in Palladium-Catalyzed Redox-Relay Heck Arylations of Alkenyl Alcohols”46

**Baylis-Hillman**

Yield:

* “Direct comparison of safer or sustainable alternative dipolar aprotic solvents for use in carbon–carbon bond formation”42

# “The Morita–Baylis–Hillman reaction in aqueous–organic solvent system”47

Properties important to reaction class:

* “Rate Acceleration of the Baylis−Hillman Reaction in Polar Solvents (Water and Formamide). Dominant Role of Hydrogen Bonding, Not Hydrophobic Effects, Is Implicated”48
* “A New Interpretation of the Baylis−Hillman Mechanism” 49
* “Mechanism of the Morita−Baylis−Hillman Reaction:  A Computational Investigation”50

**Buchwald-Hartwig**

Yield:

* “Green-Solvent Selection for Acyl Buchwald–Hartwig Cross-Coupling of Amides (Transamidation)”51

Properties important to reaction class:

* “Effect of Solvents on the Product Distribution and Reaction Rate of a Buchwald−Hartwig Amination Reaction”52
* “Role of the Base in Buchwald–Hartwig Amination”53

Other useful papers:

# “TPGS-750-M: A Second-Generation Amphiphile for Metal-Catalyzed Cross-Couplings in Water at Room Temperature”54

**Ester Hydrolysis**

Yield:

* “A simple method for the alkaline hydrolysis of esters”55
* “Estimation of Carboxylic Acid Ester Hydrolysis Rate Constants”56
* “Chlorinated Solvents: Their Advantages, Disadvantages, and Alternatives in Organic and Medicinal Chemistry”57

Ideally, obtain yields for a range of solvents under same conditions but not possible for all reaction classes. Aim is to highlight solvents that have previously been used for the reaction class so solvent map can be assessed, therefore when a clean dataset couldn’t be found, acceptable to suggest yield based on description of how well solvent performed. This was done for ester hydrolysis.

**Boc deprotection**

“Improved Pinner Reaction with CPME as a Solvent”58

“The greening of peptide synthesis”59

No range of replacement solvents found but these two papers gave the current solvents used and two greener alternatives. Solvents given same value for yield to show prevalence of solvent use on map.

**Chromatography**

“A convenient guide to help select replacement solvents for dichloromethane in chromatography”60

“Sustainable chromatography (an oxymoron?)”61

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