Solid phase organic reactions, part I (C-C bond formation, cyclisation reactions)
Many C-C bond-forming reactions are practicable on solid phase:

- Suzuki Couplings
- Heck Reaction
- Stille Couplings
- Sonogashira Couplings
- Reactions involving Grignard Reagents
- Olefin Metathesis
- Wittig Reaction
- Radical Reactions
- Pauson-Khand reaction
- Claisen reaction
- Knoevenagel reaction
- [2+2]-, [3+2]-, [4+2]-Cycloadditions
- etc
Suzuki Coupling
problems: homodimerization of boronic acids or arylhalides
prevention: exclusion of oxygen
Heck Reaction

usefull in preparation of new cyclic peptide structures
Stille Coupling
synthesis of 14-membered macrocycle (S)-Zearalenon
(remarkable: only E-isomer came off the solid phase by cyclisation)
Grignard Reaction

side reactions minimized by:
- rigorous drying of the resin
- use of large excess of Grignard reagent
Ring Closure Metathesis

advantage: cleavage by cyclisation enhances purity of product, for incomplete products stay bound to resin
Wittig-Type Reaction

Synthesis of makrocycles by cleavage from solid support via Wittig reaction

\[ \text{K}_2\text{CO}_3, 18\text{-crown-6} \]

\[ \text{toluene, 65}^\circ\text{C} \]

\[ n = 7, 9 \]
Synthesis of indole

1. Na$_2$S$_2$O$_4$, EtOH, reflux
2. HBr, MeOH, dioxane
Radical Cyclization

Formation of 1-alkyl-5-dihydrobenzofuran from o-iodobenzyl-vinylether

\[
\begin{align*}
&\text{HN} \quad \text{HN} \\
&\text{O} \quad \text{O} \\
&\text{I} \quad \text{O} \\
&\text{O} \quad \text{O} \\
&\text{HN} \quad \text{HN}
\end{align*}
\]

3 eq nBuSnH, 0.6 eq AlBN, benzene, reflux, 48 h

<table>
<thead>
<tr>
<th>R</th>
<th>yield (%)</th>
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<tbody>
<tr>
<td>Me</td>
<td>95</td>
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<td>OMe</td>
<td>95</td>
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Pauson-Khand-Cyclization

\[
\text{Co}_2(\text{CO})_8, \text{NMO, solvent DCM} \quad \underbrace{\text{under } \text{N}_2, 4 \text{ h}}_{\text{ }}
\]

\[
\text{TFA:DCM 1:1}
\]
Claisen Condensation

\[ \text{NaH, DMA, under N}_2, 1\text{h, 90°C} \]
Pyrazole synthesis
Benzodiazepine-2,5-dione Synthesis
Furan formation: a rhodium-mediated carbene addition
[3+2] Cycloaddition
[4+2] Cycloaddition
Diels-Alder-Reaction
References: