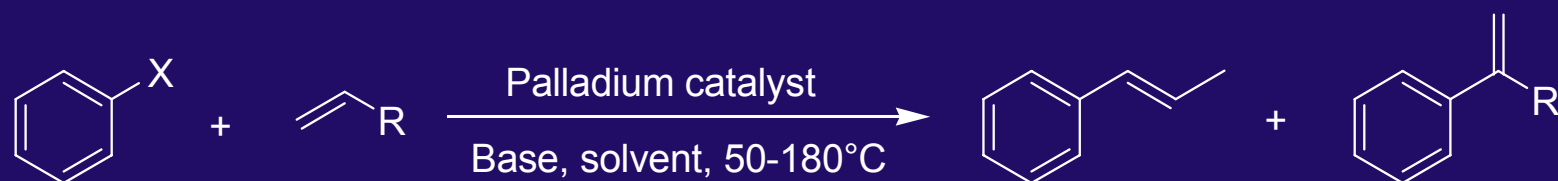


The Heck Reaction



X = I, Br, Cl, COCl, CO₂C(O)Ar, OSO₂R, N₂⁺X⁻

- Mild conditions
- High selectivity to α or β possible
- Compatible with many functional groups: *No protection deprotection necessary!*
- Applied in at least 5 industrial processes*

* J.G. de Vries, *Can. J. Chem.*, **2001**, 79, 1086-1092.

The Heck reaction

- Important problems in scaling up for production:
 - Cost of the catalyst and/or ligand
 - Separation of catalyst
 - Purification of product.
 - Salt waste
- We offer three solutions to the above problems. All three are based on the use of a *ligand-free palladium* catalyst. Absence of phosphine ligands reduces cost and simplifies purification.



Catalyst recycle in ligand-free Heck reactions

- Ligand-free Pd(OAc)₂ is a very effective catalyst for Heck reactions on aryl iodides.
- Once conversion is complete all palladium precipitates as Pd-black. A carrier material like Celite or silica is added to aid its filtration.
- This material has much lower activity than the original Pd(OAc)₂ *but it can be restored to its original activity by the addition of 2 equivalents of I₂.*
- Up to 8 recycles have been achieved in this way.

F.J. Parlevliet, A.H.M. de Vries and J.G. de Vries, Process for regenerating palladium catalysts., WO 02 00340, 03-01-02.

A.H.M. de Vries, F.J. Parlevliet, L. Schmieder-van de Vondervoort, J.H.M. Mommers, H.J.W. Henderickx, M.A.N. Walet and J.G. de Vries, *Adv. Synth. Catal.*, **2002**, 344, 996-1002.

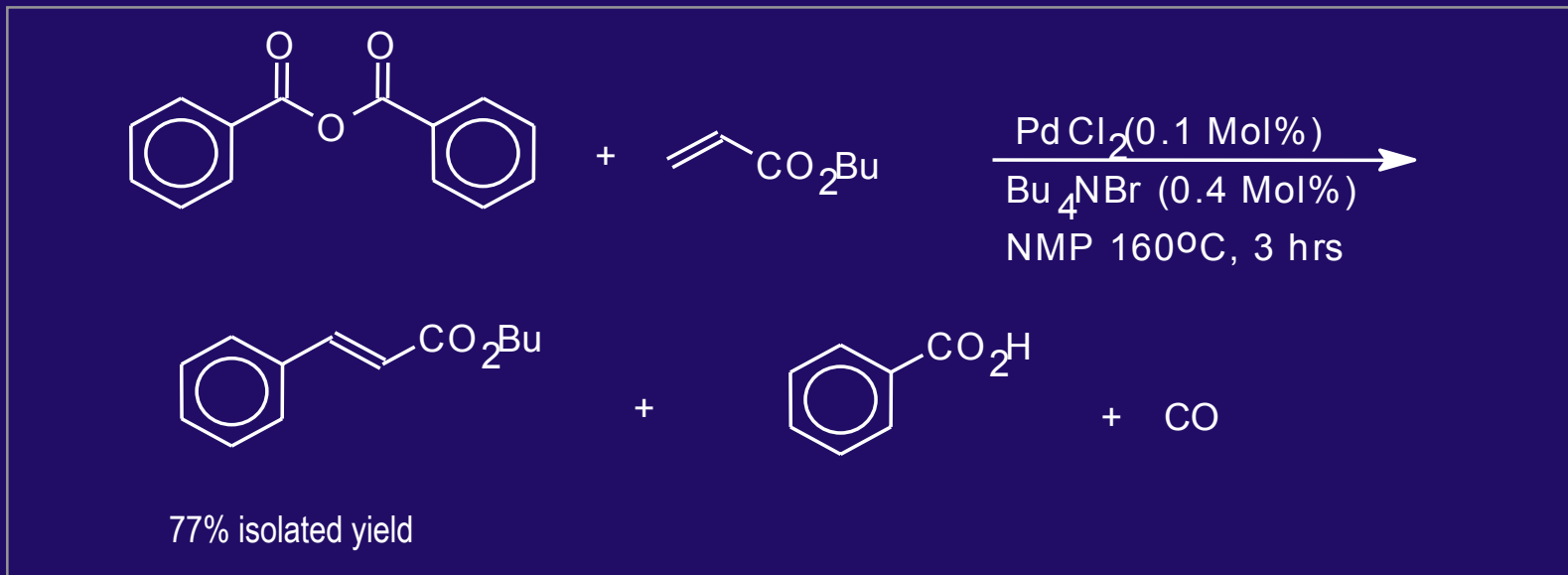
Homeopathic palladium in the Heck reaction

- Very low loading of ligand-free Pd(OAc)₂ in Heck (and Suzuki) reactions on aryl bromides is an effective means to prevent precipitation of palladium black during the reaction.
- Yet the reaction rate remains high at Pd/S = 0.01-0.05 mol%
- Ligand-free Pd is easiest in handling and work-up.
- Very cost-effective (cat < 5 € / kg product)



A.H.M. de Vries and J.G. de Vries, "Process for a catalysed C-C coupling reaction".
WO 02/057199.

Aromatic anhydrides in the Heck reaction



No salt waste! Neither base nor phosphine ligand is needed: Easy purification.

M.S. Stephan, A.J.J.M. Teunissen, G.K.M. Verzijl and J.G. de Vries, *Angew. Chem. Int. ed.*, **1998**, *37*, 662-4.

J.G. de Vries and M.S. Stephan, WO 98/49128.