IASOC 2008, Ischia, September 30, 2008

# Selective Catalytic Syntheses Steered by Palladacycles

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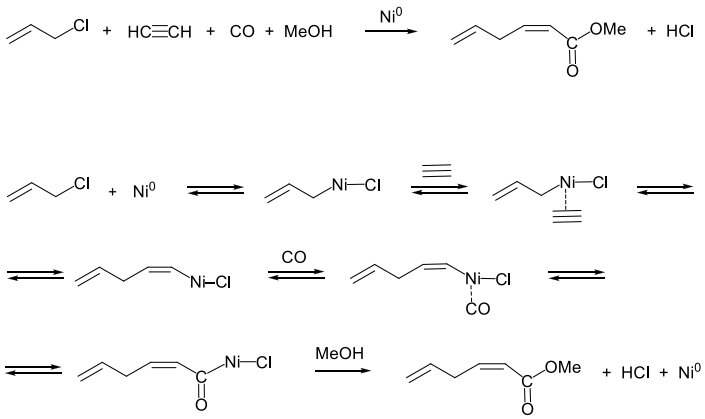
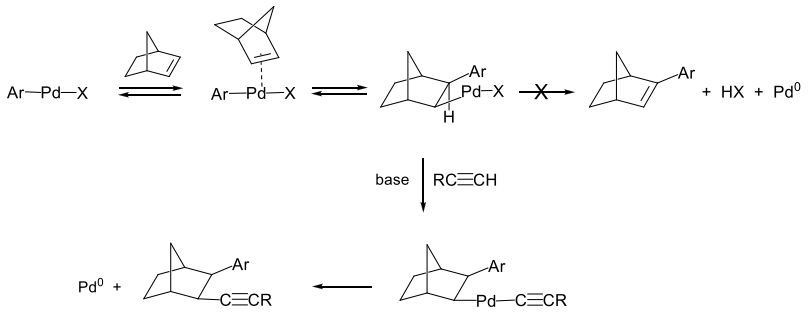
## Sequential reactions: a cascade sequence



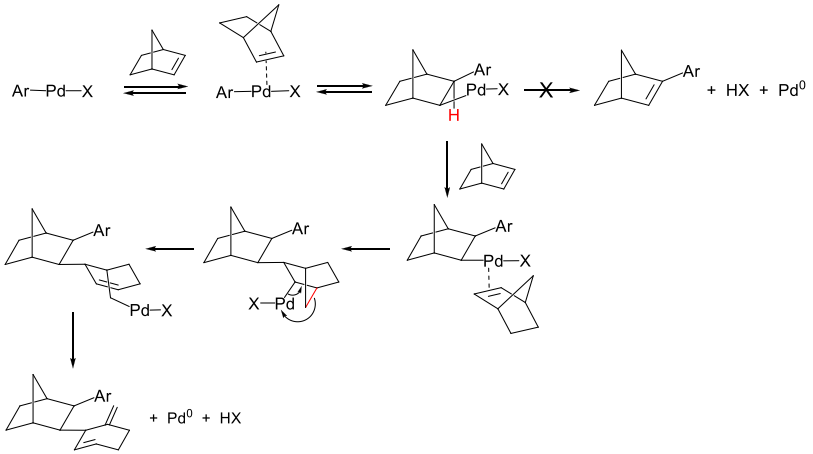

F. Guerrieri, G. P. Chiusoli, *J. Organometal. Chem*. **1968**, *15*, 209.

## Model for delaying termination



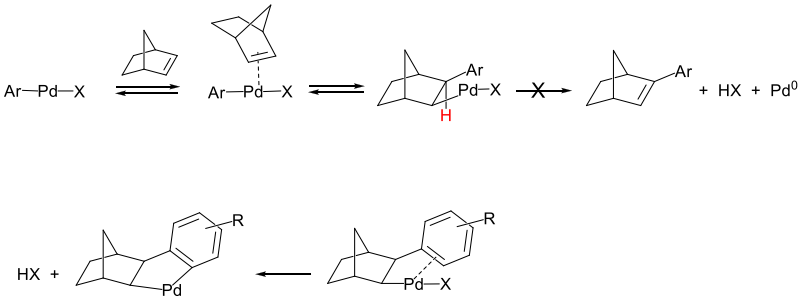

M. Catellani, *Top. Organometal. Chem*. **2005**, *14*, 21.

## Models for delaying termination



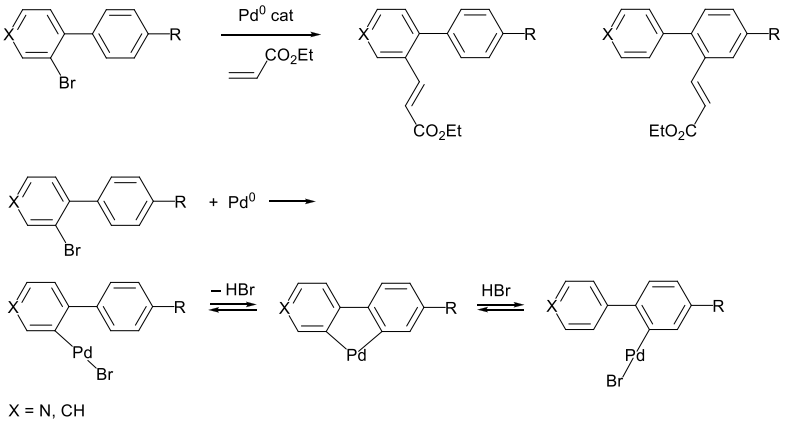

M. Catellani, G. P. Chiusoli, *J. Organometal. Chem*. **1983**, *247*, C59.

## Example of isolated metallacycles




M. Catellani, E. Motti, N. Della Ca', *Acc. Chem. Res*. **2008**.

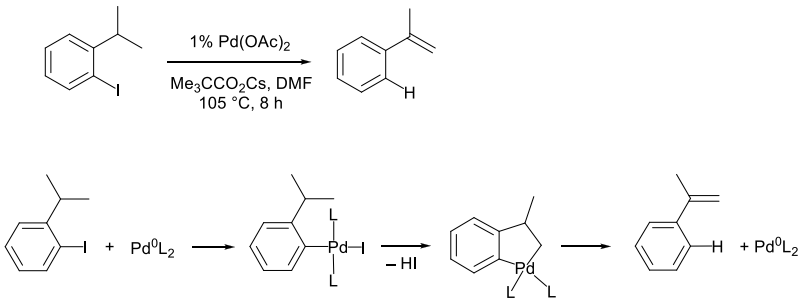
## Example of palladium migration through palladacycle




X = N, CH

M.A. Campo, H. Zhang, T. Yao, A. Ibdah, R.D. McCulla, Q. Huang, J. Zhao, W.S. Jenks, R.C. Larock, *J. Am. Chem. Soc*. **2007**, *129*, 6298. G. Karig, M.-T. Moon, N. Thasana, T. Gallagher, *Org. Lett*. **2002**, *4*, 3115. M. A. Campo, R. C. Larock, *J. Am. Chem. Soc*. **2002**, *124*, 14326.

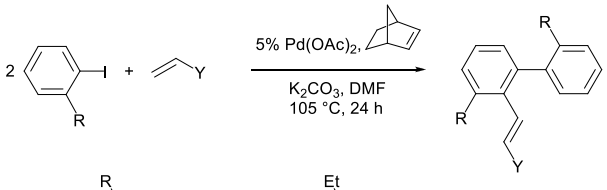
## Example of aliphatic C–H bond activation via palladacycle

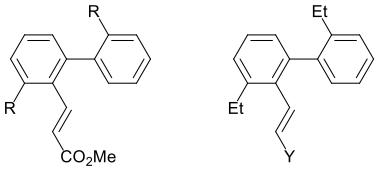



M. Catellani, E. Motti, *Adv. Synth. Catal*. **2008**, *350*, 565.

## Taking advantage of palladacyles for selective aromatic functionalization

## Synthesis of *ortho*-vinylbiaryls



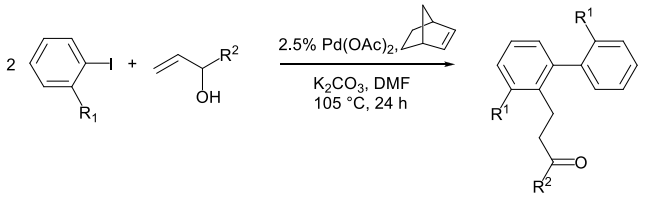





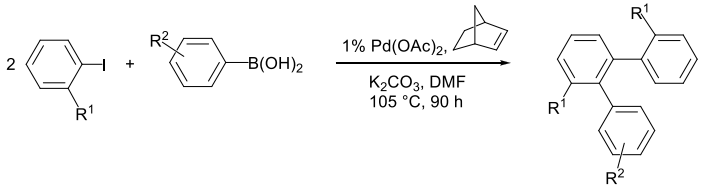
| | | | |
|---|---|---|---|
| R = *i*-Pr | 84% | Y = $CO_2Me$ | 79% |
| R = –$(CH)_4$– | 93% | Y = COMe | 79% |
| R = OMe | 88% | Y = CN | 77% |
| R = $CO_2Me$ | 87% | Y = SOPh | 81% |
| R = $NO_2$ | 94% | Y = Ph | 87% |

E. Motti, G. Ippomei, S. Deledda, M. Catellani, *Synthesis*, **2003**, 2671

## Synthesis of selectively substituted biaryls and teraryls



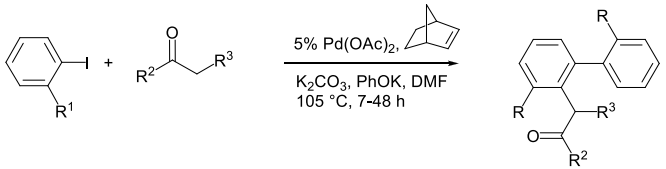

53-75%

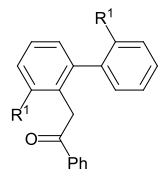


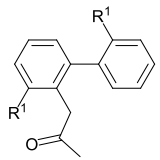

88-93%

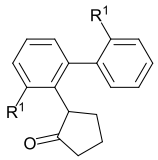
M. Catellani, S. Deledda, B. Ganchegui, F. Henin, E. Motti, J. Muzart, *J. Organomet. Chem*., **2003**, *687*, 473. E. Motti, A. Mignozzi, M. Catellani, *J. Mol. Catal. A: Chem*. **2003**, *204*, 115.

## Synthesis of biaryls containing an oxoalkyl chain





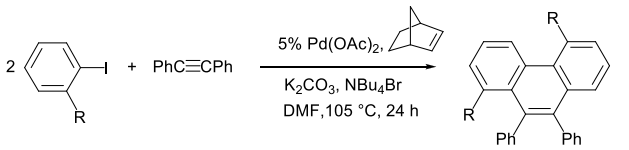


| | | | |
|---|---|---|---|
| $R^1$ = Me | 28 | $R^1$ = *i*-Pr | 70 |
| $R^1$ = Et | 74 | $R^1$ = –$(CH)_4$– | 53 |
| R1 = *i*-Pr | 77 | | |
| $R^1$ = –$(CH)_4$– | 75 | | |

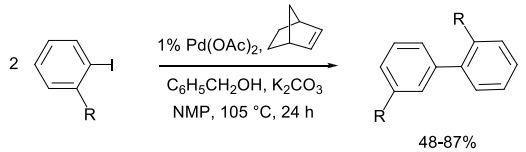
| | | | |
|---|---|---|---|
| $R^1$ = *i*-Pr | 67 | | |
| $R^1$ = –$(CH)_4$– | 71 | | |

G. Maestri, N. Della Ca', M. Catellani - submitted

## Synthesis of selectively substituted phenanthrenes and biaryls



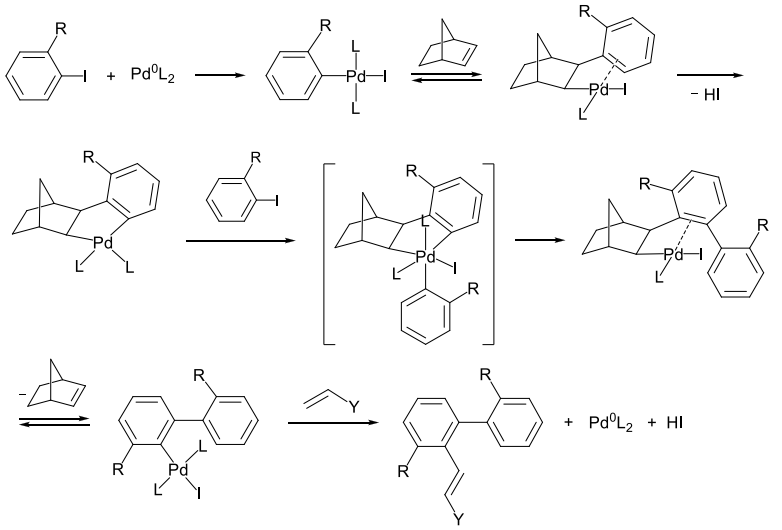

64-93%



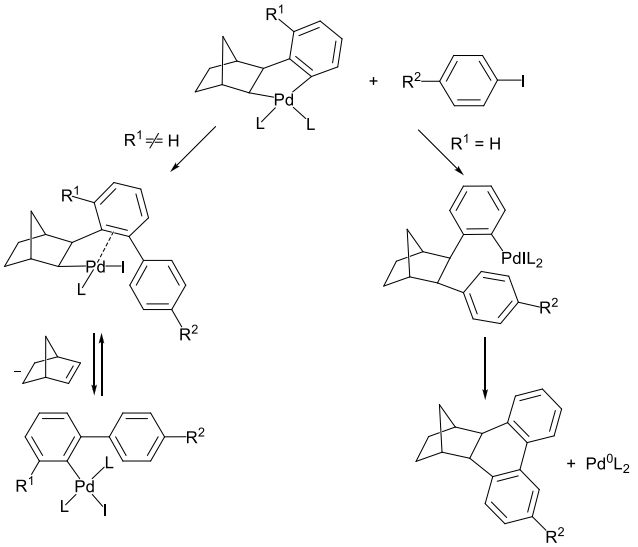

48-87%

M. Catellani, E. Motti, S. Baratta, *Org. Lett*., **2001**, *3*, 3611.
S. Deledda, E. Motti, M. Catellani, *Can. J. Chem*., **2005**, *83*, 741.

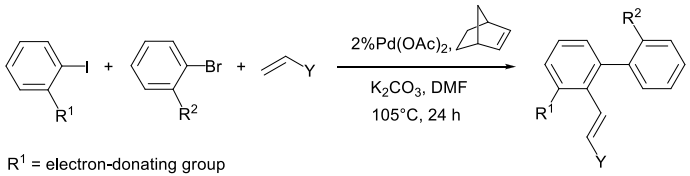
## Reaction Scheme



## *Ortho* effect

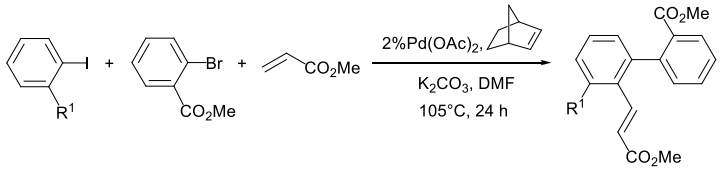


## Synthesis of vinyl derivatives of unsymmetrical biaryls



$R^1$ = electron-donating group
$R^2$ = electron-withdrawing group
Y = $CO_2Me$, Ph, $C_6H_{13}$, O-*n*-Bu

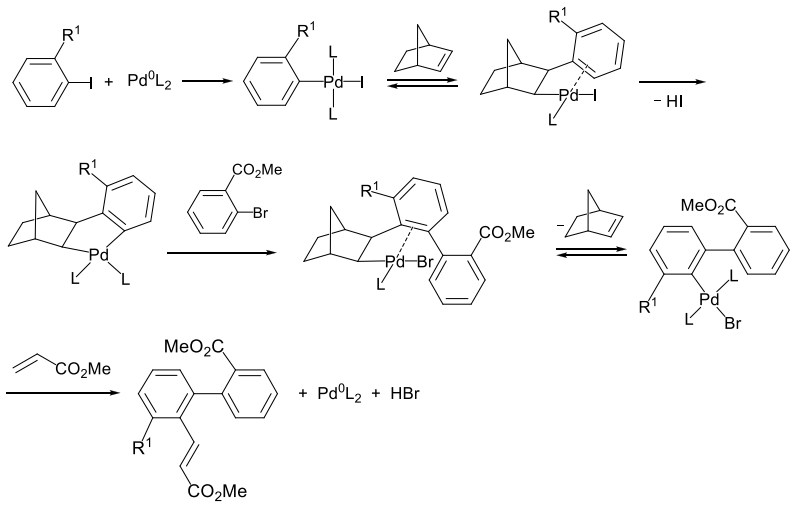
## Synthesis of vinyl derivatives of unsymmetrical biaryls



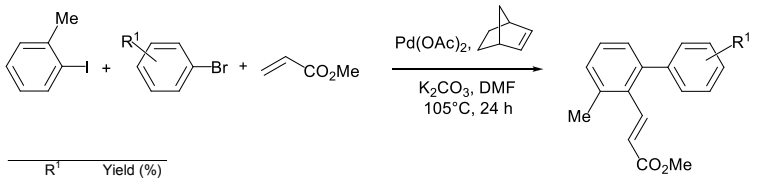
| | |
|---|---|
| $R^1$ = Me | 80% |
| $R^1$ = *i*-Pr | 74% |
| $R^1$ = Ph | 73% |
| $R^1$ = OMe | 83% |
| $R^1$ = $NMe_2$ | 82% |

F. Faccini, E. Motti, M. Catellani, *J. Am. Chem. Soc.*, **2004**, *126*, 78

## Scheme of unsymmetrical aromatic arylation

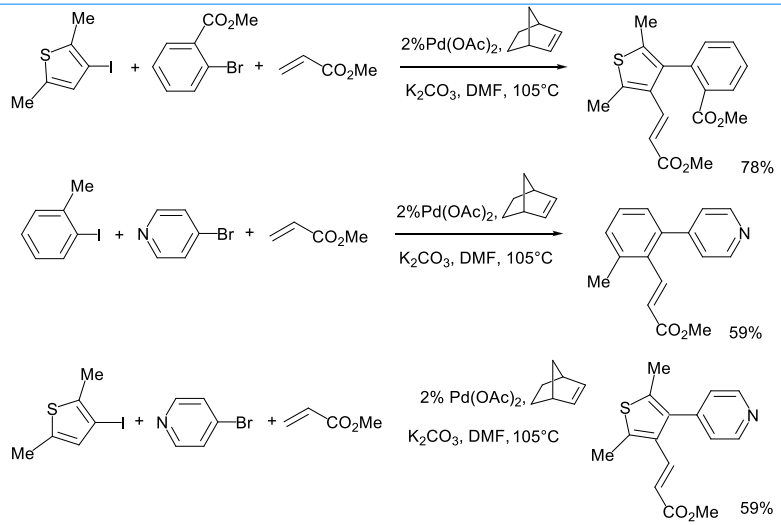



## Synthesis of vinyl derivatives of unsymmetrical biaryls



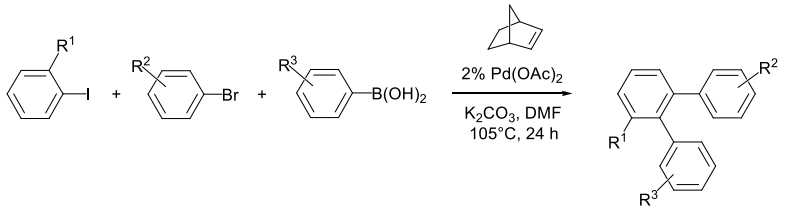

| $R^1$ | Yield (%) |
|---|---|
| *o*-$NO_2$ | 72 |
| *m*-$NO_2$ | 76 |
| *p*-$NO_2$ | 83 |
| *o*-CN | 13 |
| *m*-CN | 62 |
| *p*-CN | 79 |
| *o*-$CF_3$ | - |
| *m*-$CF_3$ | 71 |
| *p*-$CF_3$ | 80 |
| *o*-$CO_2CH_3$ | 80 |
| *m*-$CO_2CH_3$ | 37 |
| *p*-$CO_2CH_3$ | 71 |

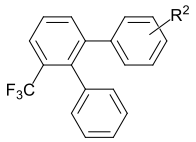
## Synthesis of vinyl derivatives of aryl-heteroaryl coupling compounds



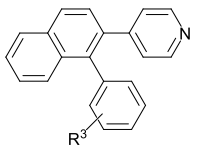

M. Catellani, E. Motti, N. Della Ca', *Acc. Chem. Res.* **2008** and unpublished results

## Synthesis of unsymmetrical teraryls



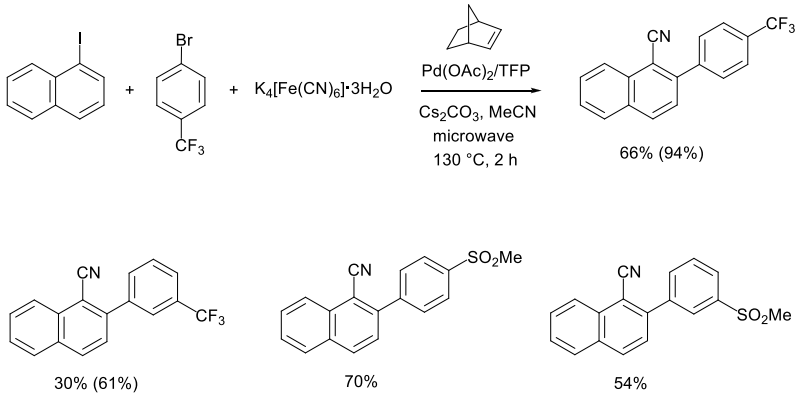

$R^2$ = 2-$CO_2$Me 83%
$R^2$ = 3-$CO_2$Me 79%
$R^2$ = 4-$CO_2$Me 90%




$R^3$ = H 75%
$R^3$ = 4-Me 73%
$R^3$ = 4-F 80%

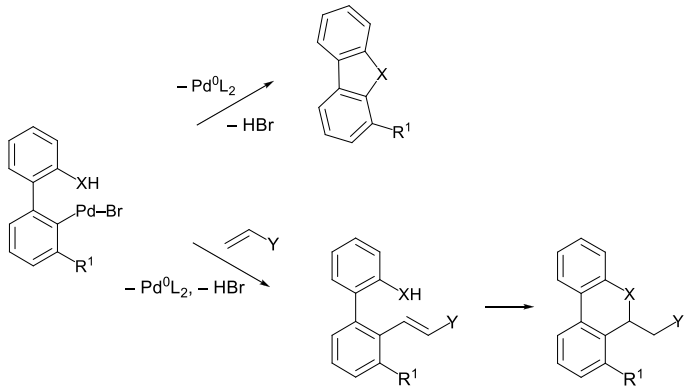
M. Catellani, E. Motti, N. Della Ca', *Acc. Chem. Res.* **2008** and unpublished results

## Synthesis of aromatic nitriles

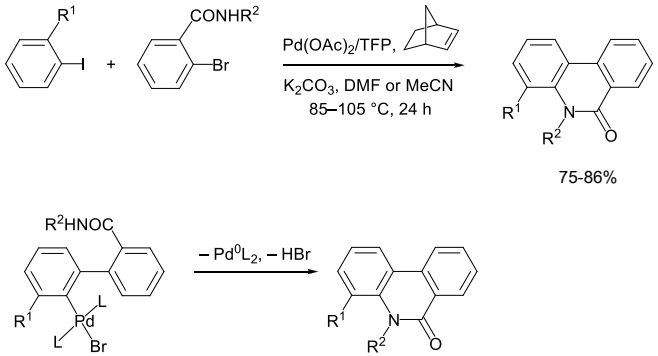



B. Marianpillai, J. Alliot, M. Li, M. Lautens, *J. Am. Chem. Soc.* **2007**, 129, 15372

## Condensed tricyclic compounds

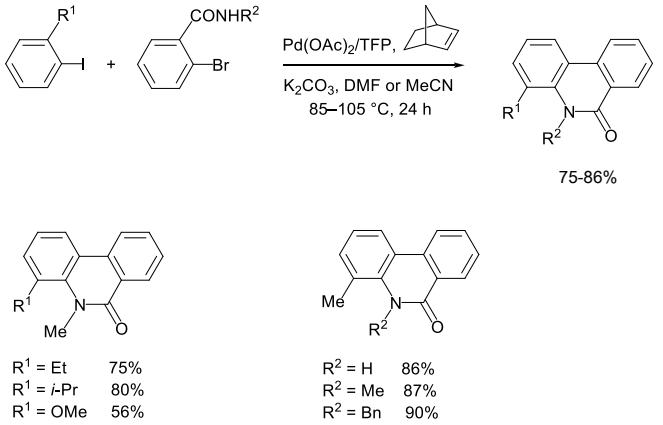



## Synthesis of phenanthridinones




R. Ferraccioli, D. Carenzi, O. Rombolà, M. Catellani, *Org. Lett.*, **2004**, *6*, 4759

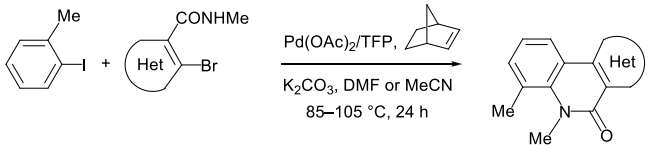
## Synthesis of phenanthridinones




| | |
|---|---|
| $R^1$ = Et | 75% |
| $R^1$ = *i*-Pr | 80% |
| $R^1$ = OMe | 56% |

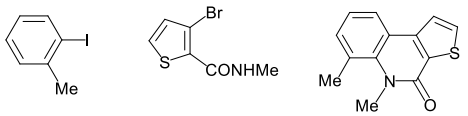
| | |
|---|---|
| $R^2$ = H | 86% |
| $R^2$ = Me | 87% |
| $R^2$ = Bn | 90% |

## Synthesis of quinolinone derivatives

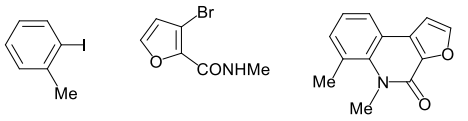



Het = electron-poor and electron-rich heterocycles

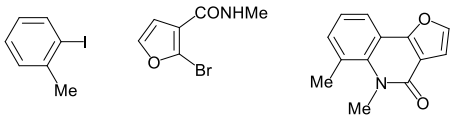
## Synthesis of quinolinone derivatives




| Solvent, T °C | Yield (%) |
|---|---|
| MeCN, 85 | 85 |
| DMF, 105 | 70 |

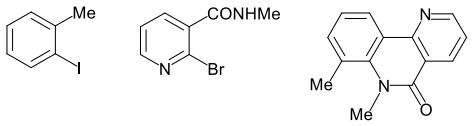



| | |
|---|---|
| MeCN, 85 | 24 |
| DMF, 85 | 82 |

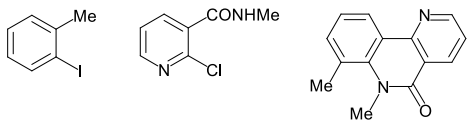



| | |
|---|---|
| DMF, 85 | 48 |

## Synthesis of quinolinone derivatives

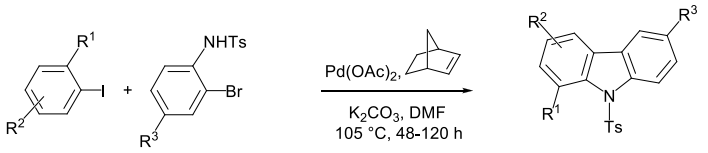



| Solvent, T °C | Isolated yield (%) |
|---|---|
| DMF, 85 | traces |

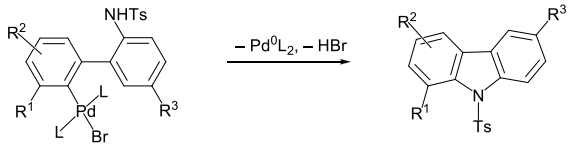



| | |
|---|---|
| DMF, 85 | 55 |

## Synthesis of carbazoles

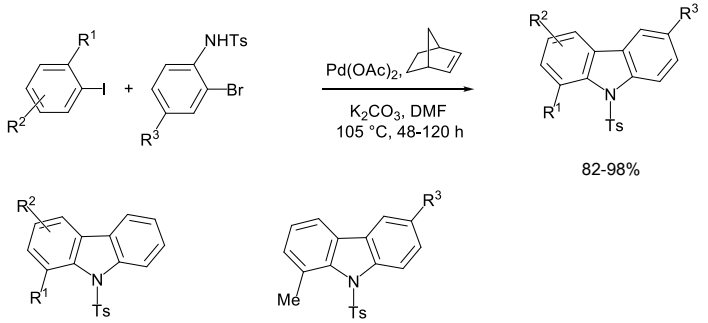



87-98%




N. Della Ca', G. Sassi, M. Catellani, *Adv. Synth. Catal*. **2008**.

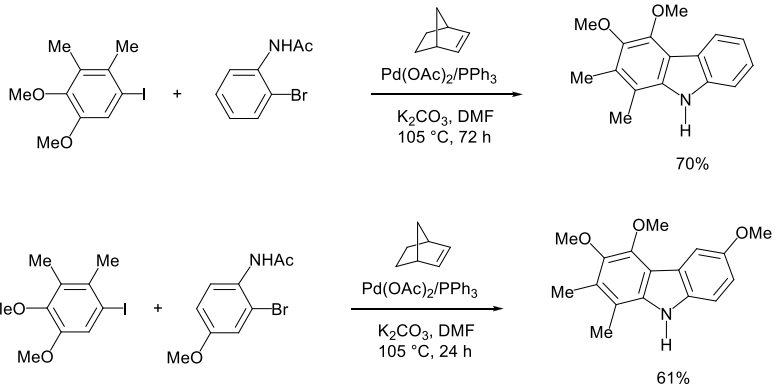
## Synthesis of carbazoles




| | |
|---|---|
| $R^1$, $R^2$ = Me, H | 93% |
| $R^1$, $R^2$ = Me, 4-Me | 91% |
| $R^1$, $R^2$ = Me, 4-OMe + 3-Me | 98% |
| $R^1$, $R^2$ = Et, H | 94% |
| $R^1$, $R^2$ = *i*-Pr, H | 82% |

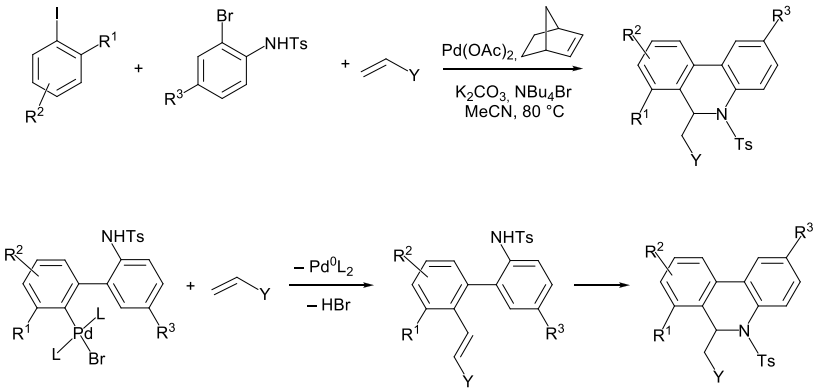
| | |
|---|---|
| $R^3$ = Me | 94% |
| $R^3$ = Cl | 90% |

## Synthesis of carbazomicyns A and D



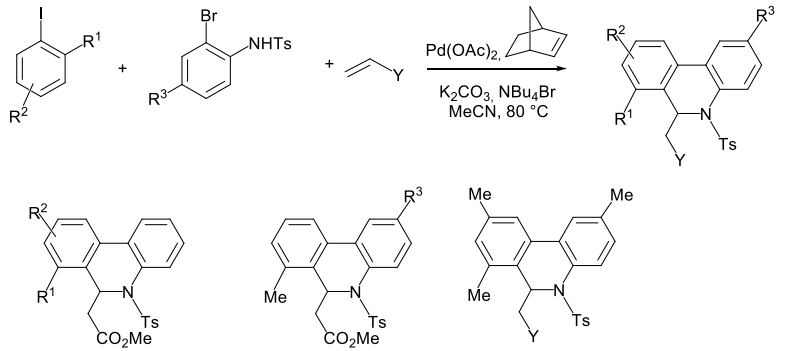

N. Della Ca', G. Sassi, M. Catellani, *Adv. Synth. Catal*. **2008** and unpublished results.

## Synthesis of phenanthridine derivatives




N. Della Ca', E. Motti, M. Catellani, *Adv. Synth. Catal.* In press.

## Synthesis of phenanthridine derivatives

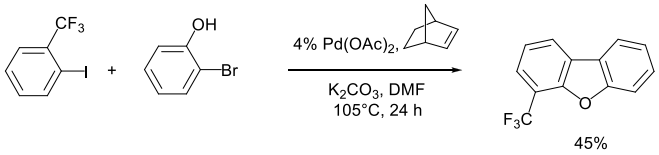



| | |
|---|---|
| $R^1$, $R^2$ = Me, H | 74% |
| $R^1$, $R^2$ = Me, 4-Me | 81% |
| $R^1$, $R^2$ = Me, 4-OMe + 3-Me | 84% |
| $R^1$, $R^2$ = *i*-Pr, H | 70% |

| | |
|---|---|
| $R^3$ = Me | 84% |
| $R^3$ = Cl | 84% |
| $R^3$ = $NO_2$ | 75% |

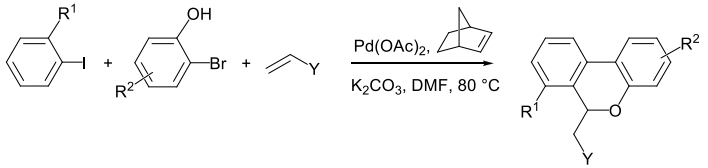
| | |
|---|---|
| Y = $CO_2Me$ | 81% |
| Y = CO | 82% |
| Y = CN | 61% |

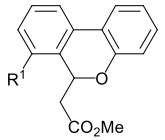
## Synthesis of dibenzofuran



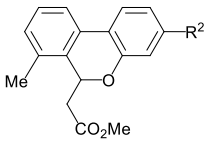

M. Catellani, E. Motti, N. Della Ca', *Acc. Chem. Res.* **2008** and unpublished results

## Synthesis of 6*H*-dibenzopyrans

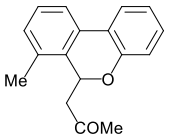



$R^1$ = Me 83%
$R^1$ = Et 64%
$R^1$ = $CF_3$ 92%
$R^1$ = 2,4-Me 88%



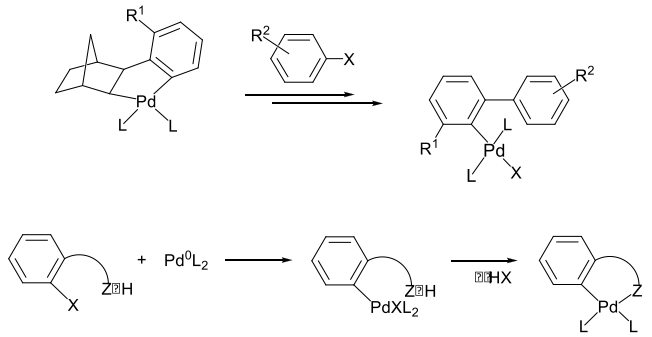

$R^2$ = Me 83%
$R^2$ = $CO_2Me$ 64%
$R^2$ = $NO_2$ 92%



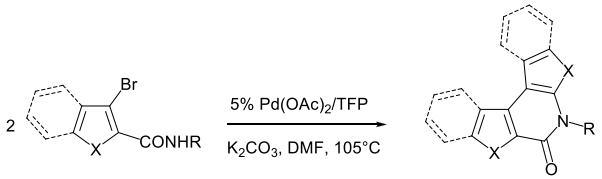

73%

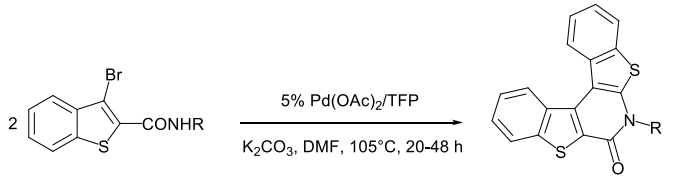
E. Motti, F. Faccini, I. Ferrari, M. Catellani, R. Ferraccioli, *Org. Lett.*, **2006**, *8*, 3967

## Other palladacycles as tools for aryl-aryl coupling




## Synthesis of pyridones

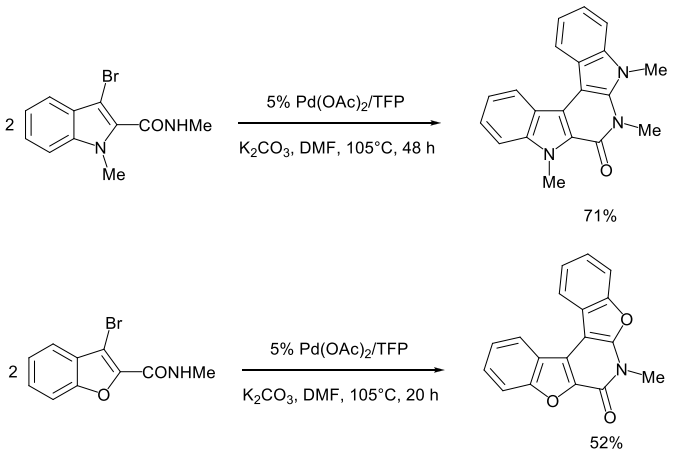


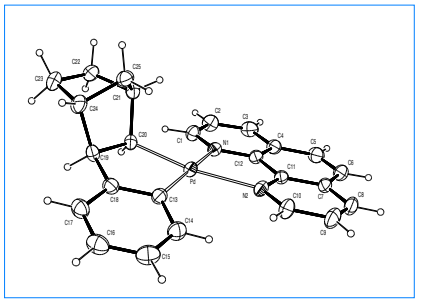




70-86%

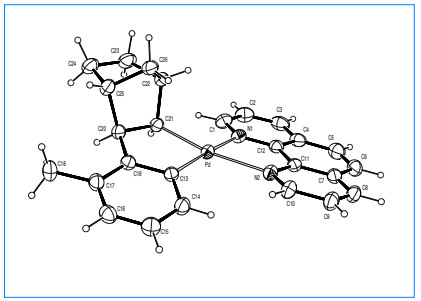
R. Ferraccioli, D. Carenzi, E. Motti, M. Catellani, *J. Am. Chem. Soc.,* **2006**, *128*, 722.

## Synthesis of pyridones



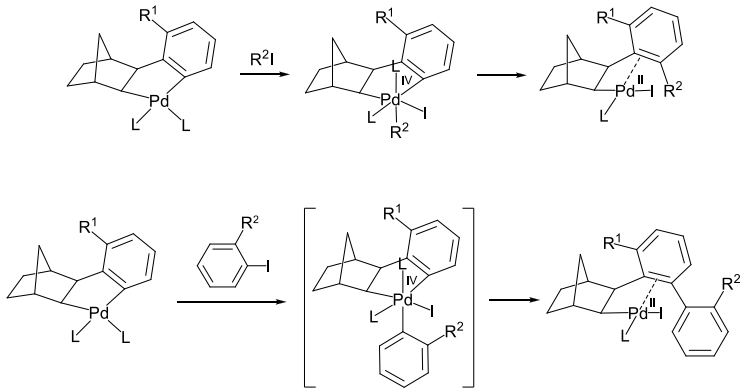
| Selected Distances (Å) | |
|---|---|
| Pd-N1 | 2.145(3) |
| Pd-N2 | 2.216(3) |
| Pd-C13 | 2.016(5) |
| Pd-C20 | 2.029(4) |



| Selected Distances (Å) | |
|---|---|
| Pd-N1 | 2.130(4) |
| Pd-N2 | 2.213(4) |
| Pd-C13 | 1.990(5) |
| Pd-C21 | 2.012(4) |

M. Catellani, A. M. Manotti Lanfredi, C. Massera, E. Motti, unpublished results.

## Comparison between alkylation and arylation pathways




## Summary

Palladacycles are particularly effective in that they bring the entire sequence under tight control of the metal center through appropriate stereochemical arrangements.

In this way it has been possible to gain access to a wide variety of aromatic structures chemo-, regio- and stereoselectively, in particular symmetrical and unsymmetrical biaryl derivatives and condensed structures containing O, N and S heteroatoms.

The identification of the organometallic structures involved has proved very useful for synthetic development. Further studies in this area will no doubt open new perspectives in mechanistic interpretations and synthetic applications.