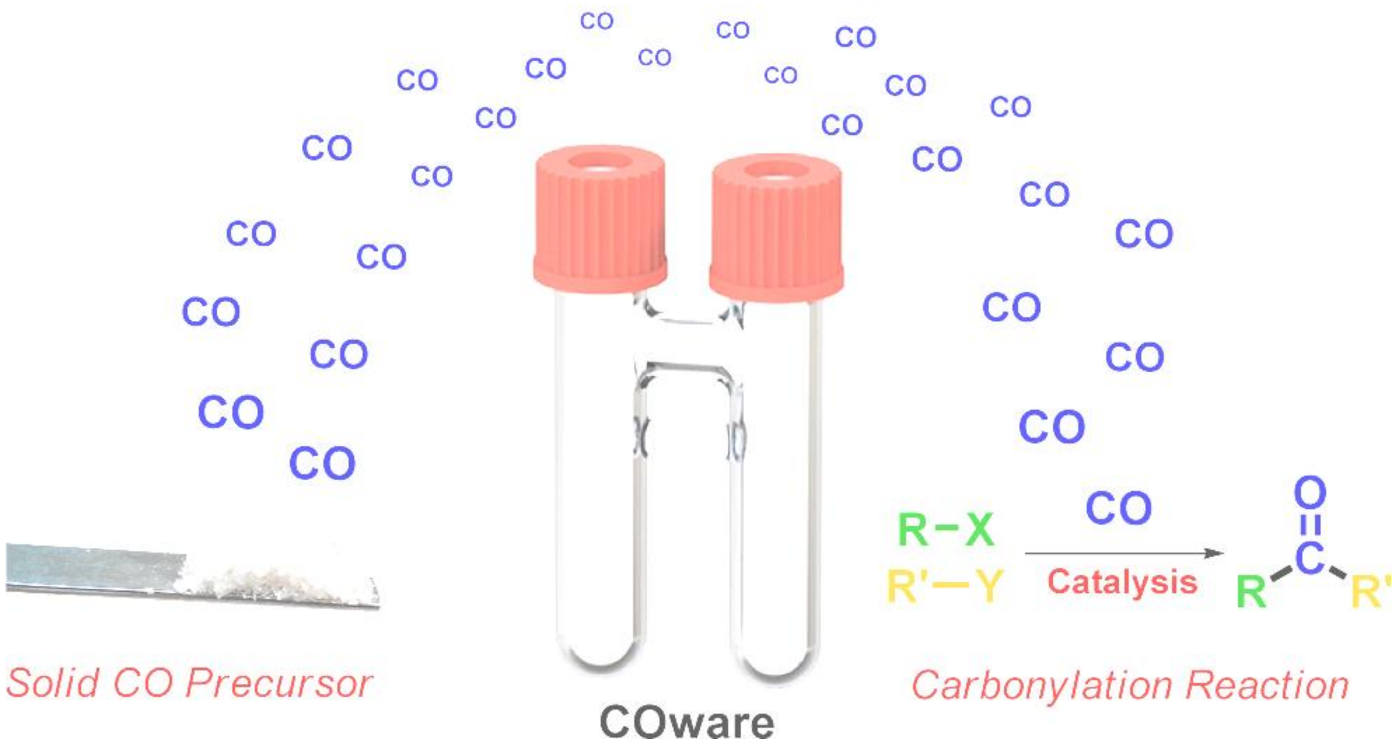
Metal-catalyzed Carbonylation Reactions : No Need for Carbon Monoxide



Literature Seminar 2017.08.26
Benjamin Ovadia

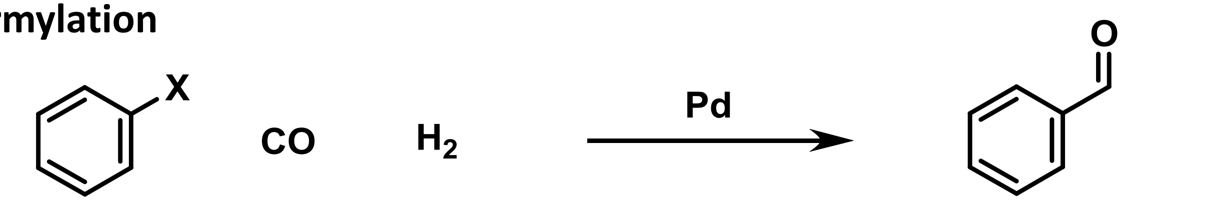
M-Catalyzed Carbonylative Coupling

- **Pioneering work by Heck in the 70s**

Pd-Catalyzed alkoxycarbonylation

Pd-Catalyzed amidocarbonylation

Pd-Catalyzed formylation

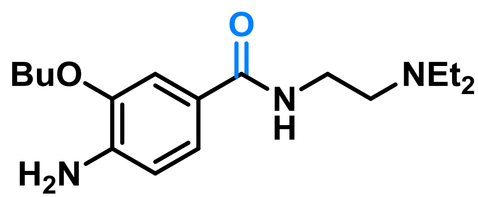


For review on Pd-ctalyzed carbonylative coupling:

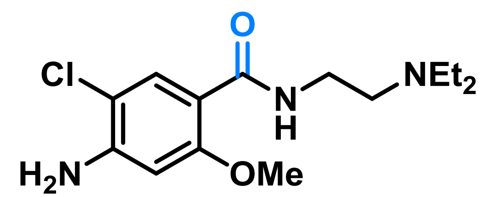
A. Brennführer, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2009**, *48*, 4114–4133.
X. F. Wu, H. Neumann, M. Beller*, Chem. Soc. Rev.* **2011**, *40*, 4986–5009.
X. F. Wu, H. Neumann, M. Beller, *Chem. Rev.* **2013**, *113*, 1–35.
Q. Liu, H. Zhang, A. Lei*, Angew. Chem. Int. Ed.* **2011**, *50*, 10788–10799

M-Catalyzed Carbonylative Coupling

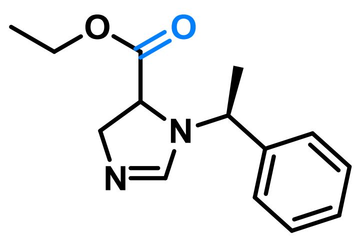
✓ CO is the most important C1 building block to introduce a carbonyle moiety
✓ Provide a straightforward access to valuable intermediates



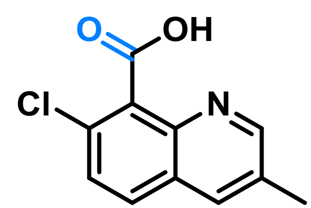
Oxybucopraine
analgesic



Metoclopramide
antiemetic



Etomidate
narcotic



Quinmerac
herbicide

X CO is a Highly toxic gas
X Carbonylation require high pressures of CO
X Extreme caution to handle, store and transport

For review on Pd-ctalyzed carbonylative coupling:
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X. F. Wu, H. Neumann, M. Beller, *Chem. Soc. Rev.* **2011**, *40*, 4986–5009.
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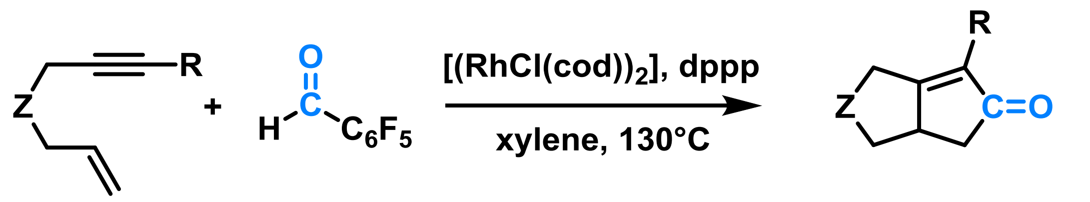
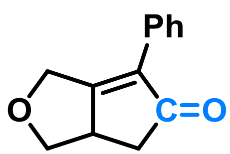
Carbonylation Reactions with CO-Surrogate

- *In-situ* generation of CO from aldehydes

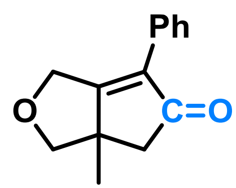
- Rh-catalyzed Pauson-Khand type reaction (Kakiuchi and Shibata, 2002)



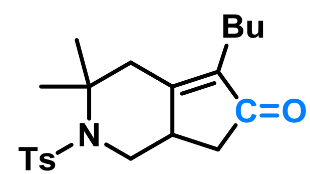
Z = C, N, O



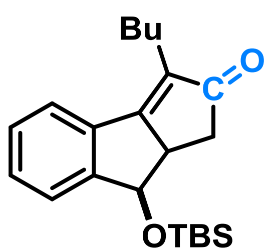
91%



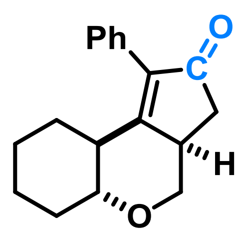
92%



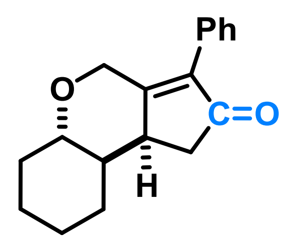
36%



88% (d.r. 11:1)



77%



90%

Morimoto, T.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. *J. Am. Chem. Soc*. **2002**, *124*, 3806
Shibata, T.; Toshida, N.; Takagi, K. *Org. Lett*. **2002**, *4*, 1619

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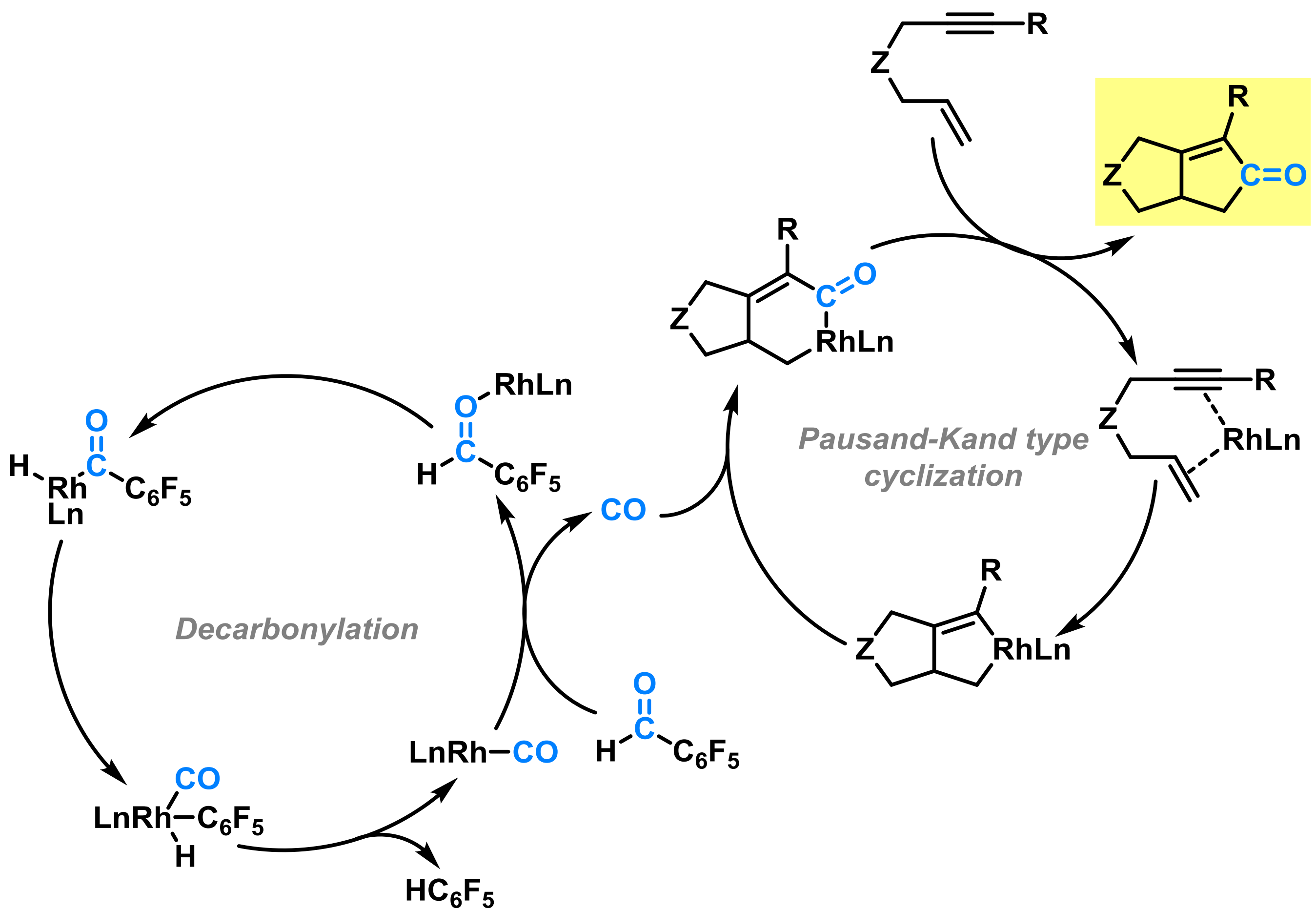
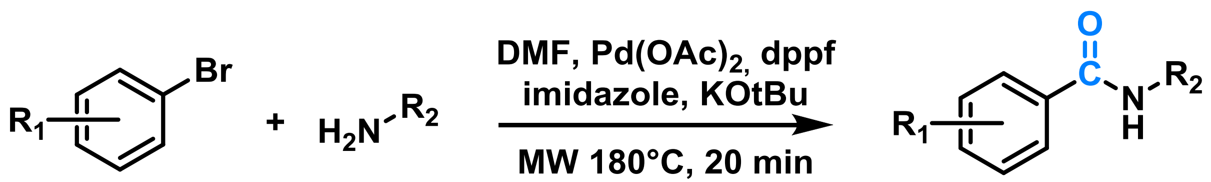


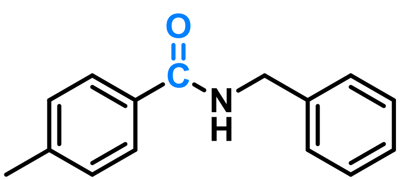
Morimoto, T.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. *J. Am. Chem. Soc*. **2002**, *124*, 3806
Shibata, T.; Toshida, N.; Takagi, K. *Org. Lett*. **2002**, *4*, 1619

Carbonylation Reactions with CO-Surrogate

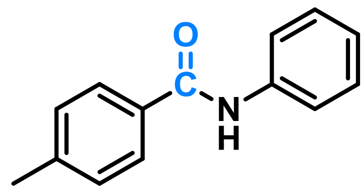
- *In-situ* generation of CO from formamides

- Pd-catalyzed aminocarbonylation of aryl bromides (Alterman, 2002)

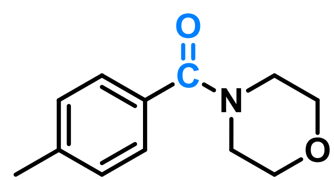




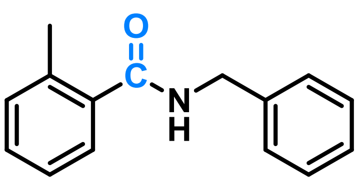
76%



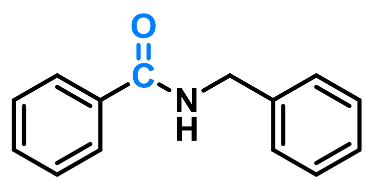
77%



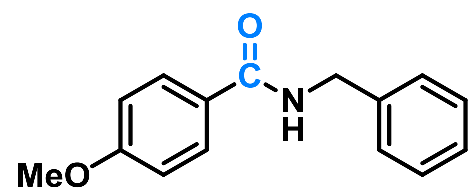
78%



94%



82%



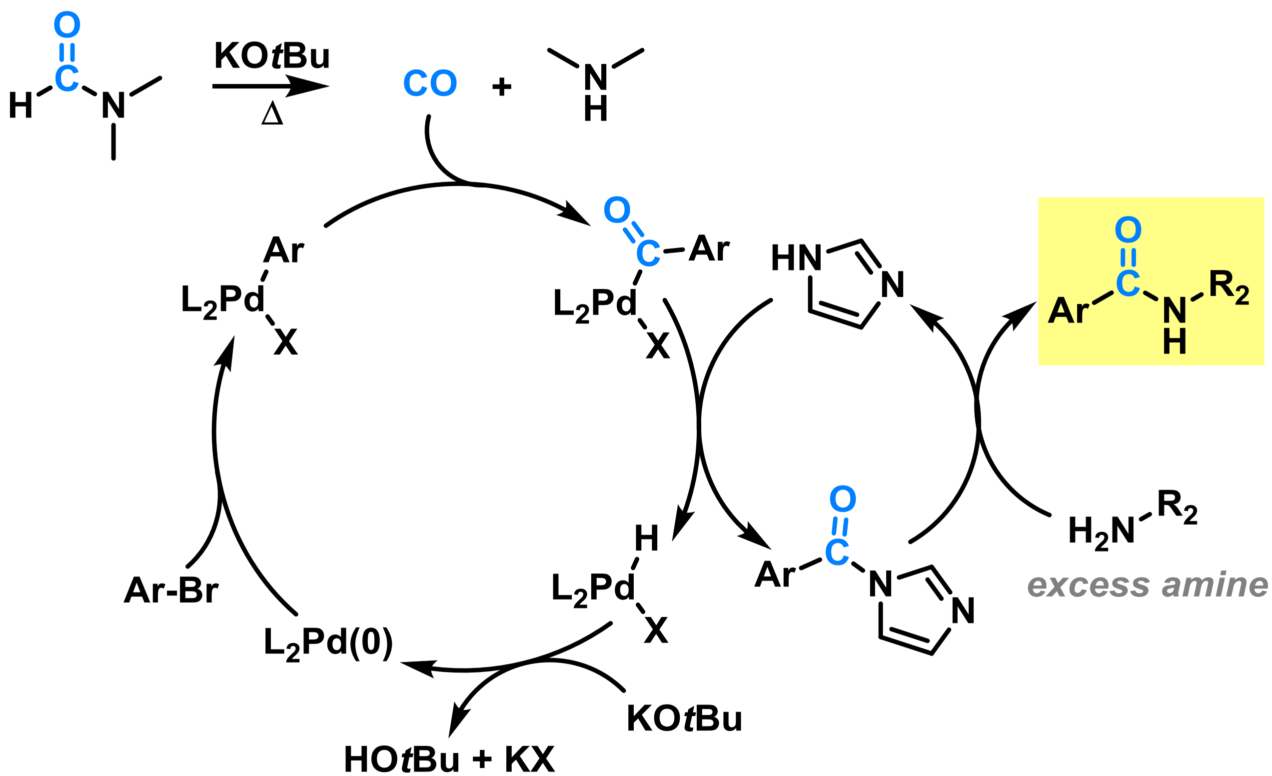
70%

Wan, Y.; Alterman, M.; Larhed, M.; Hallberg, A. *J. Org. Chem.* **2002**, *67*, 6232

Carbonylation Reactions with CO-Surrogate

- *In-situ* generation of CO from formamides

- Pd-catalyzed aminocarbonylation of aryl bromides (Alterman, 2002)

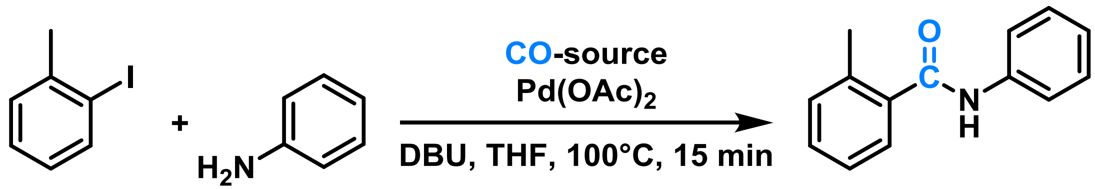


Wan, Y.; Alterman, M.; Larhed, M.; Hallberg, A. *J. Org. Chem.* **2002**, *67*, 6232

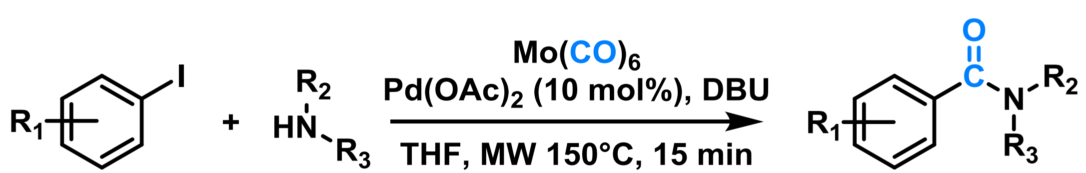
Carbonylation Reactions with CO-Surrogate

- ***In-situ* generation of CO from metal carbonyles**

- Pd-catalyzed aminocarbonylation of aryl iodide under MW irradiation (Larhed, 2003)



Entry	CO-source	Yield
1	$Cr(CO)_6$	80%
2	$Mo(CO)_6$	84%
3	$W(CO)_6$	77%
4	$Fe(CO)_5$	0%
5	$Fe_3(CO)_{12}$	0%
6	$Co_2(CO)_8$	28%

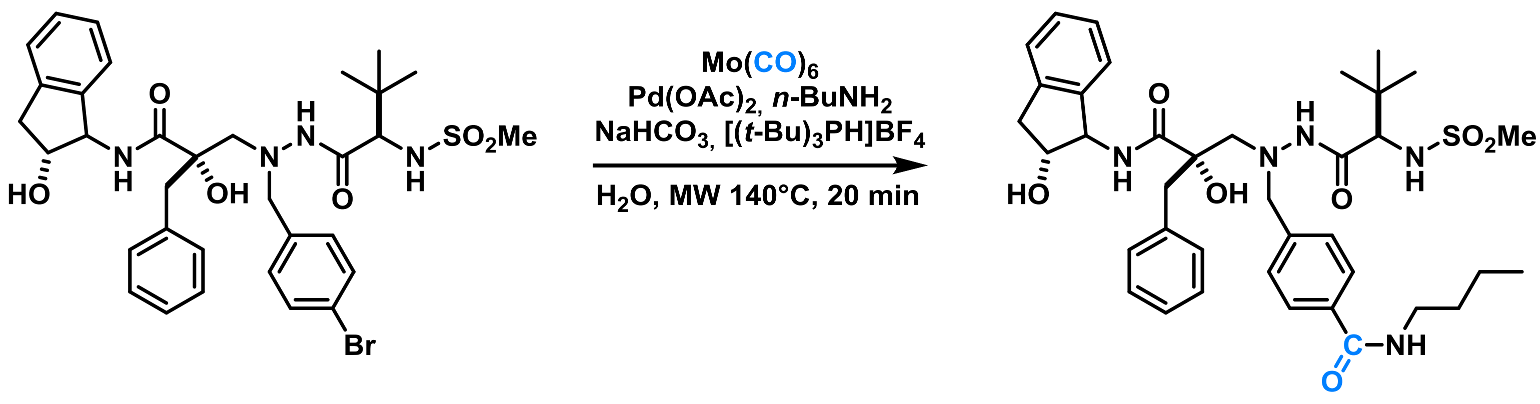


23 examples
35-95%

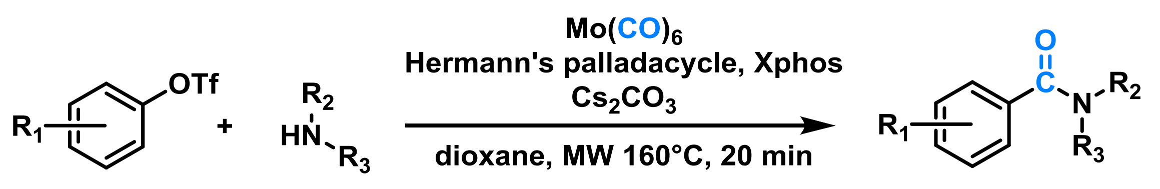
Wannberg, J.; Larhed, M. *J. Org. Chem.* **2003**, *68*, 5750

Carbonylation Reactions with CO-Surrogate

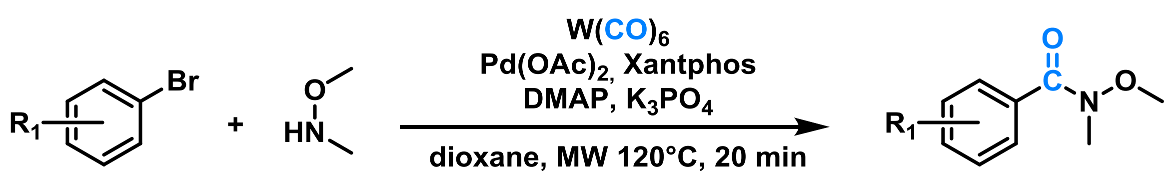
- *In-situ* generation of CO from metal carbonyles



HIV-1 protease inhibitor (35%)



21 examples
45-93%



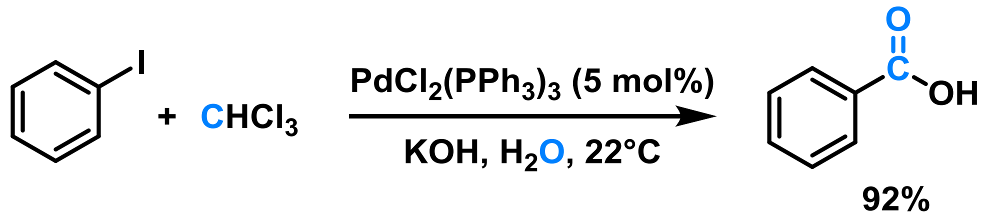
11 examples
20-94%

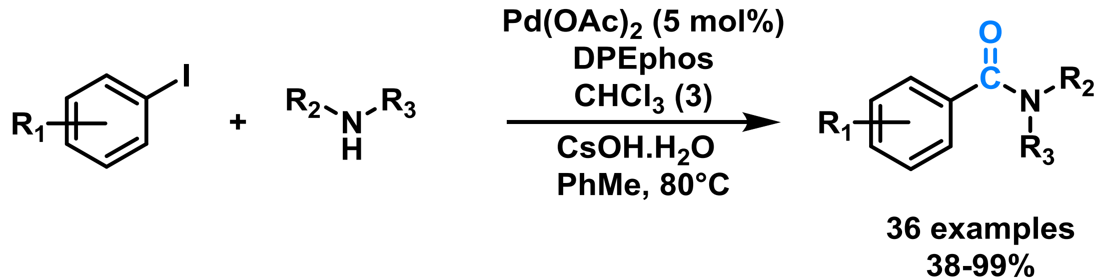
Wu, X., Ekegren, J. K., Larhed, M. *Organometallics* **2006**, *25*, 1434
Odell, L. r.; Savmarker, J.; Larhed, M. *Tetrahedron Lett.* **2008**, *49*, 6115
Wieckowska, A.; Fransson, R.; Odell, L. R., Larhed, M. *J. Org. Chem*. **2011**, *76*, 978

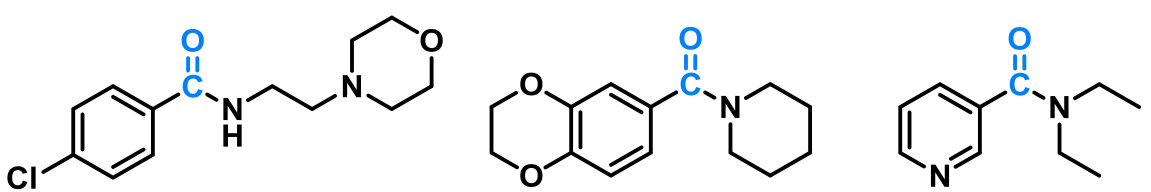
Carbonylation Reactions with CO-Surrogate

- ***In-situ*** **generation of CO from chloroform**

-Pd-catalyzed hydroxycarbonylation of aryl iodide (Alper, 1993; Hull, 2015)







Moclobemide (99%)
anti-depressant

CX-546 (99%)
schizophrenia

Nikethamide (79%)
stimulant

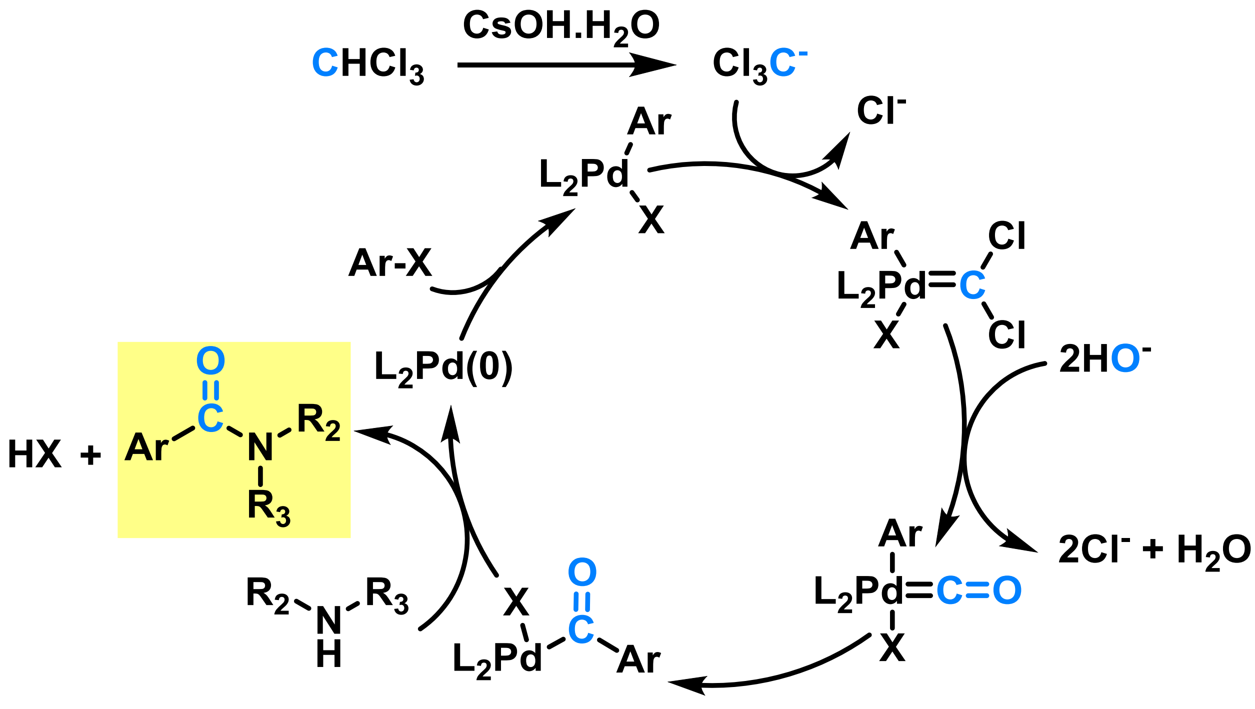
Grushin, V. V.; Alper, H. *Organometallics* **1993**, *12*, 3846
Gockel, S. N.; Hull, K. L. *Org. Lett.* **2015**, *17*, 3236

Carbonylation Reactions with CO-Surrogate

- *In-situ* generation of CO from chloroform

-Pd-catalyzed hydroxycarbonylation of aryl iodide (Alper, 1993; Hull, 2015)

Proposed mechanism for generation of CO



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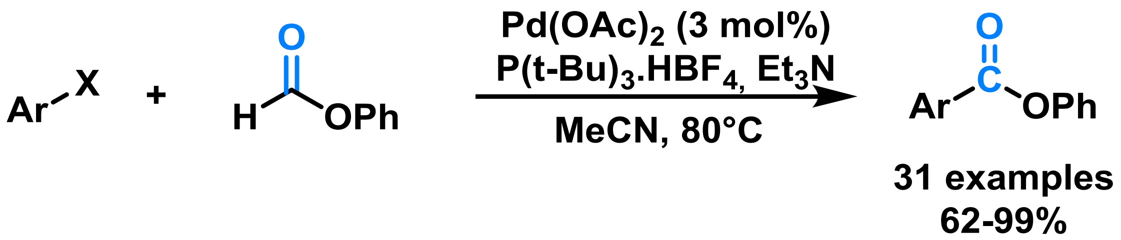
Gockel, S. N.; Hull, K. L. *Org. Lett*. **2015**, *17*, 3236

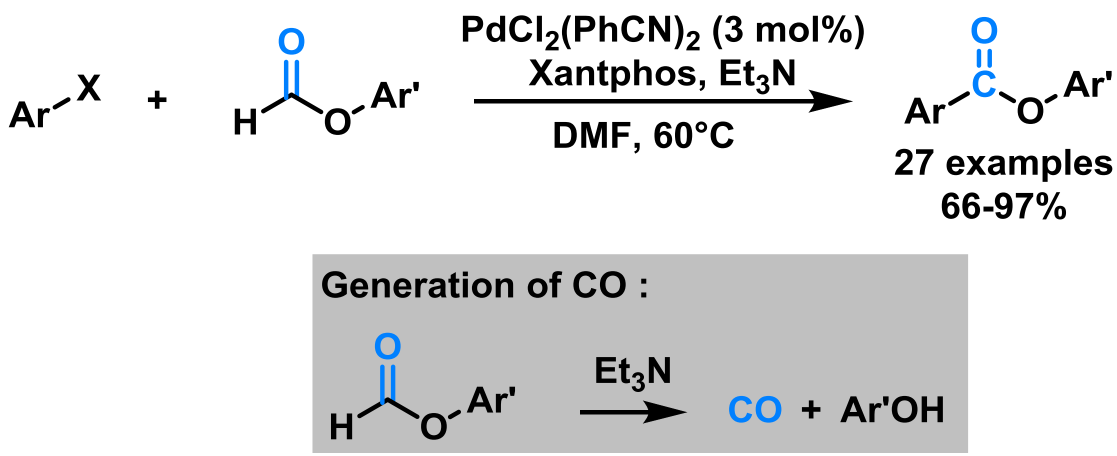
Carbonylation Reactions with CO-Surrogate

- ***In-situ* generation of CO from arylformate**

-Pd-catalyzed alcoxycarbonylation of aryl halide with phenylformate (Manabe, 2012)



-Pd-catalyzed alcoxycarbonylation of aryl halide with arylformate (Tsuji, 2012)

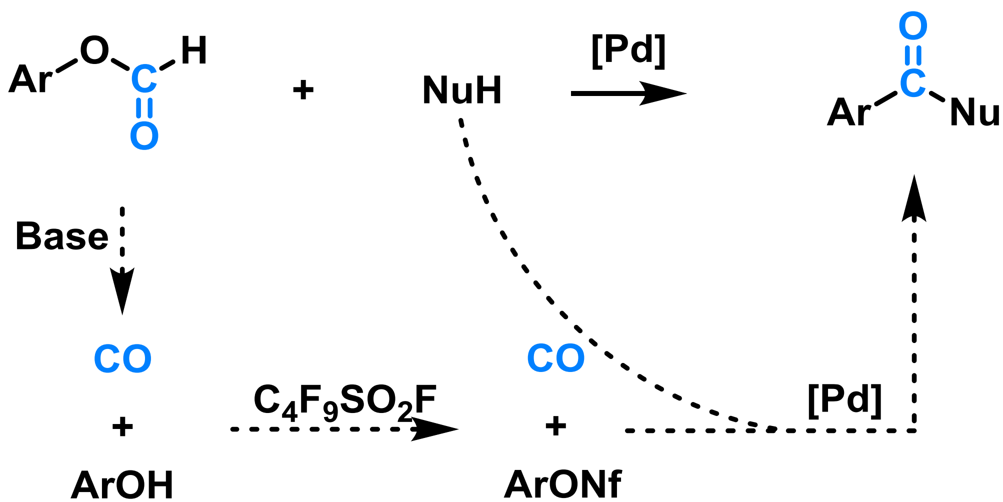


T. Ueda, H. Konishi, K. Manabe, *Org. Lett.* **2012**, *14*, 3100–3103.
T. Fujihara, T. Hosoki, Y. Katafuchi, T. Iwai, J. Terao, Y. Tsuji, *Chem. Commun.* **2012**, *48*, 8012–8014.

Carbonylation Reactions with CO-Surrogate

• ***In-situ* generation of CO from arylformate**

-Pd-catalyzed carbonylation of aryl sulfonyl with arylformate (Beller, 2014)



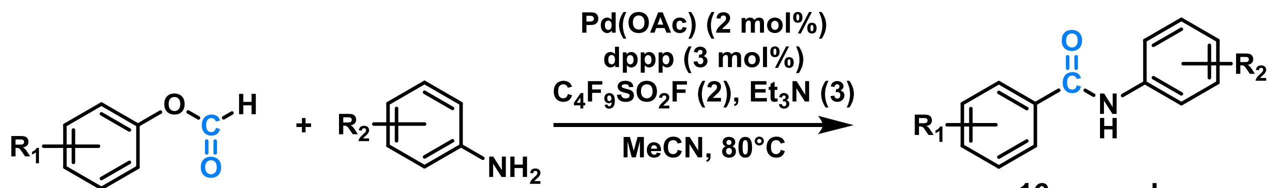
Li, H.; Neumann, H.; Beller, M.; Wu, X.-F. *Ang. Chem. Int. Ed.* **2014**, *53*, 1

Carbonylation Reactions with CO-Surrogate

- *In-situ* generation of CO from arylformate

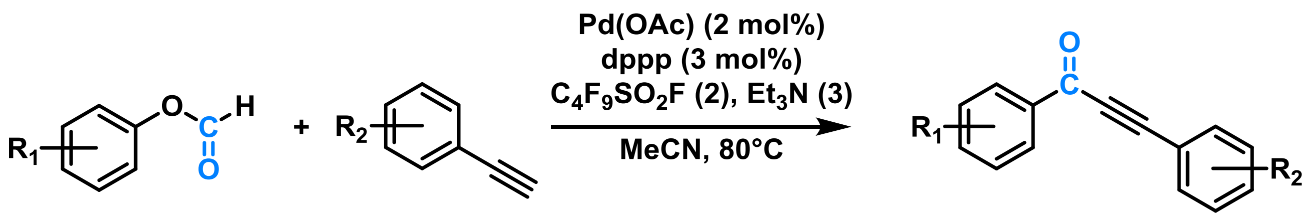
-Pd-catalyzed carbonylation of aryl sulfonyl with arylformate (Beller, 2014)

- Carbonylative synthesis of amides



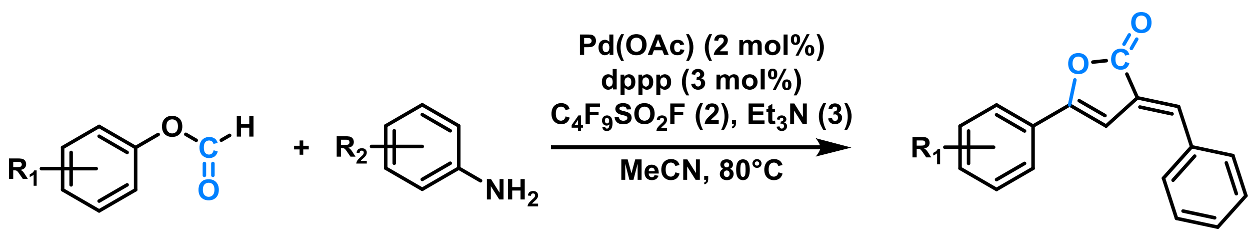
16 examples
50-96%

- Carbonylative synthesis of alkynones



14 examples
54-88%

- Carbonylative synthesis of furanones



3 examples
67-76%

Li, H.; Neumann, H.; Beller, M.; Wu, X.-F. *Ang. Chem. Int. Ed.* **2014**, *53*, 1

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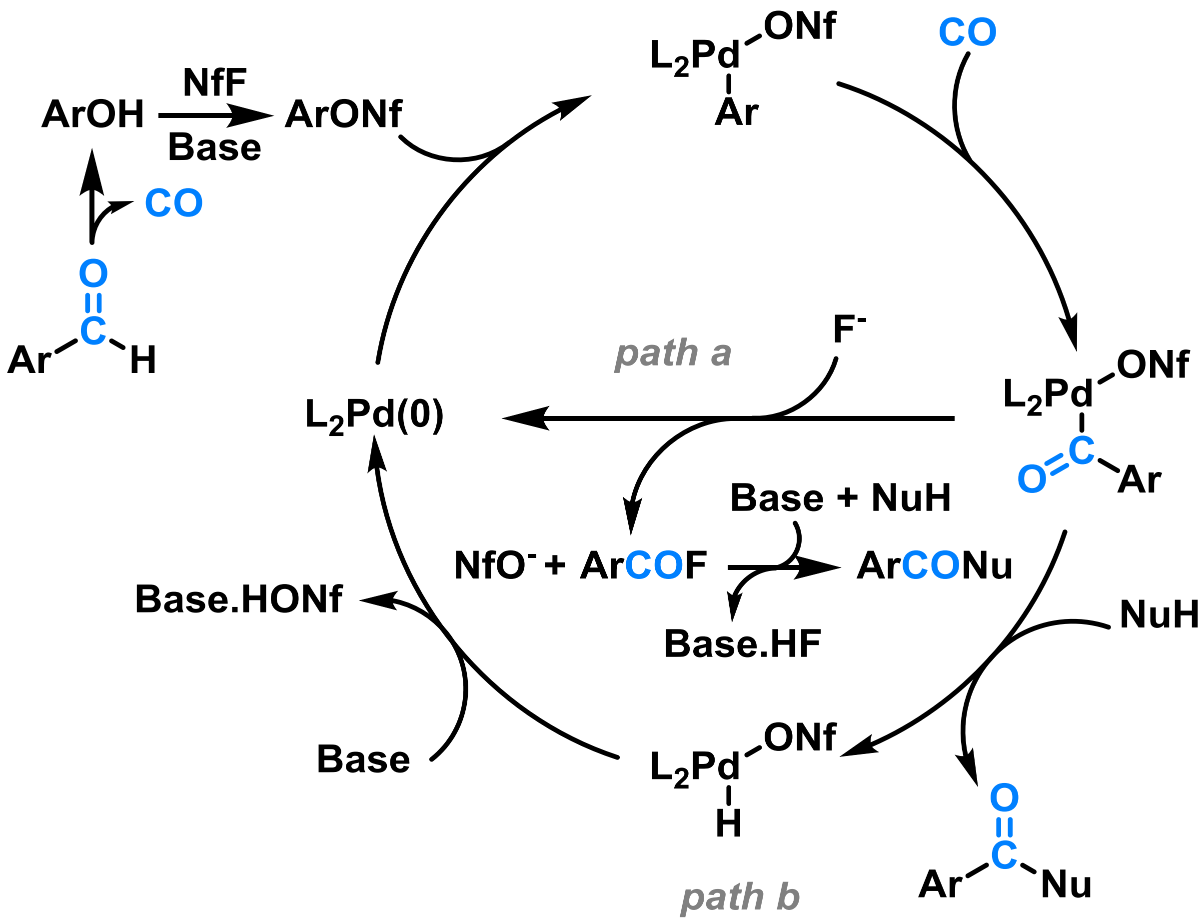
• ***In-situ* generation of CO from arylformate**

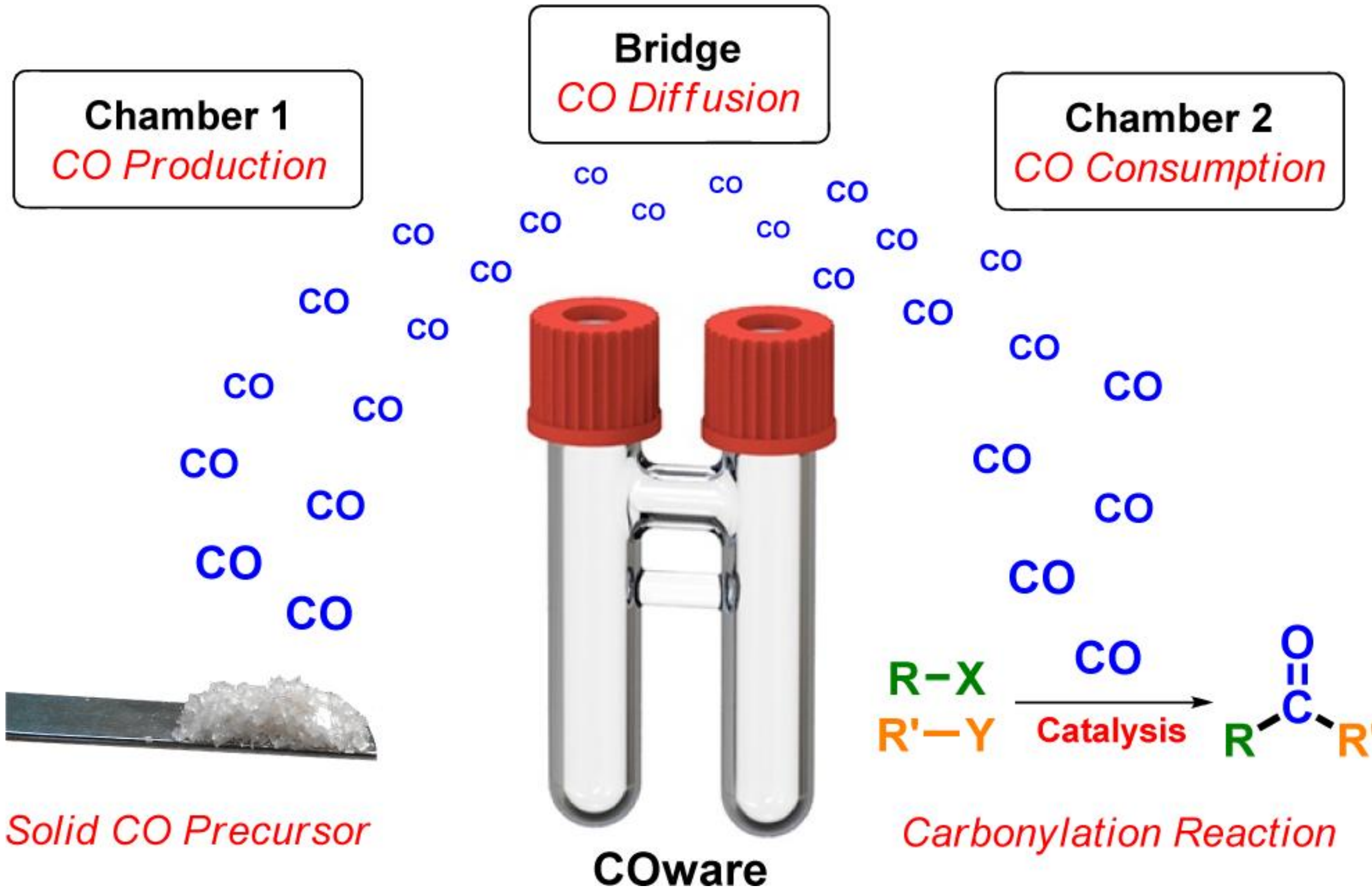
-**Pd-catalyzed carbonylation of aryl sulfonyl with arylformate (Beller, 2014)**



Li, H.; Neumann, H.; Beller, M.; Wu, X.-F. *Ang. Chem. Int. Ed.* **2014**, *53*, 1

Carbonylation Reactions with CO-Surrogate

- ***Ex-situ*** **generation of CO : Two-chamber reactors and CO precursors**



Friis, S.; Lindhardt, A. T.; Skrydstrup, T. *Acc. Chem. Res.* **2016**, *49*, 594

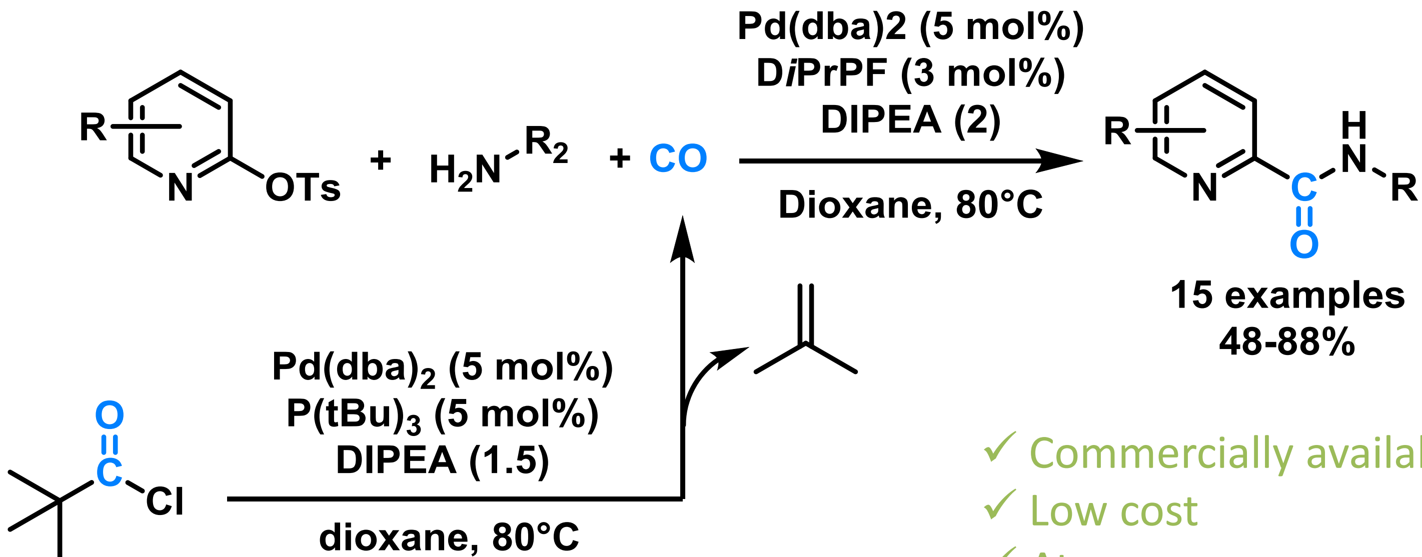
P. Hermange, A. T. Lindhardt, R. H. Taaning, K. Bjerglund, D. Lupp, T. Skrydstrup, *J. Am. Chem. Soc.* **2011**, *133*, 6061

Carbonylation Reactions with CO-Surrogate

- ***Ex-situ*** **generation of CO : Two-chamber reactors and CO precursors**

- First generation precursor : pivaloyl chloride

CO consuming chamber



CO producing chamber

✓ Commercially available
✓ Low cost
✓ Atom economy

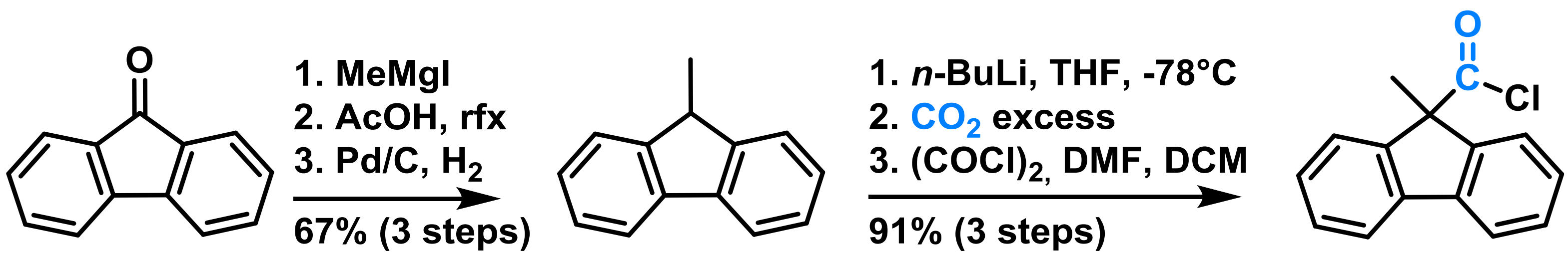
X Pollution of CO consuming chamber with isobutene gas

Friis, S.; Lindhardt, A. T.; Skrydstrup, T. *Acc. Chem. Res.* **2016**, *49*, 594
P. Hermange, A. T. Lindhardt, R. H. Taaning, K. Bjerglund, D. Lupp, T. Skrydstrup, *J. Am. Chem. Soc.* **2011**, *133*, 6061

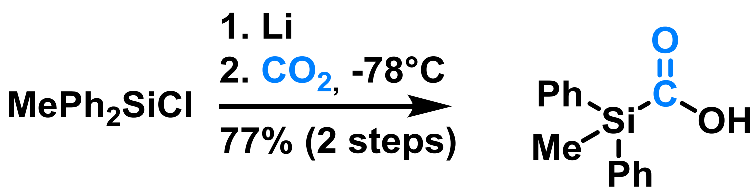
Carbonylation Reactions with CO-Surrogate

- ***Ex-situ* generation of CO : Two-chamber reactors and CO precursors**

- Second generation precursors : Cogen and SilaCogen

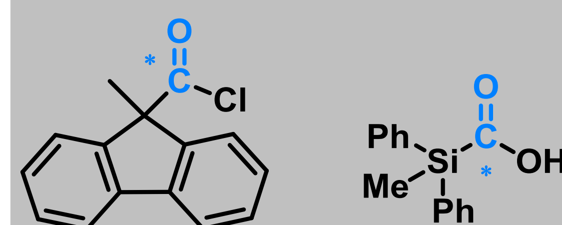


COgen
9-methylfluorene-9-carbonyl chloride



SilaCOgen
methyldiphenylsilacarboxylic acid

Labelling from $^{13}CO_2$ and $^{14}CO_2$



^{13}COgen : 73%
^{14}COgen : 88%
Sila^{13}COgen : 99%

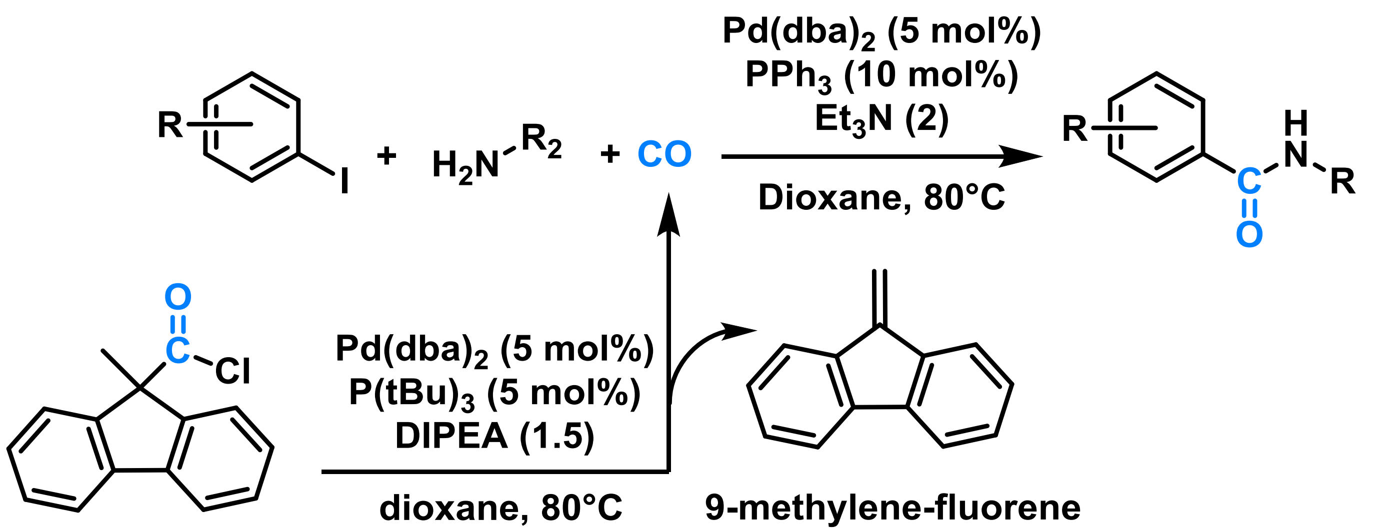
Friis, S.; Lindhardt, A. T.; Skrydstrup, T. *Acc. Chem. Res.* **2016**, *49*, 594
P. Hermange, A. T. Lindhardt, R. H. Taaning, K. Bjerglund, D. Lupp, T. Skrydstrup, *J. Am. Chem. Soc.* **2011**, *133*, 6061

Carbonylation Reactions with CO-Surrogate

- ***Ex-situ*** **generation of CO : Two-chamber reactors and CO precursors**

- Application : Pd-catalyzed aminocarbonylation of aryl halide using COgen

CO consuming chamber



CO producing chamber

Friis, S.; Lindhardt, A. T.; Skrydstrup, T. *Acc. Chem. Res.* **2016**, *49*, 594
P. Hermange, A. T. Lindhardt, R. H. Taaning, K. Bjerglund, D. Lupp, T. Skrydstrup, *J. Am. Chem. Soc.* **2011**, *133*, 6061

Carbonylation Reactions with CO-Surrogate

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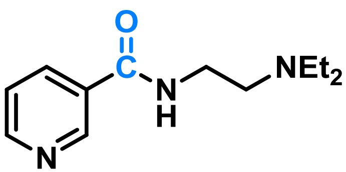
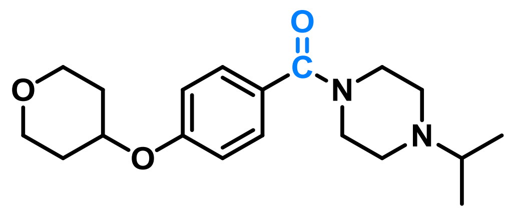
- Application : Pd-catalyzed aminocarbonylation of aryl halide using COgen

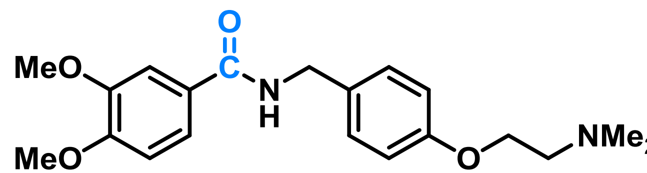
Preparation of biologically relevant structure :



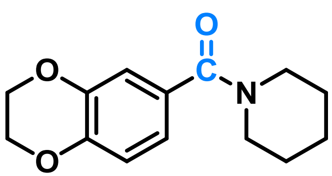
PET tracer for melanoma (86%)



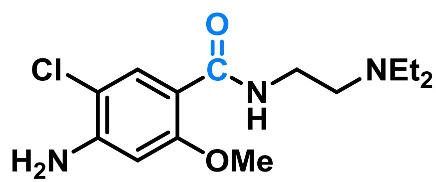
H3-receptor antagonist (83%)



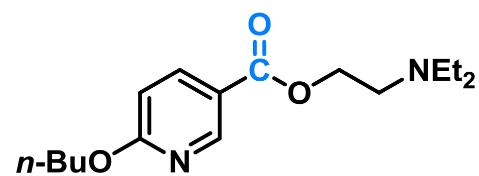
Itopride (94%)



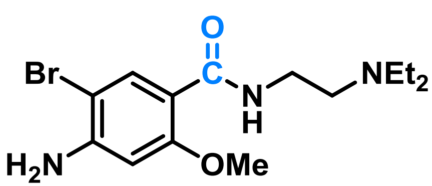
CX-546 (83%



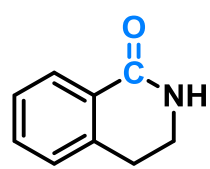
Metaclopramide (63%)



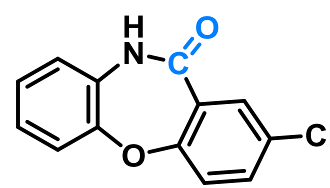
Butoxycaine (89%)



Bromopride (65%)



Core of PARP1 inh. (84%)



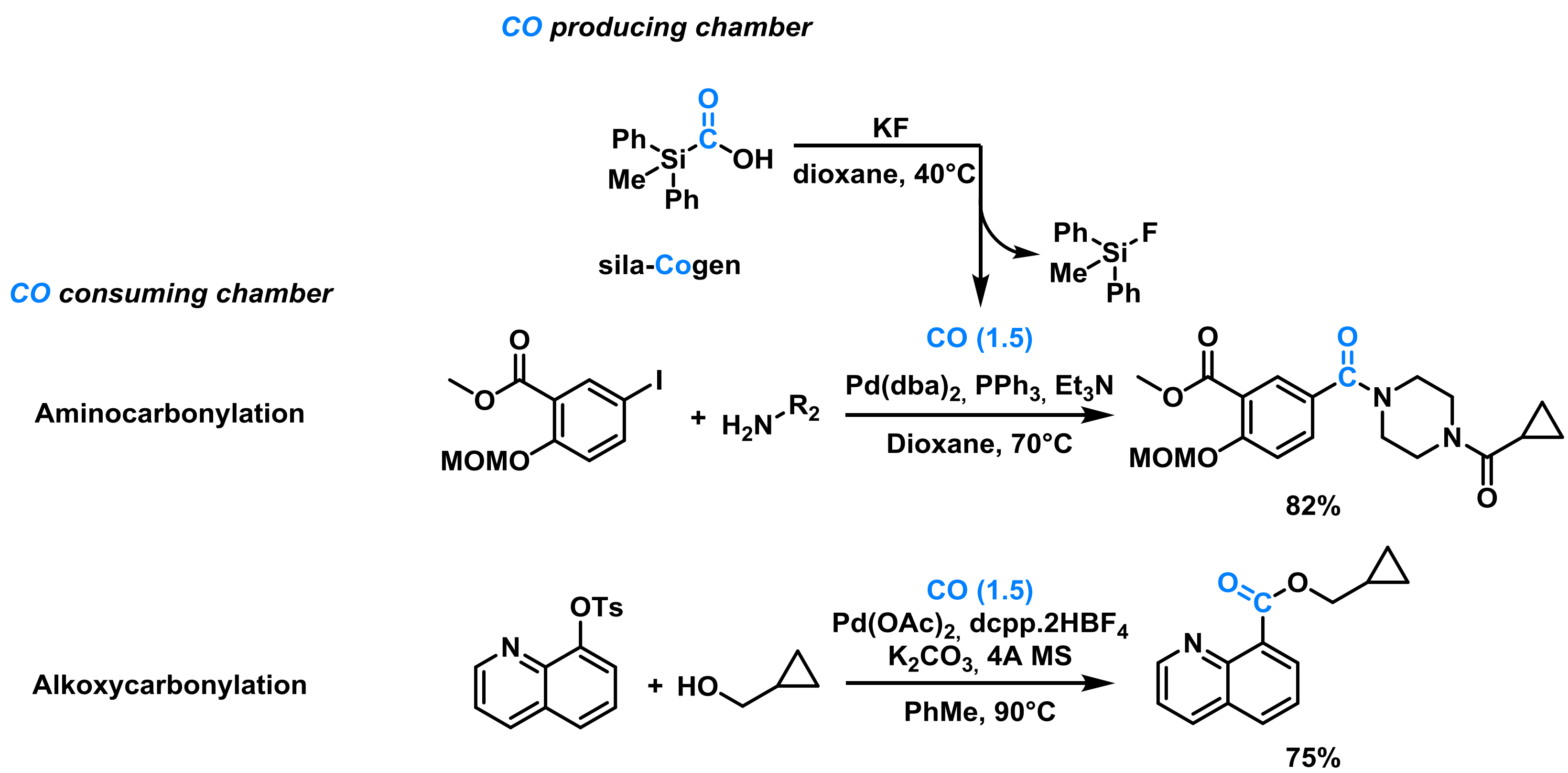
Loxapine precursor (79%)

Friis, S.; Lindhardt, A. T.; Skrydstrup, T. *Acc. Chem. Res.* **2016**, *49*, 594
P. Hermange, A. T. Lindhardt, R. H. Taaning, K. Bjerglund, D. Lupp, T. Skrydstrup, *J. Am. Chem. Soc.* **2011**, *133*, 6061

Carbonylation Reactions with CO-Surrogate

• ***Ex-situ*** **generation of CO : Two-chamber reactors and CO precursors**

- Application : Pd-catalyzed carbonylation of aryl halide using SilaCOgen



Friis, S.; Lindhardt, A. T.; Skrydstrup, T. *Acc. Chem. Res.* **2016**, *49*, 594
Friis, S.; Taaning, R. H., Lindhardt, A. T.; Skrydstrup, T. *J. Am. Chem. Soc.* **2011**, *133*, 18114

Carbonylation Reactions with CO-Surrogate

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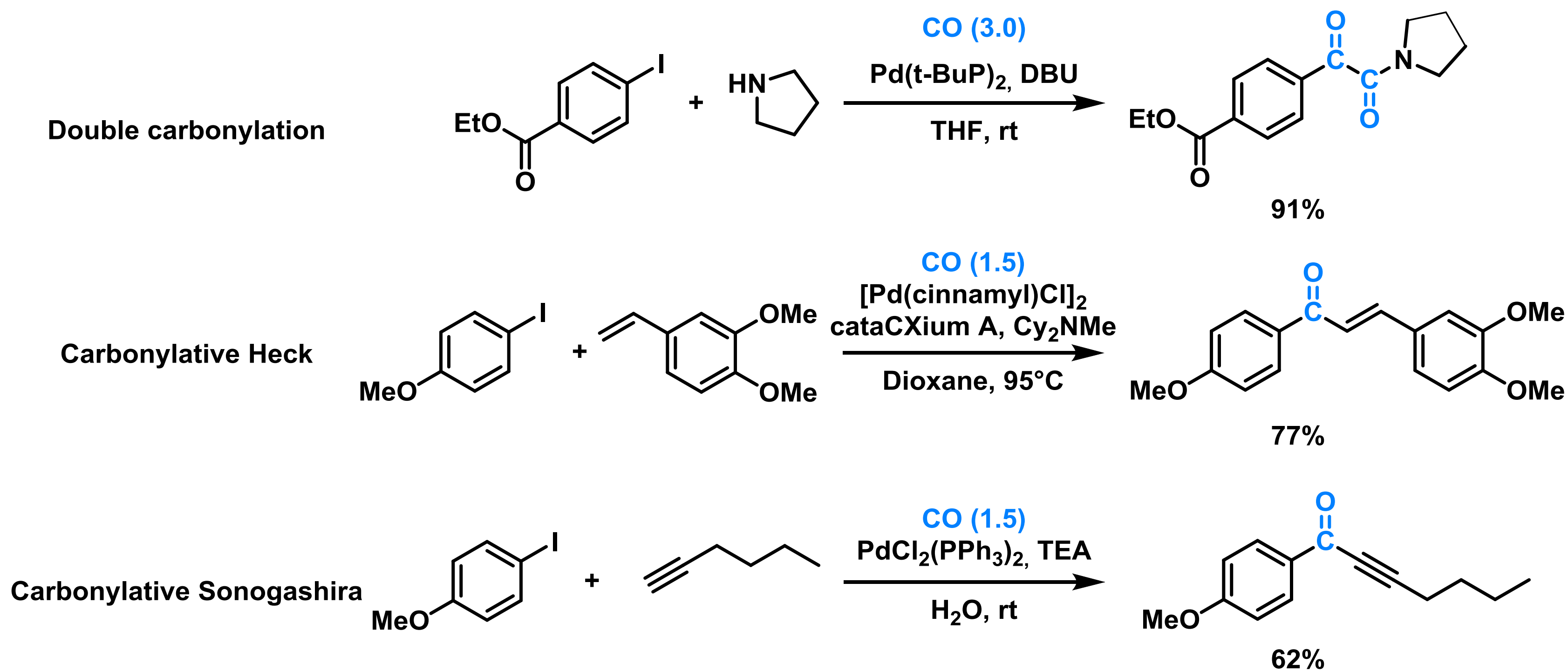
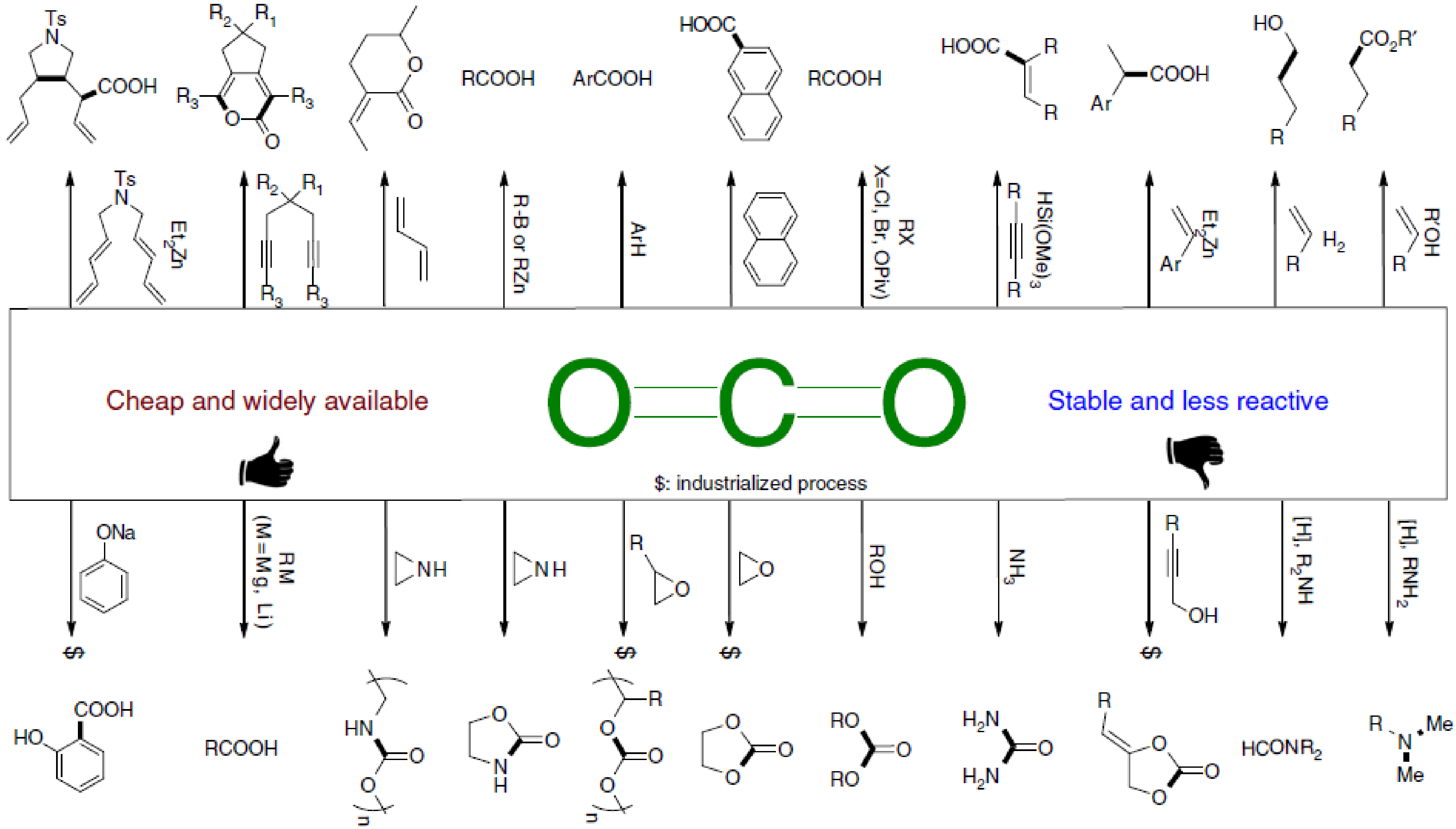


Friis, S.; Lindhardt, A. T.; Skrydstrup, T. *Acc. Chem. Res.* **2016**, *49*, 594

Friis, S.; Taaning, R. H., Lindhardt, A. T.; Skrydstrup, T. *J. Am. Chem. Soc.* **2011**, *133*, 18114

Carbonylation Reactions Using CO_2 as CO-Surrogate



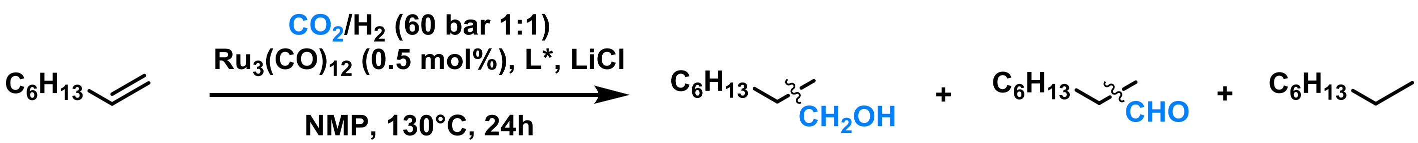
Liu, Q.; Wu, L.; Fleisher, I.; Jackstell, R.; Beller, M. *Nat. Commun*. **2014**, *6*, 5933
Morimoto, T.; Kakiuchi, K. *Angew. Chem. Int. ed.* **2004**, *43*, 5580

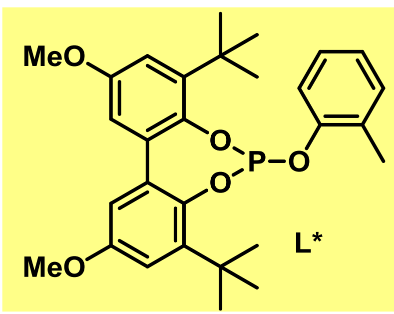
Carbonylation Reactions Using CO_2 as CO-Surrogate

- **Catalytic production of CO from reduction of CO_2**

- Using H_2 as reductant

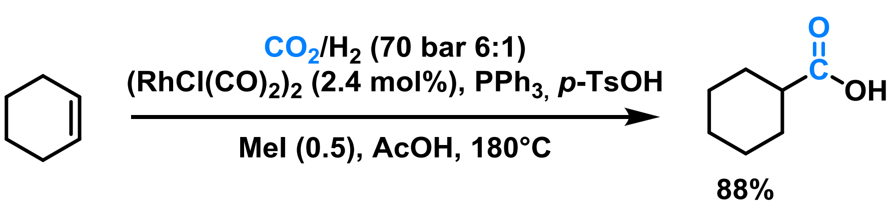
Tominaga *et al.*, 2000 and Beller *et al.*, 2014 : Ru-catalyzed hydroformylation of alkenes





L*	76% (*n*/*iso* 49:51)	1%	15%	TON_{Ru} : 200
No ligand	33% (*n*/*iso* 49:51)	6%	22%	TON_{Ru} : <20

Leitner *et al.*, 2013 : Rh- catalyzed Hydrocarboxylation of olefins



Tominaga, K.-I.; Sasaki, Y. *Cat. Commun*. **2000**, *1*, 1

Liu, Q.; Wu, L.; Fleisher, I.; Selent, D.; Franke, R.; Jackstell, R.; Beller, M. *Chem. Eur. J.* **2014**, *20*, 6888

Ostapowiz, T. G.; Schmitz, M.; Krystof, M.; Klankermayer, J.; Leitner, W. *Angew. Chem. Int. ed.* **2013**, *52*, 12119

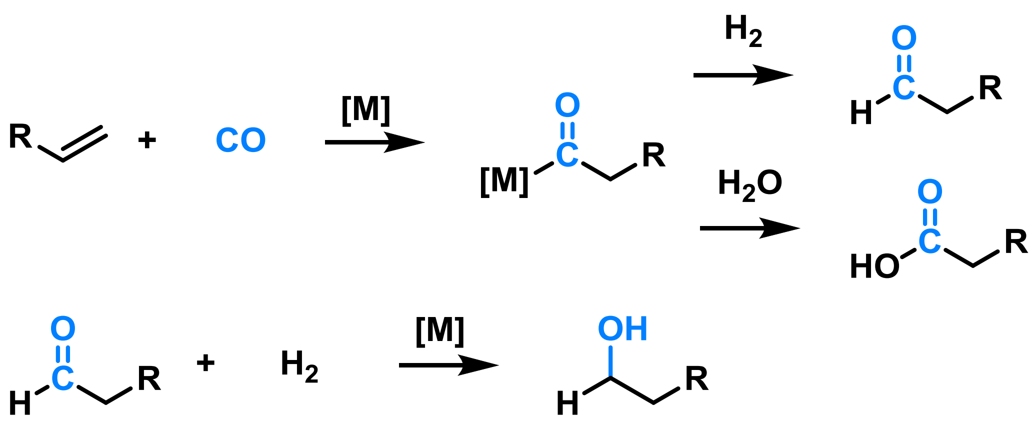
Carbonylation Reactions Using CO_2 as CO-Surrogate

- **Catalytic production of CO from reduction of CO_2**

- Using H_2 as reductant

Proposed pathway for the generation of CO :

$$CO_2 + H_2 \xrightarrow{[M]} CO + H_2O \qquad (1)$$



(2)

(3)

Tominaga, K.-I.; Sasaki, Y. *Cat. Commun*. **2000**, *1*, 1
Liu, Q.; Wu, L.; Fleisher, I.; Selent, D.; Franke, R.; Jackstell, R.; Beller, M. *Chem. Eur. J.* **2014**, *20*, 6888
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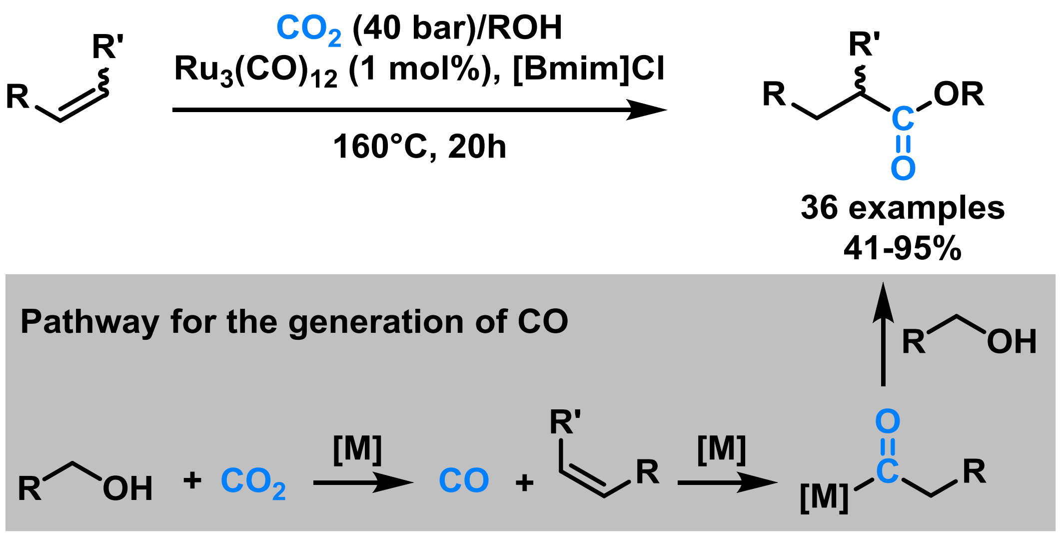
Carbonylation Reactions Using CO_2 as CO-Surrogate

- **Catalytic production of CO from reduction of CO_2**

- Using Alcohol as reductant

Beller *et al.*, 2013 : Ru-catalyzed alkoxycarbonylation of olefins with CO_2



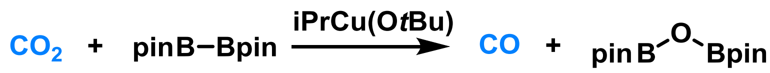
Wu, L.; Liu, Q.; Fleisher, I.; Jackstell, R.; Beller, M. *Nat. Commun.* **2013**, *5*, 1

Carbonylation Reactions Using CO_2 as CO-Surrogate

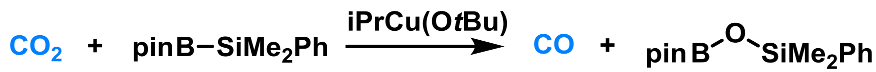
- **Catalytic production of CO from reduction of CO_2**

- Copper catalyzed oxygen abstraction of diboron or Borosilane

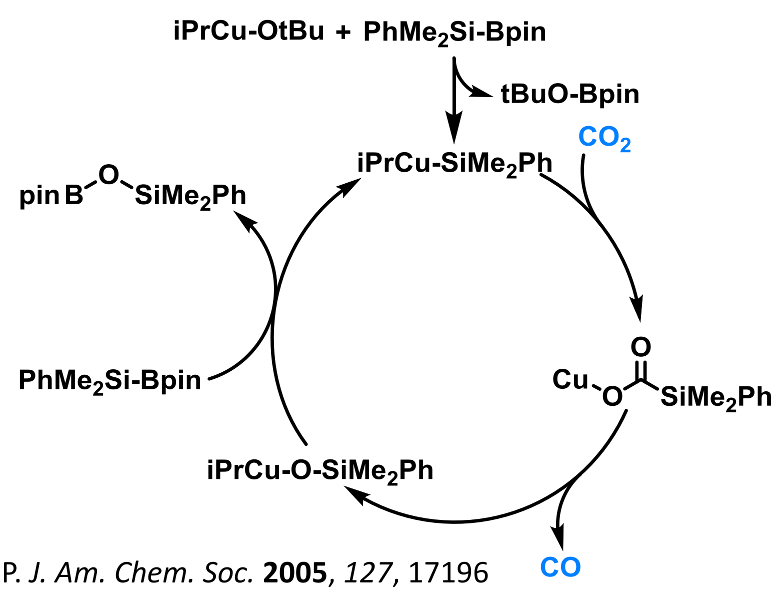
Sadighi *et al.*, 2005



Kleeberg *et al.*, 2011

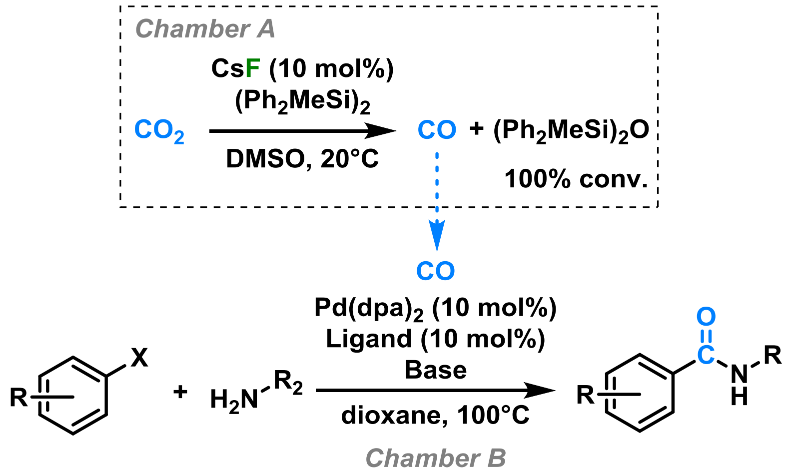


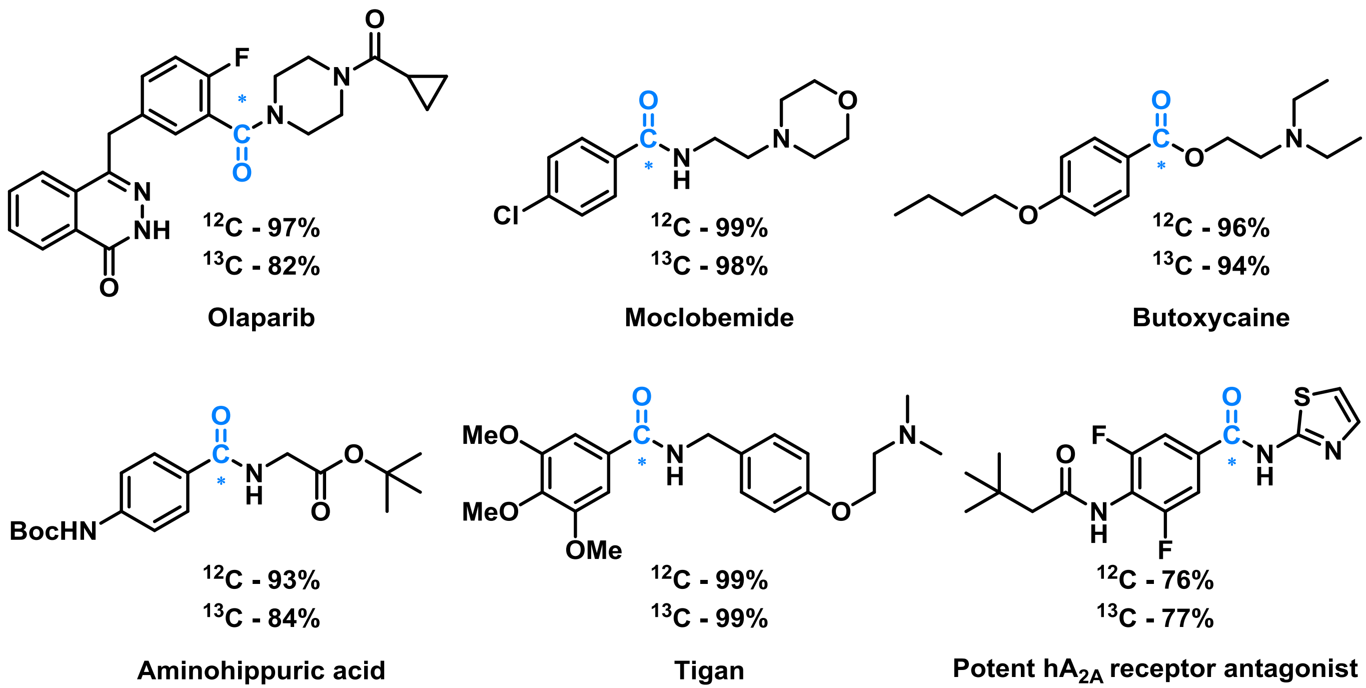
Proposed catalytic cycle for the Cu-catalyzed reduction of CO_2 to CO



Laitar, D. S.; Muller, P., Sadighi, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 17196
Kleeberg, C.; Cheung, M. S.; Lin, Z.; Marder, T. B. *J. Am. Chem. Soc.* **2011**, *133*, 19060

Fluoride-Catalyzed Conversion of CO_2 to CO Using Disilanes





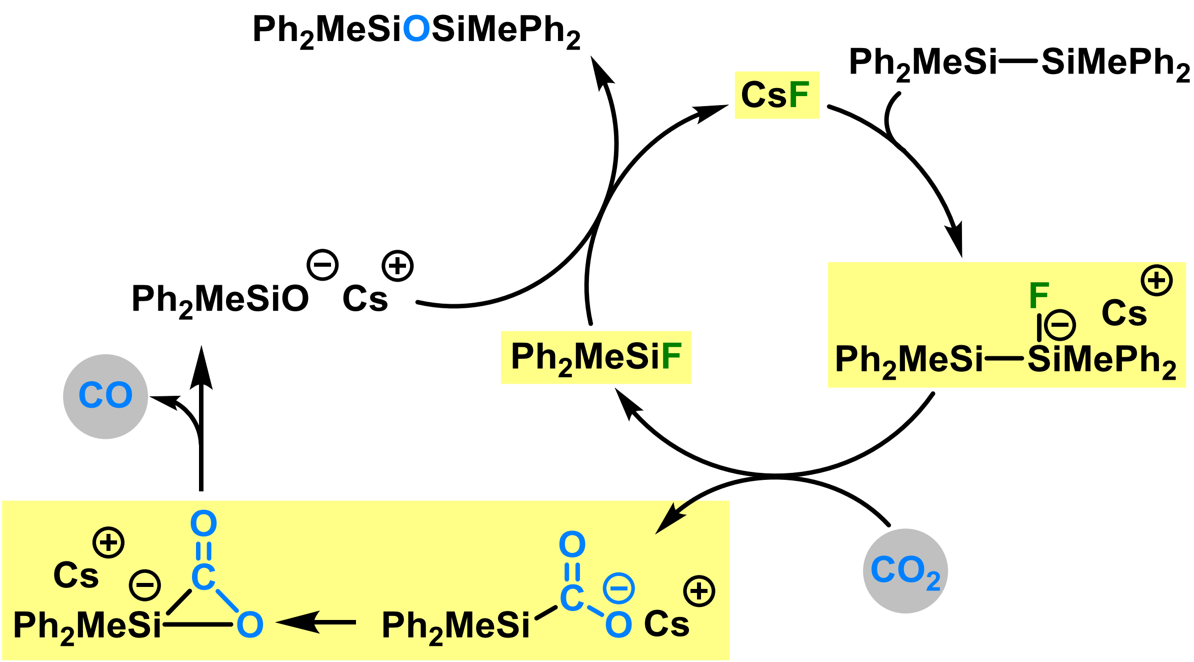
Lescot, C.; Nielsen, D. U.; Makarov, I. S.; Lindhart, A. T.; Daasbjerg, K., Skrydstrup, T. *J. Am. Chem. Soc.* **2014**, *136*, 6142

Fluoride-Catalyzed Conversion of CO_2 to CO Using Disilanes

- **Catalytic production of CO from reduction of CO_2**

- Proposed pathway

Stoechiometric silicon by-product



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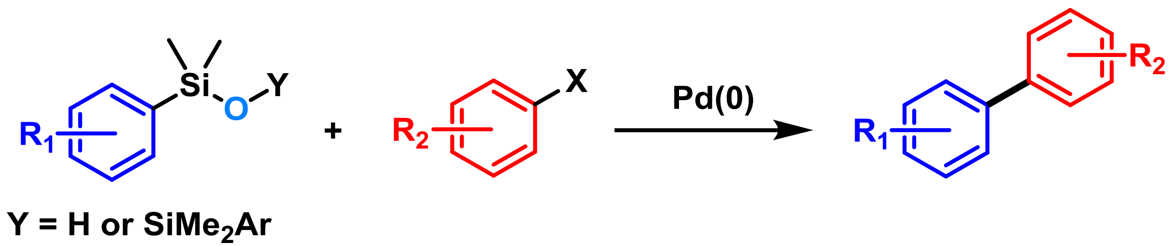
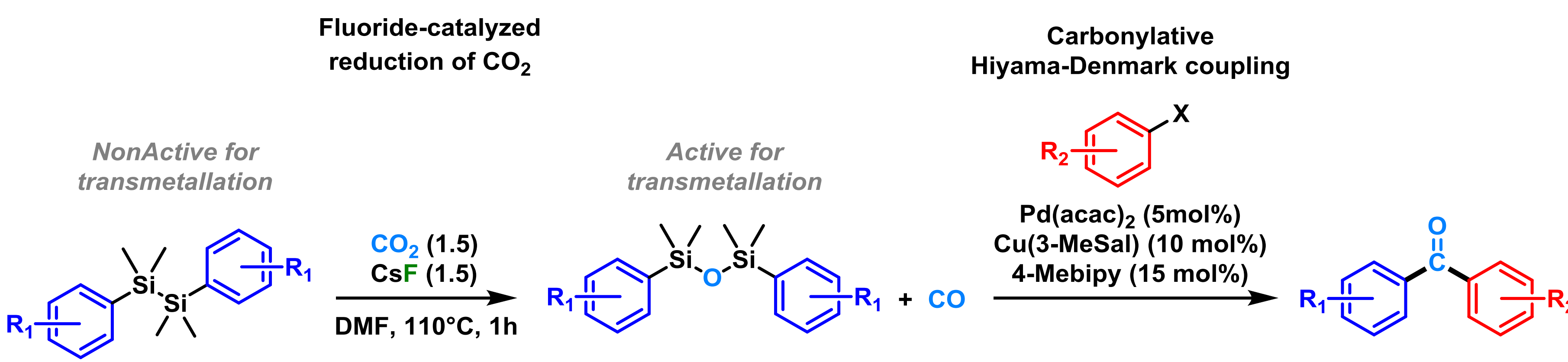
Fluoride-Catalyzed Conversion of CO_2 to CO Using Disilanes

- **Hiyama-Denmark cross-coupling**



- **Cooperative redox activation of CO_2/Carbonylative Hiyama-Denmark coupling**



Lian, Z.; Nielsen, D. U.; Lindhart, A. T.; Daasbjerg, K., Skrydstrup, T. *Nat. Commun*. **2016**, *7*, 13782

Fluoride-Catalyzed Conversion of CO_2 to CO Using Disilanes

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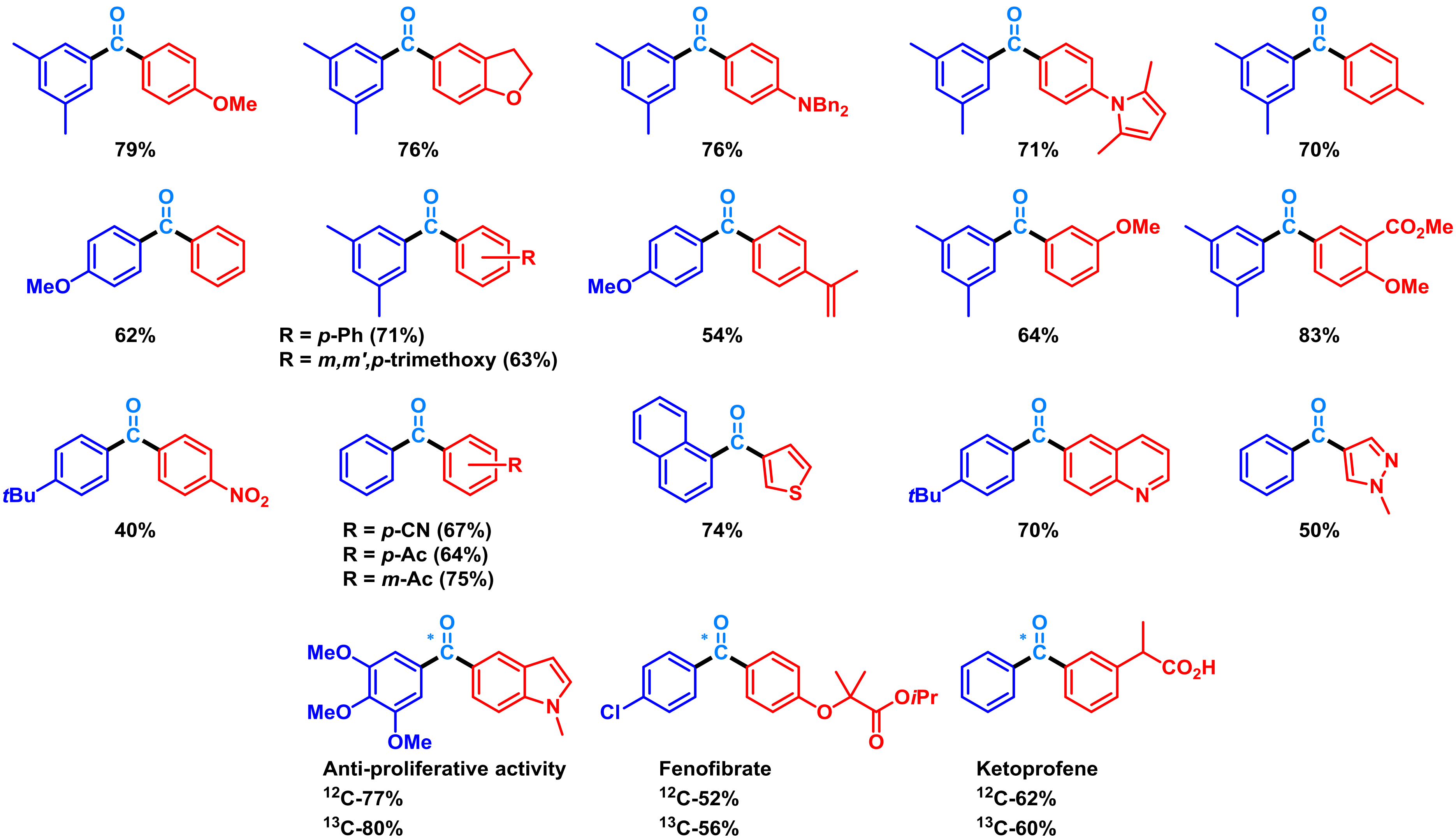

Lian, Z.; Nielsen, D. U.; Lindhart, A. T.; Daasbjerg, K., Skrydstrup, T. *Nat. Commun*. **2016**, *7*, 13782

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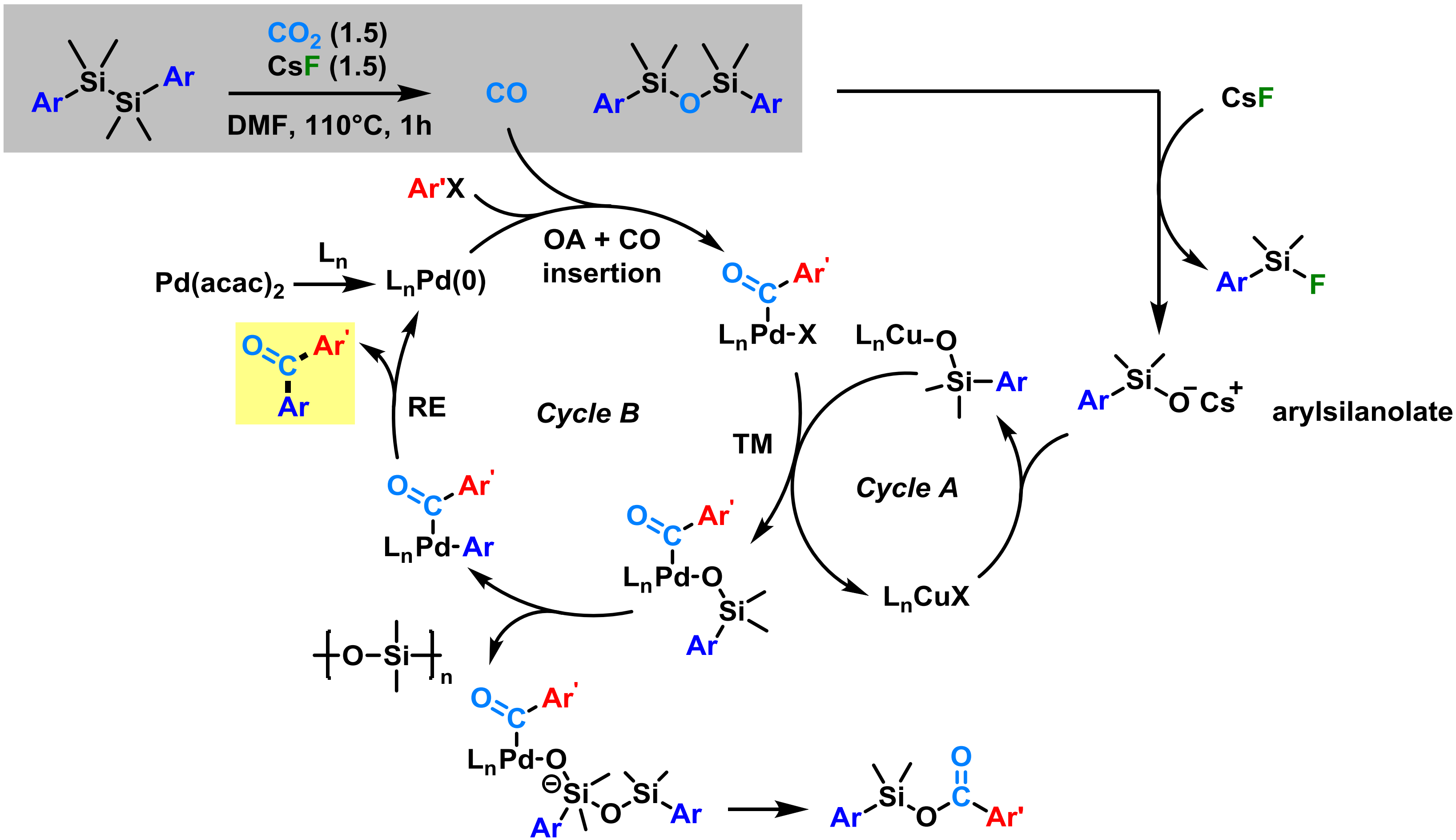
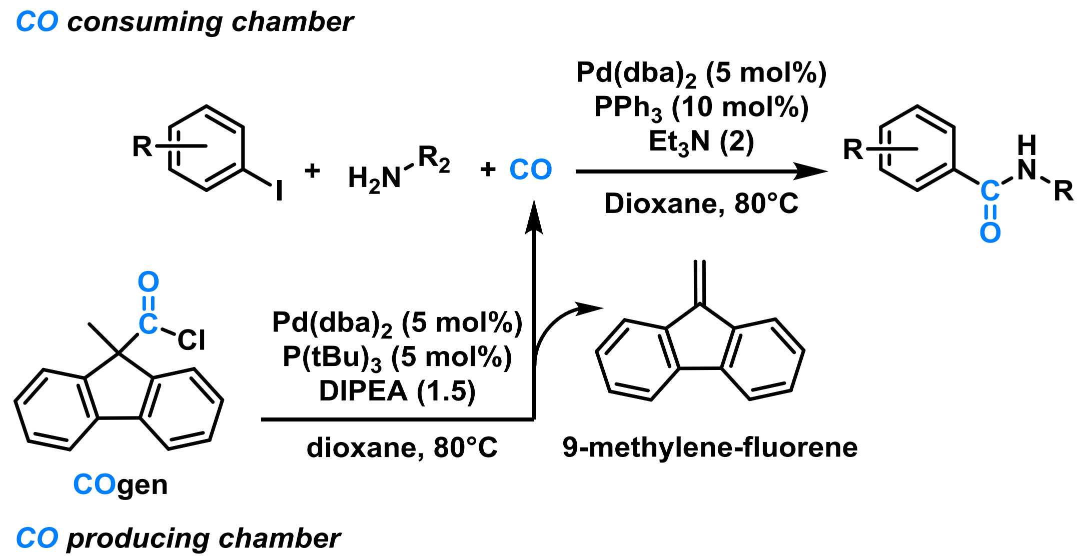


Lian, Z.; Nielsen, D. U.; Lindhart, A. T.; Daasbjerg, K., Skrydstrup, T. *Nat. Commun*. **2016**, *7*, 13782

Conclusion

- *Ex-situ* generation of CO using CO precursor in a double chamber



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