

Harnessing non-covalent interactions to exert control over regioselectivity and site-selectivity in catalytic reactions

Holly J. Davis and Robert J. Phipps*

*Reporter: Li Li
Supervisor: Yong Huang
Date: 2017-9-11*

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2 Control of regioselectivity in catalytic reactions

- 2.1 Regioselective functionalisation of arenes
- 2.2 Regioselective functionalisation of alkynes
- 2.3 Regioselective functionalisation of alkenes
- 2.4 Regioselective functionalisation of ketones

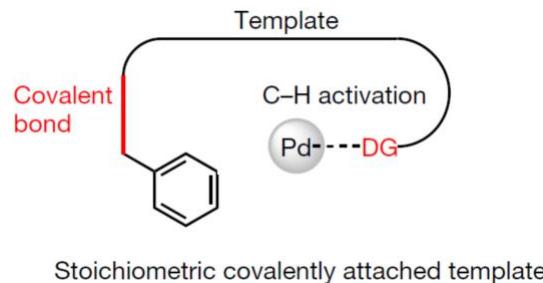
3 Control of site-selectivity in catalytic reactions

- 3.1 Site-selective aliphatic C–H functionalisation
- 3.2 Site-selective alkene functionalisation

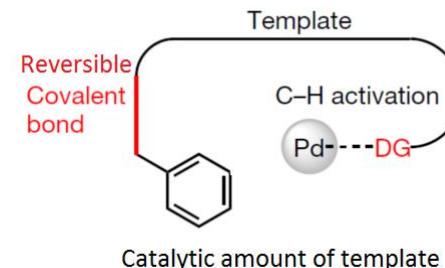
4 Conclude and acknowledge

1 Introduction

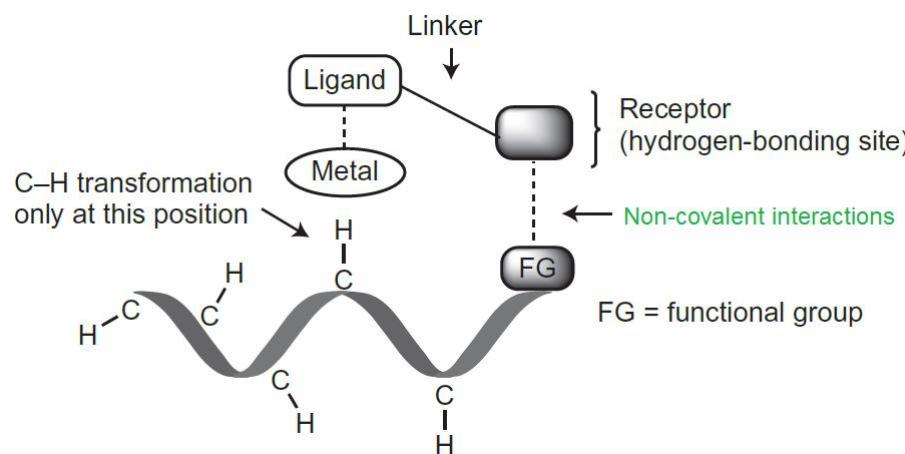
Type I



Type II

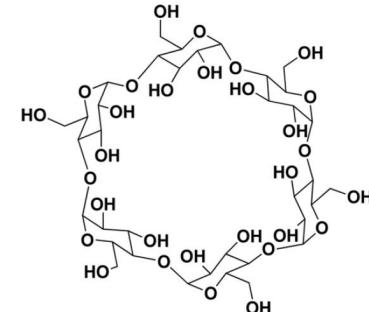
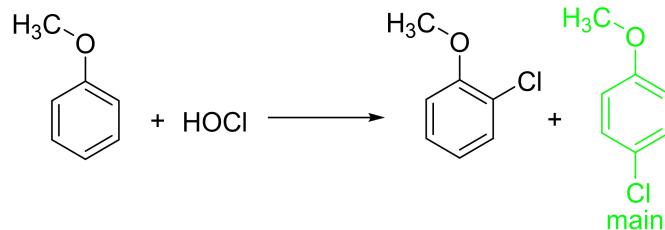


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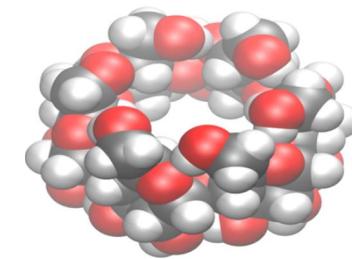
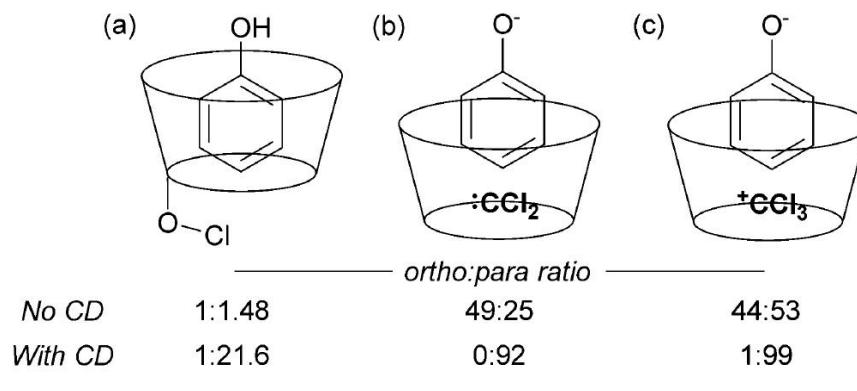


1 Introduction

R. Breslow



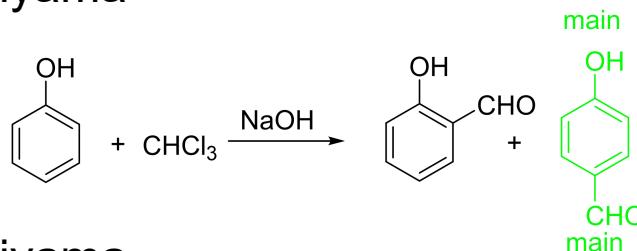
cyclodextrin:
schematic structure



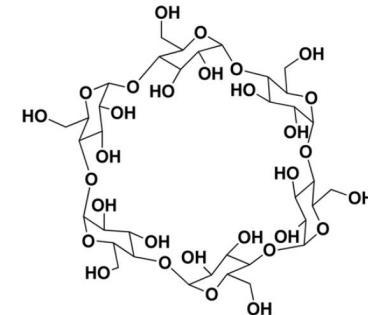
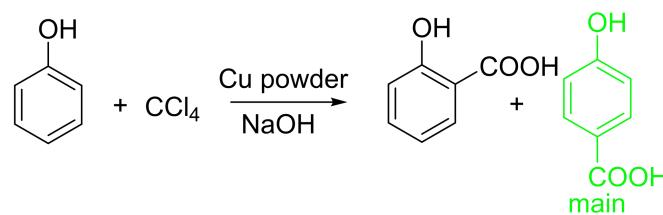
cyclodextrin:
space-filling structure

1 Introduction

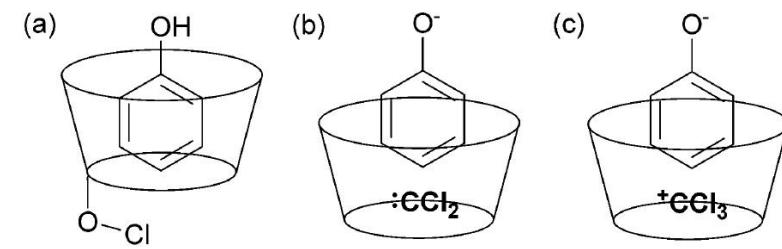
M. Komiya



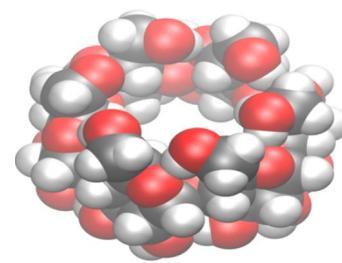
M. Komiya



cyclodextrin:
schematic structure



	ortho:para ratio	
No CD	1:1.48	
With CD	1:21.6	



cyclodextrin:
space-filling structure

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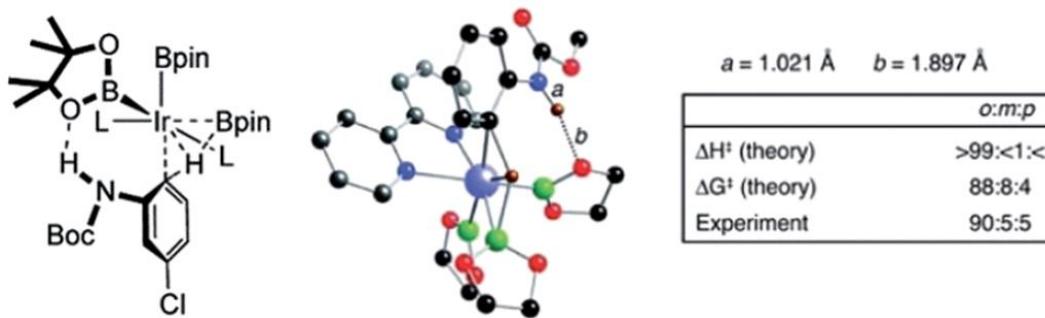
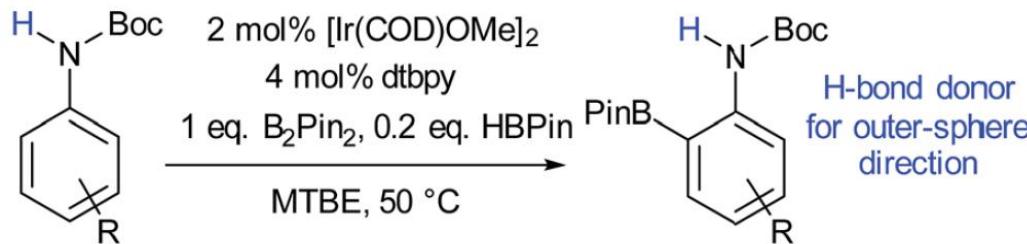
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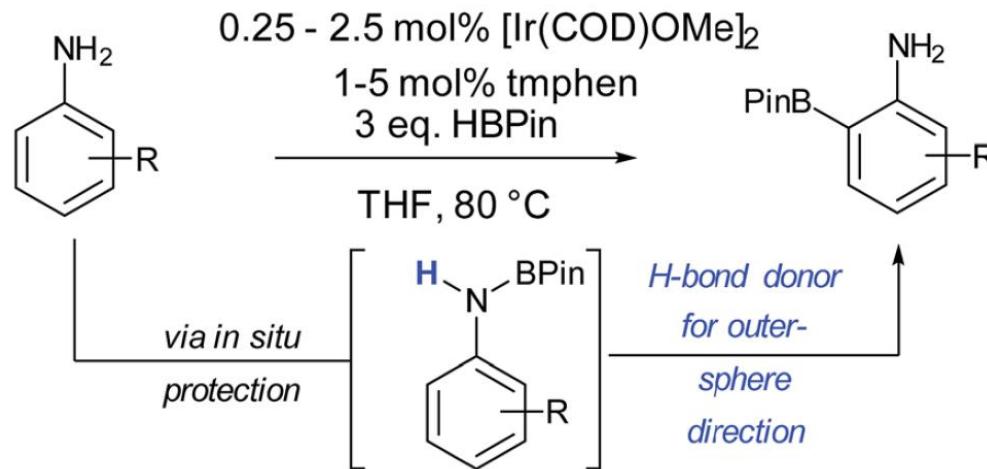
M. R. Smith



Proposed transition state (theoretical predictions and calculations of N–H and O–H bond distances in the TS.)

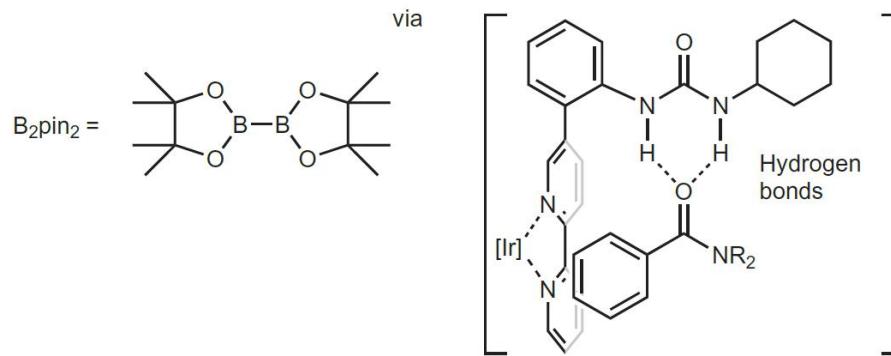
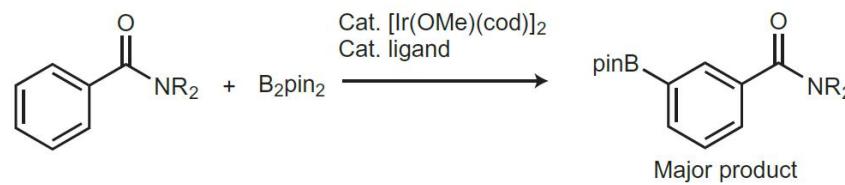
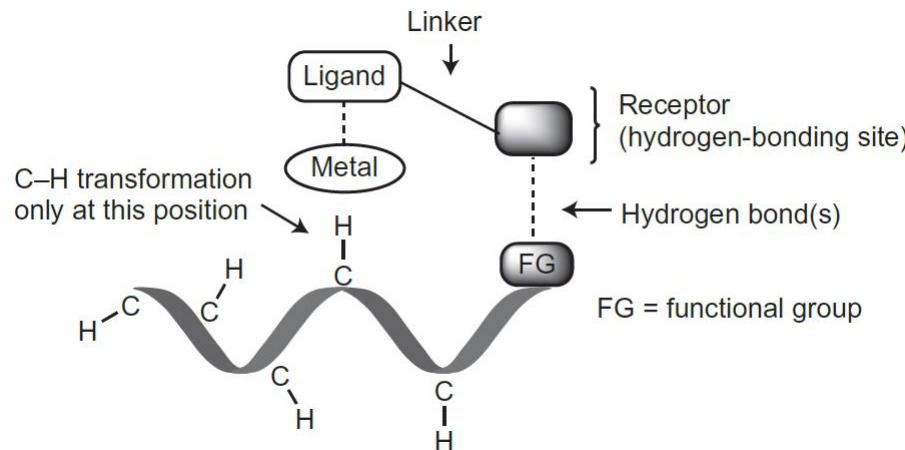
2.1 Regioselective functionalisation of arenes

M. R. Smith

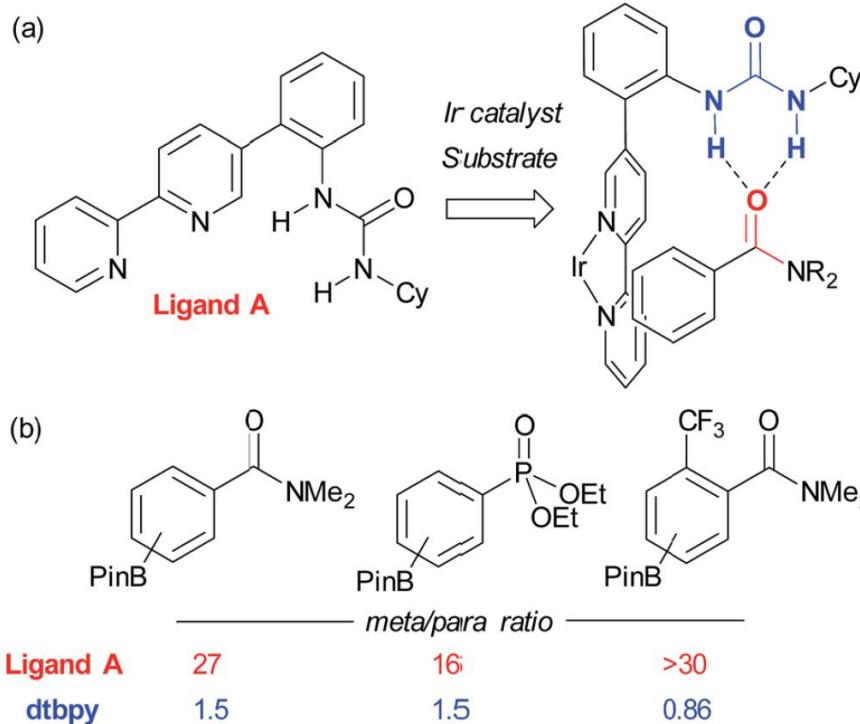


ortho-Selective borylation of anilines
(*in situ* formation of N-BPin derivative)

2.1 Regioselective functionalisation of arenes



2.1 Regioselective functionalisation of arenes

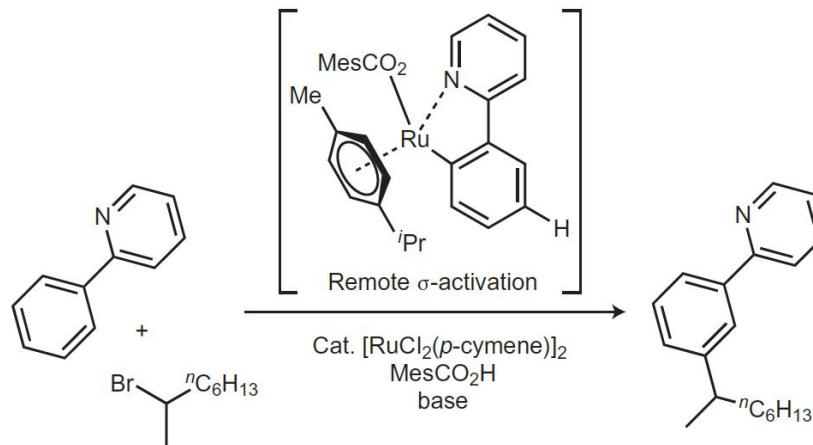


Typical Reaction conditions: 1.5 mol% $[\text{Ir}(\text{COD})\text{OMe}]_2$, 3 mol% Ligand A,
1.5 eq. IB_2Pin_2 , *p*-Xylene, 25 °C

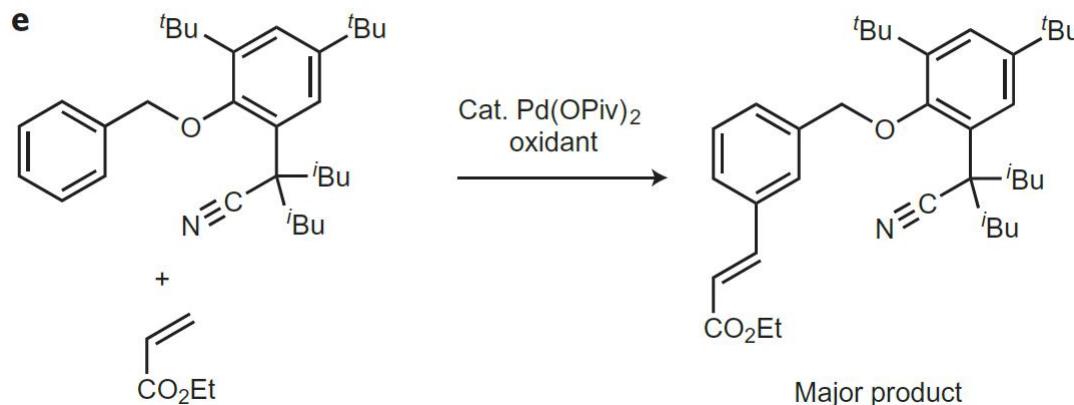
A selection of substrates, highlighting *meta:para* selectivity for both the optimal bifunctional ligand and standard borylation ligand dtbpy

2.1 Regioselective functionalisation of arenes

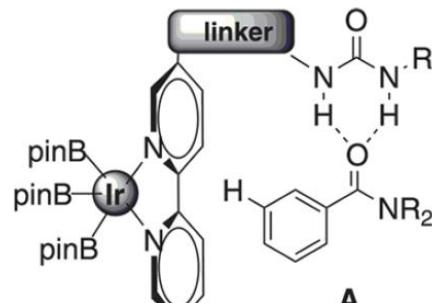
A strong *para*-directing effect from the ruthenium centre



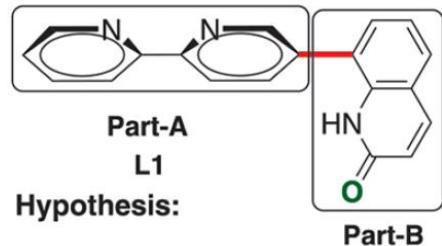
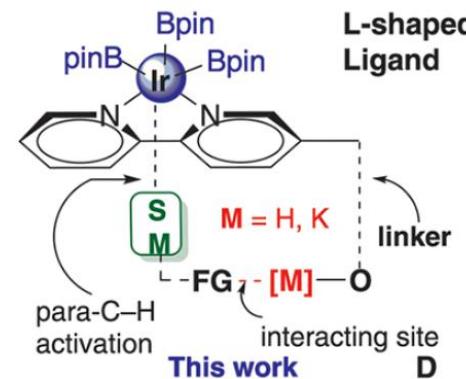
A directing group



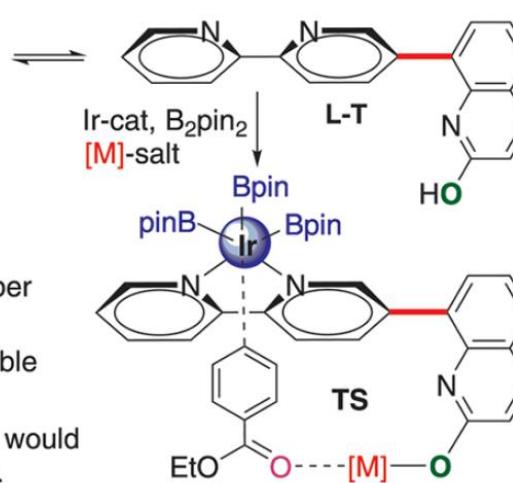
2.1 Regioselective functionalisation of arenes



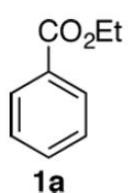
hydrogen bond directed
Kanai & Kuninobu



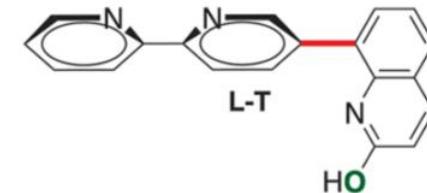
- L-shape is essential for the proper non-covalent interaction.
- L1 should produce the more stable L-T form upon tautomerization.
- OH or in situ formed O-M group would recognize the ester functionality.



2.1 Regioselective functionalisation of arenes



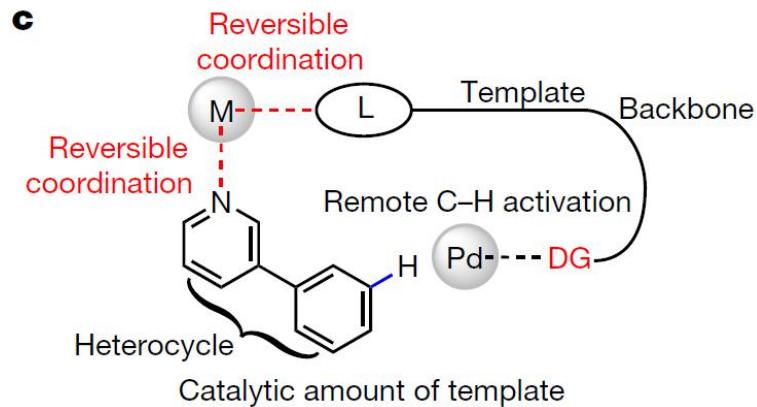
1.5 mol% $[\text{Ir}(\text{cod})(\text{OMe})]_2$, 3.5 mol% L,
1.0 equiv. B_2pin_2 , 4.5 mol% MO^tBu ,
THF, 25–80 °C, 12 h



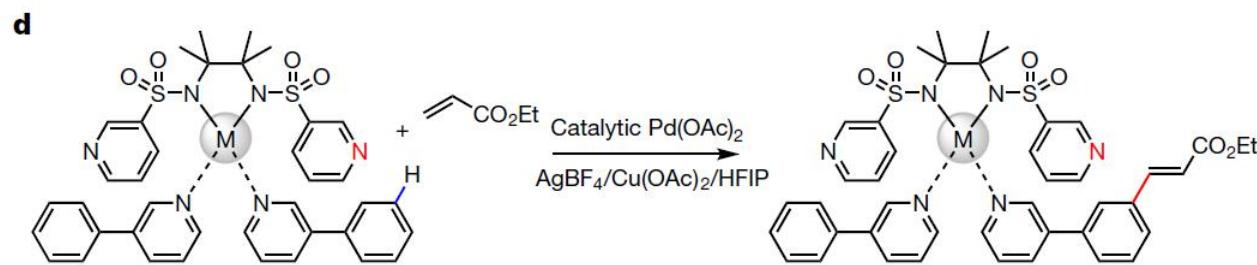
no.	ligand	T, °C	MO^tBu	conv. (%)	<i>m,m</i> -di(%)	para/meta
1	dtbpy	25	—	89	40	1.2/1.0
2	dtbpy	80	—	93	31	1.1/1.0
3	L1	25	—	97	12	6.1/1.0
4	L1	50	—	98	13	5.7/1.0
5	L1	80	—	98	17	3.0/1.0
6	L1	50	LiO^tBu	0	—	—
7	L1	50	NaO^tBu	75	—	3.8/1.0
8	L1	50	KO^tBu	95 (92)	—	32.3/1.0
9	L1	80	KO^tBu	99	—	24/1.0
10	dtbpy	50	KO^tBu	95	20	1.4/1.0

^aReaction scale 0.2 mmol. GC ratios; conversions are based on dodecane as internal standard. In parentheses, isolated yields.

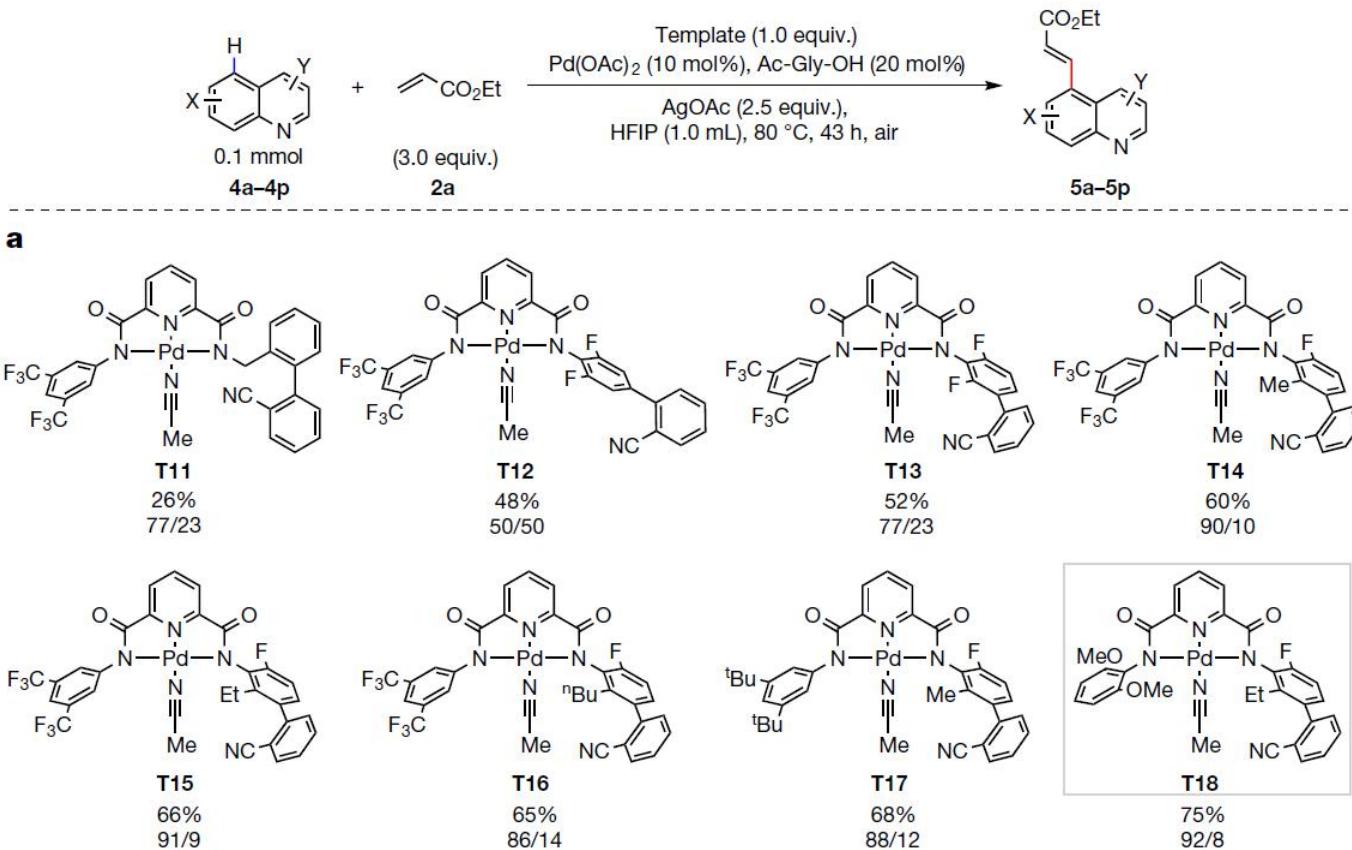
2.1 Regioselective functionalisation of arenes



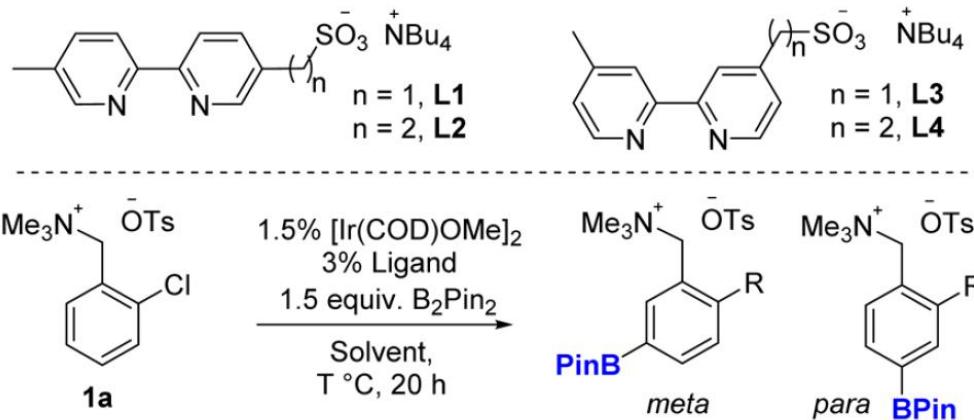
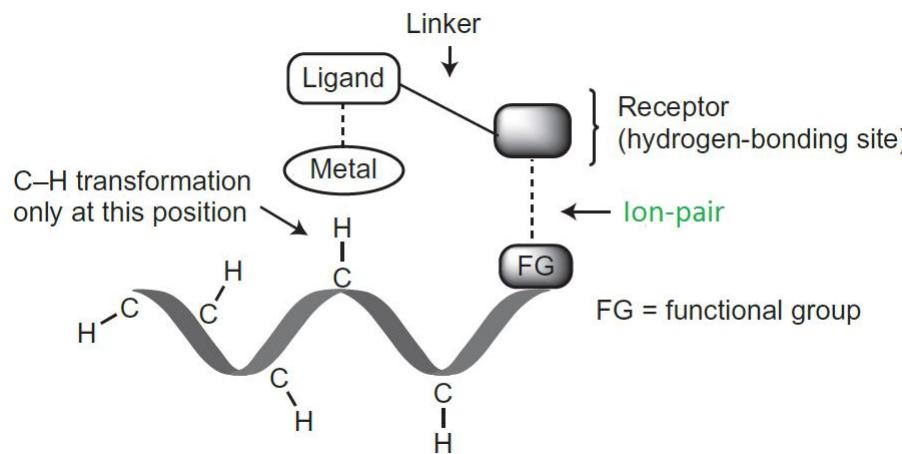
Catalytic bifunctional template



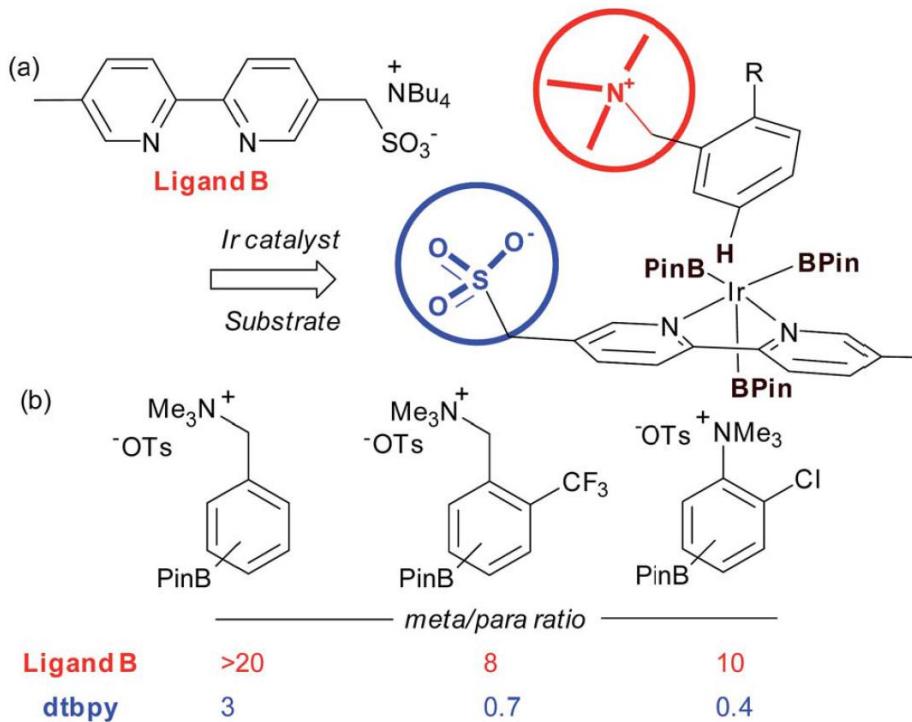
2.1 Regioselective functionalisation of arenes



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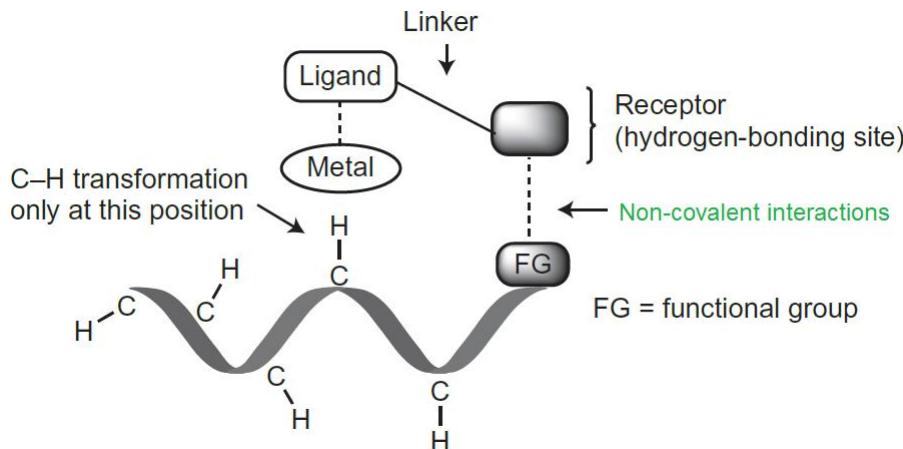
2.1 Regioselective functionalisation of arenes



Typical Reaction conditions: 1.5 mol% $[\text{Ir}(\text{COD})\text{OMe}]_2$, 3 mol% Ligand B, 1.5 - 3.0 eq. B_2Pin_2 , THF, 50 °C

(a) Optimal ligand design. (b) Selection of substrates, highlighting meta:para selectivity for both the anionic ligand B and dtbpy.

2.1 Regioselective functionalisation of arenes



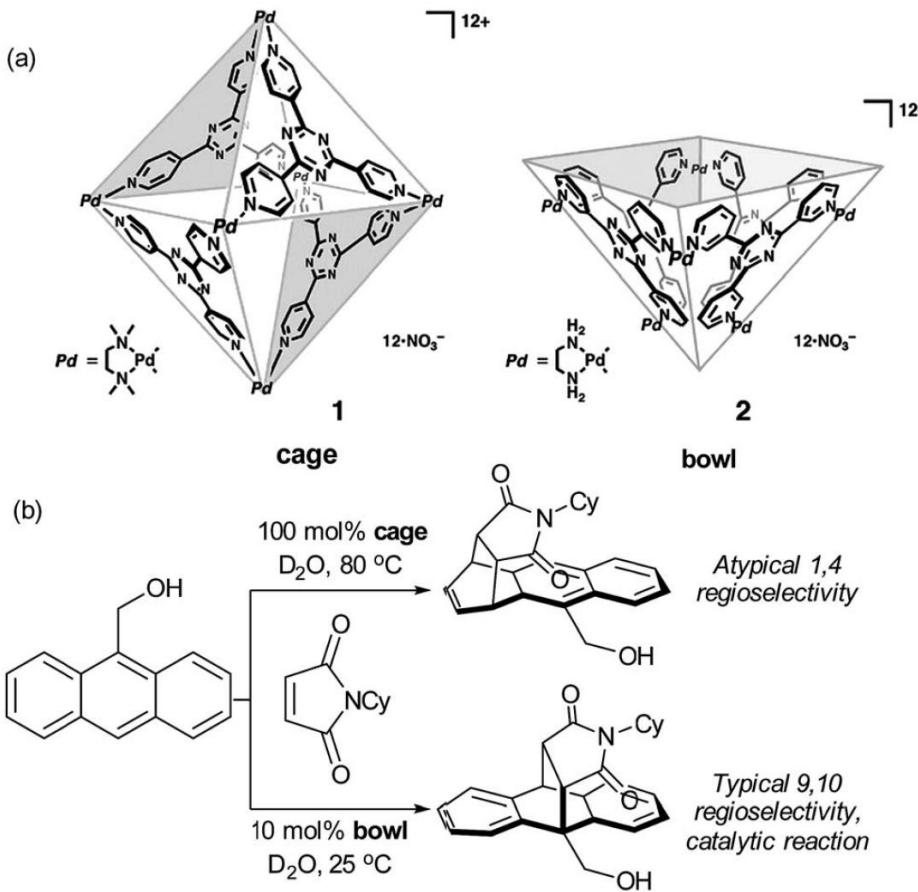
Iridium-catalysed borylation (brief summary)

- 1 mild conditions,
- 2 compatibility with non-polar reaction solvents
- 3 lack of requirement for acidic additives

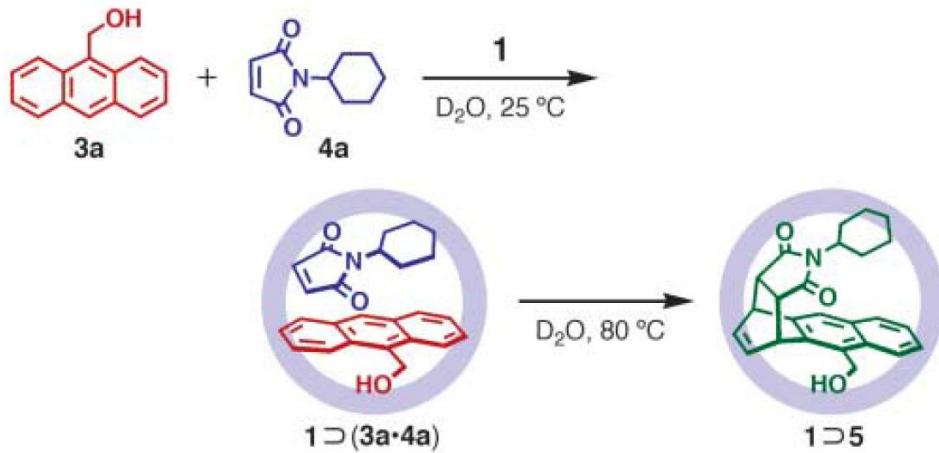
Then: combination with potentially subtle directing effects such as hydrogen bonds or ion pairs

2.1 Regioselective functionalisation of arenes

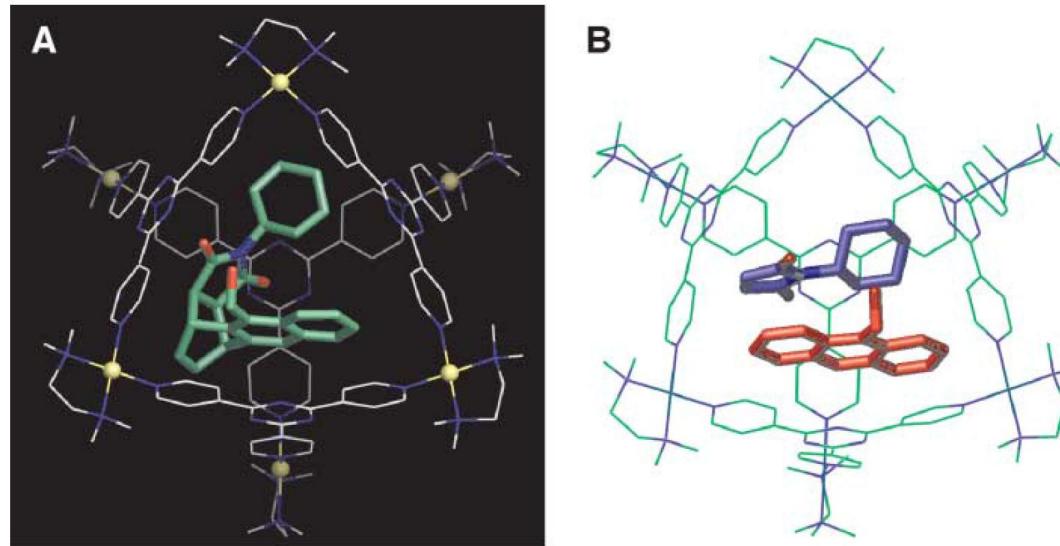
M. Fujita



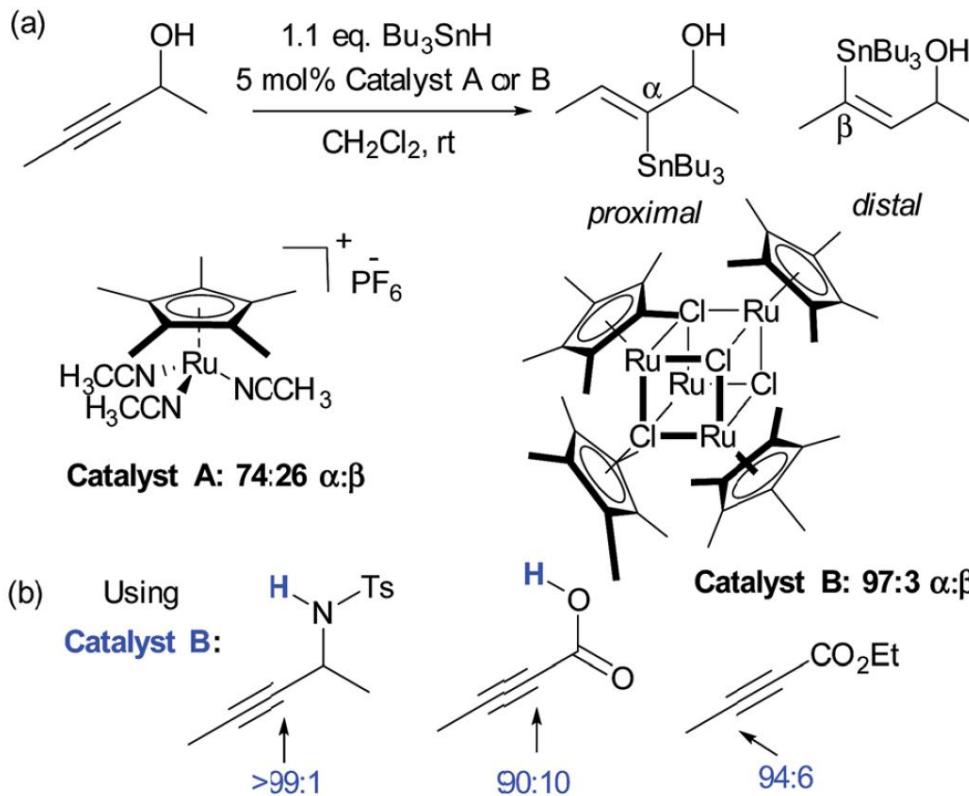
2.1 Regioselective functionalisation of arenes



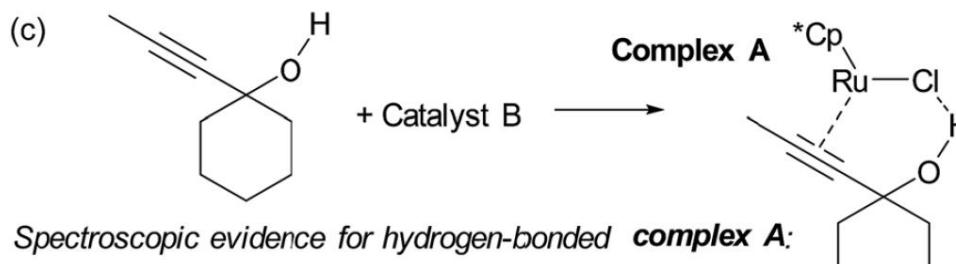
Mechanism: aromatic stacking interactions



2.2 Regioselective functionalisation of alkynes



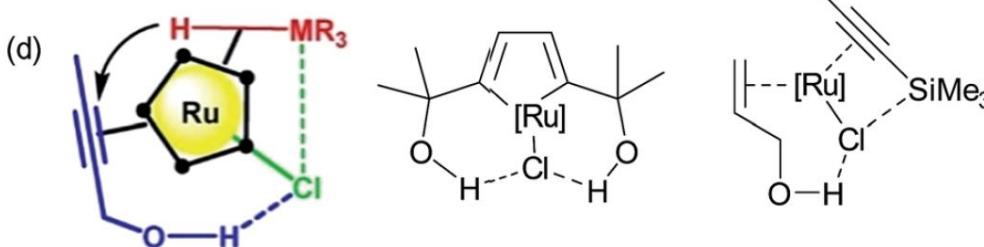
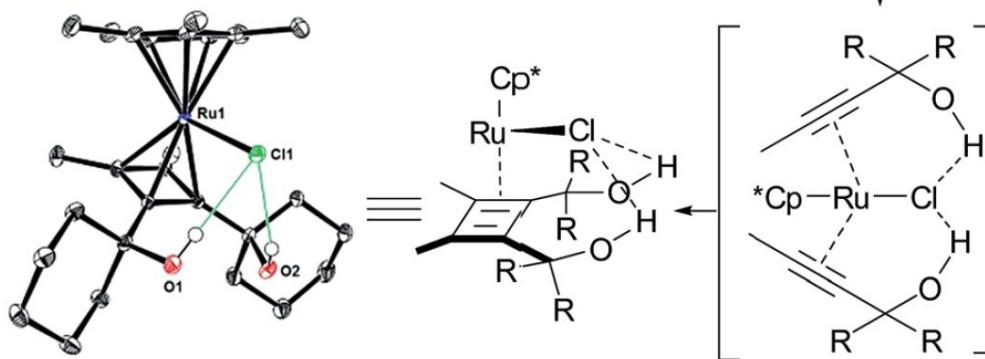
2.2 Regioselective functionalisation of alkynes



*Spectroscopic evidence for hydrogen-bonded **complex A**:*

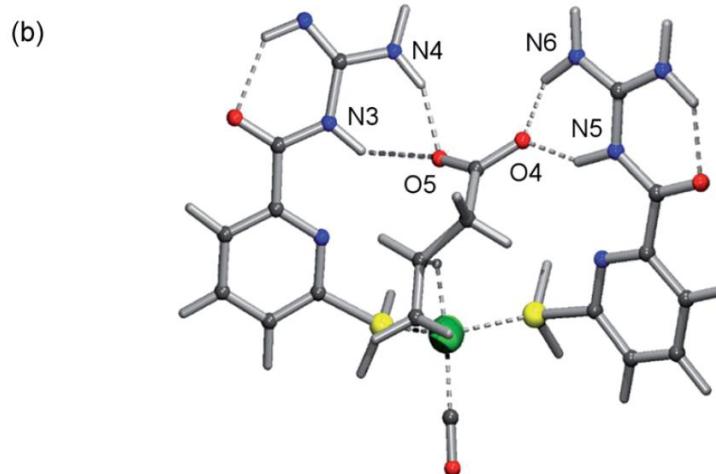
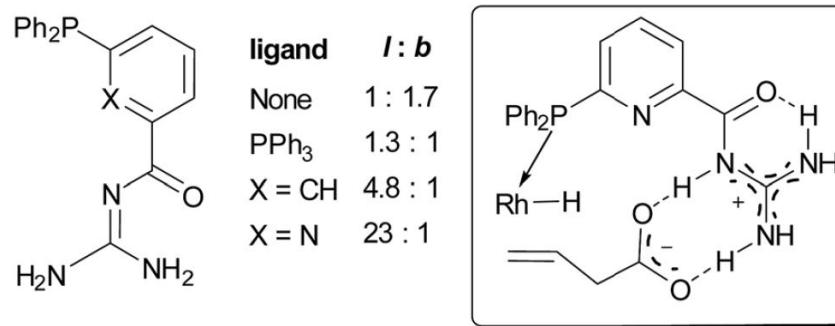
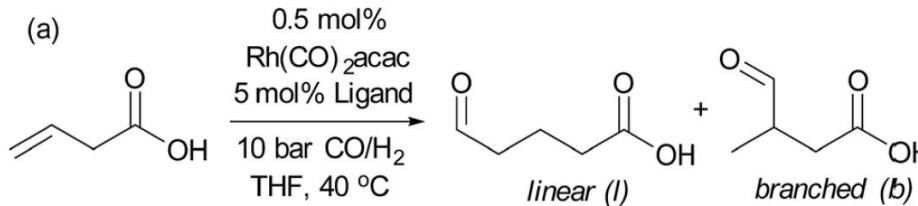
$^1\text{H-NMR}$: Hydroxyl peak shifts from 2.0 ppm to 5.1 ppm,

$^{13}\text{C-NMR}$: Alkyne peaks shift from 80/83 ppm to 130/155 ppm



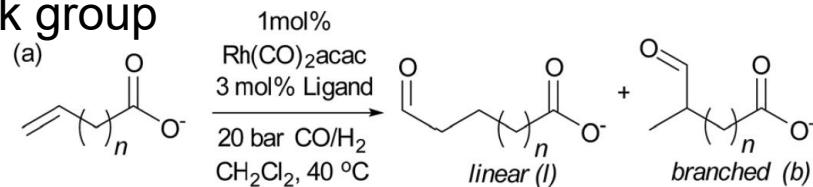
2.3 Regioselective functionalisation of alkenes

Bernhard Breit

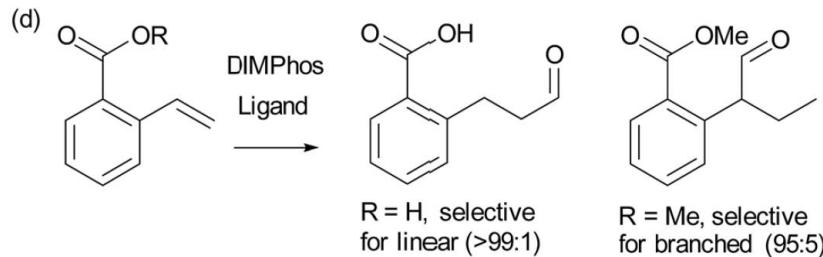
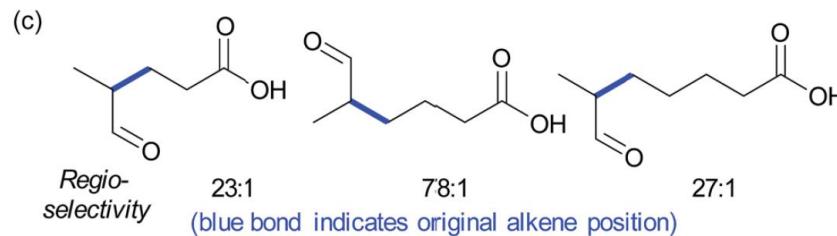


2.3 Regioselective functionalisation of alkenes

The Reek group

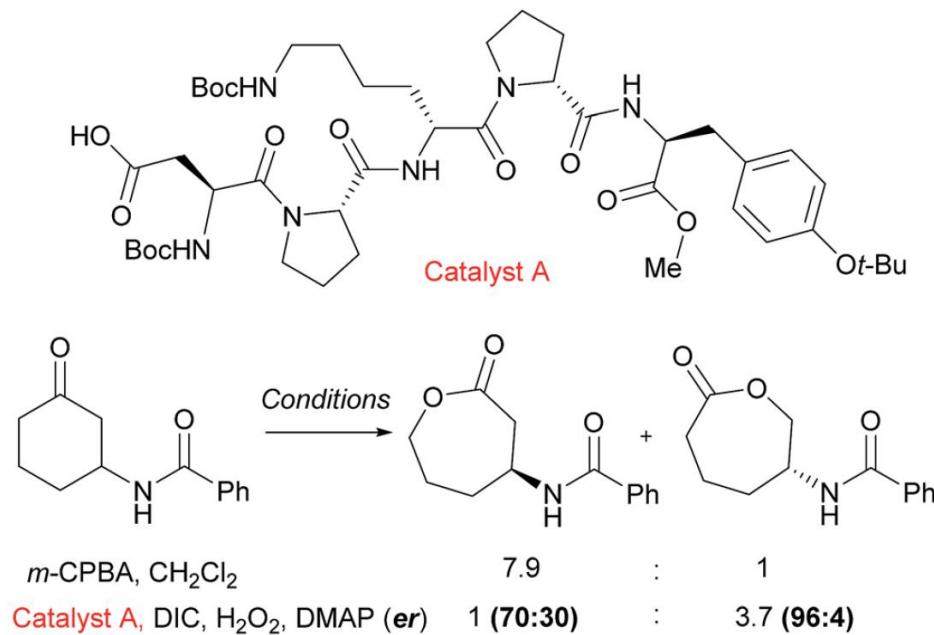


<i>n</i>	ligand	<i>l:b</i>
1	PPh_3	3 : 1
1	DIMPPhos	3 : 1
2	PPh_3	3 : 1
2	DIMPPhos	40 : 1
3	PPh_3	3 : 1
3	DIMPPhos	22 : 1



2.3 Regioselective functionalisation of ketones

The Miller group



Reversal of regioselectivity observed in Baeyer–Villiger oxidation of particular cyclic ketones using catalyst A when compared with mCPBA

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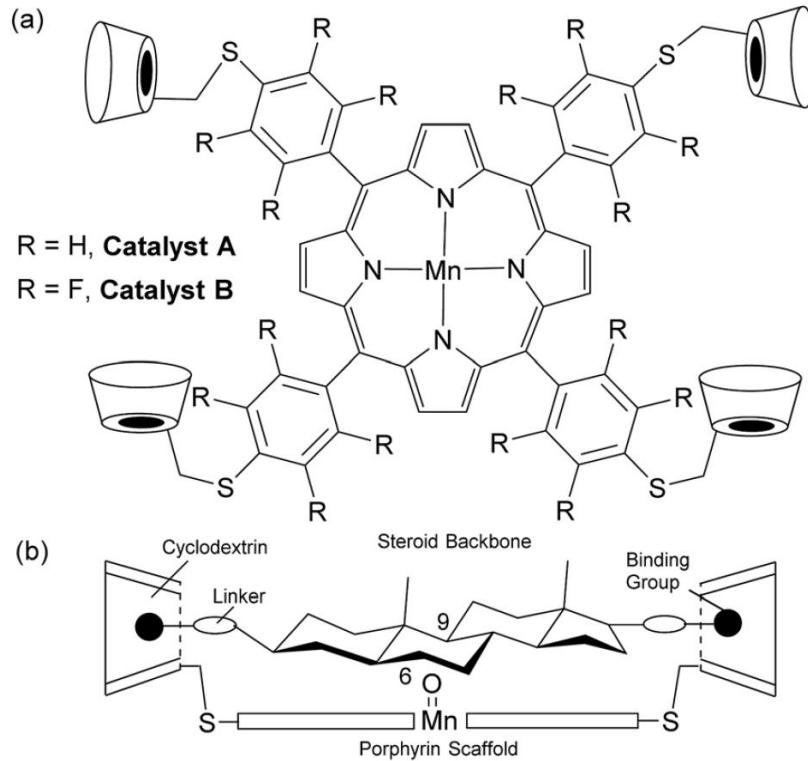
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4 Conclude and acknowledge

3.1 Site-selective aliphatic C–H functionalisation

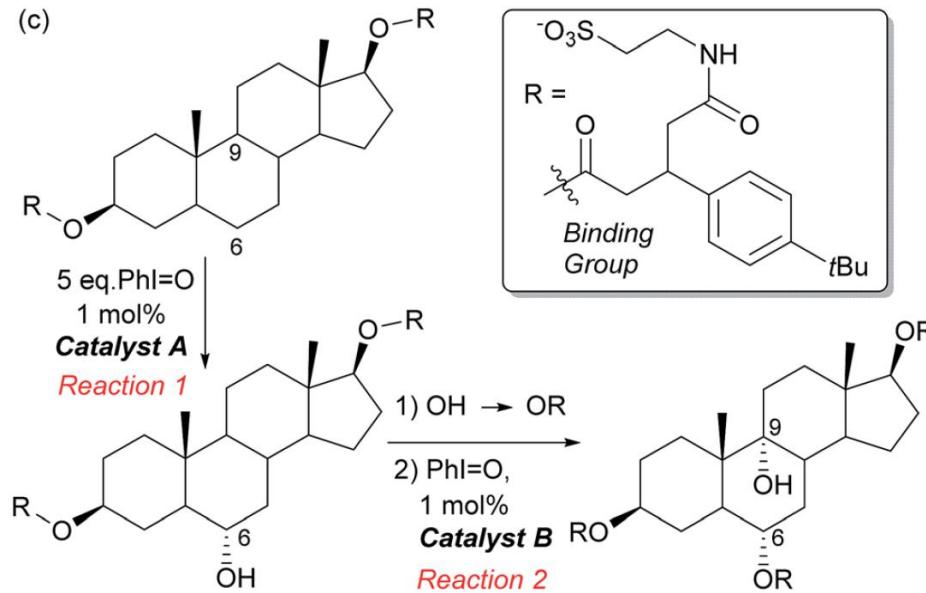
The R. Breslow group



Structure of manganese porphyrin catalysts developed for steroid functionalisation

3.1 Site-selective aliphatic C–H functionalisation

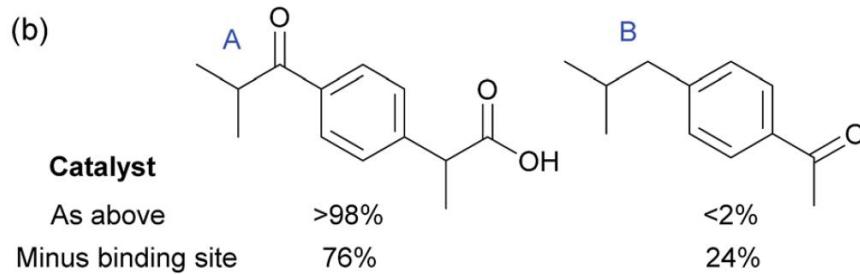
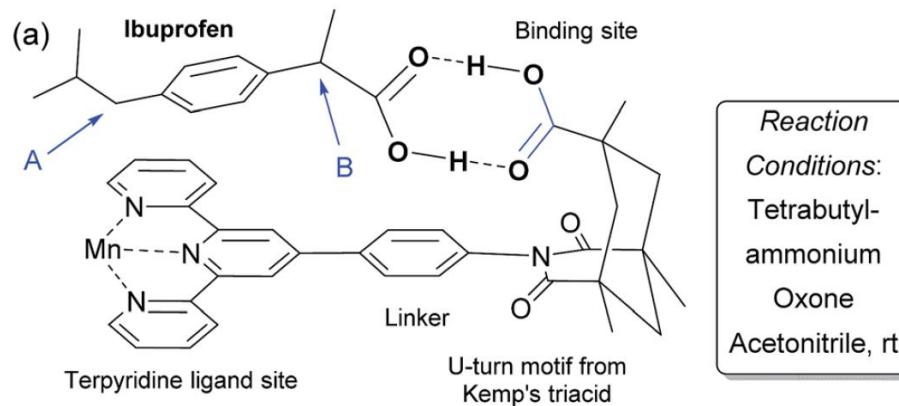
The R. Breslow group



Selective oxidation at C-6 followed by installation of a further binding group then selective oxidation at C-9.

3.1 Site-selective aliphatic C–H functionalisation

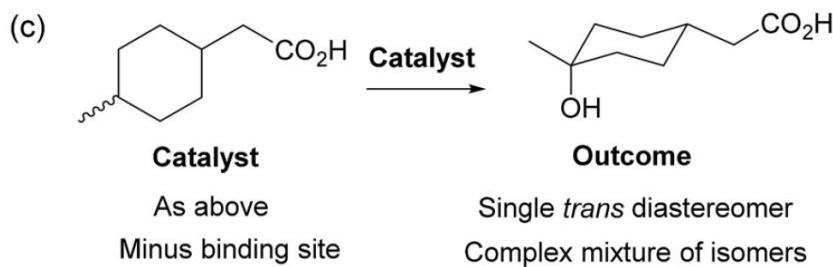
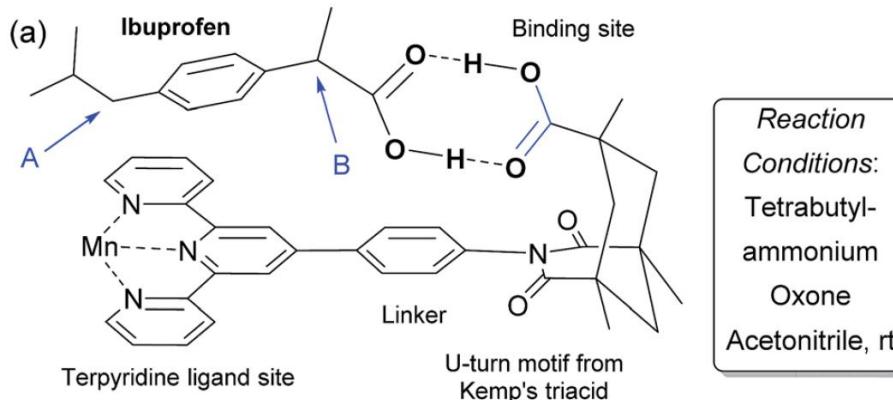
Robert H. Crabtree group



Results for oxidation of ibuprofen

3.1 Site-selective aliphatic C–H functionalisation

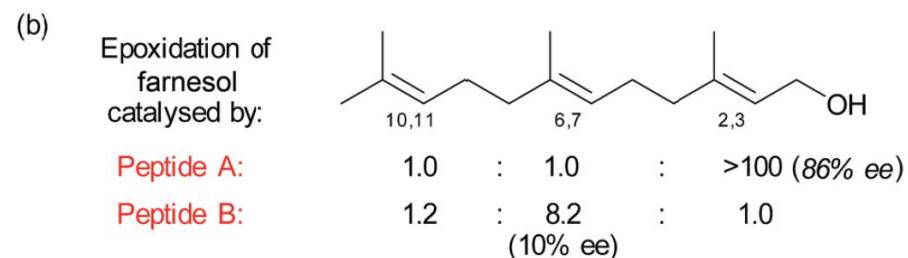
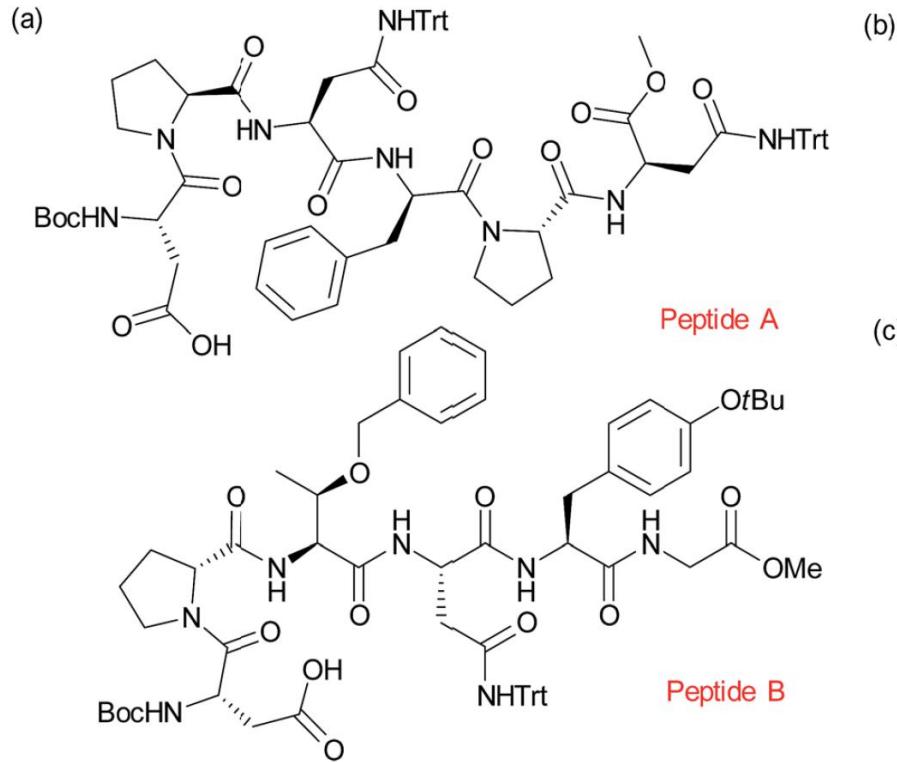
Robert H. Crabtree group



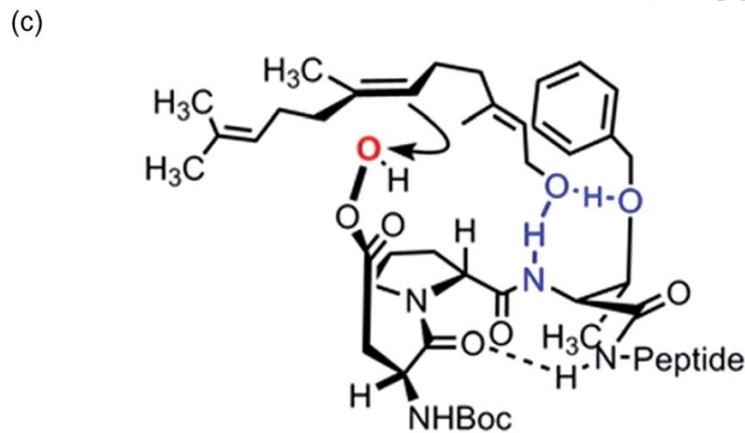
Outcome of oxidation of a mixture of cis and trans 4-methylcyclohexyl acetic acid using the same two catalysts

3.2 Site-selective alkene functionalisation

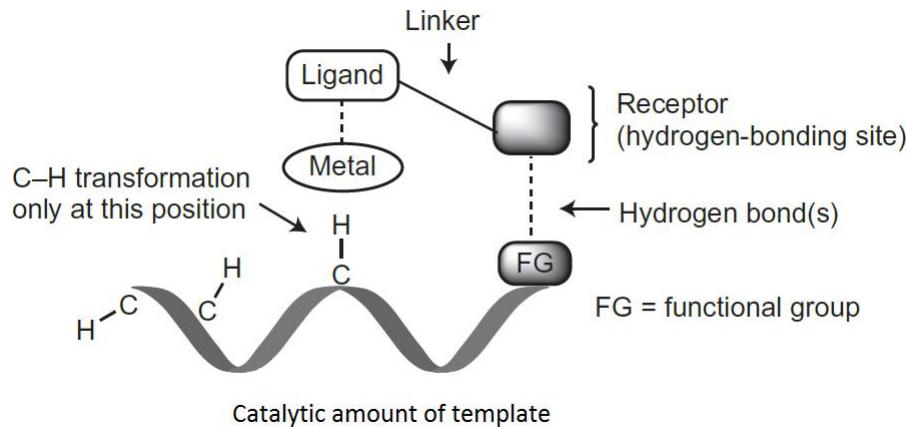
S. J. Miller group



Reaction conditions: *N,N*-diisopropylureaHOBT, DMAP (1 eq. each), H₂O₂, DCM, 4 °C



Summary



1 Highlights using non-covalent interactions to address regiocontrol and site-selectivity in catalytic reactions.

2 Most C-H activation reactions operate under mild, neutral conditions.

Acknowledgments

THANK YOU

- Prof. Huang
- All members here

Thanks for your attention!