ICCOM-CNR
Istituto di Chimica dei Composti OrganoMetallici

ISTITUTO DI CHIMICA DEI COMPOSTI ORGANOMETALLICI

From PTA to novel CAP: application of water soluble phosphines in catalysis and medicinal chemistry

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DSCTM

Young Investigator Award 2018

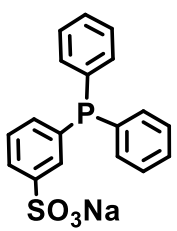
Conferenza di Dipartimento 2018

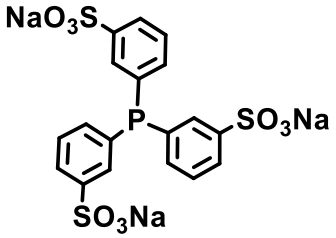
Water: green solvent for homogeneous and biphasic catalytic processes

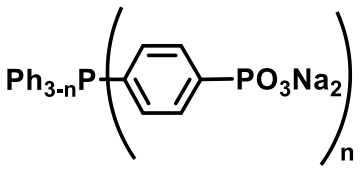
ADVANTAGES

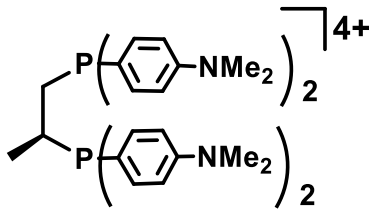
- environmentally benign (not volatile and not toxic)
- replacement of organic solvents and their disposal
- reduction of risks (not flammable)
- separation of organic products from catalysts (recovery and recycling)
- low cost, abundant

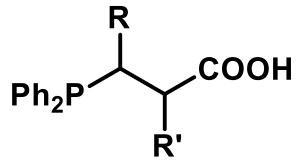
WATER SOLUBLE *P*- LIGANDS



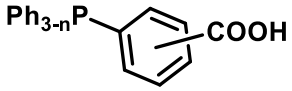


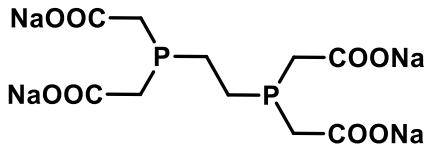


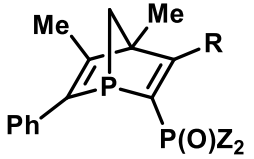




(R = H, COOH;
R' = H, Me)







Z = NEt_2, OEt_2, OH, ONa;
R = H, Ph

Shaughnessy, K.H. *Chem. Rev. 109* (**2009**) 643

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PTA: the long story of a versatile water soluble phosphine

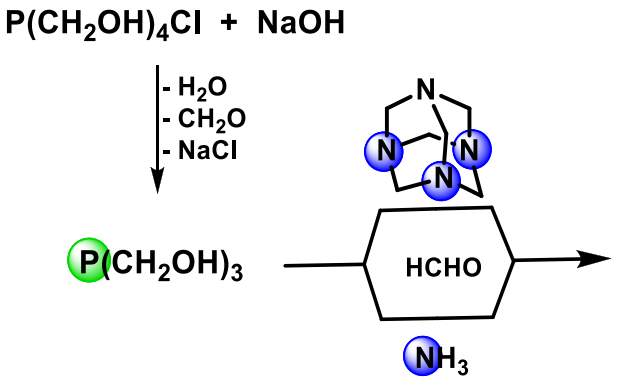
1. **"Soft metal " coordination**: catalysis and biological activities

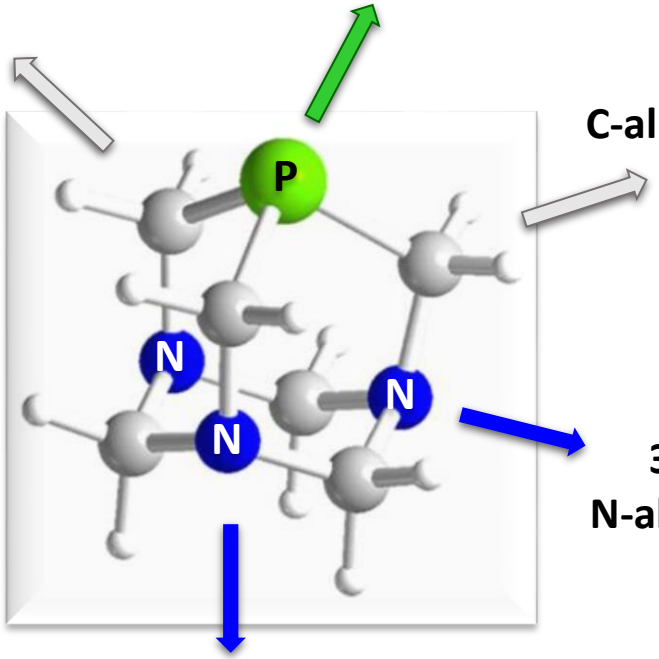
2. **Upper rim functionalisation** with C-alkylation: bidentate ligands and introduction of a stereocentre

3. **Lower rim functionalisation** with N-alkylation: catalysis (hydroformylation)

4. **"Hard metal " coordination**: grafting, heterogenisation, polymerization

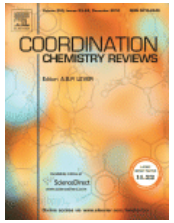
5. **Cage opening**: P,N chelates for catalysis





PTA: 1,3,5-triaza-7-phosphadamantane

- Neutral phosphine synthesized in 80-90% yield
- Thermally stable (dec. Temp. >260°C)
- Solid stable to air and moisture
- Soluble in water (*S* = ca. 235 g/L)
- Small cone angle (103°)



Phillips, A. D. et al., *Coord Chem Rev* (**2004**) *248*, 955
Bravo, J. et al., *Coord Chem Rev* (**2010**) *254*, 555
Guerriero, A. et al., *Coord Chem Rev* (**2018**) *355*, 328

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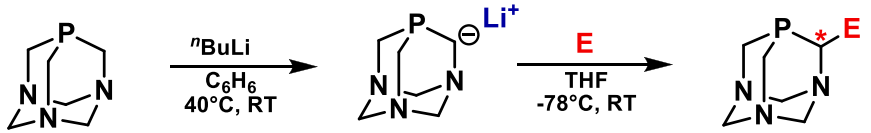
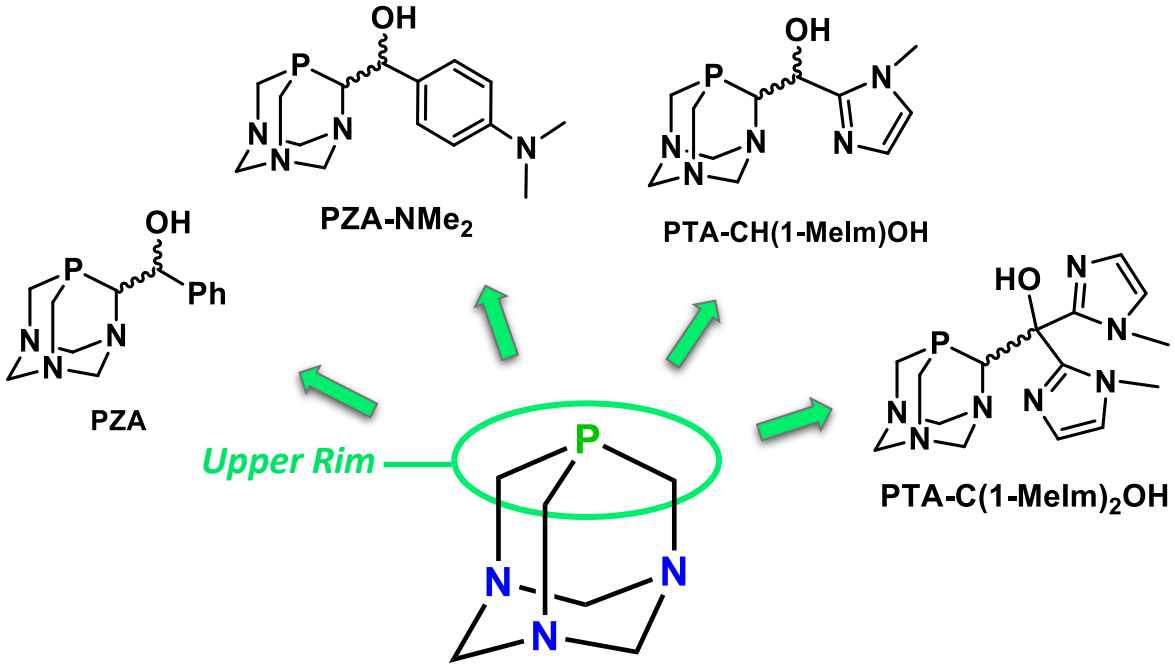
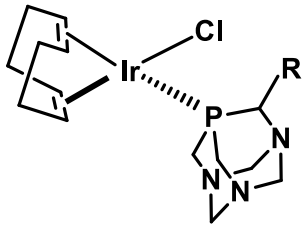
PTA upper rim functionalisation

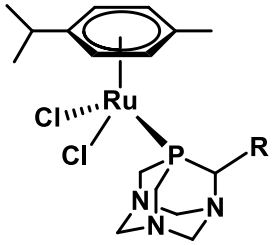


GENERAL SYNTHETIC ROUTE



Synthesis of Ir(I) and Ru(II) Complexes





Solubility in water @ 20 °C (g/L)	
PZA= 1050	PZA-NMe$_2$= 1.8
PTA-CH(1MeIm)OH= 320	PTA-C(1MeIm)$_2$OH= 78

Guerriero A., Erlandsson, M., et al. *Organometallics* (**2011**) *30*, 1874

Krogstad, D.A.; Guerriero,A., et al. *Organometallics* (**2011**) *30*, 6292

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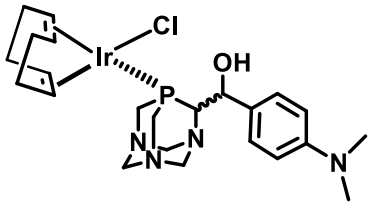
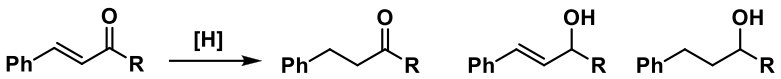
Ir(I) and Ru(II) Complexes for *Transfer Hydrogenation* Reactions

CATALYSTS

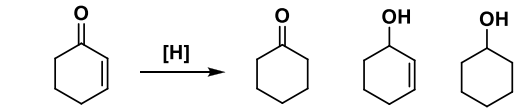


SUBSTRATES



CNA: R= H

BZA: R= CH_3



2-cyclohexen-1-one

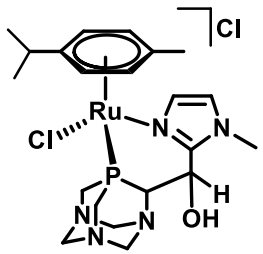
***TH* PROTOCOLS**

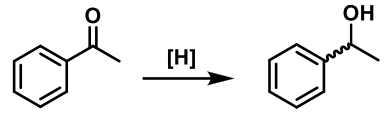
$HCOONa/H_2O/MeOH$

- **CNA→ conv. 96.6% (6h) @40 °C [cat/sub 1:100]**
  C=O selectivity
- **BZA→ conv. 55.1% (24h) @60 °C [cat/sub 1:100]**
  C=C selectivity

KOH/^{i}PrOH

- **conv. 83.3% (5h) @80 °C [cat/sub 1:500]**
  C=O and C=C hydrogenation





acetophenone → 1-phenylethanol

^{t}BuOK/^{i}PrOH
pH_2(30 bar)

- **conv. 84.1% (4h) @25 °C [cat/sub 1:250]**
- **conv. 97.9% (4h) @40 °C [cat/sub 1:500]**
- **conv. 89.7% (4h) @40 °C [cat/sub 1:1000]**

Guerriero A., Erlandsson, M., et al. *Organometallics* (**2011**) *30*, 1874

Krogstad, D.A.; Guerriero,A., et al. *Organometallics* (**2011**) *30*, 6292

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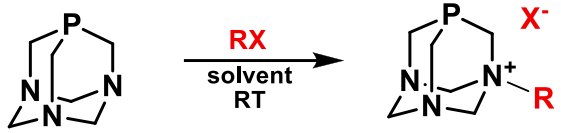
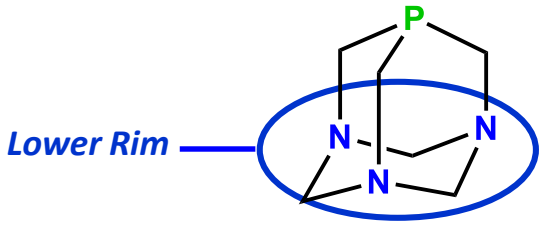
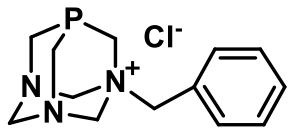
Lower rim functionalisation

GENERAL SYNTHETIC ROUTE

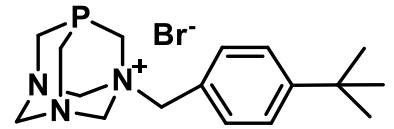


- Easily synthesised
- Design of steric and electronic properties
- Tunable water solubility



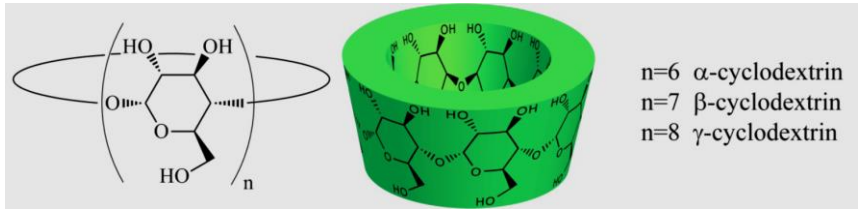


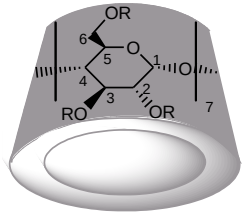
(*N*-Bz-PTA)Cl



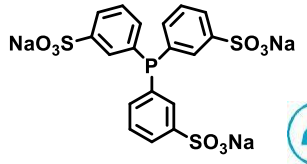
(*N-tert*-butyl-Bz-PTA)Br

Long-chain alkene biphasic HF with cyclodextrins (CDs) as *mass transfer promoters*





Native β-CD: R = H
RAME- β -CD: R = H o CH_3
(substitution degree= 1.7
Per glucopyranose unit)
RAME=randomly methylated

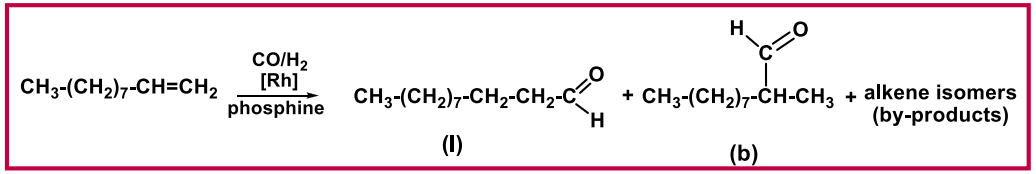


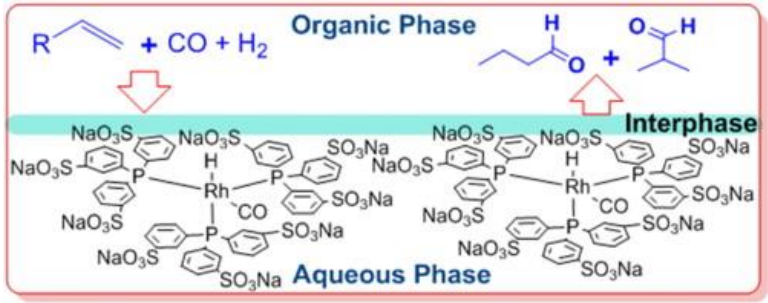
m-TPPTS

RHÔNE-POULENC

Formation of ADDUCTS (CD/Substrate and CD/catalyst)

- **van der Waals interactions**
- **hydrophobic interactions**
- **electrostatic forces**
- **steric effects**





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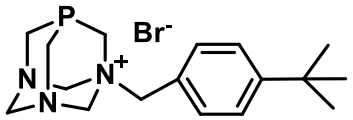
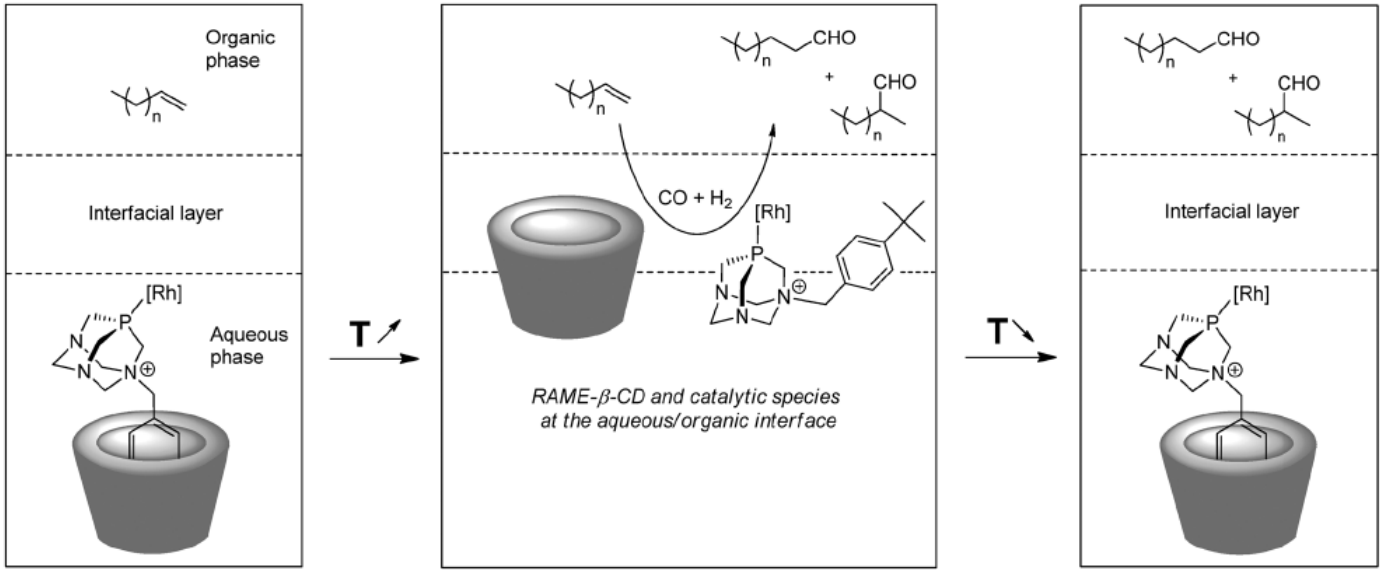
Legrand, F.-X., Guerriero, A., et al. *Appl. Cat. A: Gen.* (**2009**) *362*, 62

Six, N.; Guerriero, A., et al. *Catal. Sci. Technol.* (**2011**) *1*, 1347

Rh-catalysed hydroformylation of long chain olefins in biphasic media



- basicity > [N-Bz-PTA]Cl ($^1J_{P\text{-}Se}$= 815 Hz)
- **$S(H_2O)_{20°C}$= 10 g/L**
- interaction between *tert*-butyl group and RAME-β-CD



before reaction | **during reaction** | **after reaction**

Hydrophobic part included in CD cavity

Ligand not included and substrate included in CD cavity

Ligand included in CD cavity

Low surface activity and adsorption ability at the interface

High surface activity and increase of catalytic activity at the interface

No emulsions and rapid separation through decantation

Low conversion
T= 80 °C (K_{ass}= 5447 M^{-1})

High conversion
T > 80 °C (K_{ass} decreases)

Good phase separation
T< 80 °C (K_{ass}= 5447 M^{-1})

CD-based thermocontrolled catalytic process

Olefin	CD	T (°C)	Conv.(%)[b]	Sel. (%)[c]	l/b[d]
1-decene	–	80	26	99	2.1
1-decene	RAME-β-CD	80	10	97	1.8
1-decene	–	100	56	99	1.7
1-decene	RAME-β-CD	100	72	99	2.0
1-decene	RAME-β-CD	120	98	99	1.8
1-dodecene	RAME-β-CD	80	11	99	1.7
1-dodecene	RAME-β-CD	100	75	99	1.7
1-tetradecene	RAME-β-CD	80	14	95	1.6
1-tetradecene	RAME-β-CD	100	88	97	1.9

[a] Experimental conditions: $Rh(acac)(CO)_2$ (4.07×10^{-2} mmol), water-soluble ligand (0.21 mmol), CD (0.48 mmol), H_2O (11.5 mL), 1-alkene (20.35 mmol), 1500 rpm, CO/H_2 (1/1): 50 bar, 6 h. [b] Calculated with respect to the starting olefin. [c] (mol. of aldehydes)/(mol of converted olefins) × 100. The side products were mainly isomeric olefins. [d] Ratio of linear to branched aldehyde product.

Six, N.; Guerriero, A., et al. *Catal. Sci. Technol.* (**2011**) *1*, 1347

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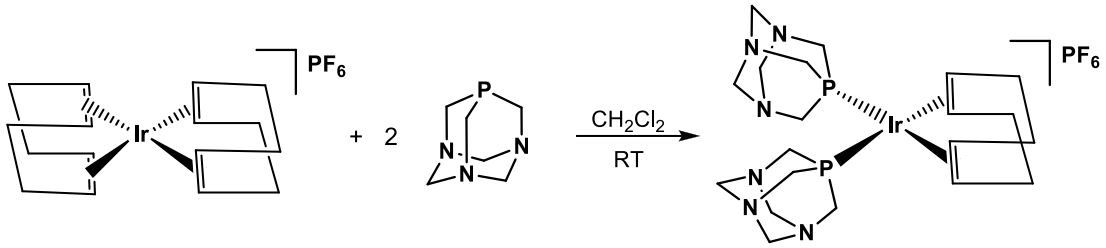
Immobilization of Ir-PTA complex on DOWEX resins



$S(H_2O)_{20°C}$= 1.85 g/L

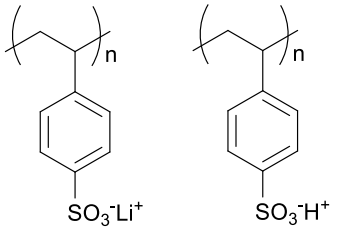
Not very stable in H_2O at T=80 °C

^{31}P (CP MAS)= – 87.3 ppm (br m)
– 142.2 ppm (sept, PF_6^-)

ION –EXCHANGE RESINS AS CATALYST CARRIERS:

- Water tolerant
- Swell in water giving a porous structure
- Commercially available and low cost
- Resistence to thermal, mechanical and chemical stress
- Easy separation

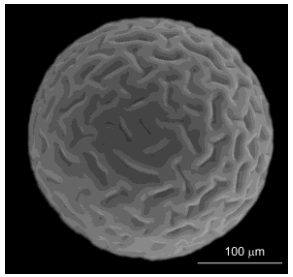
DOWEX resin sulfonated gel-type



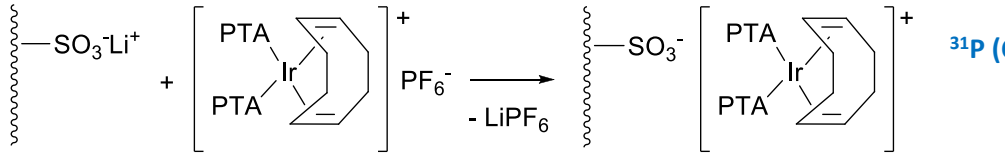
Dowex-Li+ Dowex-H+

Tethered catalysts	Ir loading (w/w)[b] (%)	Ir immobilised (%)
H^+-D50WX2	1.73 (1)	64.3%
Li^+-D50WX2	1.68 (1)	62.4%

[a] Experimental conditions: resin 700 mg (3.36 meq. Ion exchange capacity), metal complex 0.102 mmol, **H_2O:MeOH=3:1, 24h, r.t.** [b] ICP-OES value

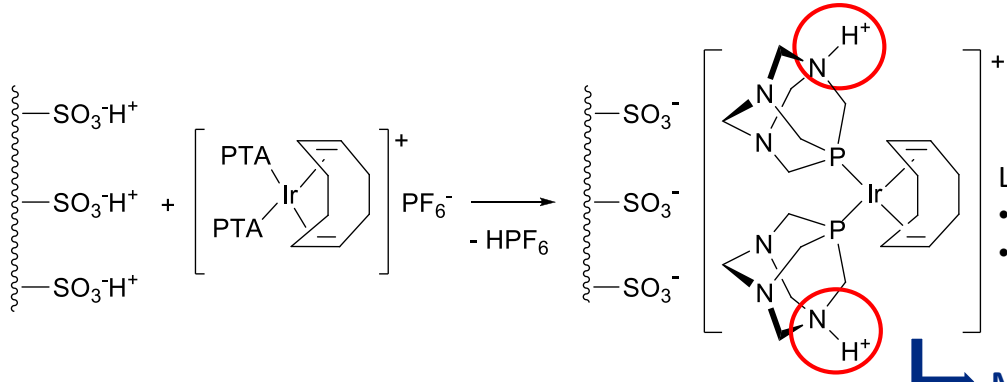


ESEM image (secondary electrons, 700 magnifications, 25 kV, 1 torr) of a 50WX2/Ir complex bead (H^+, 50-100 mesh, 1.73% Ir complex)



Li-resin Li-resin

^{31}P (CP MAS) = -83.2 ppm (NO PF_6^- signal)



H-resin H-resin

^{31}P (CP MAS) = -69.5 ppm (NO PF_6^- signal)

Larger downfield shift due:
- ionic interactions
- acid-base interactions

MORE ROBUST CATALYST

Guerriero, A,; Liguori, F. et al. *Green Chem.* (**2012**), 14, 3211

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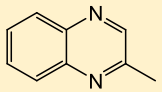
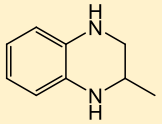
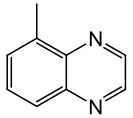
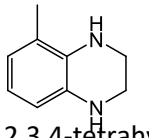
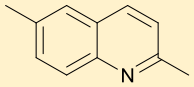
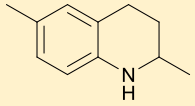
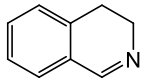
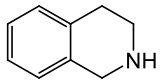
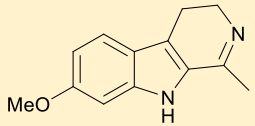
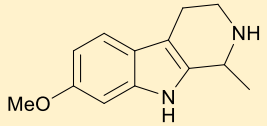
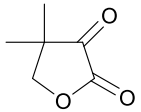
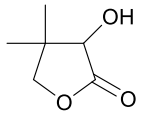
C=N and C=O hydrogenation with Ir-DowexH$^+$ resin

Substrate	Product	Phase	Yield (%) [time h]	TOF (h^{-1})	Leaching (ppm)[i]
 2-methylquinoxaline	 2-methyl-1,2,3,4-tetrahydroquinoline	Hetero[b] Homo[b]	92.2 [22] 91.1 [16]	6 9	0.2 –
 5-methylquinoxaline	 5-methyl-1,2,3,4-tetrahydroquinoline	Hetero[c] Homo[c]	89.2 [22] 32.0 [17]	6 3	0.32 –
 2,6-dimethylquinoline	 2,6-dimethyl-1,2,3,4-tetrahydroquinoline	Hetero[d] Homo[d]	26.0 [29] 3.5 [29]	1 1	0.08 –
 3,4-dihydroisoquinoline	 1,2,3,4-tetrahydroisoquinoline	Hetero[e] Homo[e] Hetero[g]	99.9 [1] 11.0 [1] 89.7 [2]	300 34 374	7.6 – 4.0
 Harmaline	 Leptaflorine	Hetero[f] Homo[f]	99.1 [24] 9.3 [22]	4 5	8.5 –
 4,4'-dimethylfuran-2,3-dione	 Pantolactone	Hetero[h] Homo[h]	89.0 [4] 99.9 [4]	22 25	0.37 –

[a] Experimental batch conditions: **P = 20 bar H_2, T = 80 °C**; [b] H_2O, S/C = 150; [c] H_2O, S/C = 150; [d] **50 bar H_2**, H_2O: MeOH = 4:1, S/C = 50; [e] H_2O, S/C = 305; [f] H_2O:MeOH = 1.5:1, S/C = 100; [g] H_2O, S/C = 830; [h] H_2O, S/C = 100; [i] determined by ICP-OES.

RESULTS

- 100% selectivity to desired products in all cases
- heterogenized catalyst more active than the homogeneous ones
- no catalytic activity shown by the solution recovered after catalysis (minor metal leaching)
- easy and quantitative recovery of the resin by decantation

➡ **Pharmaceutically relevant molecules: antidepressants, antitumoral, antibiotics etc.**

Guerriero, A,; Liguori, F. et al. *Green Chem.* (**2012**), 14, 3211

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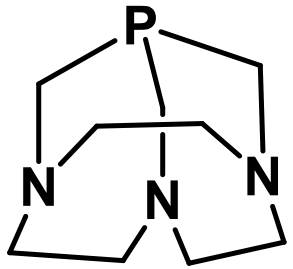
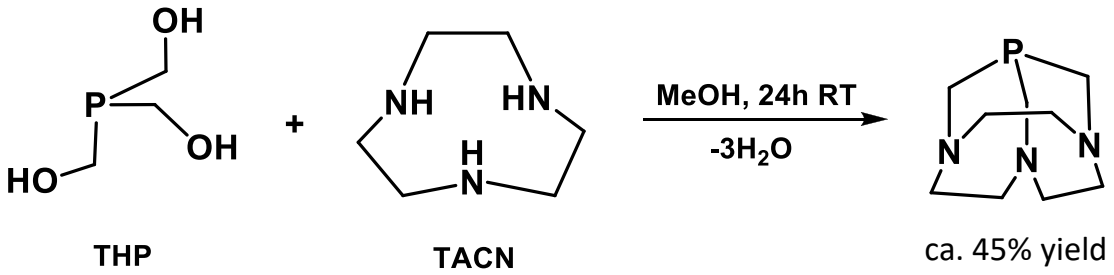
New ligand CAP: the higher homologue of PTA

Nine-membered macrocycle



- Stable to air and moisture as solid and in solution
- Soluble in water (*S* = ca. 2 g/100 mL)
- Thermal stability comparable with that of PTA
- Small cone angle (109°)
- Soluble in MeOH, EtOH, ^{i}PrOH, CH_3CN
- Highly soluble in $CHCl_3$, CH_2Cl_2 (*S* = ca. 10 g/100 mL)

CAP: 1,4,7-triaza-9-phosphatricyclo[5.3.2.1]tridecane



THP TACN ca. 45% yield

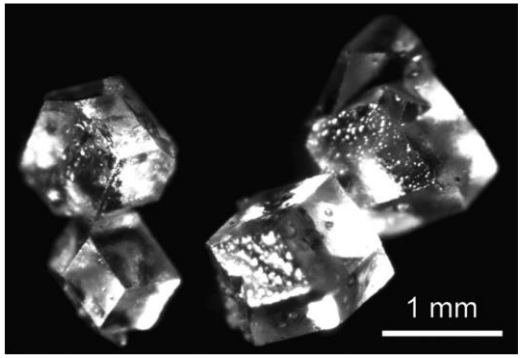


Figure 1. Dodecahedral crystals of free ligand CAP (adapted from original ref.)

THP = tris-(hydroxymethyl)phosphine
TACN = 1,4,7-triazacyclononane

- **MeOH best solvent choice**
- **No reaction in THF or acetone**
- **Formation of amorphous byproducts**

Britvin, S.N; Lotnyk, A. *J. Am. Chem. Soc.* (**2015**) *137*, 5526

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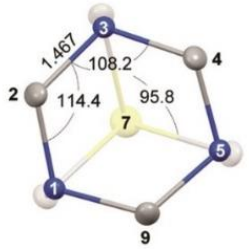
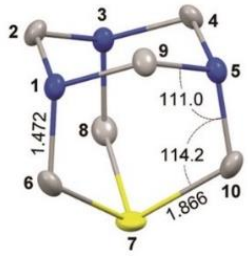
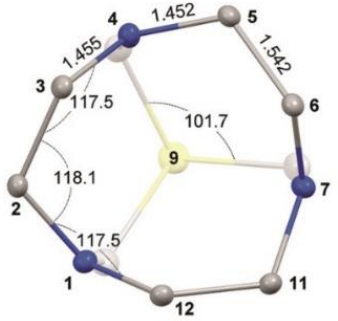
CAP cage architecture: a stereochemically intermediate between PTA and Verkade's ligand



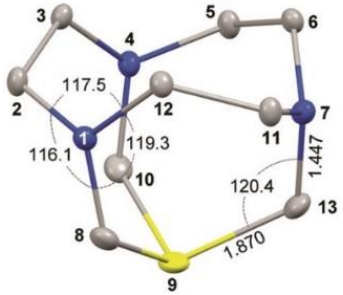
PTA



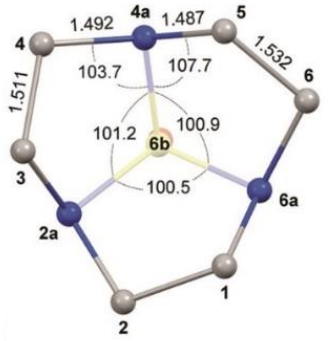
Same environment at P
(bridging P-***C***-N)



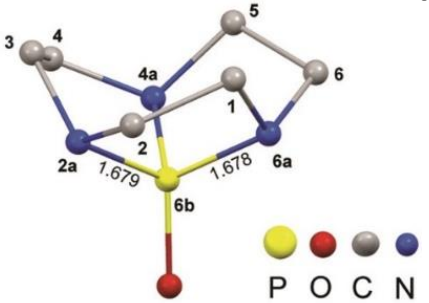
CAP



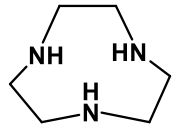
TACN macrocycle
embedded in the cage



P=O Verkade's aminophosphine



- **SAME CONFORMATION OF TACN**
- **HIGH CONFORMATIONAL FLEXIBILITY**



TACN

Britvin, S.N; Lotnyk, A. *J. Am. Chem. Soc.* (**2015**) *137*, 5526

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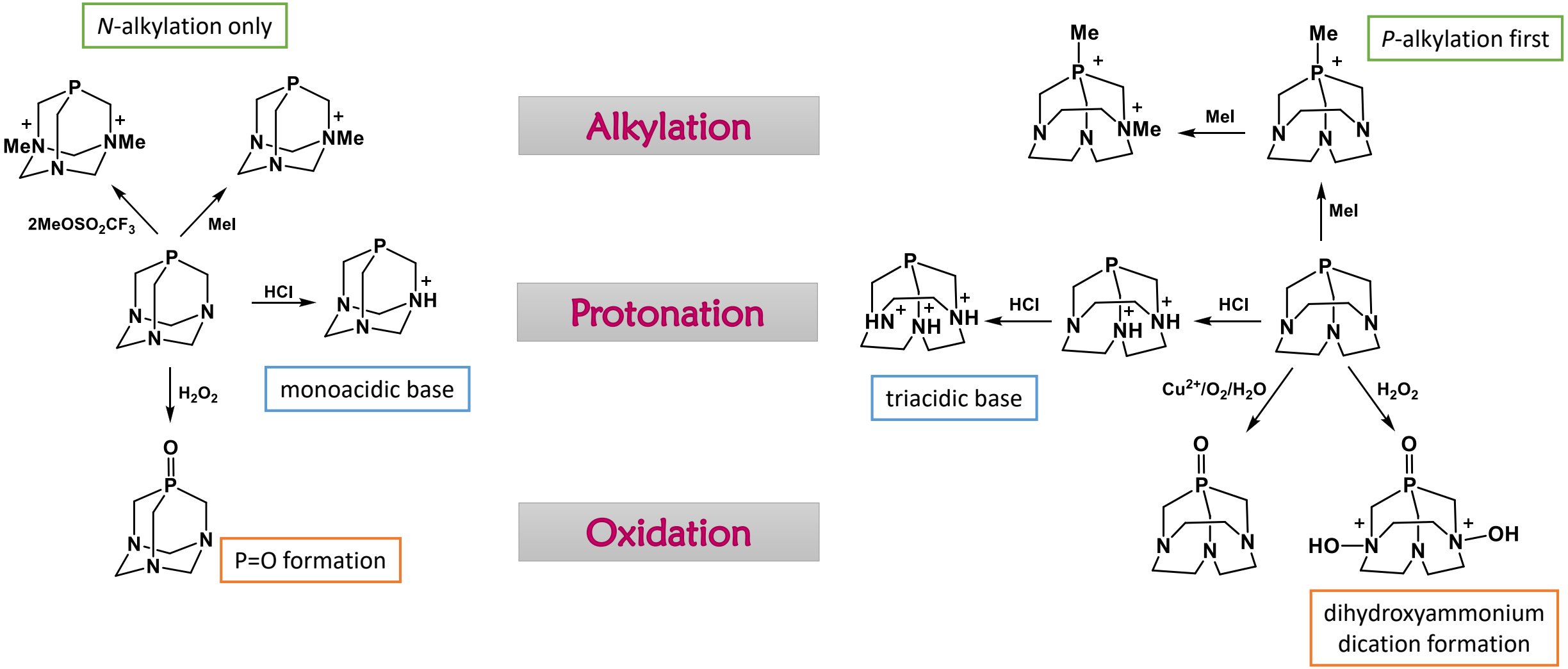
Different reactivity between CAP and PTA



Britvin, S.N., et al. *Chem. Eur. J.* (**2016**) *22*, 14227

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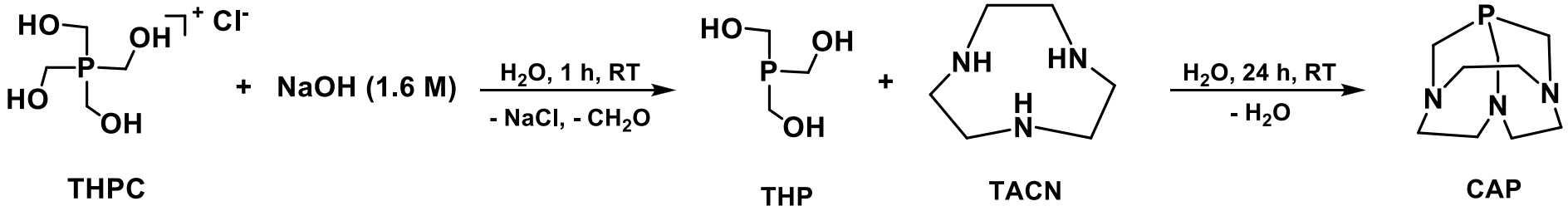
Improvement of CAP synthesis



THPC (80% in H_2O)

- air-stable
- commercially available

THP

- air-sensitive
- not isolated

TACN

CAP

- easy workup
- high purity

ca. 25% yield after recrystallization in hot EtOH

Two steps reaction in aqueous solution

THPC= *tetrakis*-(hydroxymethyl)phosphonium chloride
THP = tris-(hydroxymethyl)phosphine
TACN = 1,4,7-triazacyclononane

Guerriero, A., et al. *Inorg. Chem.* (**2017**) *56*, 5514

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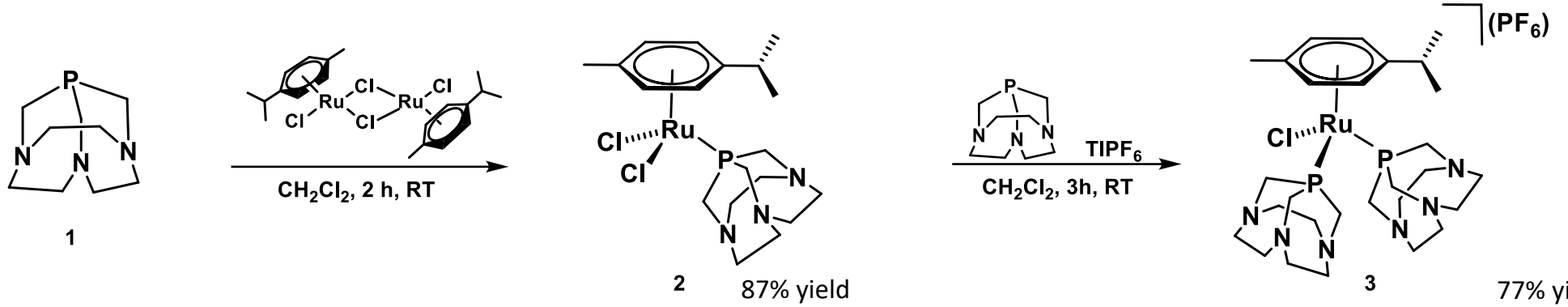
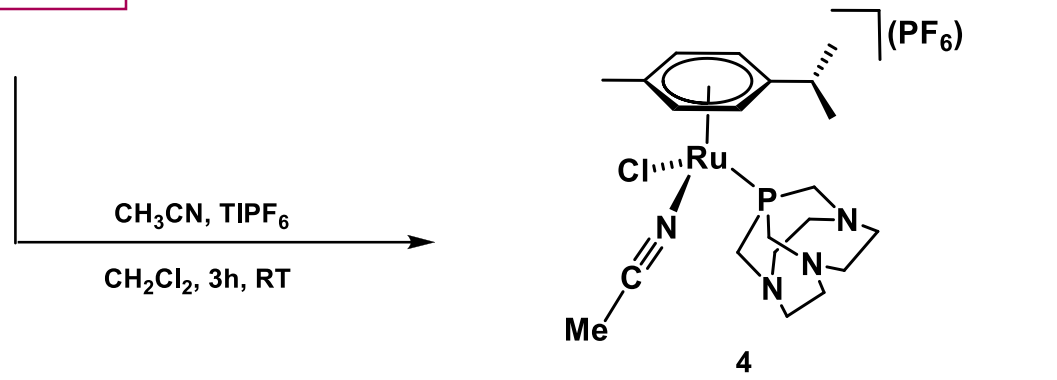
Synthesis of Ru(II) CAP complexes

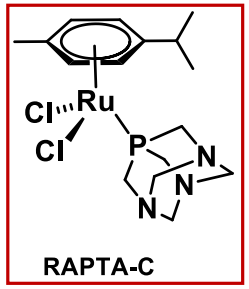


RACAP-C



Comparison of $^{31}P\{^1H\}$ NMR chemical shifts and water solubility values.

	$^{31}P\{^1H\}$ NMR (ppm)	$S(H_2O)_{20°C}$ (g L^{-1})
CAP	47.80 (s), $CDCl_3$ 46.72 (s), D_2O	20.0
PTA	–102.34 (s), $CDCl_3$ – 98.61 (s), D_2O	230.0
2	52.83 (s), $CDCl_3$ 57.48 (s), D_2O	0.86
3	51.60 (s) -144.26 (sept, J_{PF}=707.5 Hz), acetone-d_6 56.80 (s) -145.10 (sept, J_{PF} = 707.5 Hz), D_2O	1.20
4	48.17 (s) -144.27 (sept, J_{PF}=707.8 Hz), acetone-d_6 56.80 (s) -145.10 (sept, J_{PF} = 707.5 Hz), D_2O	1.10
RAPTA-C	–36.63 (s) in $CDCl_3$	10.0



Guerriero, A., et al. *Inorg. Chem.* (**2017**) *56*, 5514

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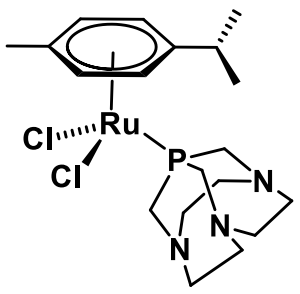
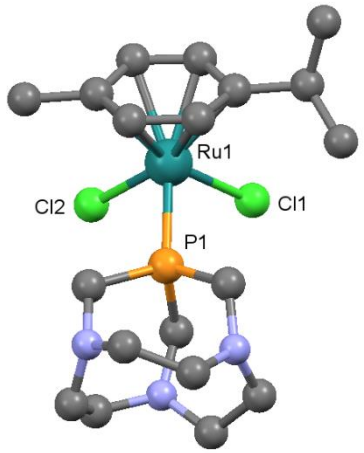
Solid-state characterisation of Ru(II) compounds

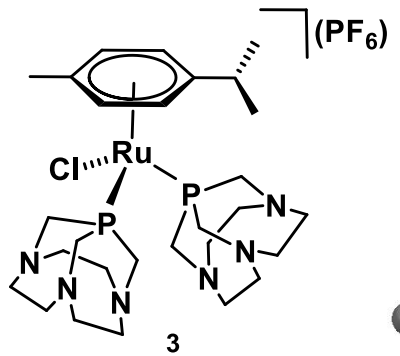
RACAP-C



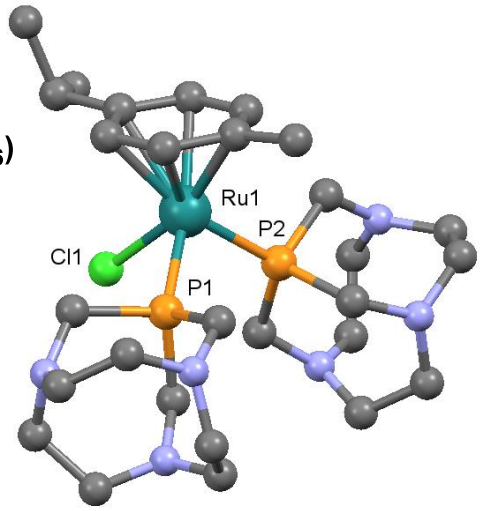
2



CRYSTALS GROWN FROM EtOH/CH_2Cl_2



3



- CAP with same [333] conformation of free ligand
- Same PN and NN distances as in free ligand
- Ru-P bond length longer than RAPTA-C
- Ru-C bond lengths longer than RAPTA-C

- Same CAP conformation of **2**
- Ru-P and Ru-C bond lengths longer than in **2** (less strong Ru-*p*-cymene interaction)
- Ru-Cl bond lengths shorter than in **2**

RACAP-C. Selected bond distances (Å) and angles (deg): Ru-Cl1=2.4184(5), Ru-Cl2=2.4205(5); Ru-P=2.3180(5); Ru-centroid(C1-C6)=1.709; Cl1-Ru-Cl2=87.601(19); Cl1-Ru-P=86.937 (19); Cl2-Ru-P=83.775(18)

Compound 3 2MeOH/H_2O. Selected bond distances (Å) and angles (deg): Ru-Cl=2.4026(7); Ru-P1=2.3254(7); Ru-P2=2.3353(7); Ru-centroid(C1-C6)=1.768; Cl-Ru-P1=83.59(2); Cl-Ru-P2=87.90(3); P1-Ru-P2=93.37(3)

Guerriero, A., et al. *Inorg. Chem.* (**2017**) *56*, 5514

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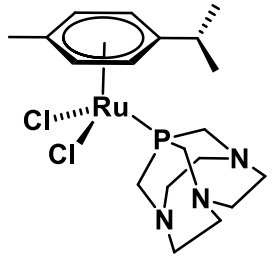
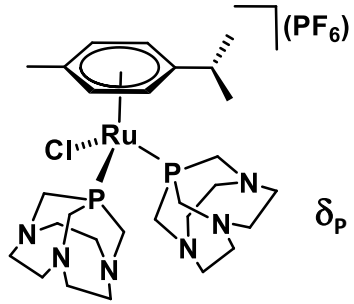
Stability tests of new Ru(II) complexes



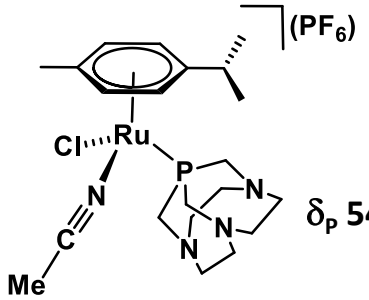
2

δ_P 57,31 ppm



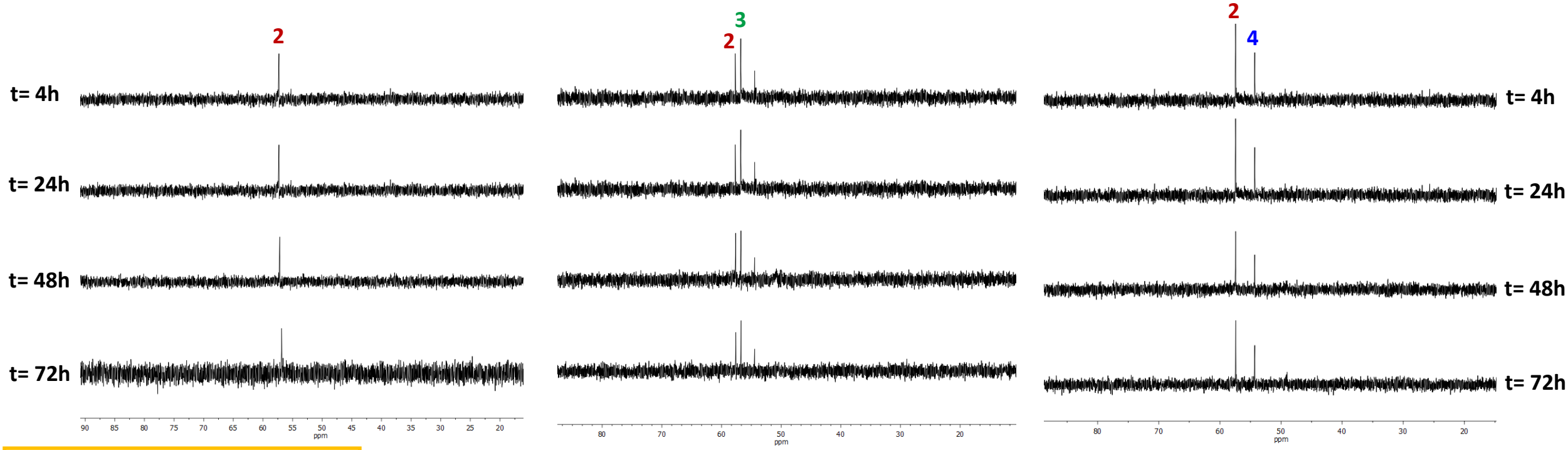
3

δ_P 56,77 ppm



4

δ_P 54,30 ppm



Pseudo-pharmacological conditions:

- NaCl/D_2O (100 mM)
- Complexes (4 mM) in NaCl/D_2O
- T= 37 °C

Details of $^{31}P\{^1H\}$ NMR spectra of complexes in NaCl/D_2O @ 37 °C

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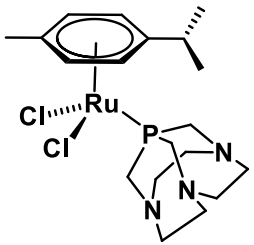
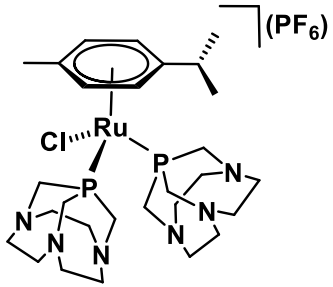
Ru(II)-CAP complexes: in vitro antitumor tests



2



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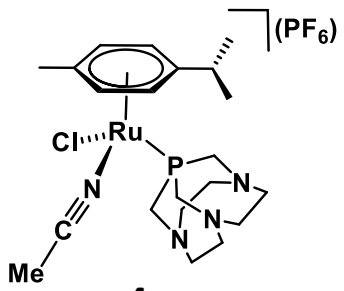
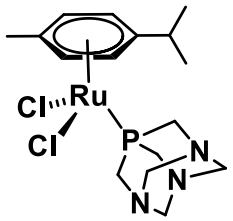


4

- Only minor cytotoxicity effects of **CAP**
- Similar IC_{50} values of **2**-**4** due to the same species in solution
- Equal cytotoxicity of **4** toward A2780 and A2780cisR
- High cell selectivity of **2**-**4** against A2780 compared to HEK293
- Higher cytotoxicity of **2**-**4** compared to **RAPTA-C**



RAPTA-C

Cytotoxicity tests (IC_{50}, μM, 72 h) of CAP and its complexes.

	A2780	A2780cisR	HEK293
CAP	>200	>200	>200
2	55.3 ± 18.6	108 ± 10	102 ± 26
3	48.1 ± 2.2	99.2 ± 15.9	80.7 ± 12.4
4	65.2 ± 18.0	70.6 ± 3.1	163 ± 46
RAPTA-C	230	270	>1000

Cytotoxicity determined by the MTT (3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide) cell viability assay. For each testing, compounds were freshly prepared as a DMSO solution of 0.5% v/v. A 100 µL portion of drug solution was added to each well and the plates were incubated at 37°C for 72 h.

A2780 = human ovarian carcinoma cells
A2780cisR = cells resistant to cisplatin
HEK293 = noncancerous human embryonic kidney cells

Guerriero, A., et al. *Inorg. Chem.* (**2017**) *56*, 5514

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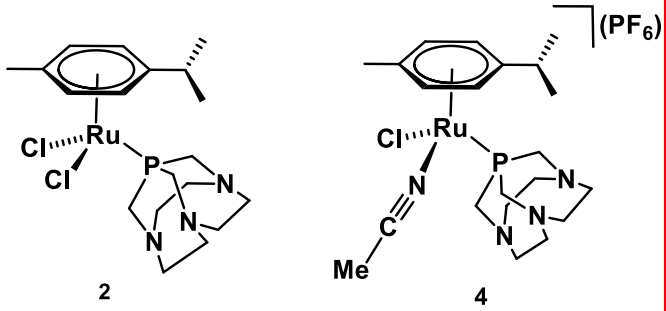
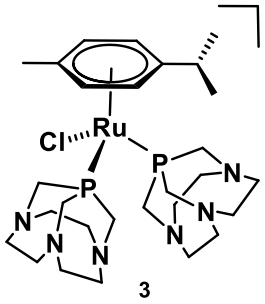
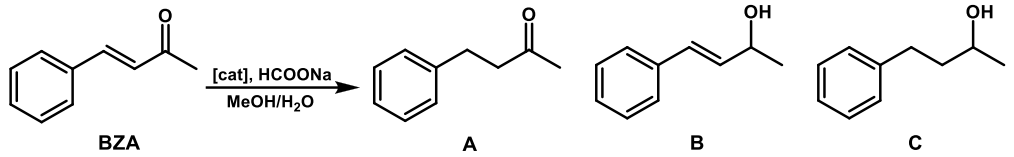
Ru(II)-CAP complexes: catalytic *transfer hydrogenation* of BZA



- Active @80°C
- Poorly stable
- More active than RAPTA-C
- Selective for C=C bond reduction



- Active @80°C
- Highly stable
- Lower reaction rate
- Selectivity for C=C bond



Catalytic transfer hydrogenation of BZA with compounds **2** – **4**

Entry	Catalyst	T (°C)	% conv.	time (h)	yield A (%)[b]	yield B (%) [b]	yield C (%) [b]
1	**2**	60	60.0	24	45.3	13.0	1.7
2[c]	**2**	60	18.7	24	14.2	4.4	0.1
3	**2**	80	99.4	4	82.0	5.2	12.2
4[c]	**2**	80	76.3	4	61.7	12.8	1.8
5	**4**	80	82.6	4	68.9	11.5	2.2
6[c]	**4**	80	51.9	4	40.4	10.8	0.7
7	**3**	80	71.8	24	52.3	15.8	3.7
			96.0	48	68.7	13.5	13.8
8[c]	**3**	80	66.5	24	46.6	17.8	2.1
			92.5	48	73.5	13.0	6.0
9	**RAPTA-C**	80	99.5	24	93.2	3.2	3.1
10[c]	**RAPTA-C**	80	30.0	24	23.8	6.0	0.2

[a]General conditions: catalyst, 9.8 x 10^{-3} mmol; BZA, 0.98 mmol; HCOONa, 9.8 mmol; **MeOH:H_2O (1:/1)**, 6 mL; **catalyst/substrate/HCOONa= 1:100:1000**. [b] GC values based on pure samples: A = 4-phenyl-2-butanone; B = 4-phenyl-3-buten-2-ol; C = 4-phenyl-2-butanol. [c] Hg(0) added (one drop).

Guerriero, A., et al. *Catalysts* (**2018**) *8*, 88

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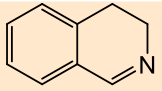
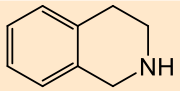
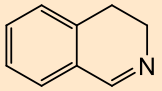
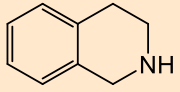
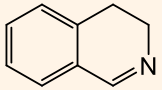
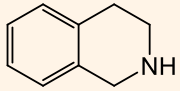
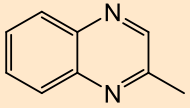
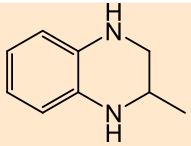
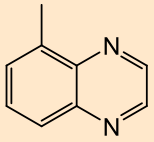
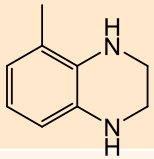
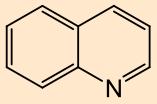
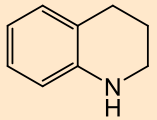
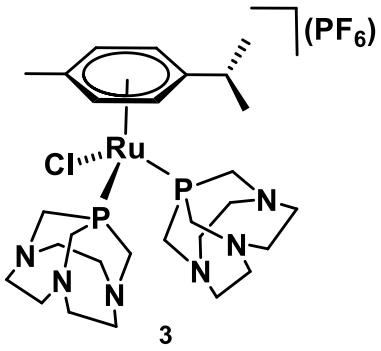
Ru(II)-CAP complex: transfer hydrogenation of cyclic imines

Catalytic transfer hydrogenation of cyclic imines with complex **3**.

Entry	T (°C)	solvent	Substrate	Product[b]	yield[c]	time (h)
1	80	H_2O			39.9	24
			3,4-dihydroisoquinoline	1,2,3,4-tetrahydroisoquinoline		
2	60	MeOH/H_2O 1:1			10.9	24
3	80	MeOH/H_2O 1:1			**74.1** **92.5**	**24** **48**
4	80	MeOH/H_2O 1:1			0.4	24
			2-methylquinoxaline	2-methyl-1,2,3,4-tetrahydroquinoxaline		
5	80	MeOH/H_2O 1:1			–	48
			5-methylquinoxaline	5-methyl-1,2,3,4-tetrahydroquinoxaline		
6	80	MeOH/H_2O 1:1			1.5 3.0	24 48
			quinoline	1,2,3,4-tetrahydroquinoline		

[a]General conditions: catalyst, 1.0 x 10^{-2} mmol; substrate, 1.0 mmol; HCOONa, 10.0 mmol; **MeOH:H_2O (1:/1)**, 6 mL.; **catalyst/substrate/HCOONa= 1:100:1000**. [b] Products confirmed by GC and GC-MS analyses. [c] GC values based on pure samples.



- active @80°C
- good conversion
- mild reduction protocol

Guerriero, A., et al. *Catalysts* (**2018**) *8*, 88

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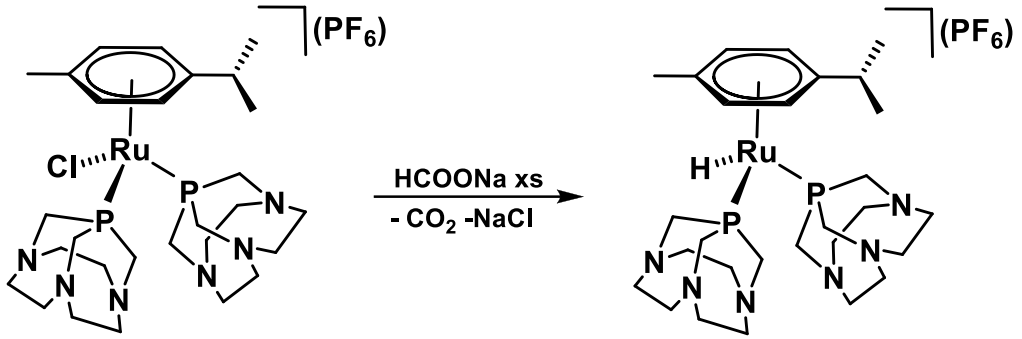
Investigation of catalytically active species



3

δ_P **55,77 ppm**

-144.45 ppm

4

δ_P **78.26 ppm**

-144.48 ppm

I. NMR scale experiment under pseudo-catalytic conditions:

3 + **HCOONa (50 eq)** $\xrightarrow{\text{MeOH/H}_2\text{O (1:1)}}$ **4**

- T = 60 °C → 100% conv. after 24 h
- T = 80 °C → 100% conv. after 17 h

II. Independent synthesis:

3 + **HCOONa (50 eq)** $\xrightarrow[\text{80 °C}]{\text{MeOH/H}_2\text{O (1:1)}}$ **4**

100% conv. after 28 h

$[RuH(p\text{-}cym)(CAP)_2]PF_6$

δ_H - 12.23 ppm ($^2J_{HP}$= 35.5 Hz)

$[RuCp(H)(PTA)_2]$

δ_H - 14.36 ppm ($^2J_{HP}$= 36.6 Hz)

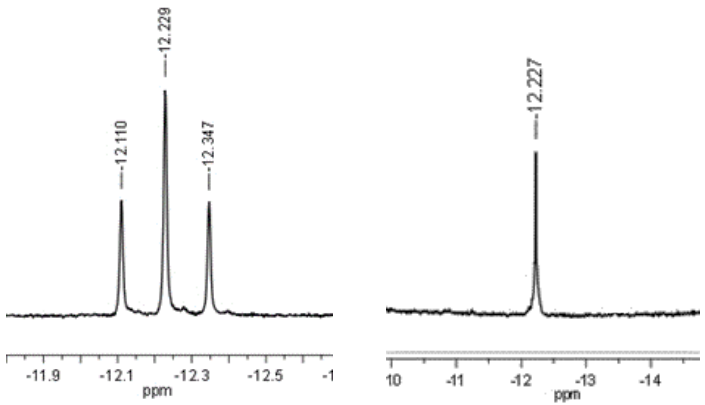


Figure 4. ^{1}H (left) and ^{1}H{^{31}P} NMR (right) spectra (negative region only, CD_2Cl_2) showing the change from triplet to singlet for the Ru-H signal in **4**.

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Guerriero, A., et al. *Catalysts* (**2018**) *8*, 88

Summary of results

PTA

- Synthesis of a library of PTA upper-rim and lower-rim modified ligands
- Homogeneous Ru and Ir catalyzed C=O and C=C bond hydrogenations
- Biphasic Rh-catalyzed olefin hydroformylation with CDs
- Heterogeneous Ir-catalyzed C=N and C=O bond hydrogenations

CAP

- Improved synthesis of CAP
- Anticancer activity in vitro of Ru-CAP complexes
- Ru-CAP complexes active in catalytic TH reactions using HCOONa

Future perspectives of CAP project

- To explore the coordination properties of CAP to other TMs
- To study the capability of CAP to bind by both P and N donors to different metals and assess the structural properties of the materials obtained
- To test the obtained complexes in other catalytic reactions
- Use of CAP to bind Ag(I) and test the compounds as antimicrobial agents

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