Новые тенденции в катализе органических реакций

- Нанокатализ
- Катализ кислотами Бренстеда
- Катализ кислотами Льюиса
- Органокатализ
- Катализ солями непереходных металлов

И.П. Белецкая

15-19.05.2017, г. Иркутск

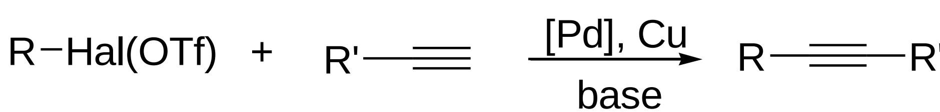
Cross-coupling reactions

R-M + Ar(Het), vinyl, alkynyl -X $\xrightarrow{\text{cat}}$ R-Ar(Het), vinyl, alkynyl

Kumada, Corriu (1972)

M = MgX (Tamao - Kumada)
= SnR_3 (Migita - Kosugi - Stille)
= ZnX (Negishi)
= $B(OH)_2$ (Suzuki - Miyaura)
= SiR_3 (Hiyama)

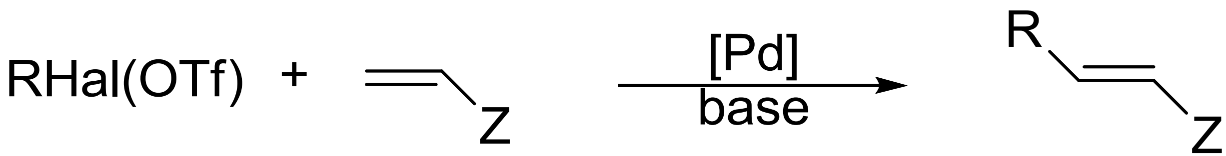
Sonogashira - Hagihara



R=Ar, Vinyl; R'=Ar, Alk

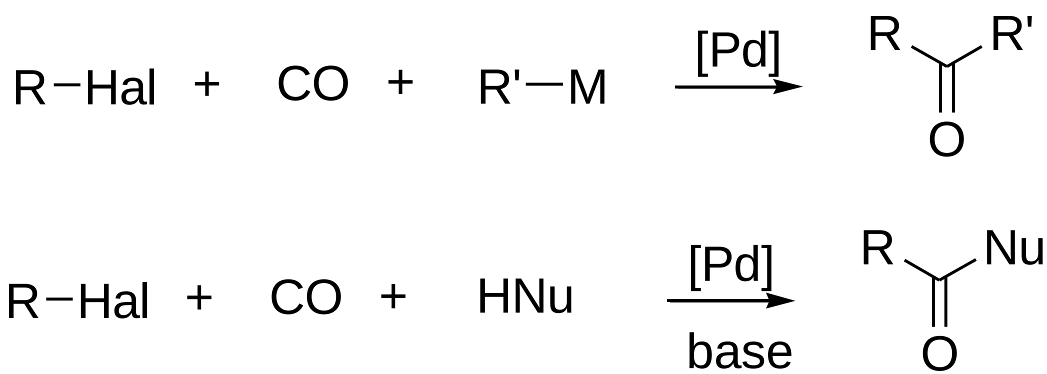
Cross-coupling reactions

Mizoroki - Heck reaction



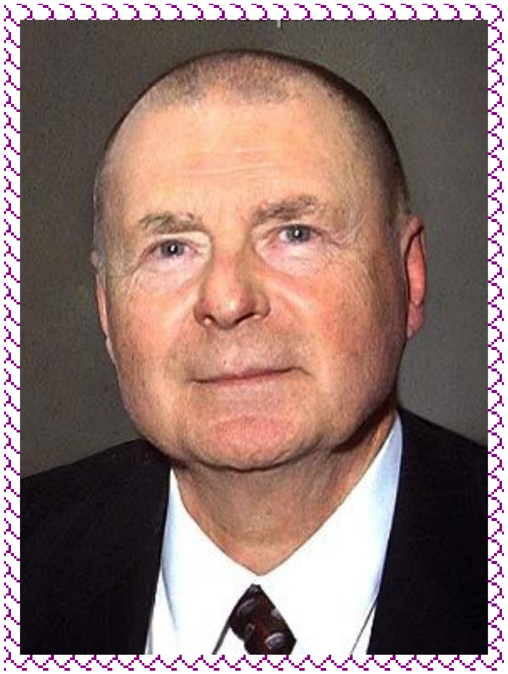
R = Ar, vinyl
Z = Ar, COOH, COOR, CN

Carbonylation



R=Ar, Vinyl;
HNu = H_2O, ROH, RNH_2, R_2NH, RSH

The Nobel Prize in Chemistry 2010



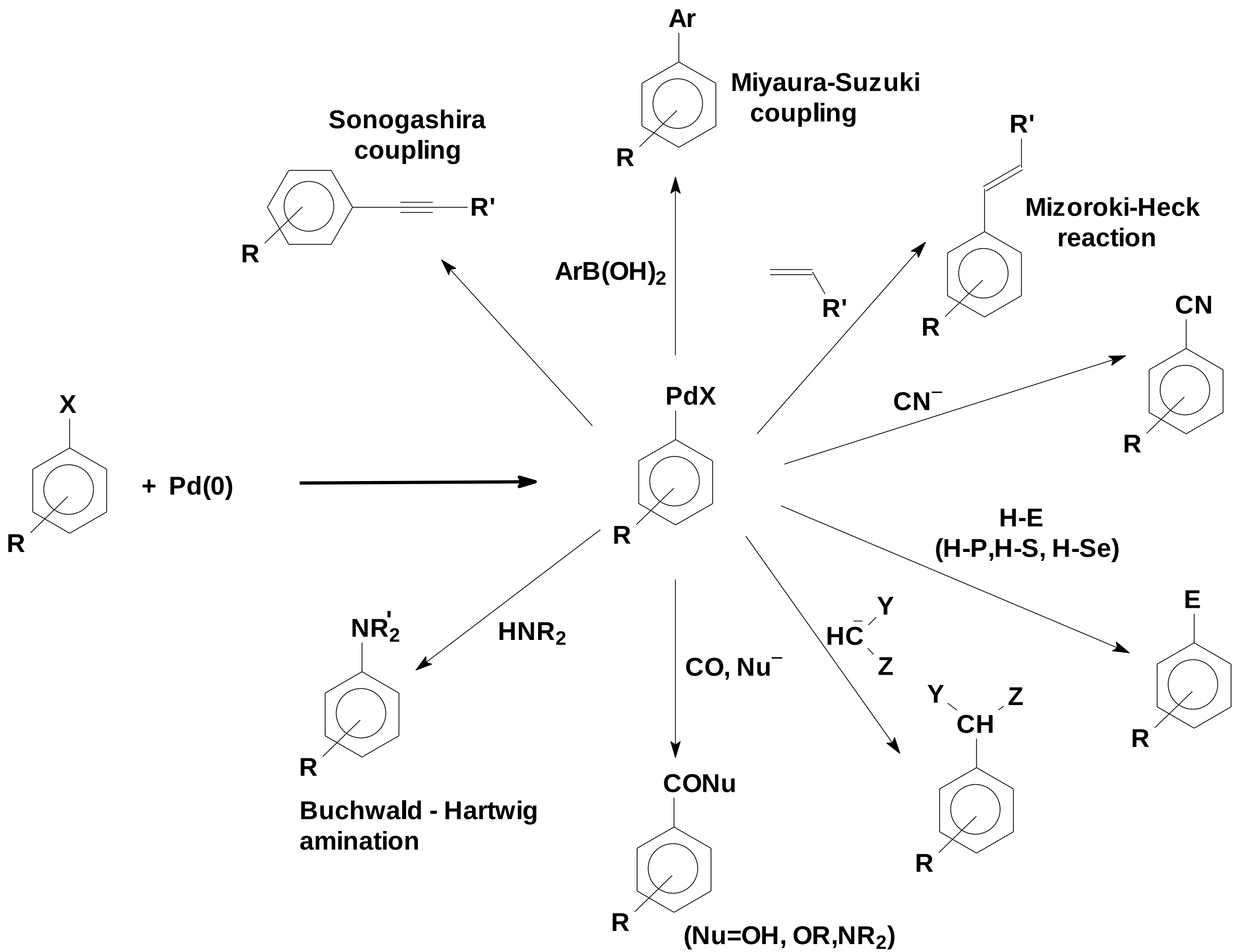
Richard F. Heck

Ei-ichi Negishi

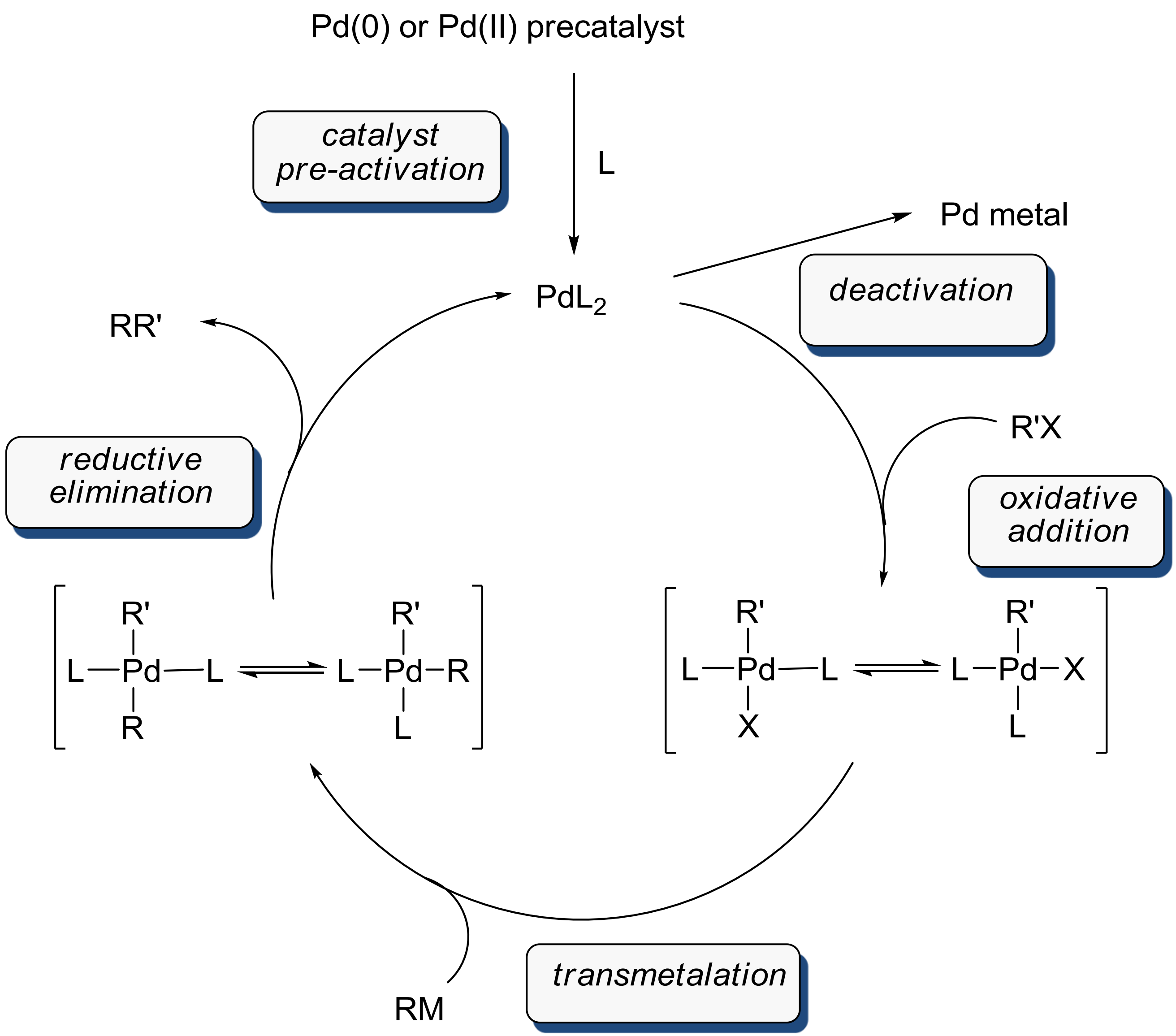
Akira Suzuki

for palladium-catalyzed cross couplings in organic synthesis

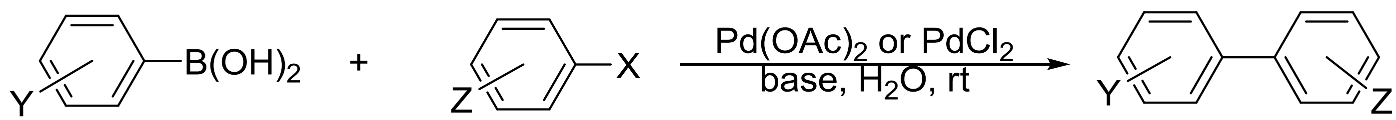
Pd-catalyzed reactions



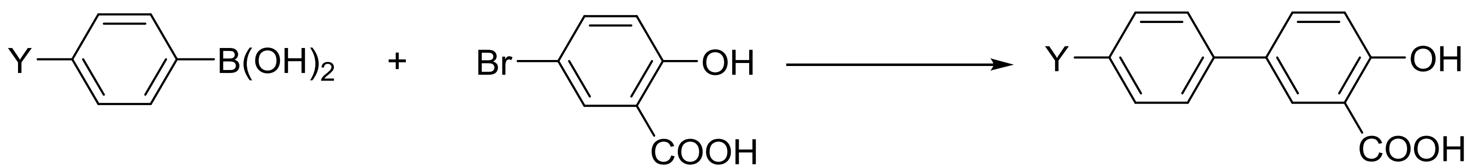
Catalytic cycle of Pd-catalyzed reactions



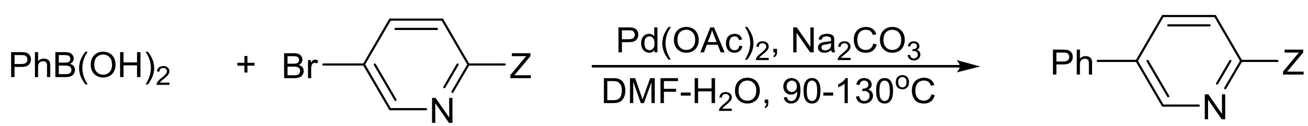
Suzuki Reaction



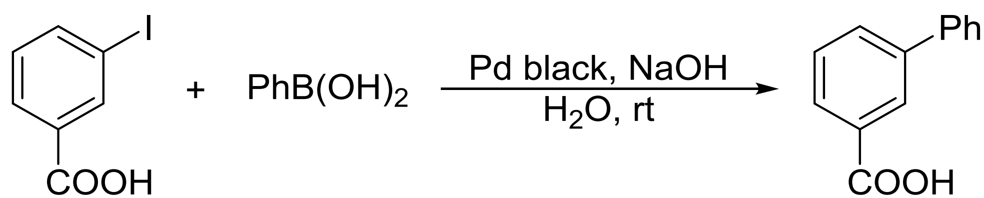
X: Br, I; Y: H, p-F, p-(4-*n*-amylcyclohexyl); Z: m-, p-OH; o-, m-, p-COOH



Y: H, F



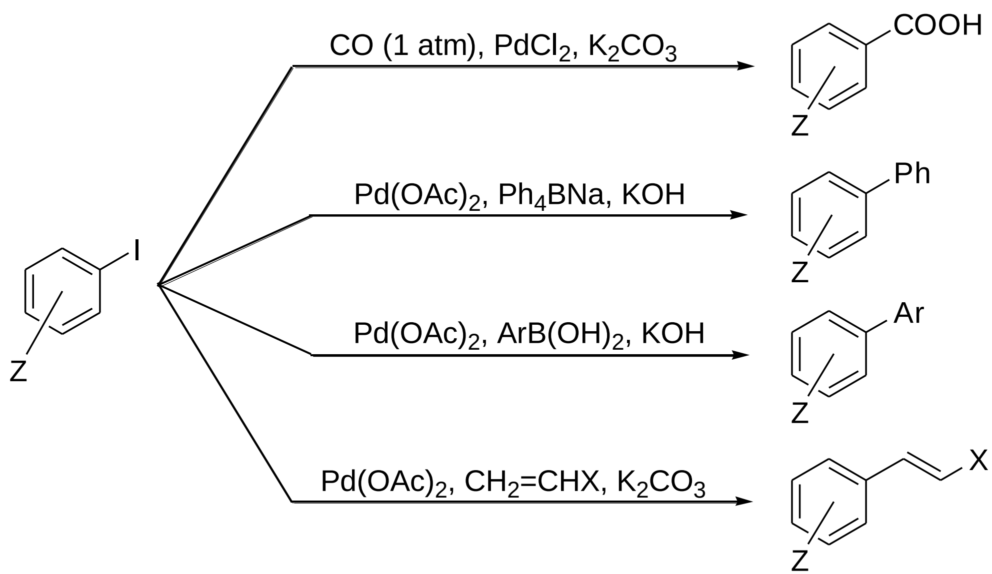
Z: NO_2, NH_2, OEt

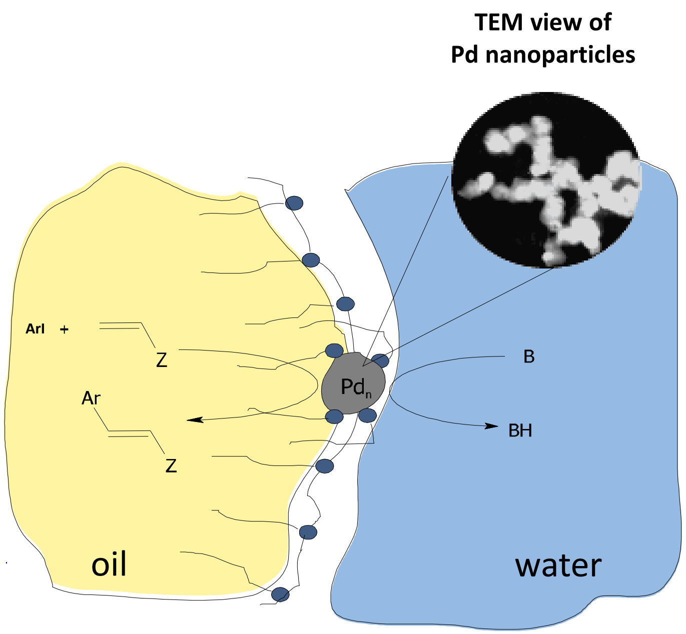


Izv. Akad. Nauk SSSR, Ser. Khim., **1989**, 2394

Reaction in microemulsion

Reactions which can be readily run
in *microemulsion media* at preparative scale

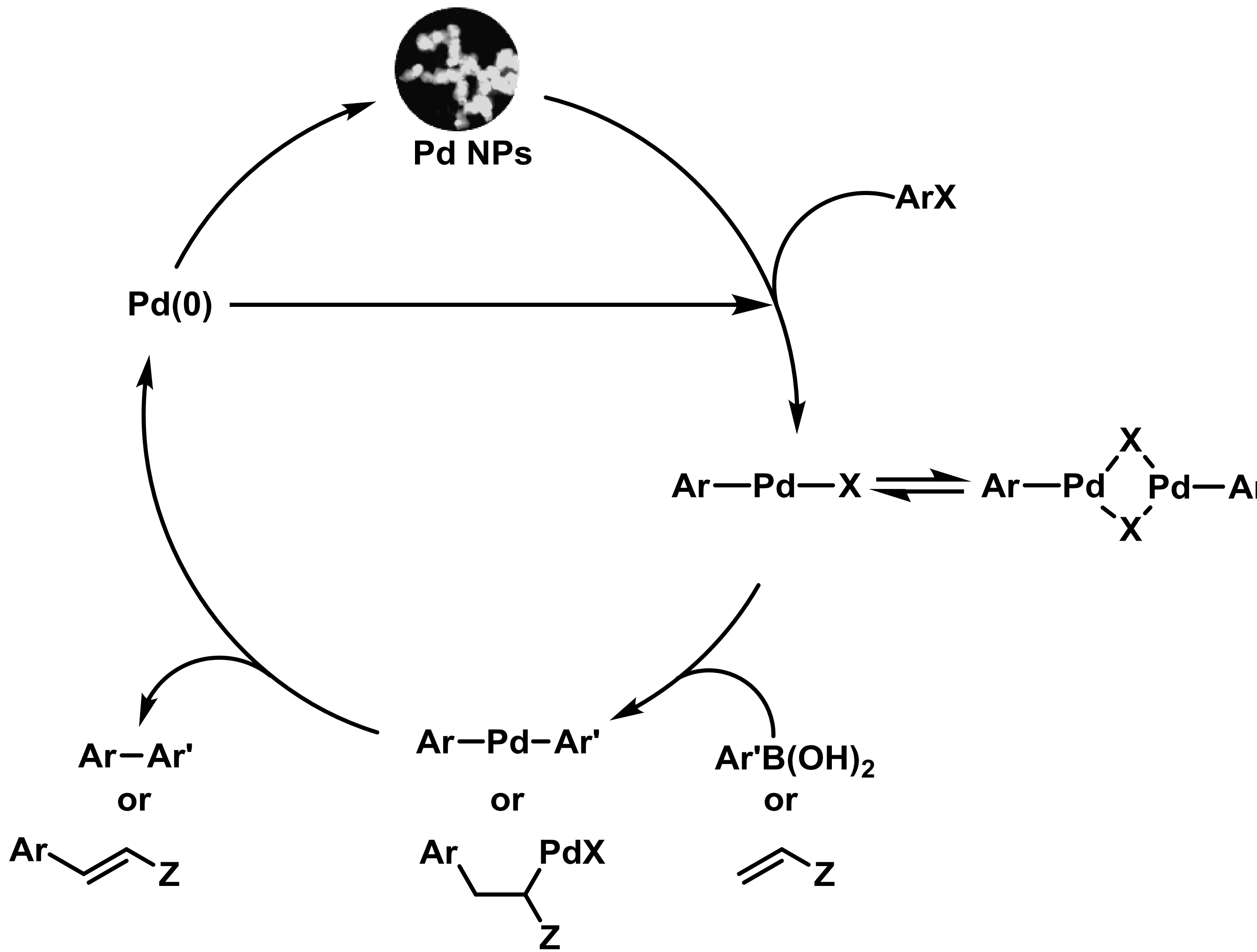




Z: Alk, NO_2, OR, COOR, CN, Hal, etc.; X = COOR, Ar, 4-Py
Microemulsion media: surfactant (anionic, cationic, or non-ionic) – co-surfactant (alkanol C_2-C_5, or alkyl ethers of mono or diethyleneglycol) – water (molar ratio 1:5-6:200)

Heck reaction

Surfactant $C_{17}H_{33}CO_2K$
$PdCl_2$ (0.01 mol%), Yield 90%

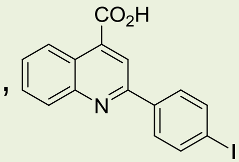


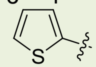
Cheprakov A.V. *Adv. Synth. Catal.,* **2015**, 357, 417

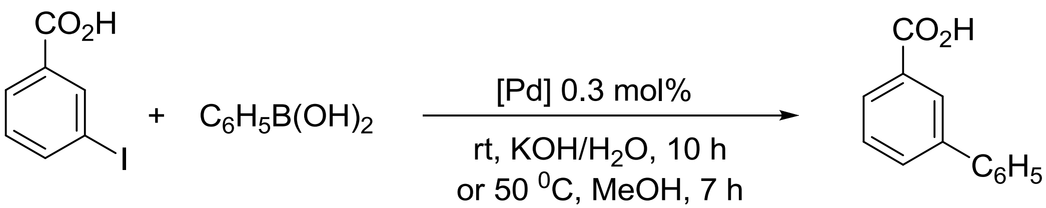
Suzuki reaction

ArHal + Ar'B(OH)$_2$ → Ar—Ar'
([Pd] 1 mol%, KOH, H_2O, 20°C or MeOH, 50°C)

up to **98%**

Ar: p-C_6H_4OH, m-$C_6H_4CO_2H$, 

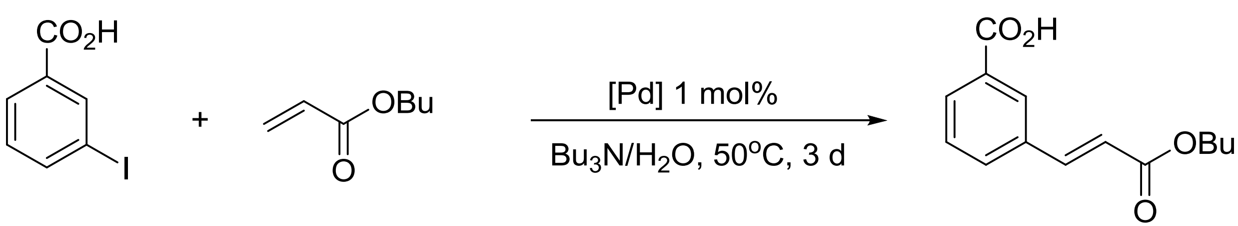
Ar': Ph, 



	Run	1	2	3	4	5
H_2O (10 h)	Yield, %	94	90	91	90	94
MeOH (7 h)		82	85	83	84	84

PS-PEO-PC-Pd

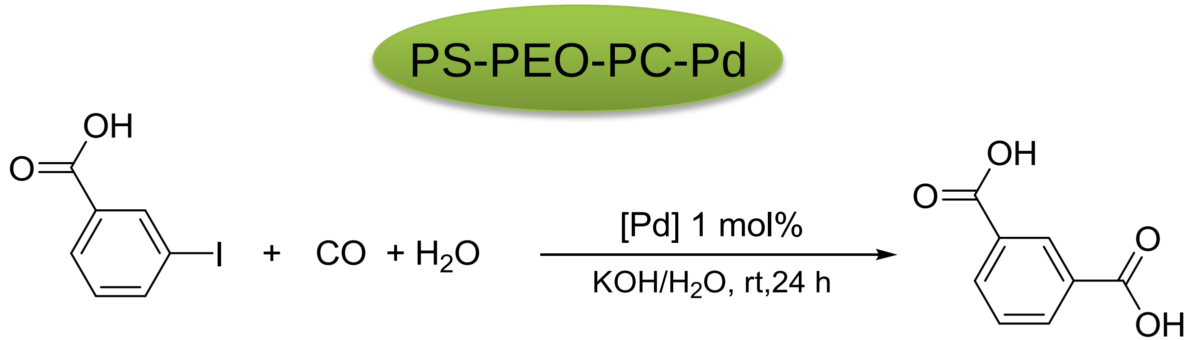
Heck reaction



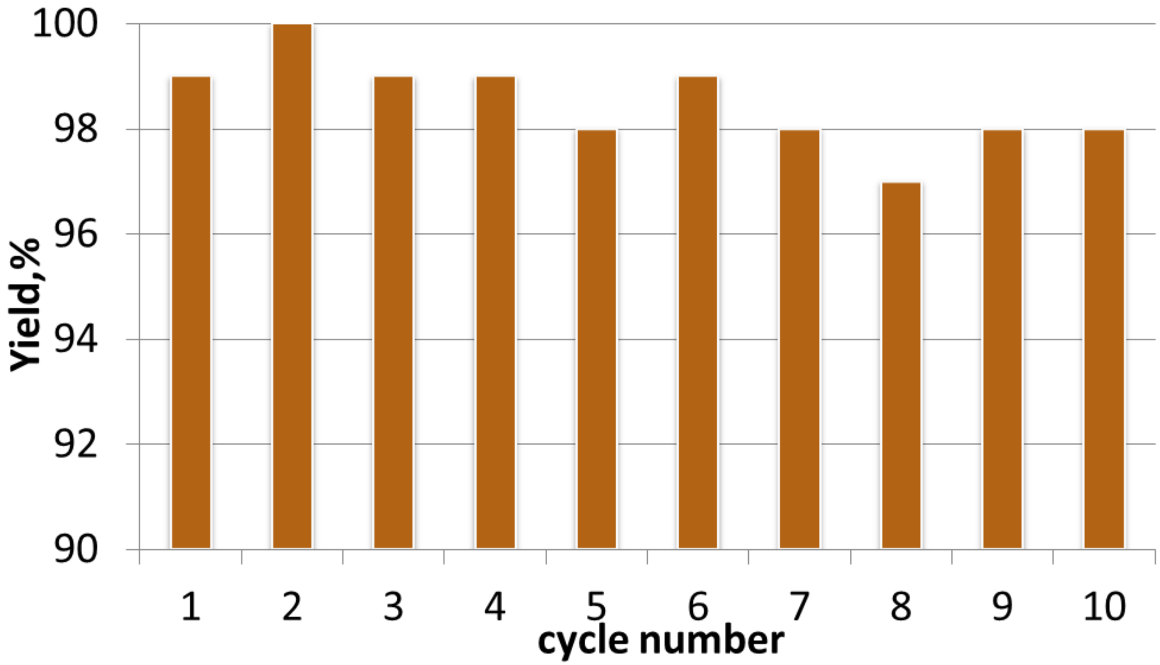
98%

A. Kashin, A. Khokhlov, *Synlett*, **2008**, 1547

Carbonylation



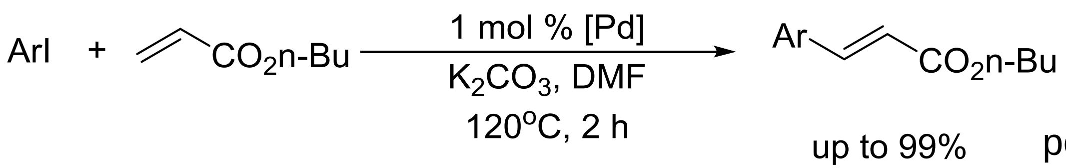
Catalyst recycling (ultrafiltration)



O. Ganina, *Reac. Kinet. Mech. Cat.*, **2010**, *99*, 1547

Heck reaction

Pd-PVI-PVC



[Pd]: $PdCl_2$ / PVI-PVC

poly(N-vinylimidazole-co-N-vinylcaprolactam)

Ar = Ph	**Run**	**1**	**2**	**3**	**4**	**5**
	Yield, %	99	99	91	94	98

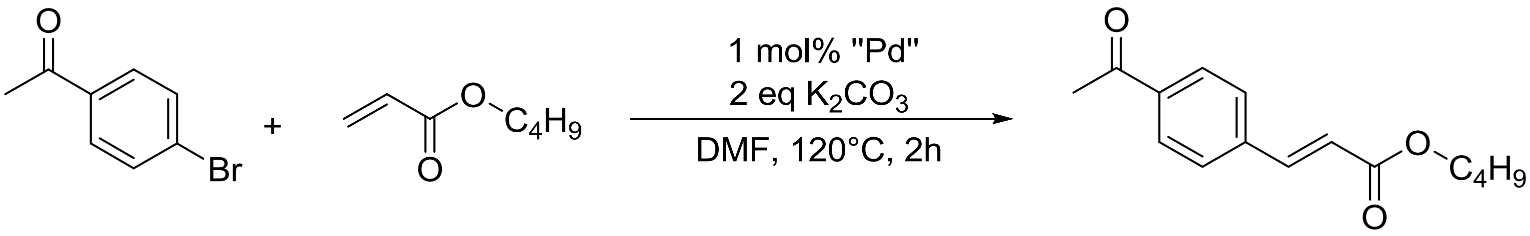
p-X	OMe	Me	MeCO	MeO_2C	CN
Yield, %	86	93	91	95	94

ArBr: Ph (84%, 24h), p-MeCO (95%, 2h)

E. Tarasenko, *J. Organomet. Chem.*, **2007**, *692*, 4402

Reactions of n-butyl acrylate with p-acetylphenyl bromide

Pd-PVI-PVC

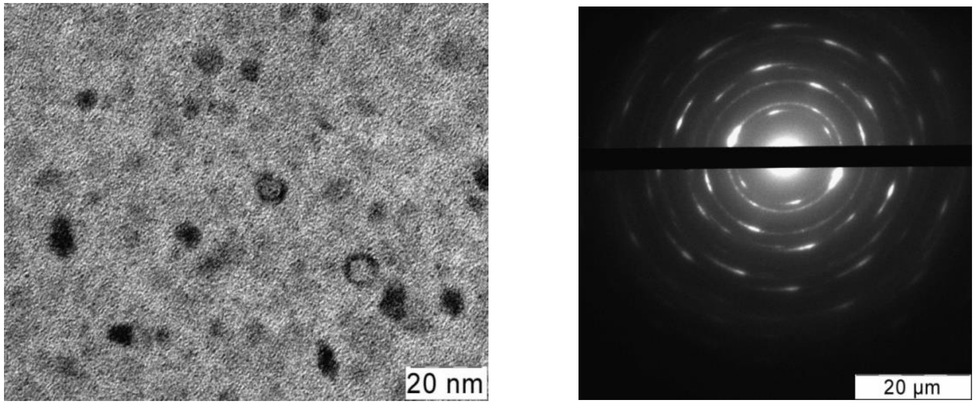


"Pd" = $PdCl_2$/PVI-PVC=1:5

[Pd]: $PdCl_2$ / PVI-PVC

Run	**1**	**2**	**3**	**4**	**5**
Yield, %	99	99	93	92	98

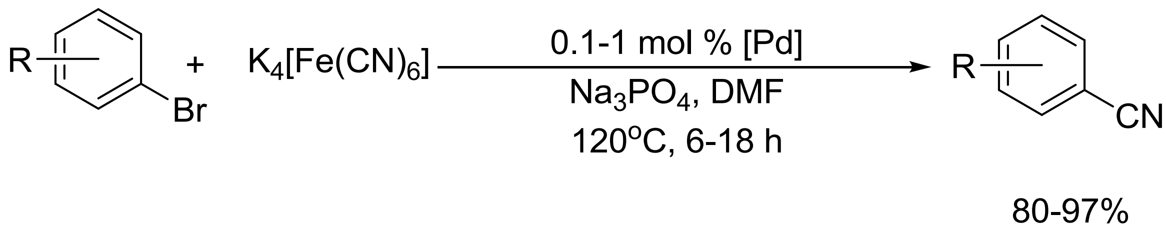
TEM images of the palladium nanoparticles

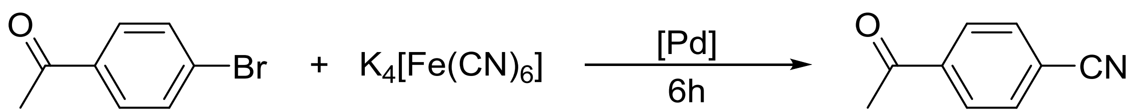


E. Tarasenko, *J.Organomet.Chem.* **2007**, 692, 4402

New recyclable catalyst for the cyanation of arylbromides

Pd-PVI-PVC

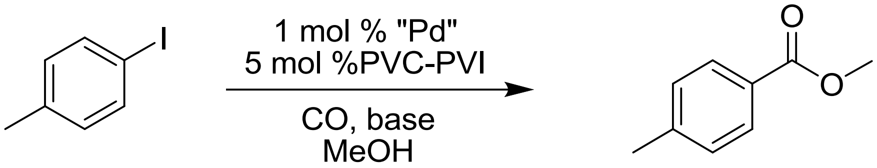




Run	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Yield, %	93	93	90	99	90	99	97	93	95	89

A. Selivanova, *Russ. J. Org. Chem.*, **2010**, *46*, 157

Alkoxycarbonylation of aryl iodides catalyzed by polymer-supported palladium



PVI-PVC = poly(N-vinylimidazole-co-N-vinylcaprolactam)

Entry	Catalyst	Base	Temp, °C	Pressure of CO, atm	Yield, %
Influence of base and catalyst					
1	H_2PdCl_4	KOH	50	1	11
2	H_2PdCl_4	K_2CO_3	50	1	18
3	H_2PdCl_4	Et_3N	50	1	32
4	K_2PdCl_4	KOH	50	1	45
5	K_2PdCl_4	K_2CO_3	50	1	53
6	K_2PdCl_4	Et_3N	50	1	85
Influence of CO pressure					
7	K_2PdCl_4	Et_3N	50	1	70
8	K_2PdCl_4	Et_3N	50	5	48
9	K_2PdCl_4	Et_3N	50	30	41
Influence of temperature					
10	K_2PdCl_4	Et_3N	25	1	8
11	K_2PdCl_4	Et_3N	40	1	63
12	K_2PdCl_4	Et_3N	55	1	92

5 cycles (entry 12)

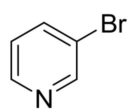
O. Ganina, *Reac. Kinet. Mech. Cat.*, **2010**, *99*, 1547

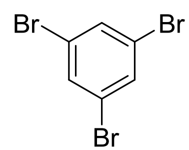
Suzuki reaction

Pd-PVI-PVC

$$ArBr + PhB(OH)_2 \xrightarrow[\text{PdCl}_2\text{/PVI-PVC=1:5, solvent, base}]{\text{1 mol\% "Pd"}} Ar{-}Ph$$

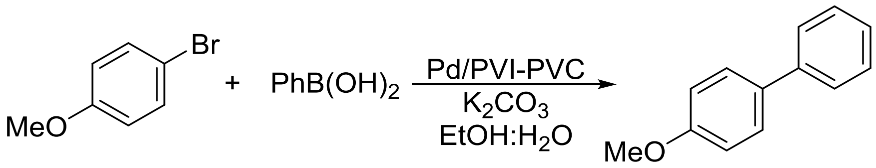
p-CH_3CO	DMF, K_2CO_3, 120°C	~90%
	EtOH:H_2O, K_2CO_3, 80°C	>99%

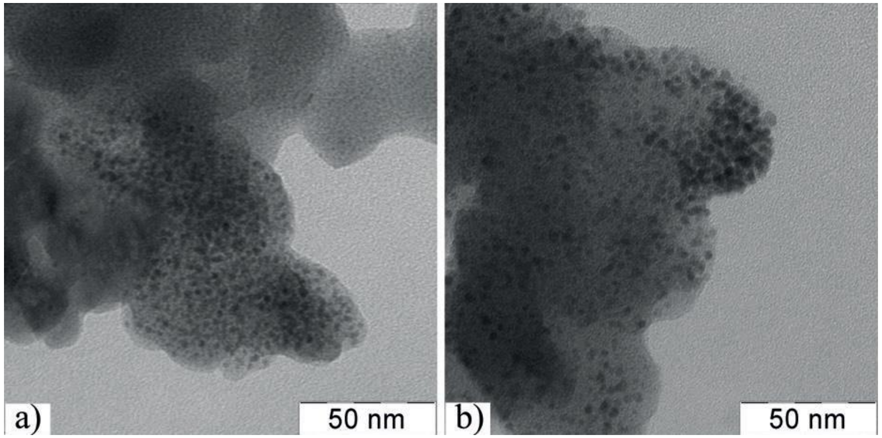
Ph (95%), p-Tol (80%), p-MeOPh (89%), m-CF_3Ph (83%),p-FPh (91%), p-ClPh (90%), 

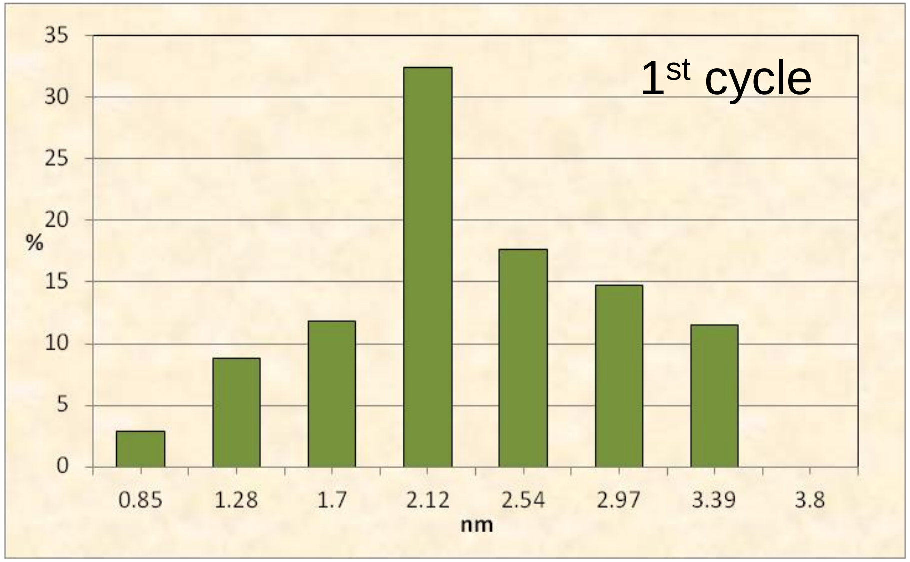
(73%), 

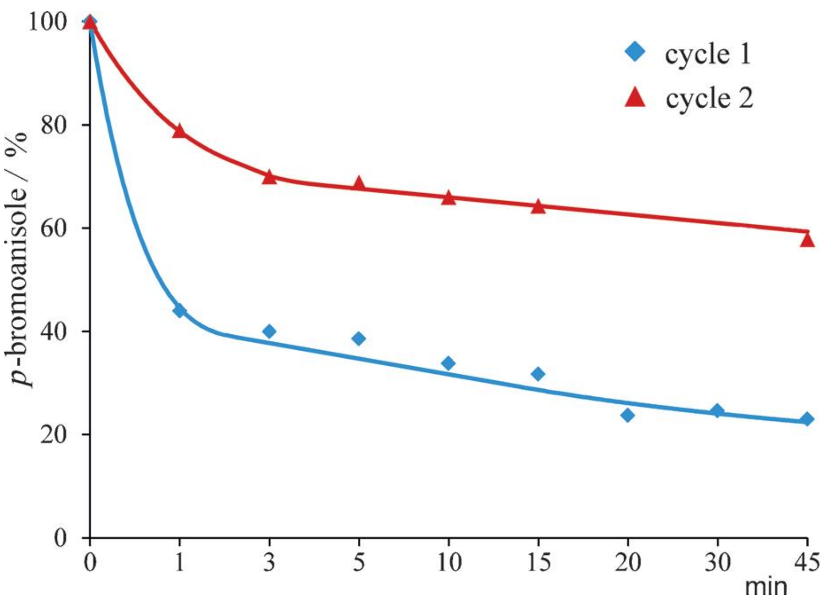
(62%+14% diarylation + 6% mono)

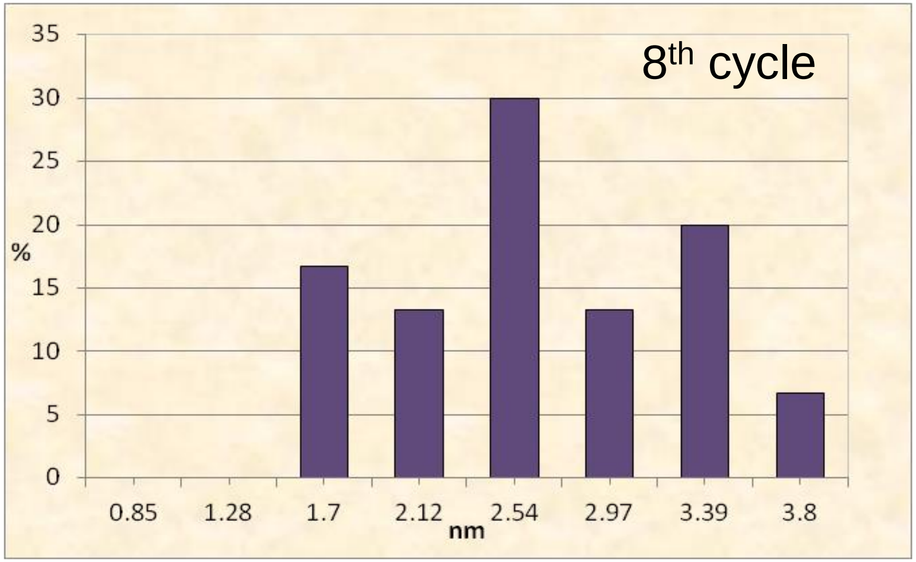
Run	1	2	3	4	5	6	7	8
Yield, %	>99	92	99	99	>99	>99	>99	98



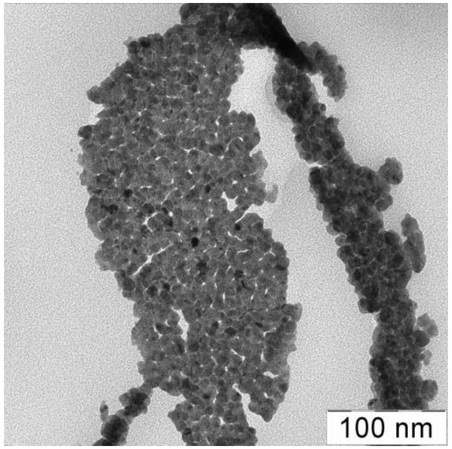


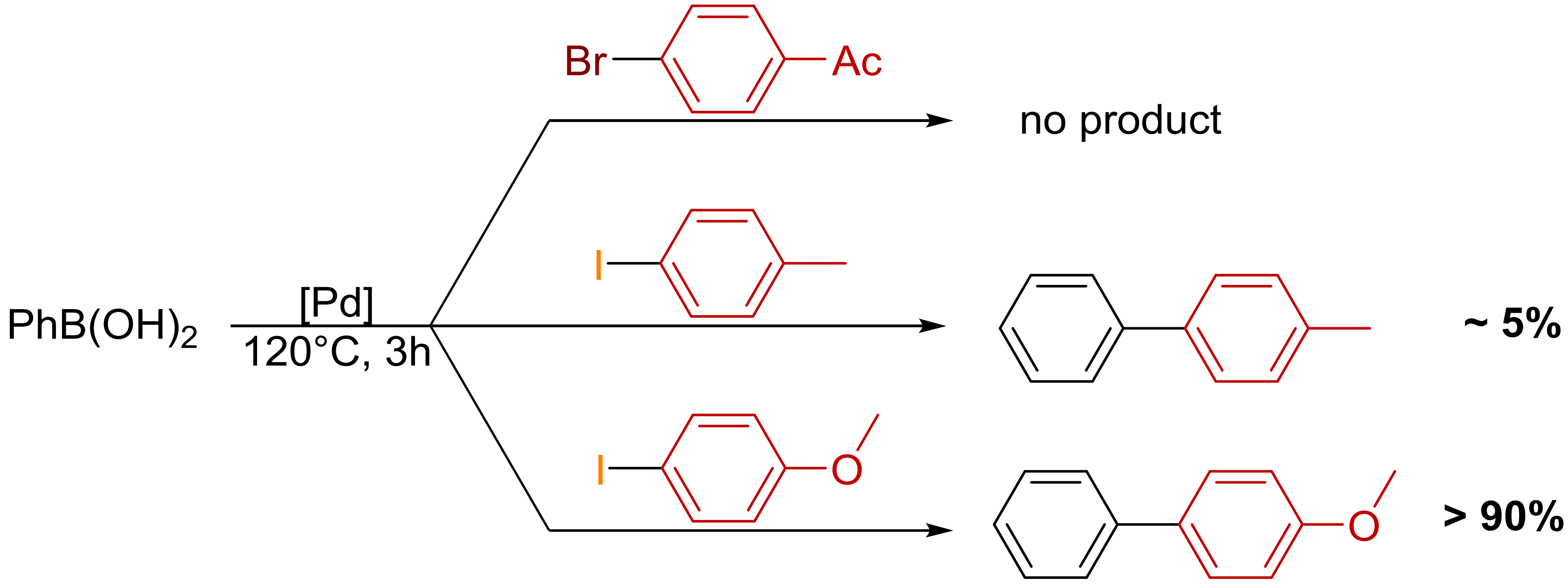




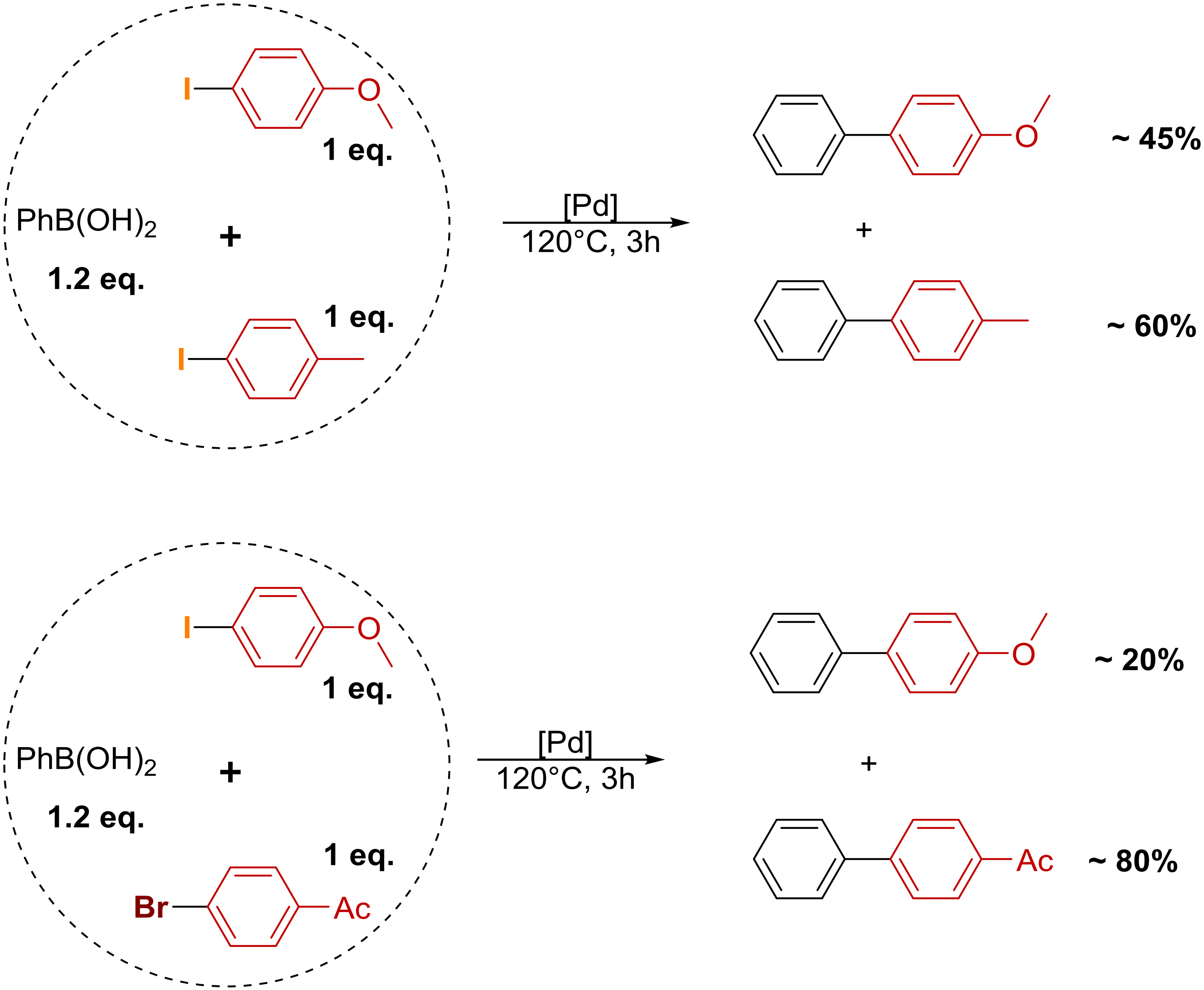


Selivanova A.V., *ChemPlusChem*, **2014**, *79*, 1278





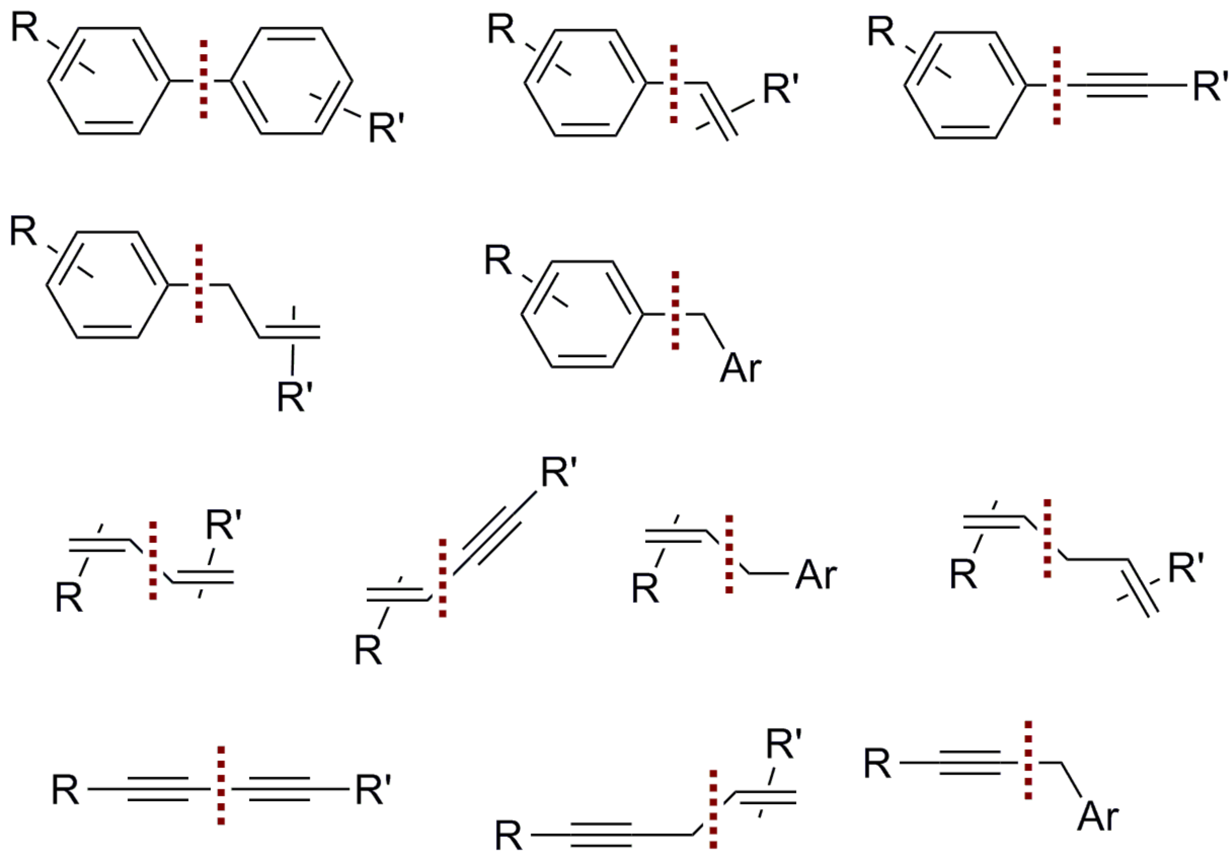
ChemCatChem., **2015**, 7, 2113-2121



ChemCatChem., **2015**, 7, 2113-2121


サイエンスセンタービル１号館
MCOS-XI SYMPOSIUM
THIRT
THE CROSS-COUPLING RE
17:00-20:00 Atrium (1F)
17:20

Scope of cross-coupling reactions



Transition metal catalysis made nucleophilic substitution at sp^2 and sp carbon atoms a routine procedure

Copper

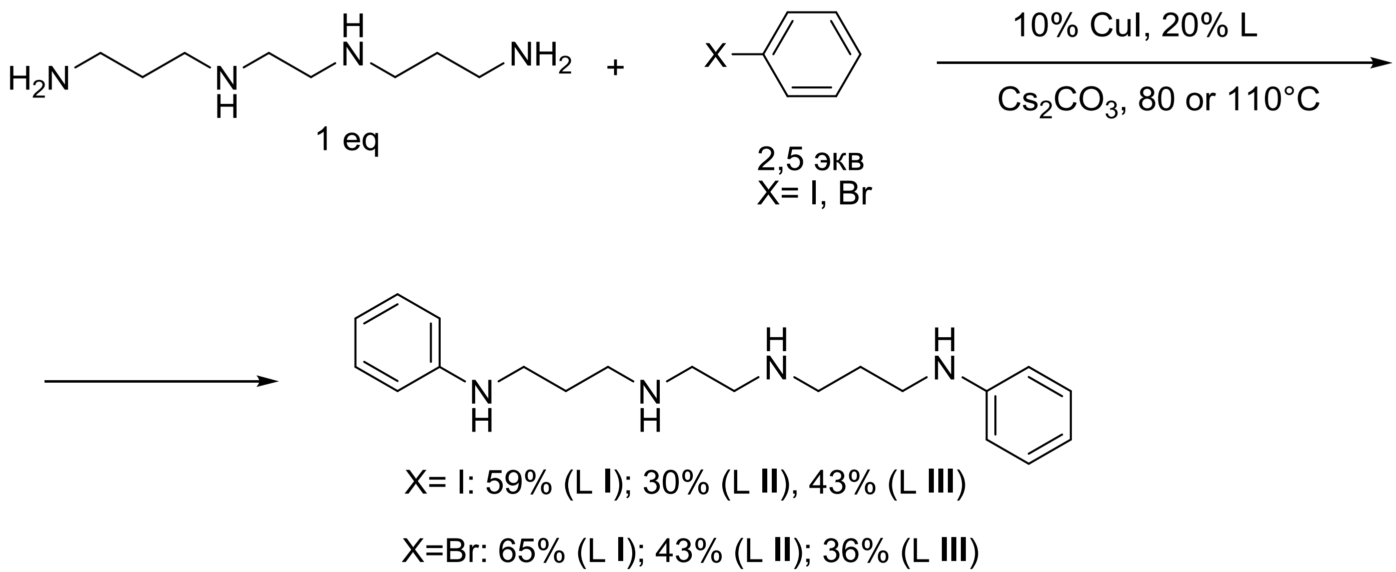
Cu

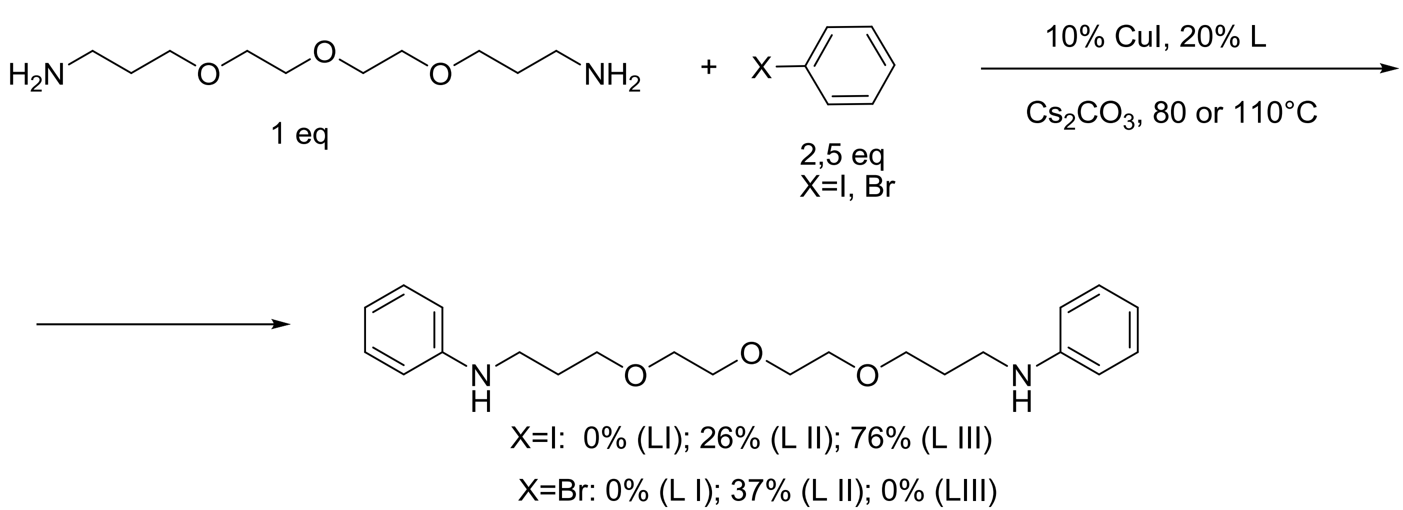
Chemical copper means:

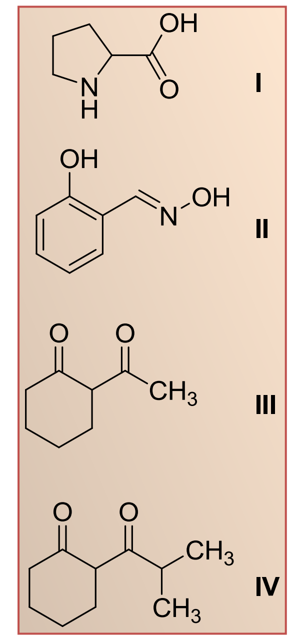
1. **Electrical engineering, telecommunications**
2. **Automotive**
3. **Plumbing: tube, pipe and fittings**
4. **Jewelry, coins**
5. **Chemistry: catalysts and reagents**
6. **Copper alloys for marine applications and more …**

The Cyprian "cyprium" meaning "bronze"

Copper catalyzed arylation of polyamines and oxadiamines

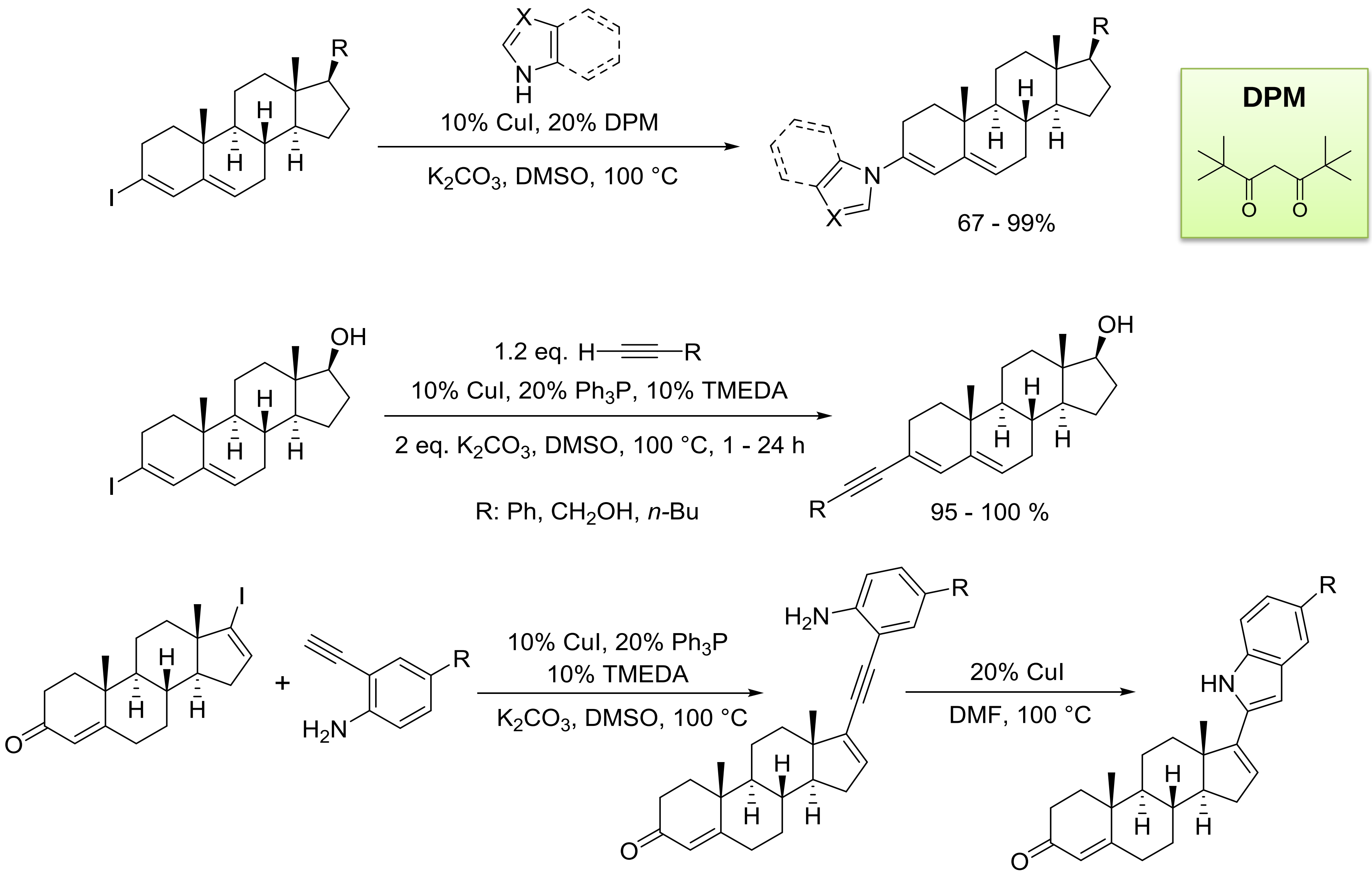






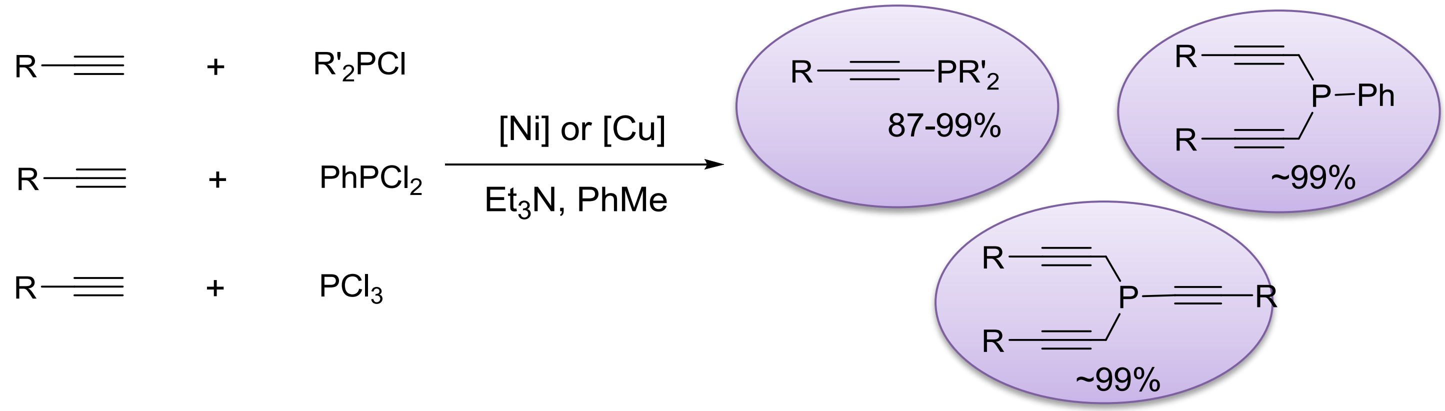
Eur. J. Org. Chem., **2011**, *31*, 6240

Catalytic approach to steroids bearing heterocyclic moieties



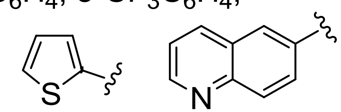
Kotovshchikov Yu.N., Latyshev G.V., *Eur. J. Org. Chem.*, **2013**, 7823; *Org. Bio. Chem.*, **2015**, 13, 5542

Ni- and Cu-catalyzed C-P bond formation

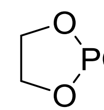


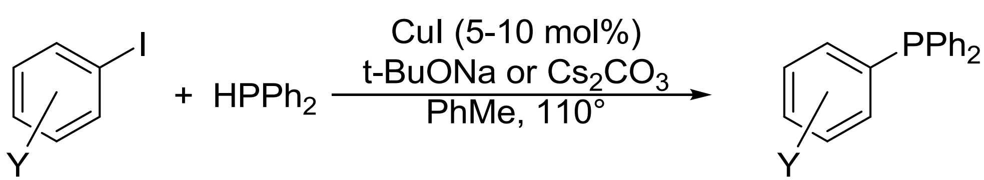
Cat. = $Ni(acac)_2$, $Ni(PPh_3)_2Br_2$, $Ni(COD)_2$, CuI

R = Pr, Am, 4-$MeOC_6H_4$, 4-$Me_2NC_6H_4$, 3-$CF_3C_6H_4$, $MeOCH_2$, Me_2NCH_2, 2-Py,



R'_nPCl_{3-n}: Ph_2PCl, *i*-Pr_2PCl, t-Bu_2PCl, (i-PrO)$_2$PCl, $(Et_2N)_2PCl$, $PhPCl_2$, PCl_3,

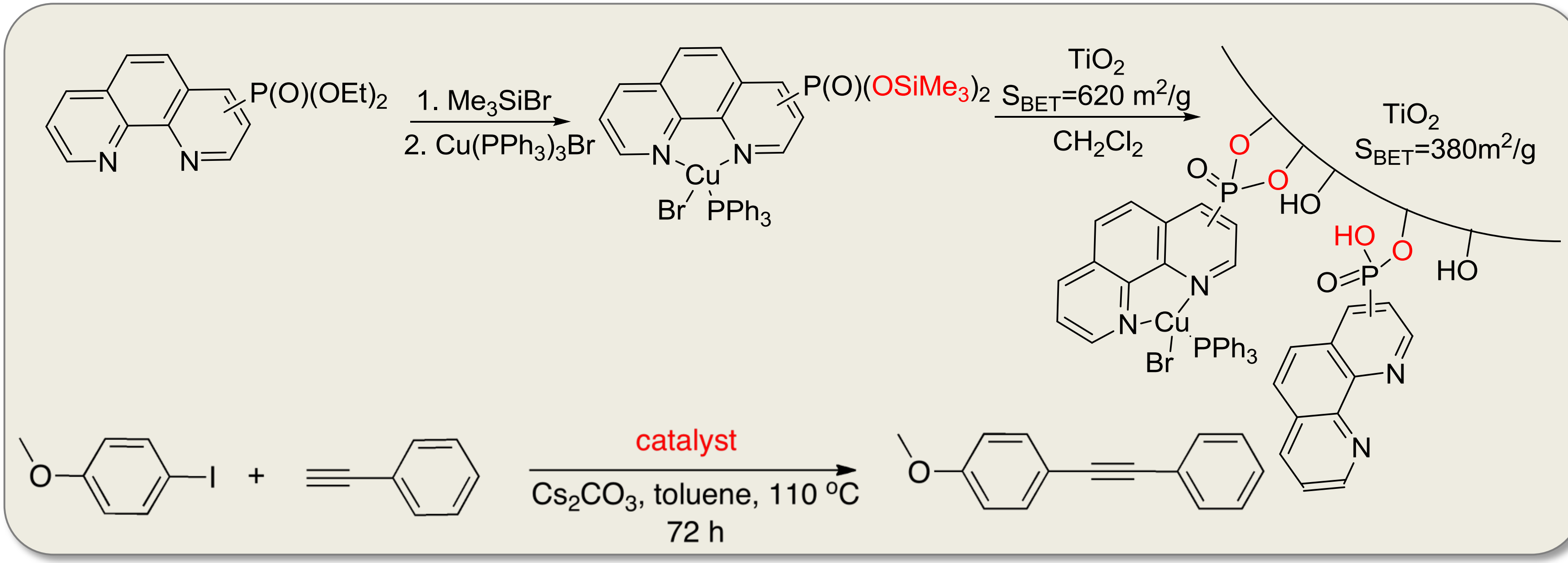




$$RX + HP(O)(OBu)_2 \xrightarrow[\text{PhMe, 110°}]{\text{CuI (5 mol\%), 4L, } Cs_2CO_3} RP(O)(OBu)_2$$

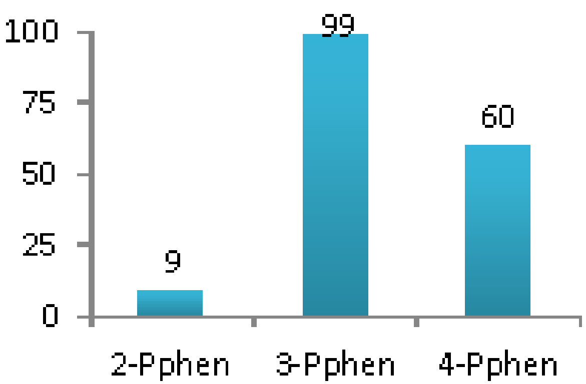
Synthesis, **2003,** 2835,
Org. Lett, **2003,** 5, 4309,

Immobilization of heteroleptic copper(I) complexes on TiO_2

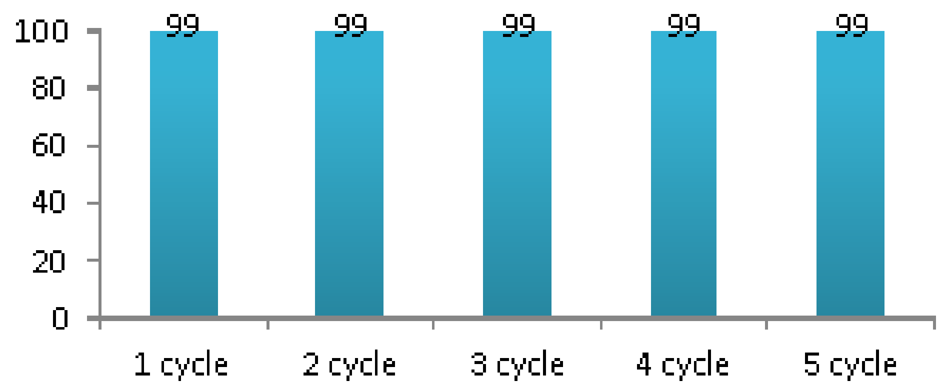


Sonogashira-type reaction

Testing of supported complexes

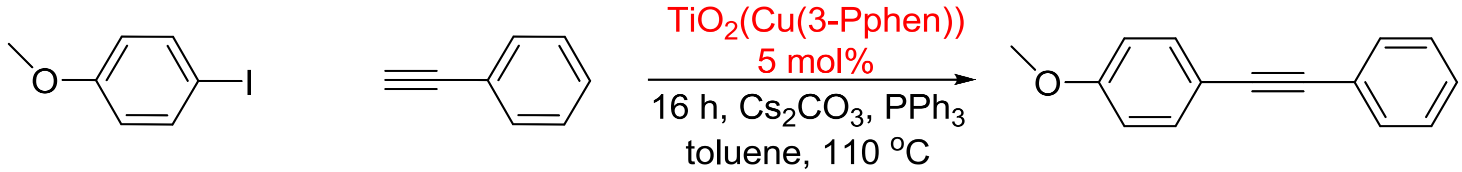


Recyclization experiments with the best catalyst



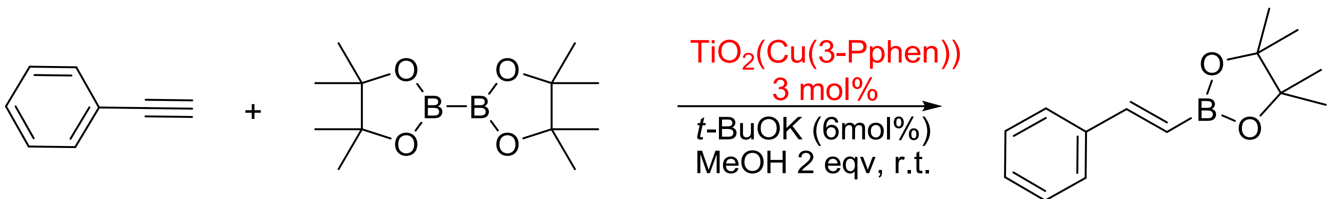
Inorganica Chimica Acta, **2015**, 431, 297–301

- **Sonogashira-type reaction**

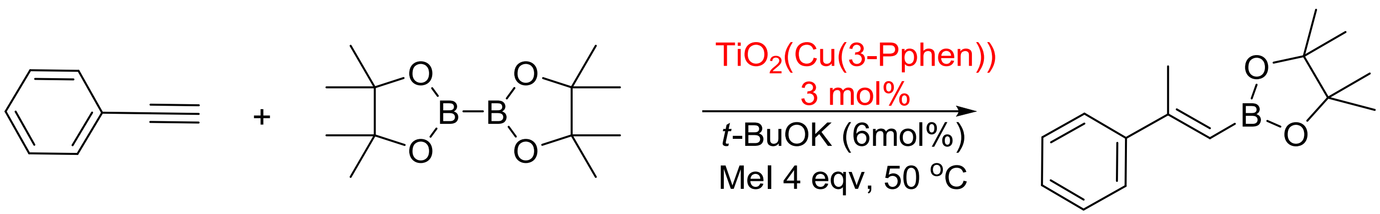


99%, 5 cycles, without loss of activity

- **borylcupration reaction**

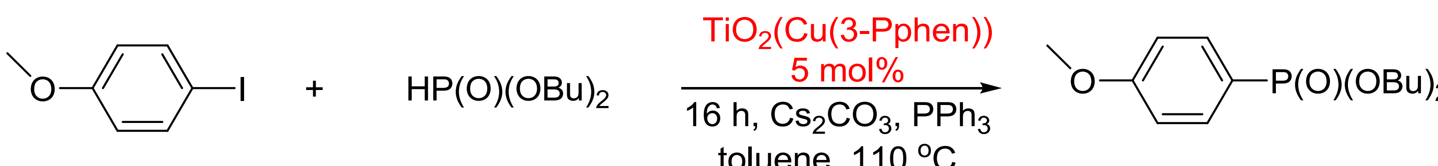


95-98%, 5 cycles, without loss of activity



60%

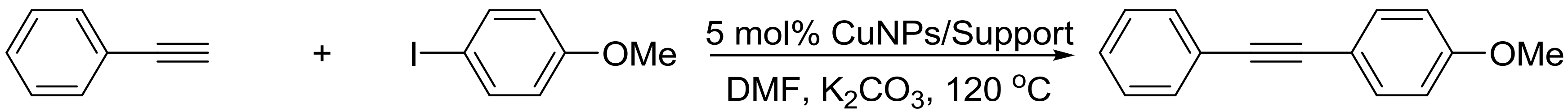
- **phosphorylation reaction**



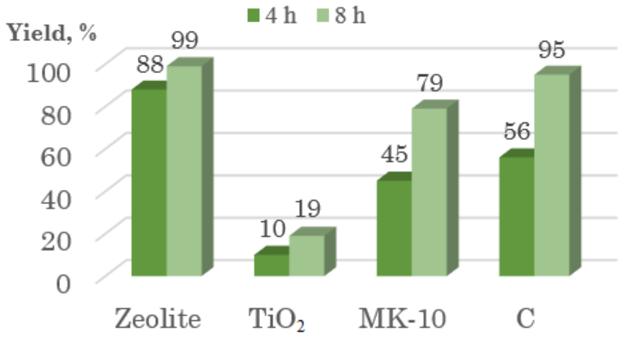
58%

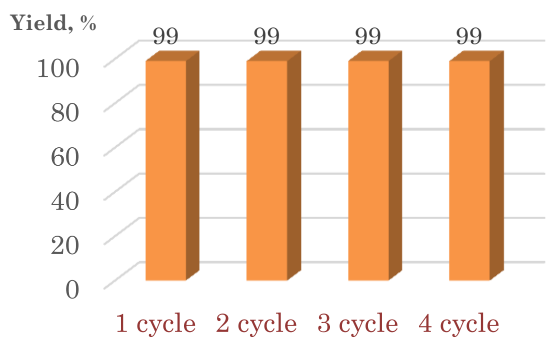
Supported copper nanoparticles in cross-coupling

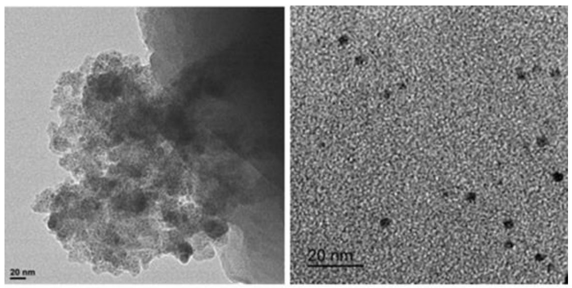
Sonogashira reaction



Entry	Catalyst	Conversion (%)
1	Cu(0)	0
2	Cu_2O	8
3	CuO	0
4	CuCl	5
5	$CuCl_2$	8
6	CuBr	0
7	CuI	4
8	CuOAc	9
9	$Cu(OAc)_2$	7
10	CuOTf	50[c]
11	$Cu(OTf)_2$	67[c]
12	$CuBr\cdot SMe_2$	4
13	CuNPs/ZY	99



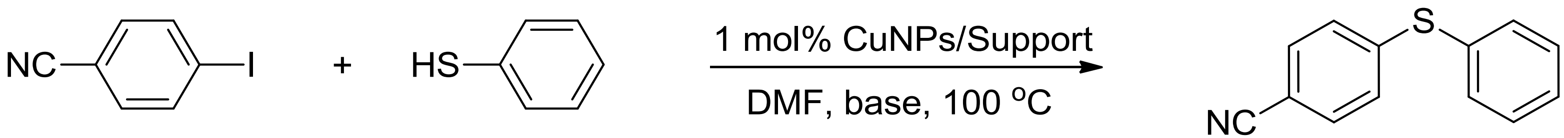




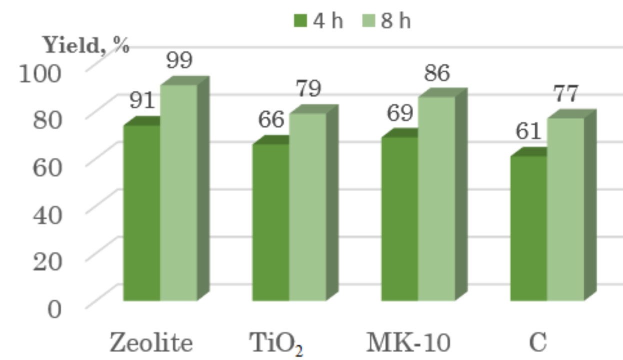
TEM micrograph of **CuNPs/ZY**
d(CuNPs = 2.0±0,9 nm)

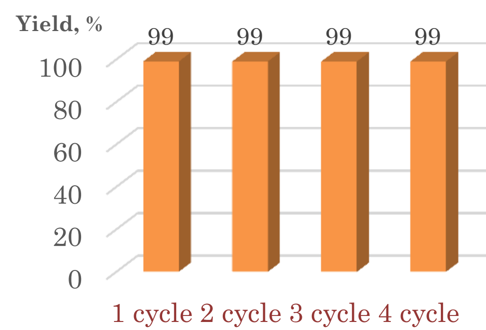
Supported copper nanoparticles in cross-coupling

Thiol arylation



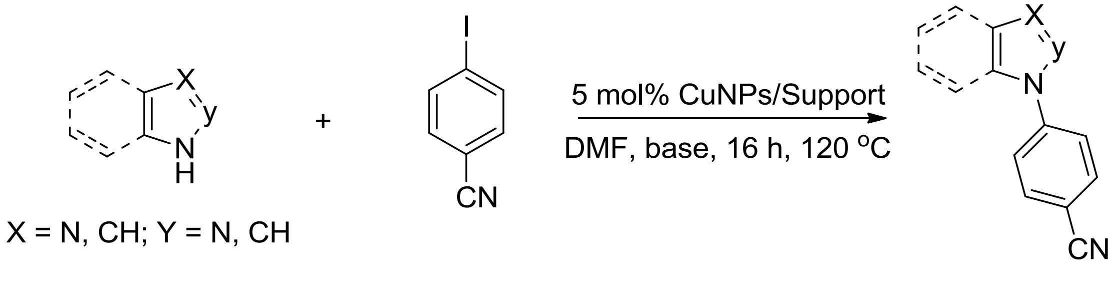
Entry	Catalyst	Conversion (%)
1	Cu(0)	25
2	Cu_2O	23
3	CuO	32
4	CuCl	54
5	$CuCl_2$	64
6	CuBr	38
7	CuI	50
8	CuOAc	63
9	$Cu(OAc)_2$	91
10	CuOTf	77
11	$Cu(OTf)_2$	82
12	$CuBr·SMe_2$	77
13	**CuNPs/ZY**	**94**





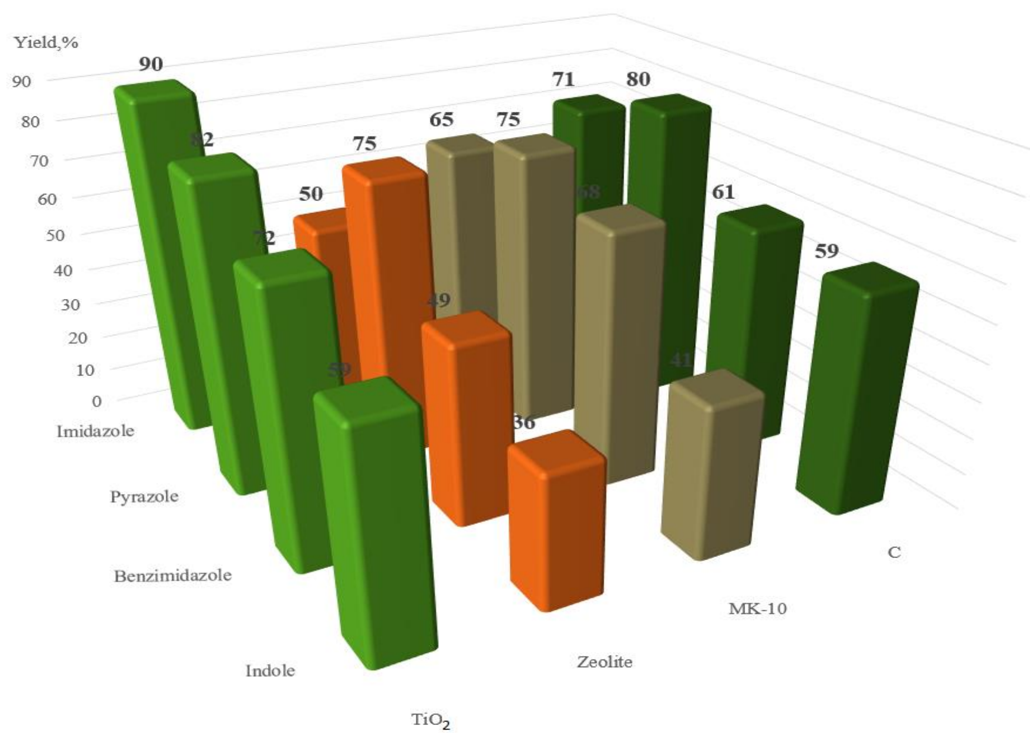
Supported copper nanoparticles in cross-coupling

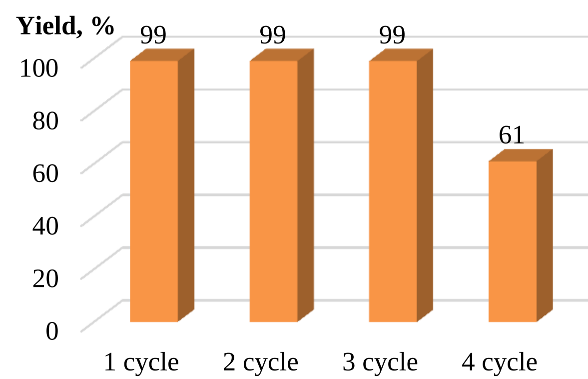
Ullmann reaction with azoles



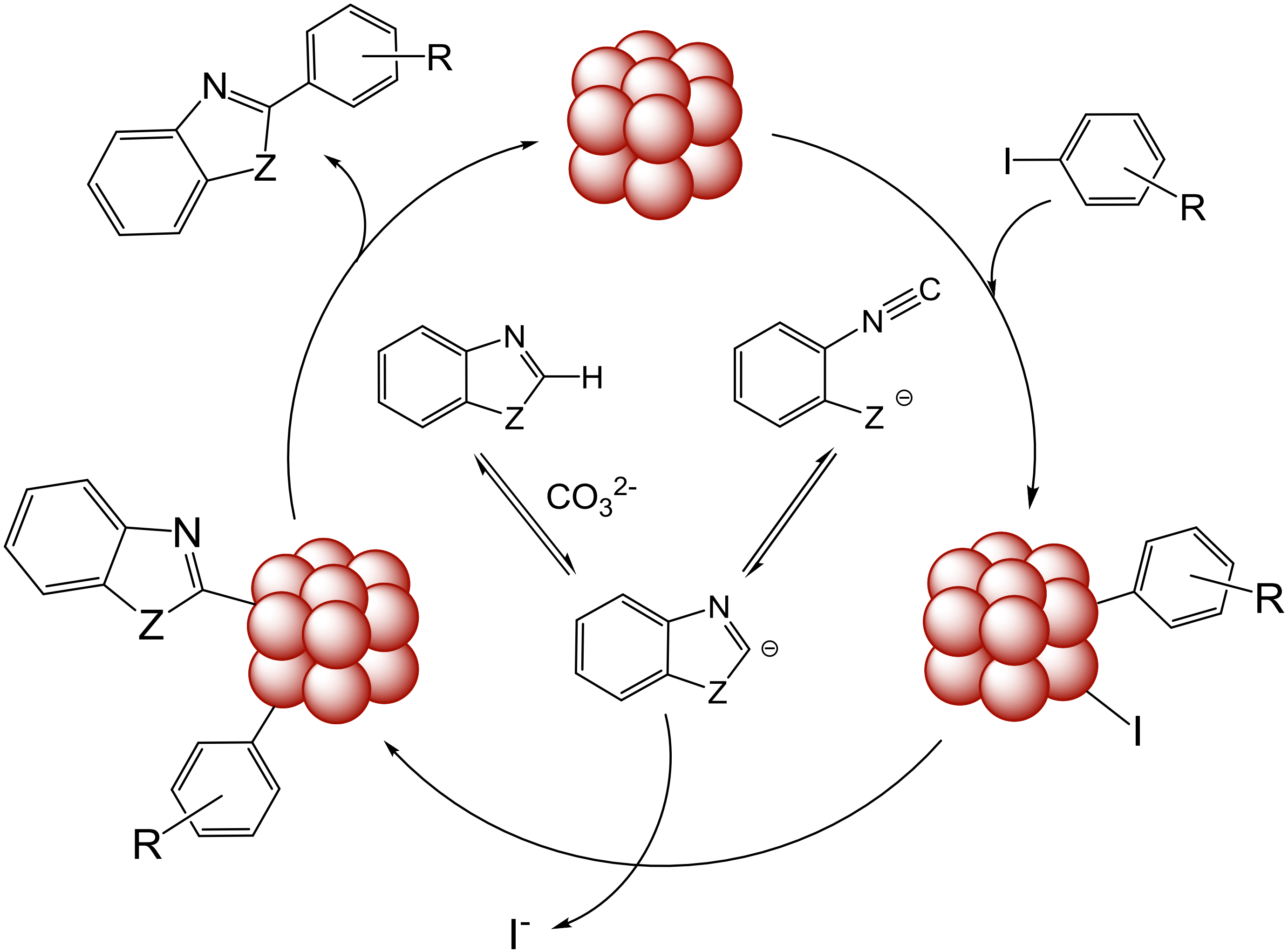
Entry	Catalyst	Conversion (%)
1	Cu(0)	28
2	Cu_2O	74
3	CuO	78
4	CuCl	44
5	$CuCl_2$	46
6	CuBr	18
7	CuI	62
8	CuOAc	25
9	$Cu(OAc)_2$	52
10	CuOTf	78
11	$Cu(OTf)_2$	67
12	$CuBr{\cdot}SMe_2$	55
13	$CuNPs/TiO_2$	99

Arylation of different azoles with supported CuNPs

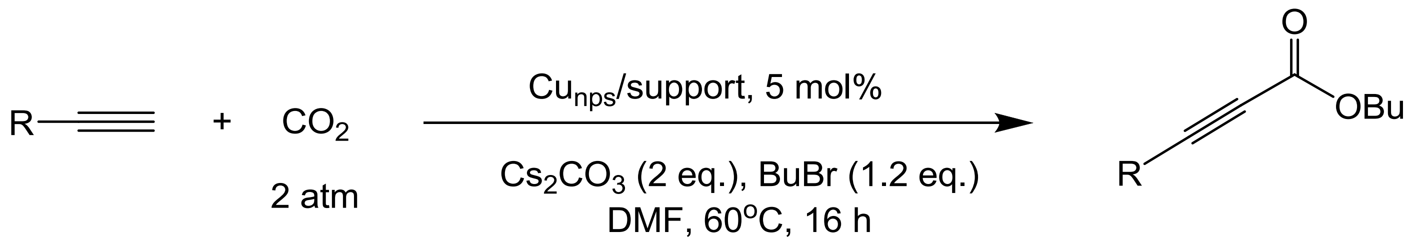


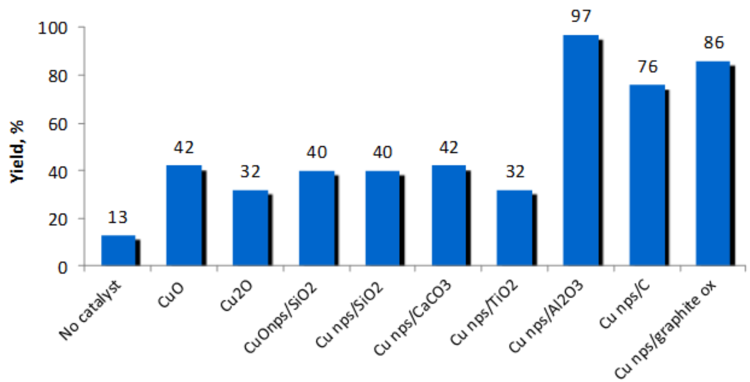


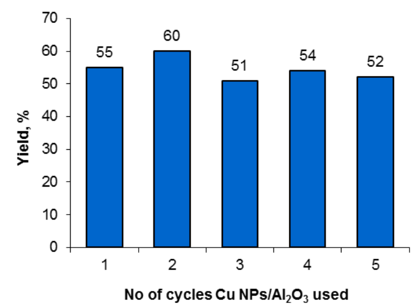
Каталитический цикл

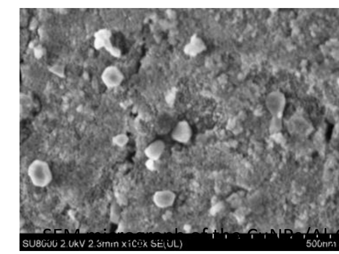


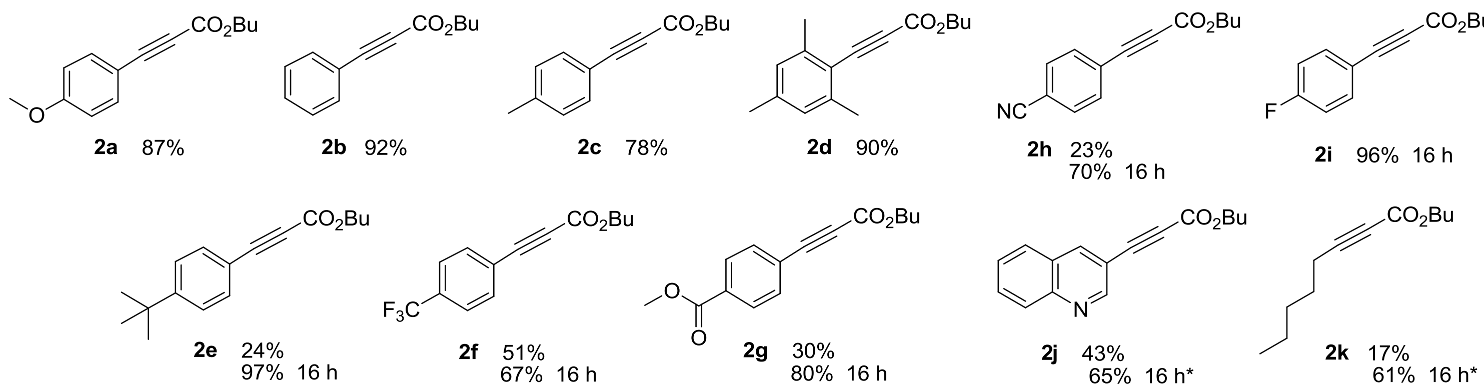
Cu(0) NPs /Al_2O_3 в катализе реакции карбоксилирования терминальных алкинов







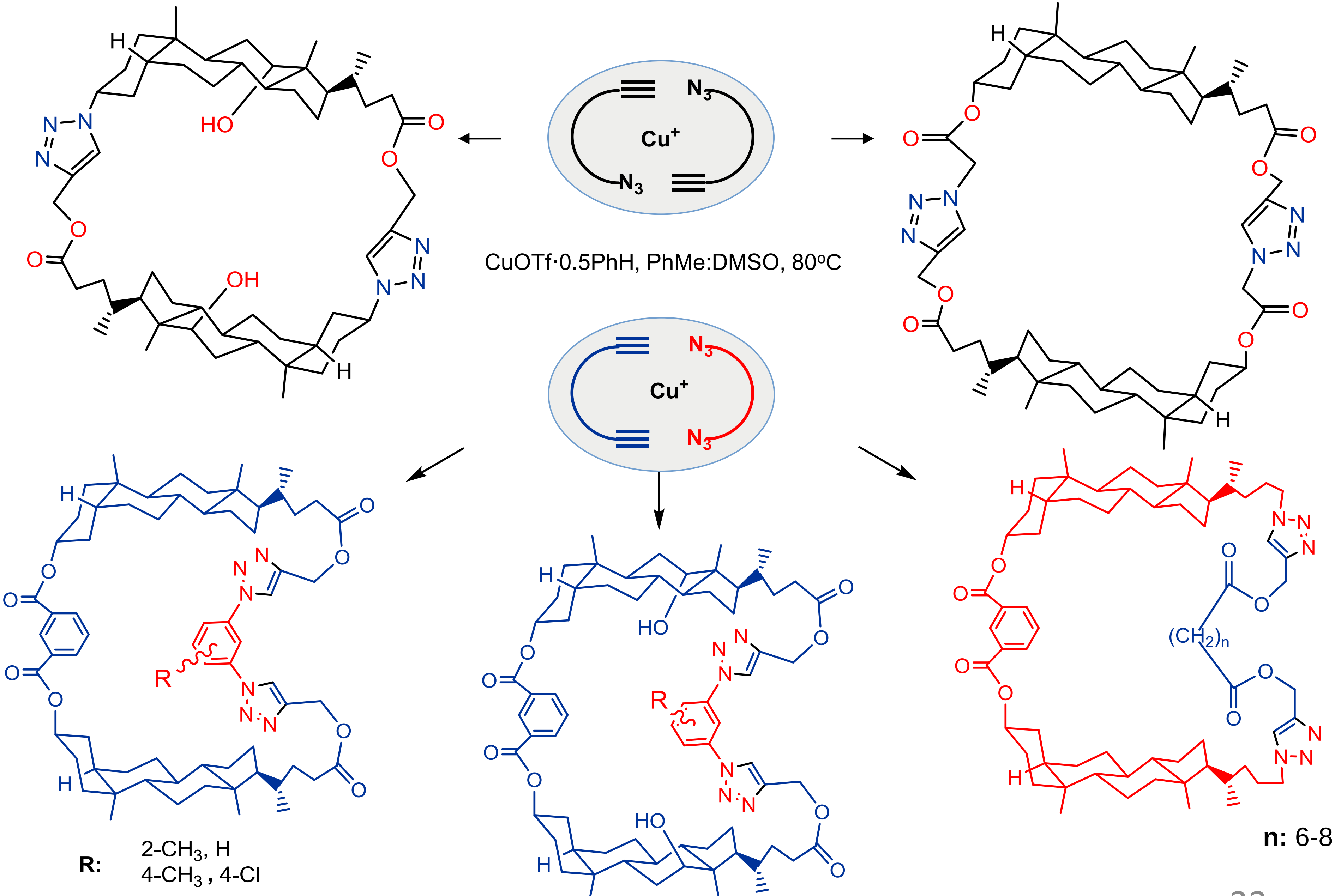




* 80°C, 4 atm CO_2

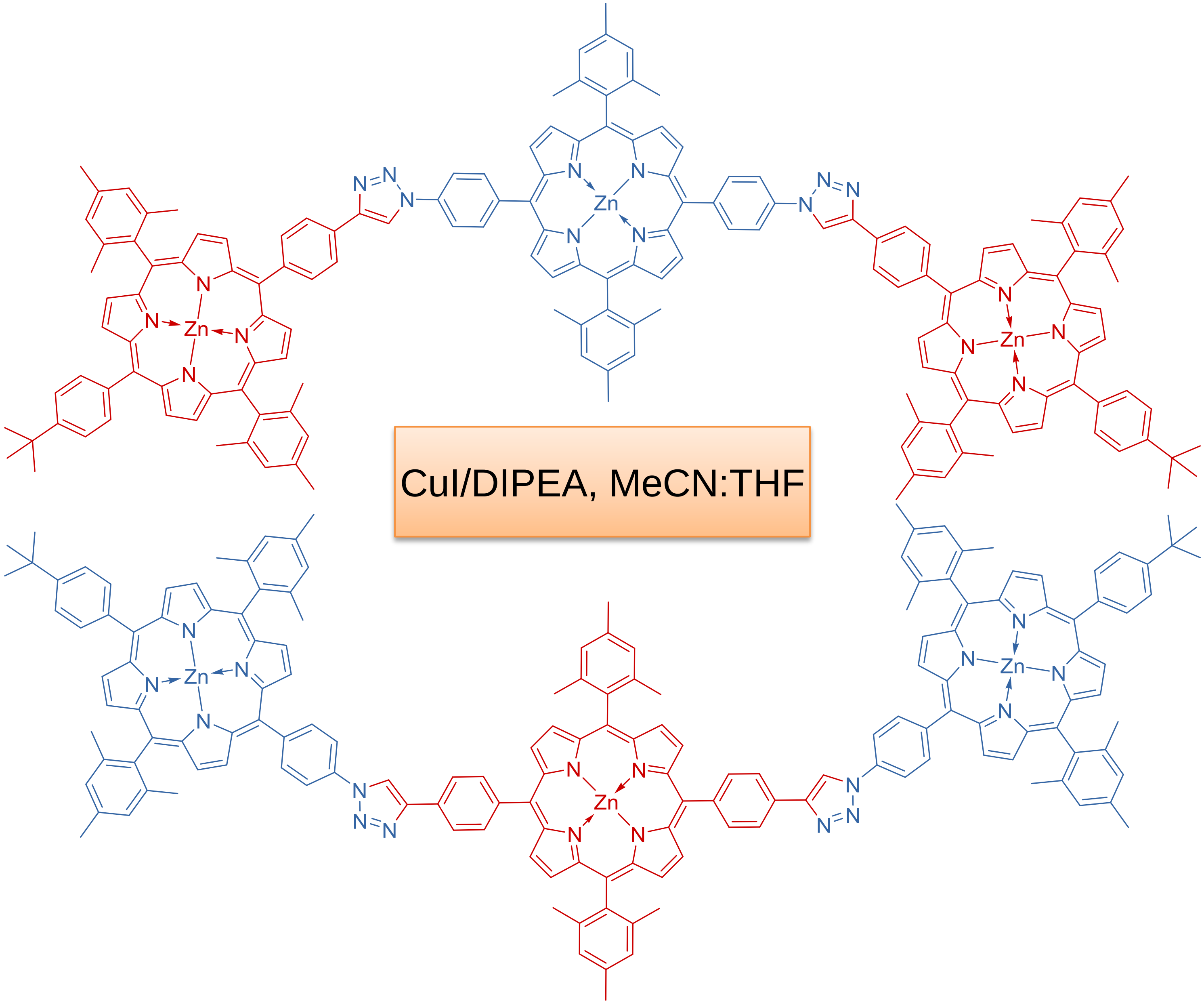
Catalysis Today, 2016 (submitted)

Click cholaphanes



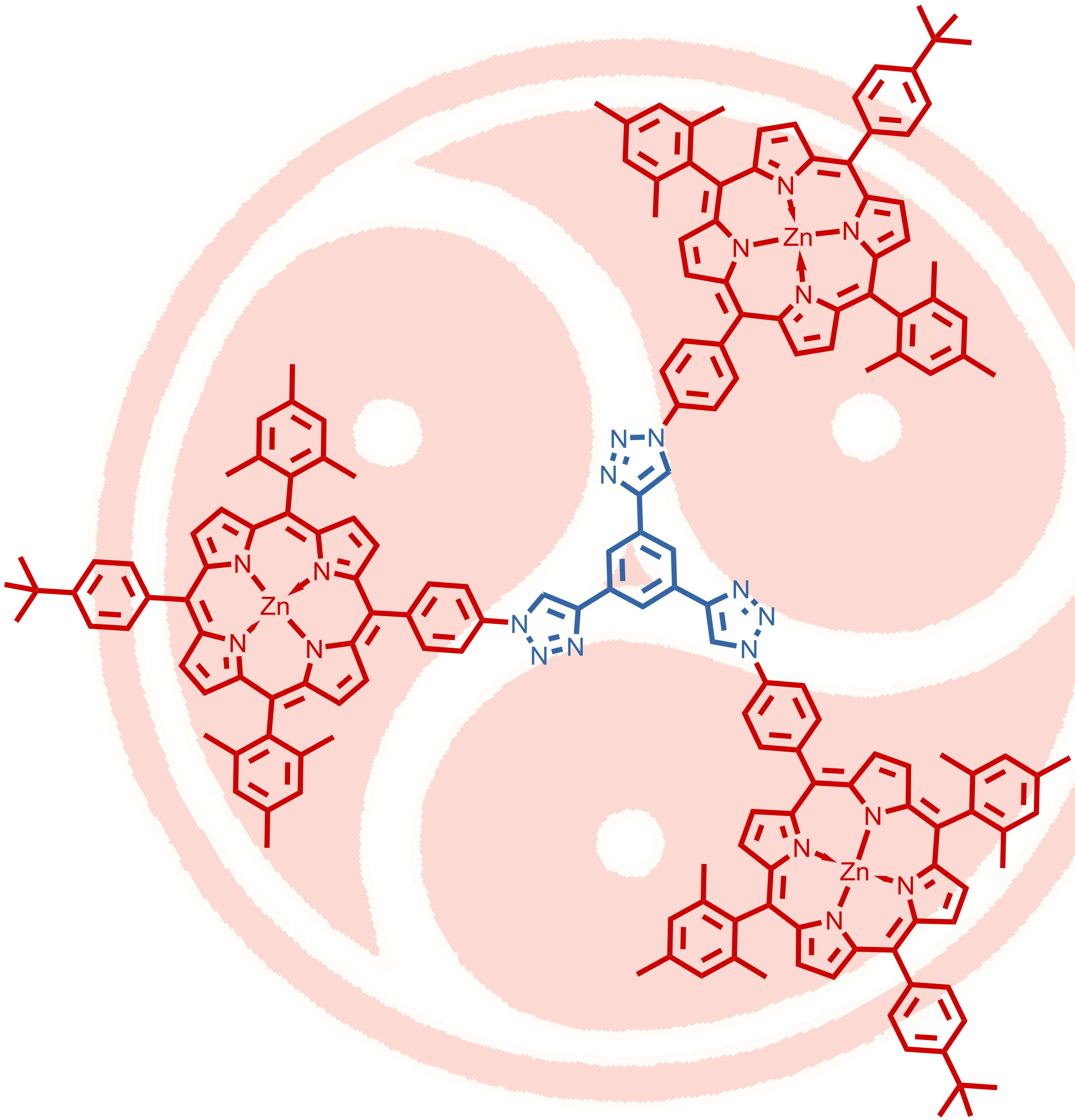
Synthesis, **2009**, 2605

Linear conjuncted Porphyrin Triad Synthesis via “click” reaction



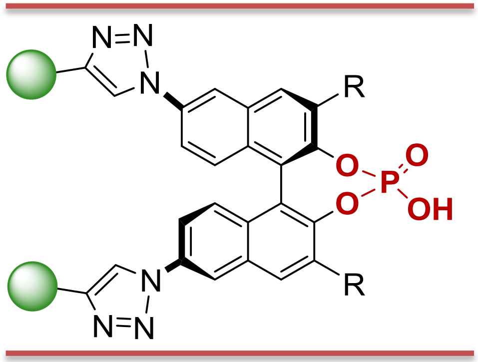
Polevaya Y.P., *J. Porphyrins Phthalocyanines*, **2014**, 18, 20-34

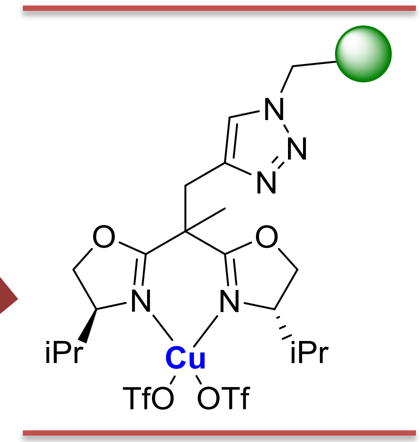
Star-shaped Porphyrin Triad

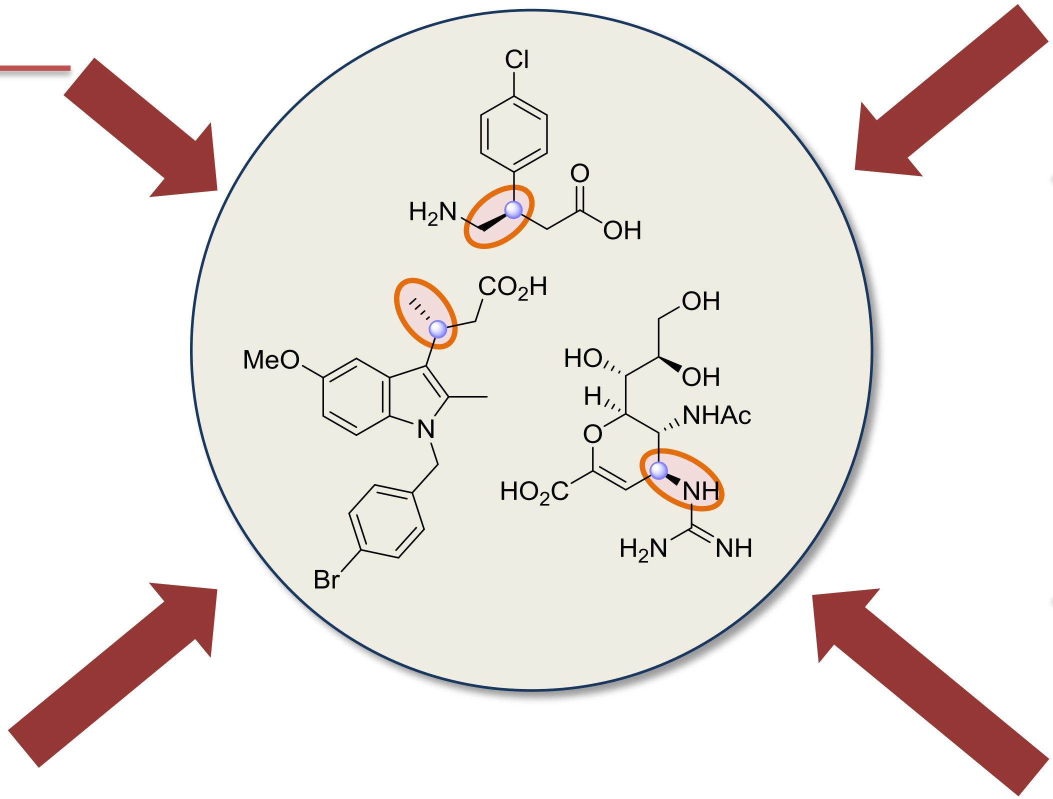


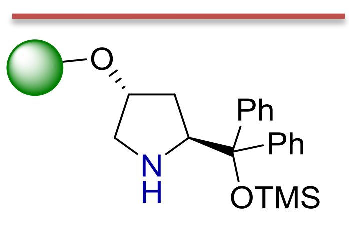
Macroheterocycles, **2012**, *5*, 302

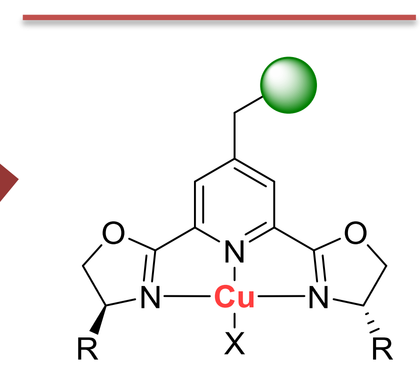
Катализ кислотами Бренстеда и Льюиса



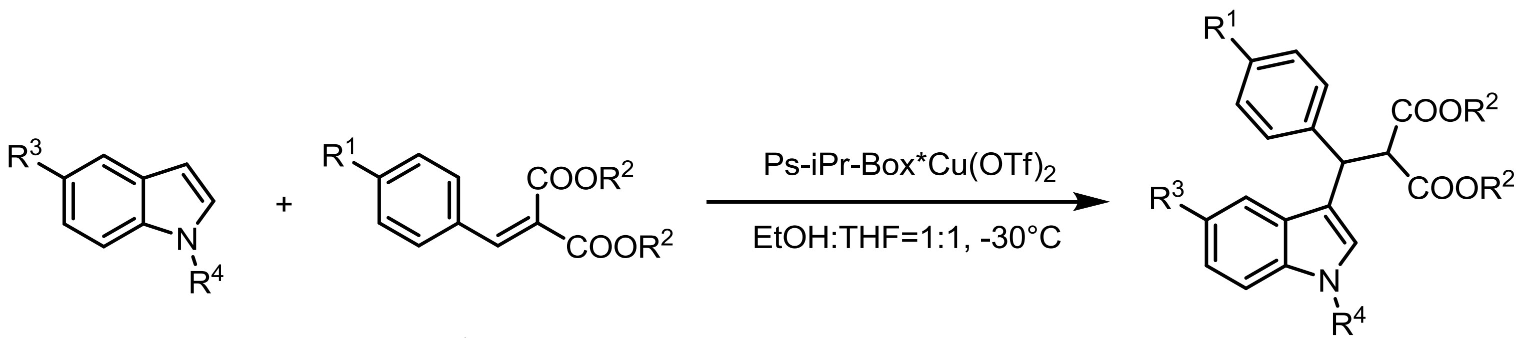








Реакции Михаэля с гетерогенным катализатором



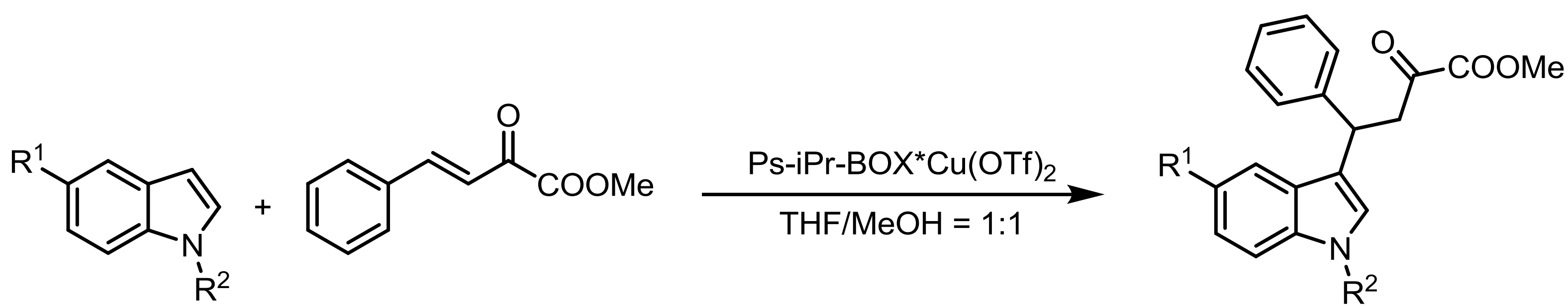
R^3 = H, OMe, Me, Br, I

R^4 = H, Me

R^1 = H, Br, NO_2

R^2 = Me, Et

up to 99%
ee up to 97%

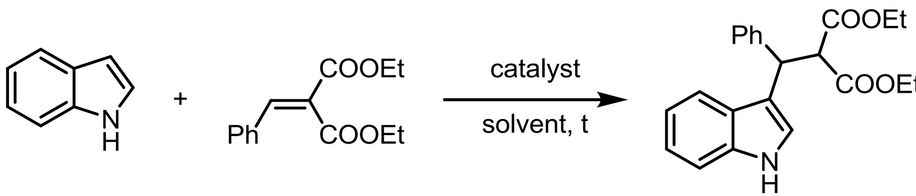


R^1 = H, OMe, Me, Br, I, CN

R^2 = H, Me

up to 94%
ee up to 49%

Реакция индола и бензалиденмалоната

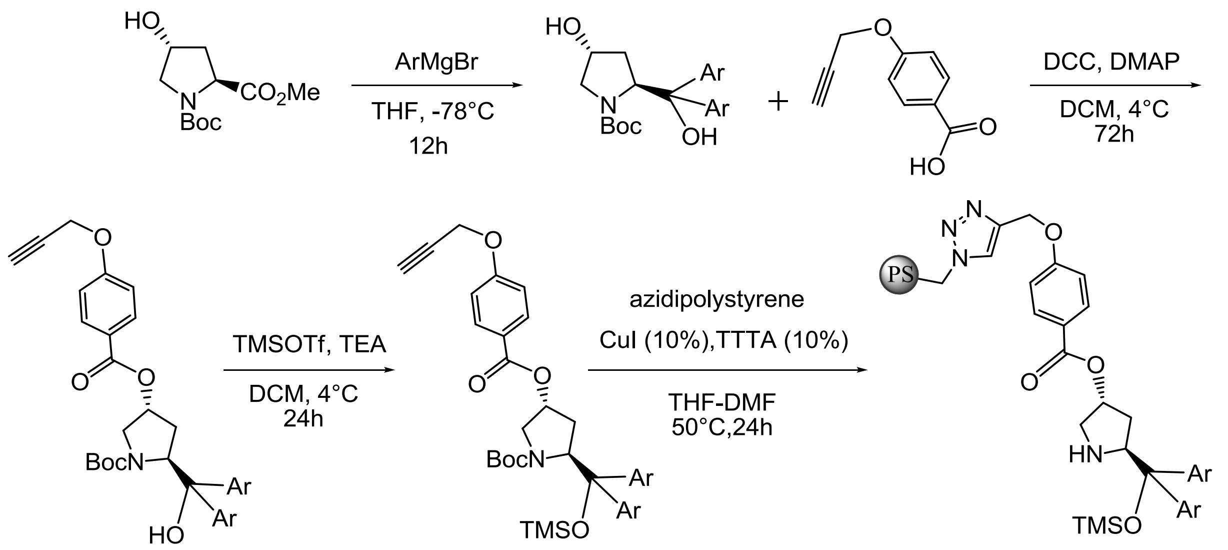


№	Катализатор	Растворитель	Температура (°C)	Выход (%)	ee (%)
1	PEG-iPr-Box*Cu(OTf)$_2$	EtOH-THF (1:1)	0˚C	0	-
2	PEG-iPr-Box*Cu(OTf)$_2$	EtOH-THF (1:1)	20˚C	0	-
3	PEG-iPr-Box*Cu(OTf)$_2$	H_2O	20˚C	0	-
4	PEG-Latex-iPr-Box*Cu(OTf)$_2$	EtOH	-30˚C	86	64
5	Ps-iPr-Box-Cu(OTf)$_2$	EtOH	0˚C	74	87
6	Ps-iPr-Box-Cu(OTf)$_2$	DCM	-30˚C	91	87
7	Ps-iPr-Box-Cu(OTf)$_2$	EtOH-THF (1:1)	-30˚C	83	92 (>99)*

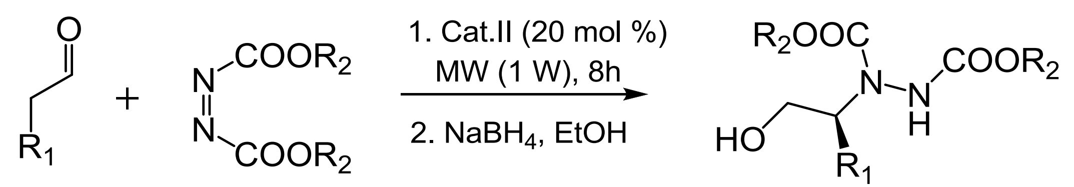
Рециклизация катализатора Ps-iPr-Box*Cu(OTf)$_2$ в реакции индола с диэтилбензалиденмалонатом

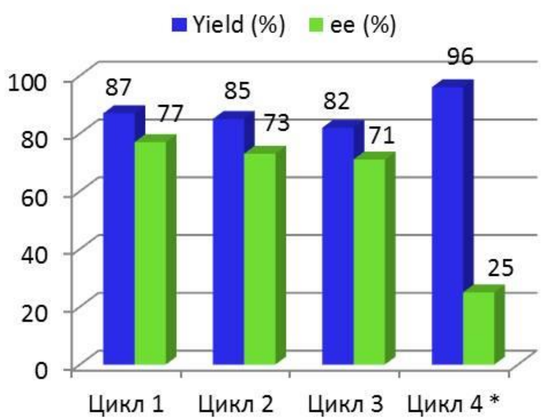
Цикл	1	2	3	4	5
Выход (%)	83	71	72	74	73
ee (%)	92	91	90	94	94

Асимметрическое α-аминирование альдегидов



Cat.II Ar = 3,5-$(CF_3)_2C_6H_3$



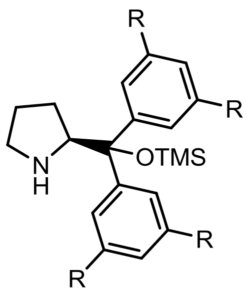


*48h

Entry	R_1	R_2	Isolated yield (%)	ee (HPLC) (%)
1	Et	Et	66	20
2	Bn	Et	84	2
3	Et	Bn	43	>99
4	^{i}Pr	Bn	55	>99

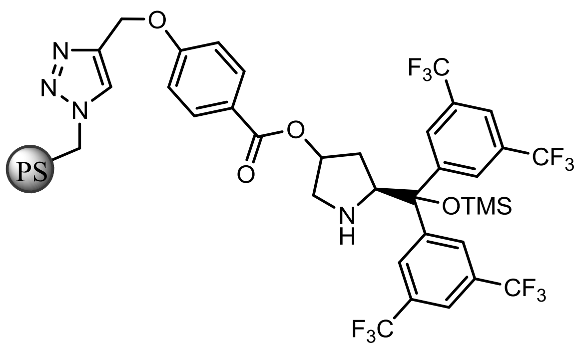
Mendeleev Commun., 2015, 25, 410–411

Катализ иммобилизованным пролином реакции диалкилмалонатов с α,β-ненасыщенными альдегидами



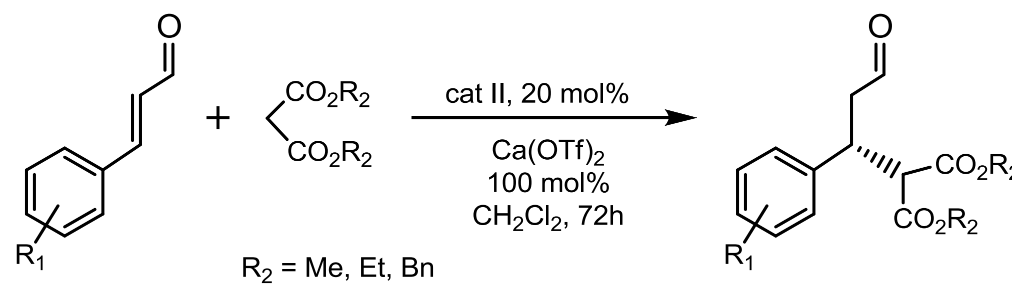
R = H, CF_3

Jorgensen-Hayashi organocatalyst I



Heterogenous Jorgensen-Hayashi organocatalyst II

Entry	Catalyst	Additive (mol%)	Solvent	Yield (%)	ee (ВЭЖХ) (%)
1	Catalyst I	-	EtOH	85	95
2	Catalyst II	-	EtOH	-	-
3	Catalyst II	-	CH_2Cl_2	-	-
4	Catalyst II	LiOAc (20)	CH_2Cl_2	-	-
5	Catalyst II	$Ca(OTf)_2$ (20)	CH_2Cl_2	56	85
6	Catalyst II	$Ca(OTf)_2$ (100)	CH_2Cl_2	62	86

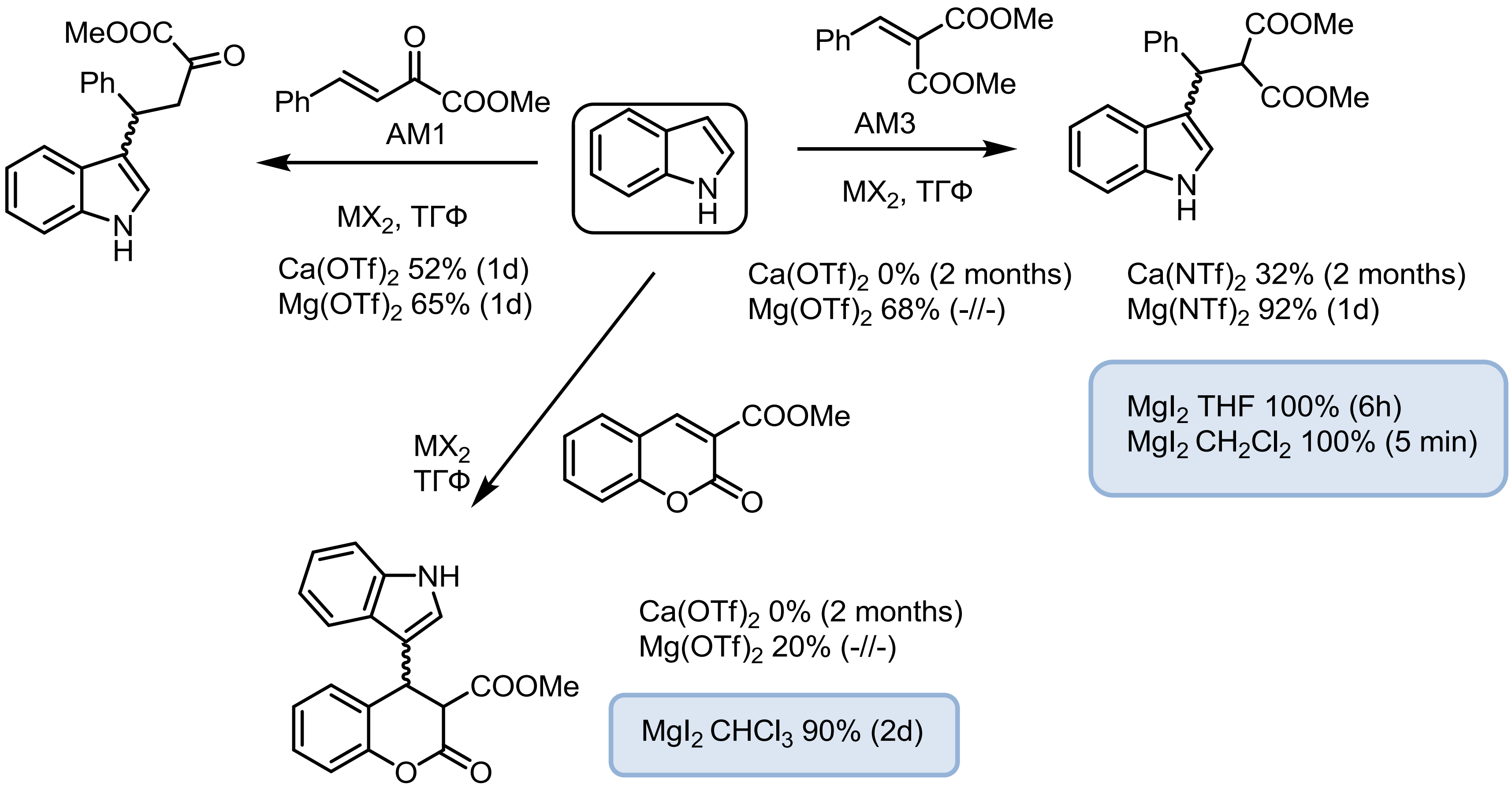


R_1 = H, p-OMe, p-Cl, p-NO_2, o-NO_2

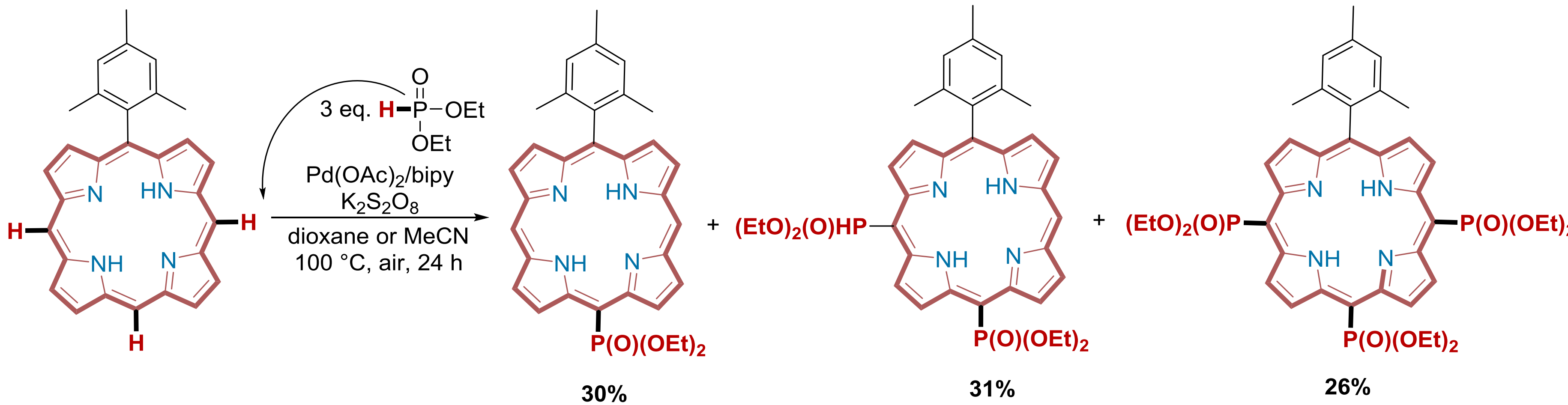
28 - 99%

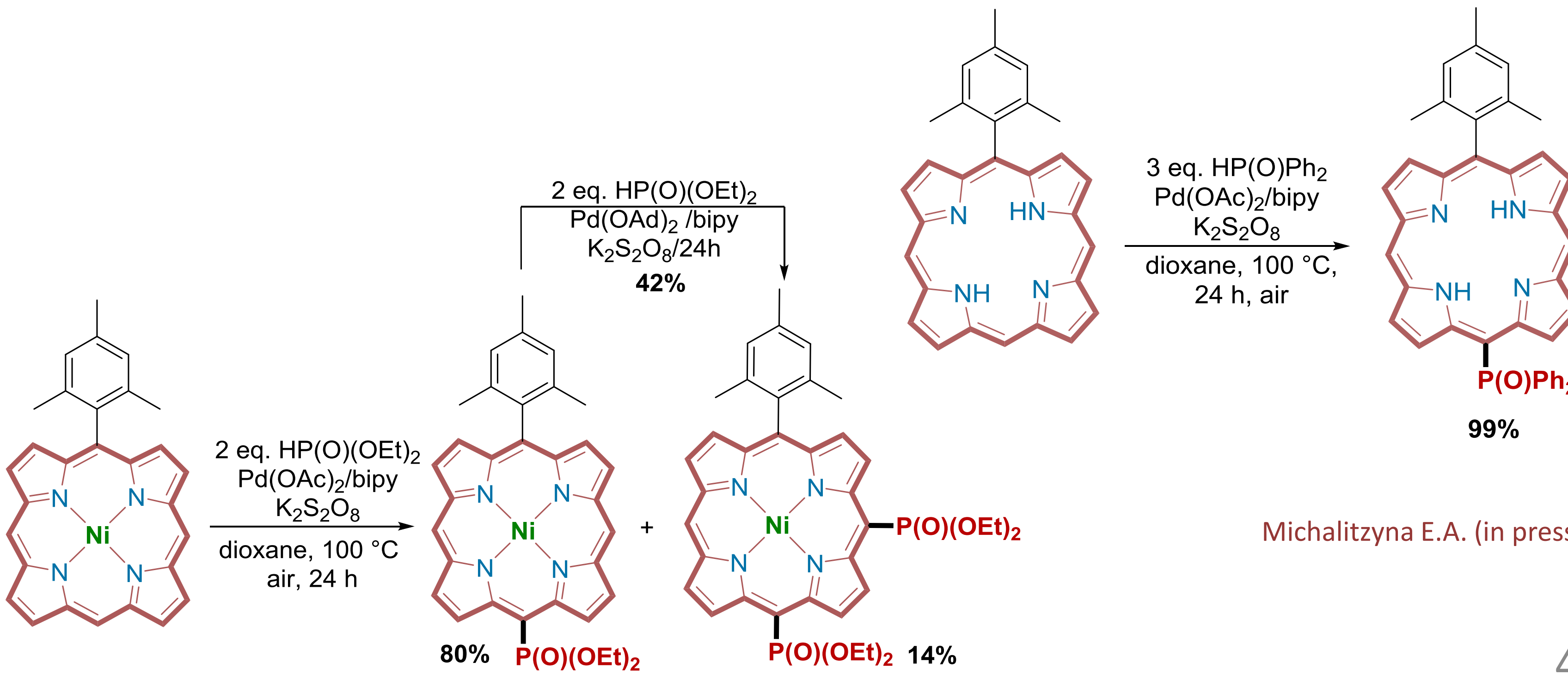
Mendeleev Comm., 2016, 26, 469

Катализ солями непереходных металлов

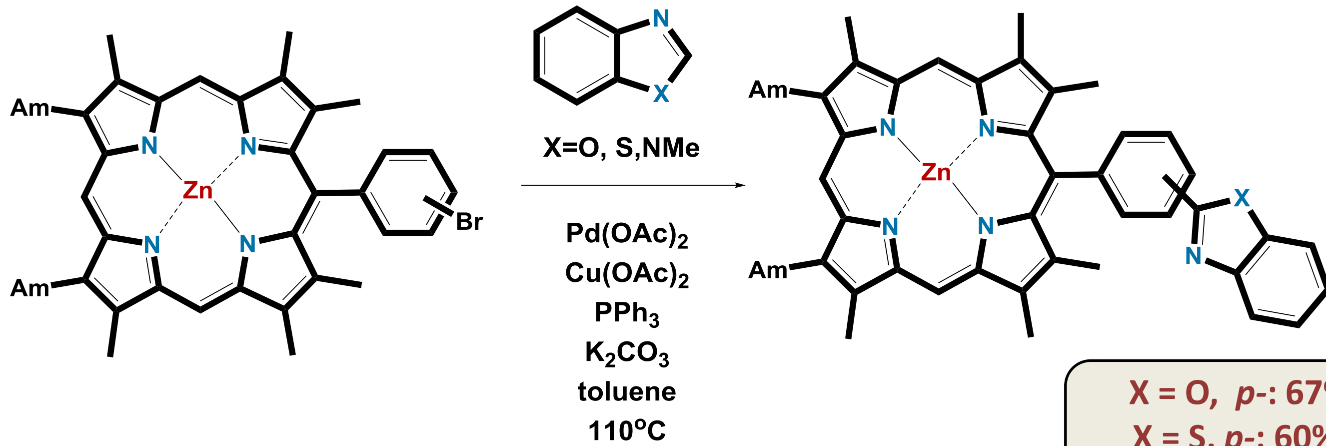


Direct C(sp^2)-H phosphonation of porphyrins in meso-position

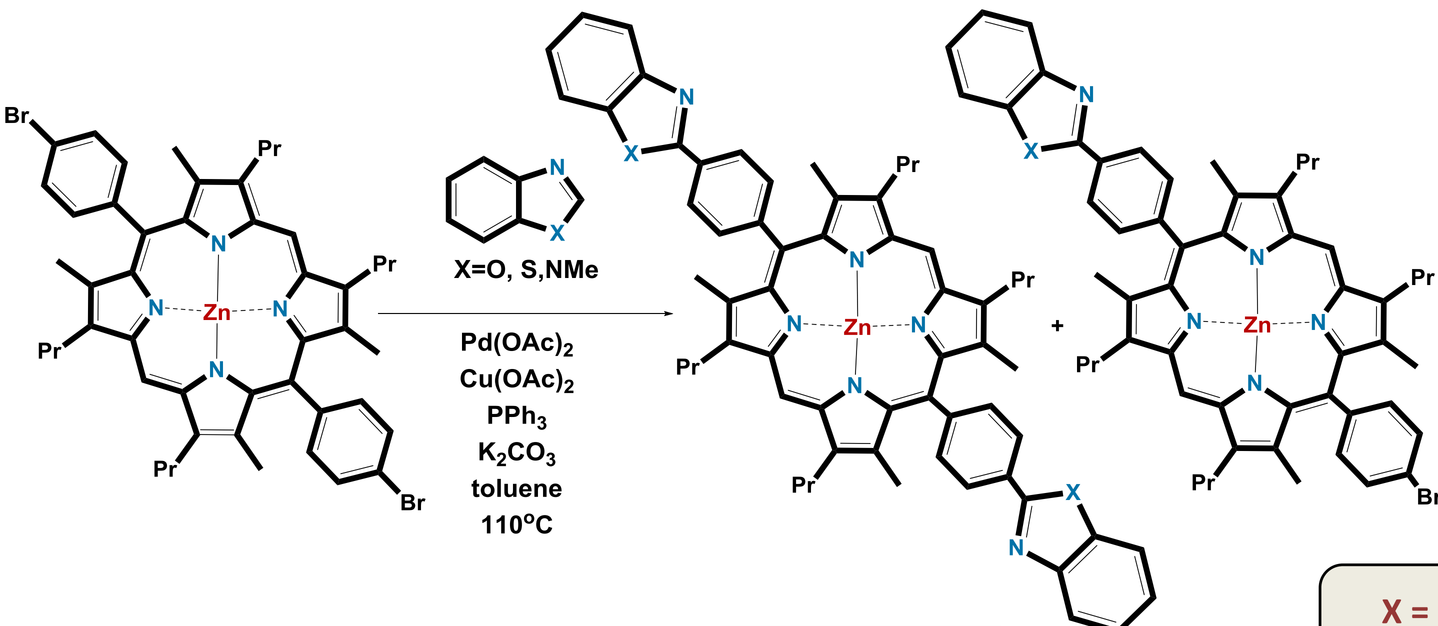




Michalitzyna E.A. (in press)



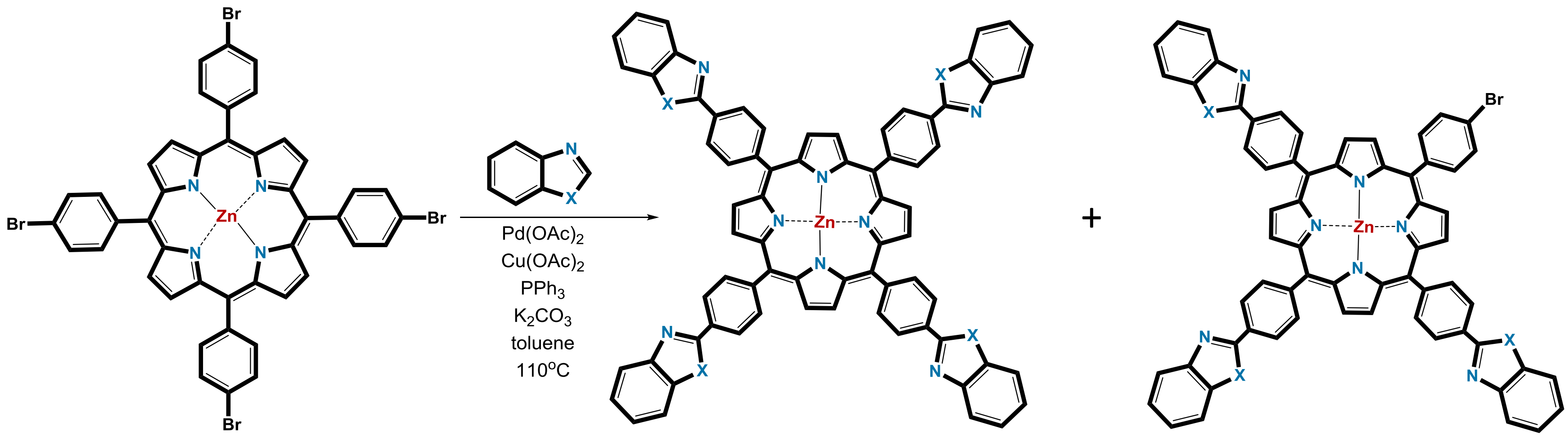
X = O, *p*-: 67%, *m*-: 50%
X = S, *p*-: 60%, *m*-: 61%
X = NMe, *p*-: 79%, *m*-: 90%



X = O, 65%
X = NMe, 78%

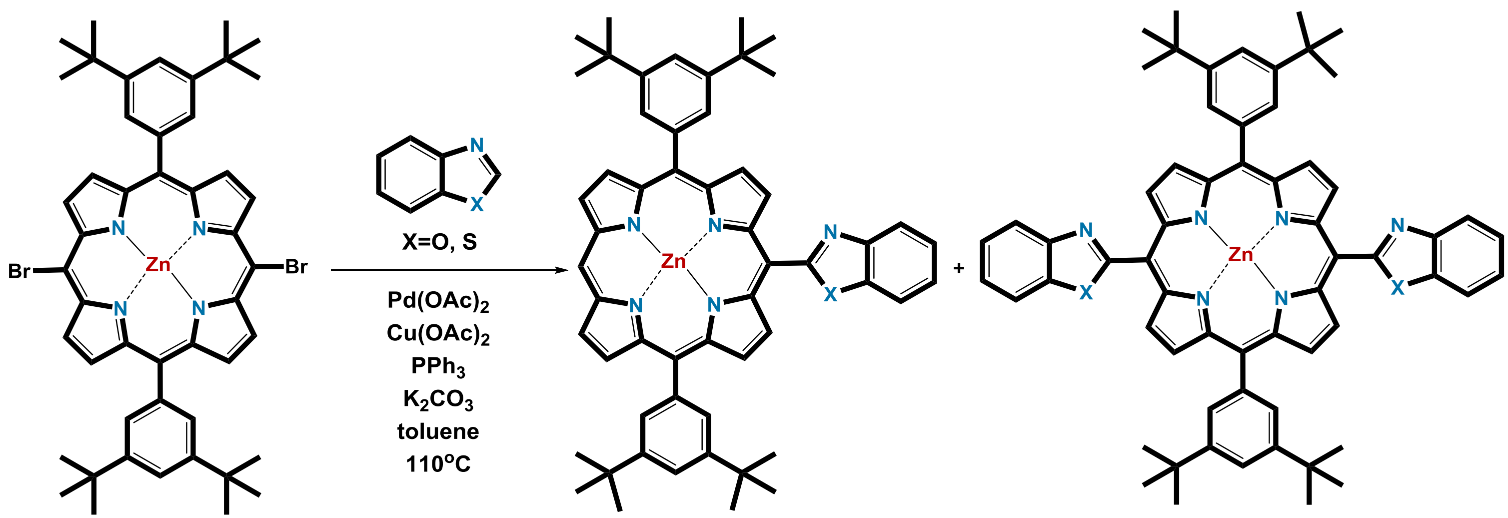
X = S, 64%
X = NMe, 22%

Kiselev A.N., (submitted)



X = O, 14%
X = S, 16%

X = O, 80%
X = S, 67%



X = S,
24%

X = O,
32%

Acknowledgements

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Anokhin M.
Bessmertnykh A.
Bondarenko G.
Cheprakov A.
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Yatshuk Yu.

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