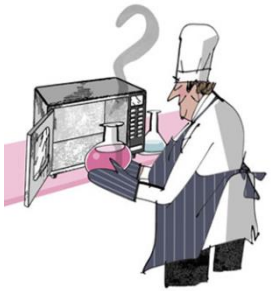
Budapest University of Technology and Economics
Department of Organic Chemistry and Technology

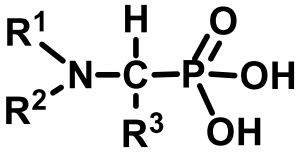
Synthesis of α-aminophosphonates and related derivatives under microwave conditions

Erika Bálint, Ádám Tajti, Anna Tripolszky and György Keglevich

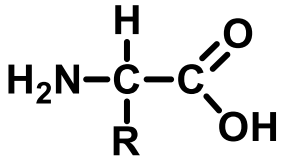


The 21st International Electronic Conference on
Synthetic Organic Chemistry
1-30 November 2017

Aminophosphonates



structural analogy



α-aminophosphonic acids

α-amino acids

High importance → more than 1600 publications

antibiotics
Phos. Heterocycles I. **2009**, *20*, 31.

antitumour agents
Curr. Med. Chem. Anticancer Agents **2001**, *1*, 301.

antiviral species
J. Antimicrob. Chemother. **1999**, *43*, 211.

anti-metabolites
Biochemistry, **2002**, *41*, 12320.

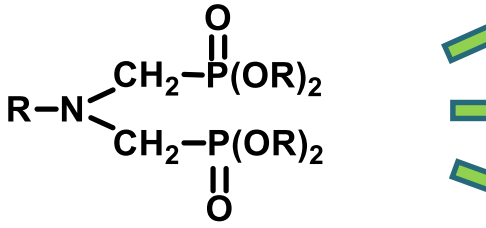
Biological activity

antihypertensives
Tetrahedron **1999**, *55*, 12237.

inhibitors of GABA-receptors
J. Med. Chem. **1994**, *37*, 158.

enzyme inhibitors
J. Med. Chem. **1989**, *32*, 1652.

pesticides, herbicides
J. Med. Chem. **1987**, *30*, 1603.



bis(α-aminophosphonates)

inhibitors of bone resorption
Phos. Heterocycles I. **2009**, *20*, 31.

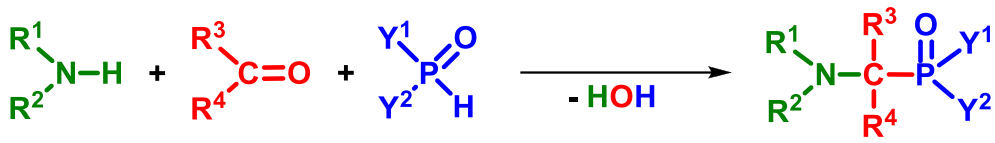
membrane transport
Russ. J. Gen. Chem., **2009**, *79*, 1480.

P-ligands
Lett. Org. Chem., **2010**, *7*, 612.

Most common synthetic routes towards α-aminophosphonates

I. Kabachnik-Fields (phospha-Mannich) reaction

M. I. Kabachnik



Kabachnik, M. I.; Medved, T. Y. *Dok. Akad. Nauk. SSSR* **1952**, *83*, 689.
Fields, E. K. *J. Am. Chem. Soc.* **1952**, *74*, 1528.

E. K. Fields

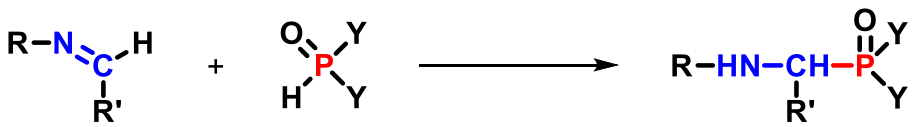
Catalyst: $SnCl_4$, $ZnCl_2$, $InCl_3$, $TaCl_5$-SiO_2, $Mg(ClO_4)_2$, GaI_3, $Bi(NO_3)_3$, $BiCl_3$, SmI_3, $Yb(OTf)_3$, $La(OTf)_3$, $Sm(OTf)_3$, $In(OTf)_3$

Solvent: dichloromethane, tetrahydrofuran, ethanol, acetonitrile, etc.

Environmental load!

II. Pudovik reaction (addition of >P(O)H reagents to imines)

A. N. Pudovik



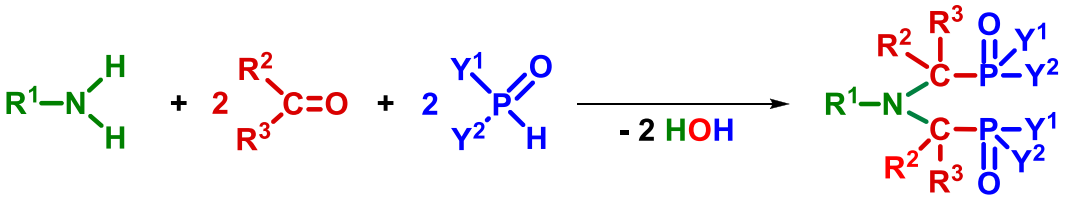
Pudovik, A. N. *Dokl. Akad. Nauk SSSR*, **1950**, *73*, 499.
Pudovik, A. N. *Dokl. Akad. Nauk SSSR*, **1952**, *83*, 865.

Environmental load!

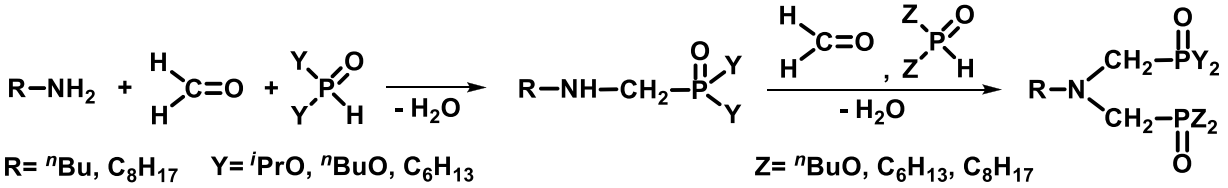
Catalyst: TsCl, HCOOH, ^{t}PcAlCl, CdI_2, K_2CO_3, TBAI, TMSCl, $LiClO_4$, TMG

Solvent: benzene, toluene, dichloromethane, ether, etc.

Double Kabachnik-Fields reactions

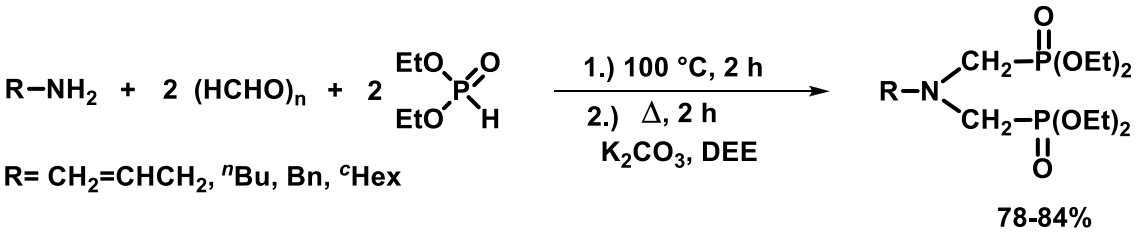


- **Synthesis of lipophilic bis(aminophosphonates)**



Cherkasov, R. A.; Garifzyanov, A. R.; Talan, A. S.; Davletshin, R. R.; Kurnosova, N. V. *Russ. J. Gen. Chem.* **2009**, *79*, 1480.

- **Double Kabachnik-Fields reactions of primary amines**



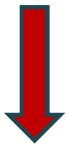
Prishchenko, A. A.; Livantsov, M. V.; Novikova, O. P.; Livantsova, L. I.; Petrosyan, V. S. *Heteroatom Chem.* **2010**, *21*, 430.

Goals of the research work

Syntheses of aminophosphonates and related derivatives

Kabachnik-Fields condensations

Pudovik reactions



Catalyst and solvent-free syntheses

Microwave technique

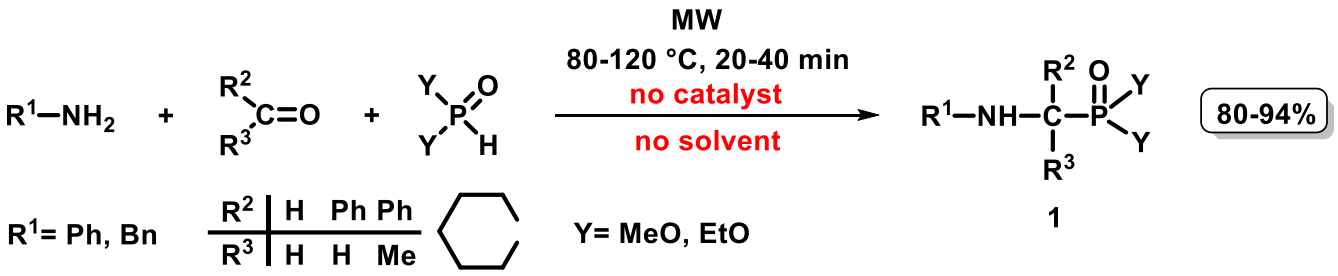
MW-assisted synthesis of aminophosphonates and related derivatives by catalyst- and solvent-free Kabachnik-Fields and Pudovik reactions

Characterization and investigation of the usability of the products

Kabachnik-Fields reaction

1.1. Microwave-assisted Kabachnik-Fields reactions using dialkyl phosphites

- **Synthesis of α-aminophosphonates**

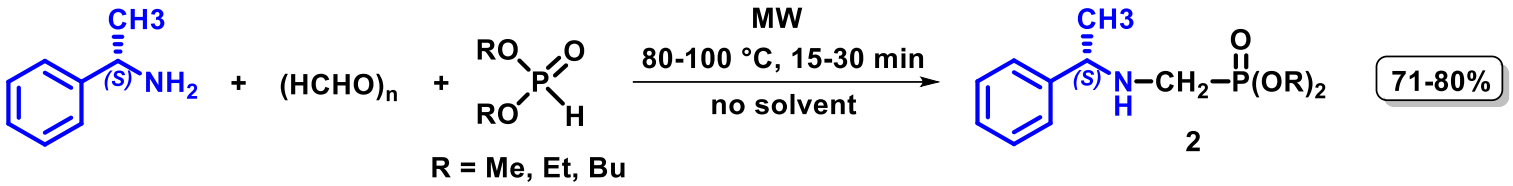


MW ⟹ **no catalyst, no solvent**

Simple, environmentally friendly and general procedure

Keglevich, G.; Szekrényi, A. *Lett. Org. Chem.* **2008**, *5*, 616-622.

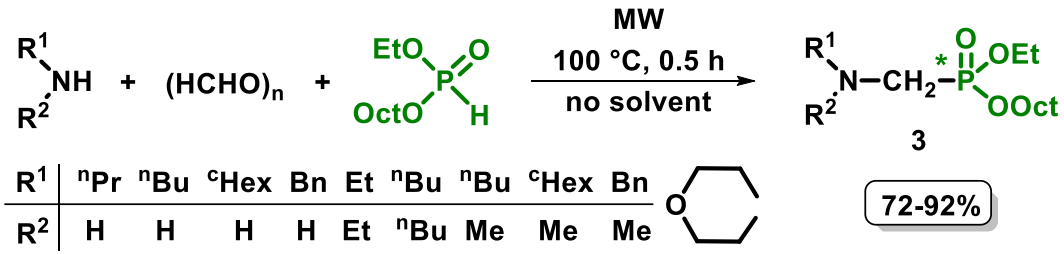
- **Synthesis of optically active α-aminophosphonates**



Bálint, E.; Tajti, Á.; Kalocsai, D.; Mátravölgyi, B.; Karaghiosoff, K.; Czugler, M.; Keglevich, G. *Tetrahedron*, **2017**, *73*, 5659-5667.

Synthesis of P-chiral α-aminophosphonates and α-aminophosphinates

- **Kabachnik-Fileds reactions with ethyl octyl phosphite**

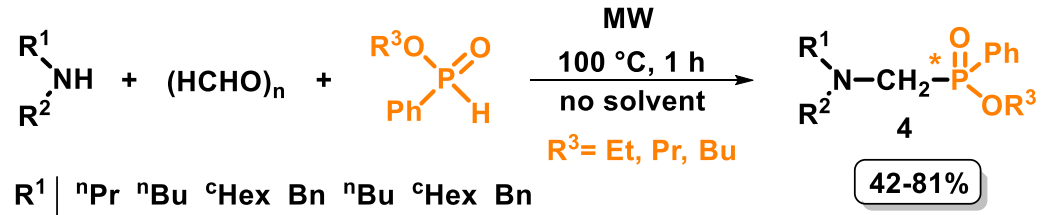


R^1	^{n}Pr	^{n}Bu	^{c}Hex	Bn	Et	^{n}Bu	^{n}Bu	^{c}Hex	Bn
R^2	H	H	H	H	Et	^{n}Bu	Me	Me	Me

New compounds

Tajti, Á.; Bálint, E.; Keglevich, G. *Curr. Org. Synth.*, **2016**, *13*, 638-645.

- **Kabachnik-Fileds reactions with alkyl phenyl-*H*-phosphinates**

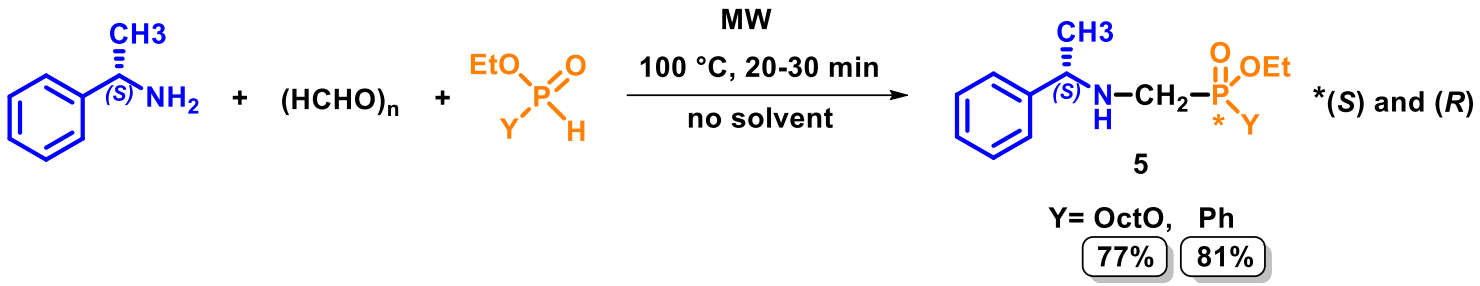


R^1	^{n}Pr	^{n}Bu	^{c}Hex	Bn	^{n}Bu	^{c}Hex	Bn
R^2	H	H	H	H	Me	Me	Me

New compounds

Bálint, E.; Tóth, R. E.; Keglevich, G. *Heteroatom Chem.*, **2016**, *27*, 323-335.

- **Synthesis of C- and P-chiral α-aminophosphonates and α-aminophosphinates**

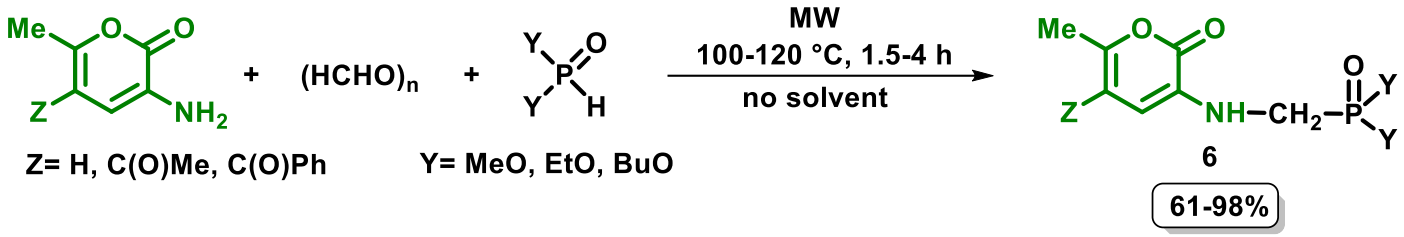


Diastereomers with two series of signals in the NMR spectra

New compounds

Bálint, E.; Tajti, Á.; Kalocsai, D.; Mátravölgyi, B.; Karaghiosoff, K.; Czugler, M.; Keglevich, G. *Tetrahedron*, **2017**, *73*, 5659-5667.

- **Synthesis of *N*-(2*H*-pyranonyl)-α-aminophosphonates**



Z= H, C(O)Me, C(O)Ph

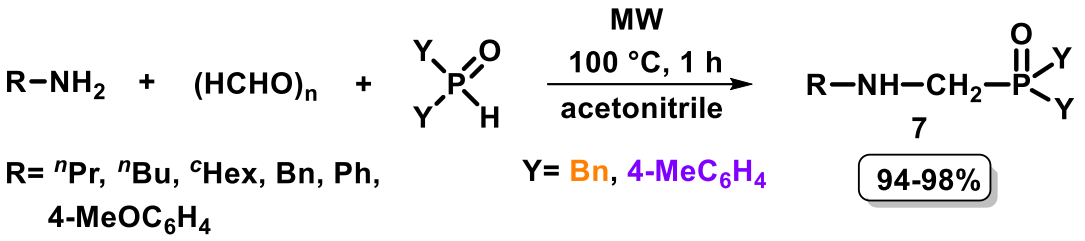
Y= MeO, EtO, BuO

New compounds

Bálint, E.; Keglevich, G.; Takács, J.; Drahos, L.; Juranovič, A.; Kočevar, M. *Heteroatom Chem.* **2013**, *24*, 221-225.

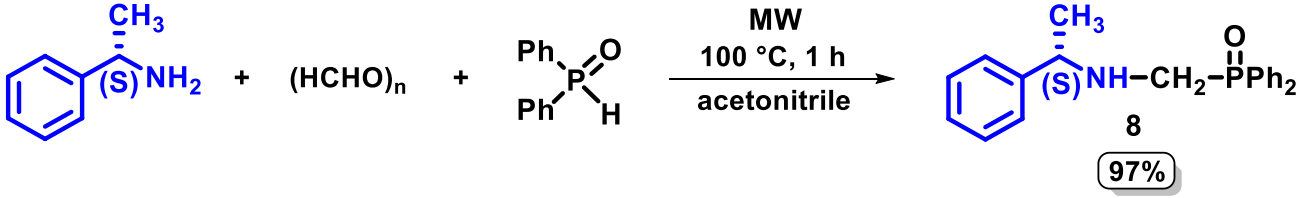
1.2. Microwave-assisted Kabachnik-Fields reactions using secondary phosphine oxides

- **Synthesis of α-aminophosphine oxides**



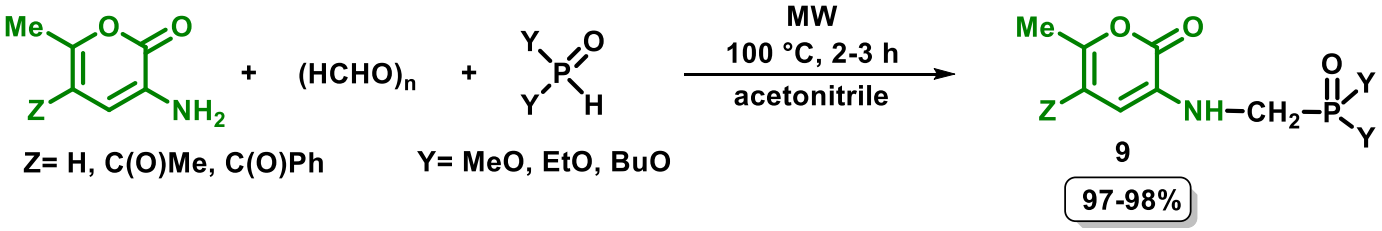
Bálint, E.; Tripolszky, A.; Jablonkai, E.; Karaghiosoff, K.; Czugler, M.; Mucsi, Z.; Kollár, L.; Pongrácz, P.; Keglevich G. *J. Organomet. Chem.* **2016**, *801*, 111-121.

- **Synthesis of optically active α-aminophosphine oxides**



Bálint, E.; Tajti, Á.; Kalocsai, D.; Mátravölgyi, B.; Karaghiosoff, K.; Czugler, M.; Keglevich, G. *Tetrahedron*, **2017**, *73*, 5659-5667.

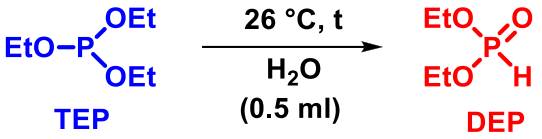
- **Synthesis of *N*-(2*H*-pyranonyl)-α-aminophosphine oxides**



Bálint, E.; Keglevich, G.; Takács, J.; Drahos, L.; Juranovič, A.; Kočevar, M. *Heteroatom Chem.* **2013**, *24*, 221-225.

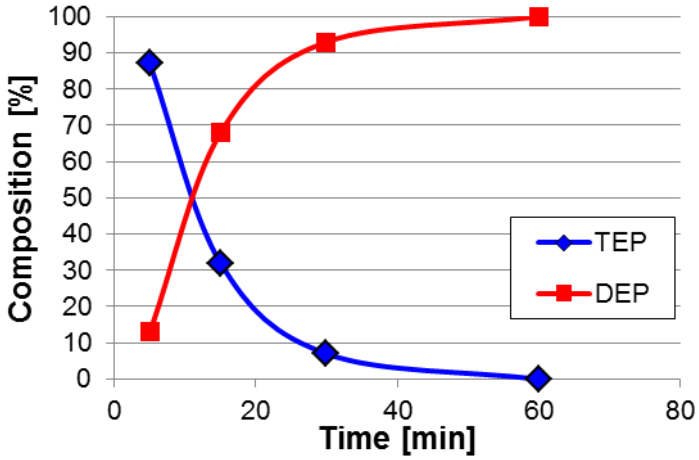
1.3. Aqueous Kabachnik-Fields reactions using triethyl- or diethyl phosphite

- **Hydrolysis of triethyl phosphite[a]**



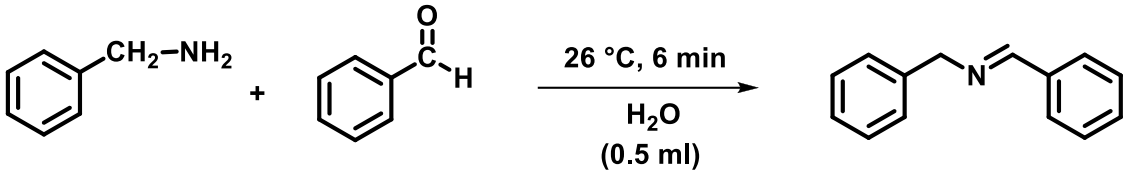
Entry	Additive	Time [min]	Composition [%][b] TEP	DEP
1	–	5	87	13
2	–	15	32	68
3	–	30	7	93
4	–	60	0	100
5	10% PTSA	2.5	0	100

[a]Stirring 0.20 mL TEP in 0.5 mL of water. [b]On the basis of GC.



relatively fast

- **Formation of imine**



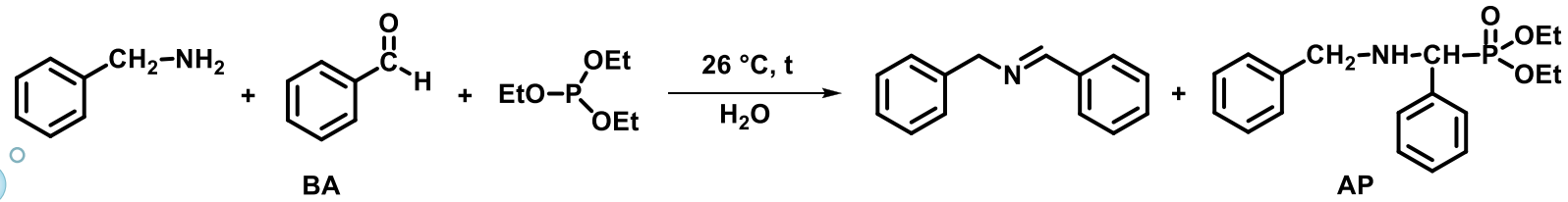
really fast

- **Kabachnik-Fields reactions with TEP in water**

In the literature	In our experiments
Large excess of water	Small amount of water
Environmental load catalysts	PTSA

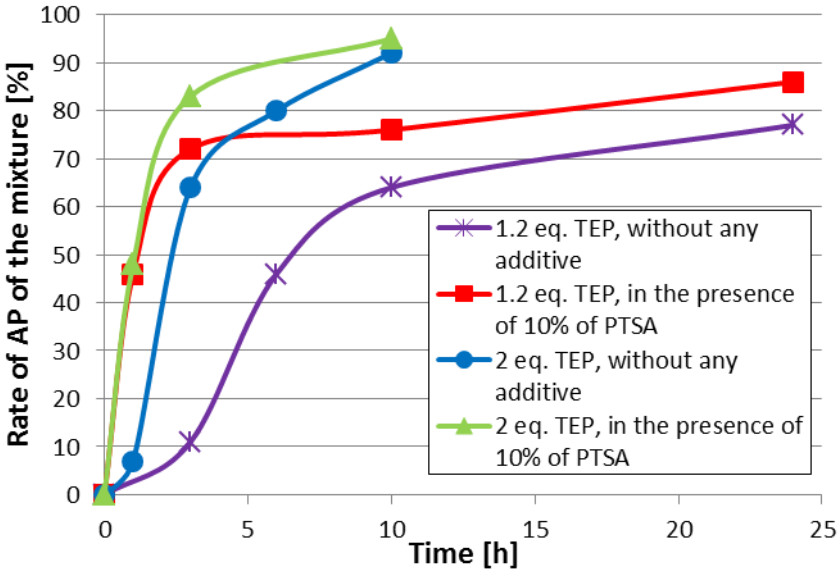
Keglevich, G.; Bálint, E.; Kangyal, R.; Bálint, M.; Milen, M. *Heteroatom Chem.* **2014**, *25*, 282-289.

Kabachnik-Fields reaction of benzyl amine, benzaldehyde and TEP in water



Entry	Additive	TEP [equiv]	Time	Composition [%][a] BA	imine	AP
1/1			3 h	3	86	11
1/2	–	1.2	10 h	3	33	64
1/3			1 day	4	19	77[b]
2/1			3 h	5	31	64
2/2	–	2	6 h	3	17	80
2/3			10 h	4	4	92[b]
3/1			3 h	4	24	72
3/2	10% PTSA	1.2	10 h	6	18	76
3/3			1 day	4	10	86[b]
4/1	10% PTSA	2	3 h	4	13	83
4/2			10 h	2	3	95[b]

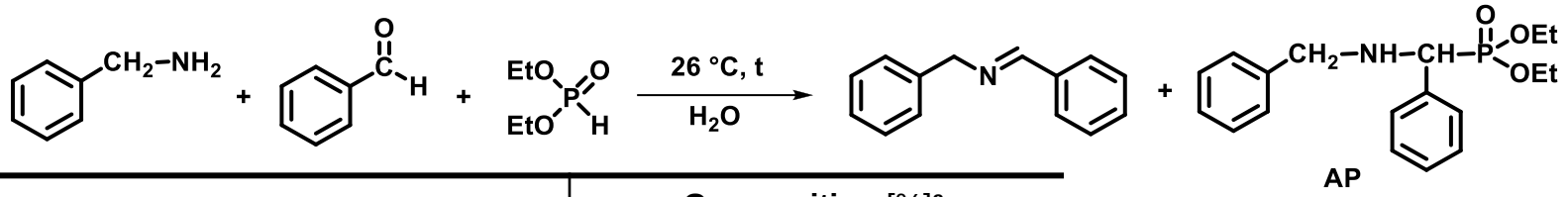
[a]On the basis of GC. [b]There was no change for further stirring.



- PTSA accelerated the process
- The TEP excess also accelerated the process
- conversion: 94-98% → max. composition of AP was 95%
- In these condensations, DEP is an in situ formed reagent concurring with TEP, and replacing it at a certain point

Keglevich, G.; Bálint, E.; Kangyal, R.; Bálint, M.; Milen, M. *Heteroatom Chem.* **2014**, *25*, 282-289.

Kabachnik-Fields reaction of benzyl amine, benzaldehyde and DEP in water



Entry	Additive	DEP [equiv]	Time	Composition [%][a] aldehyde	imine	AP
1/1	–	1.2	3 h	9	65	26
1/2			1 day	13	33	54[b]
2/1	–	2	3 h	11	68	21
2/2			1 day	16	12	72[b]
3/1	10% PTSA	1.2	3 h	9	63	28
3/2			1 day	13	24	63[b]
4/1	10% PTSA	2	3 h	10	62	28
4/2			1 day	15	9	76[b]

[a]On the basis of GC. [b]There was no change for further stirring.

- Slower process
- conversion: 84-91% → max. composition of AP 76%

DEP ⟺ TEP

1 day, 76% of AP — 10 h, 95% of AP

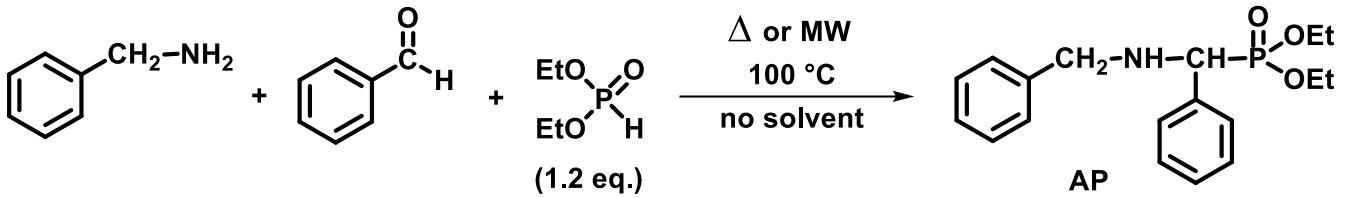
The reactions in water were not complete

Reactions under higher temperature

Entry	Additive	T [°C]	Time	Composition [%][a] aldehyde	imine	AP
1	–	40	1 day	19	30	51
2	–	80	6 h	15	26	59[b]
3	–	100	6 h	11	16	73[b]
4	10% PTSA	100	4 h	8	12	80[b]

Water inhibited the reaction of DEP

Reactions under higher temperature without solvent



Mode of heating	Time	Composition [%][a] AP
Δ	> 1 h	~100
MW	20 min	100

[a]On the basis of GC.

MW
short reaction time
∅ solvent
∅ catalyst
complete conversion

Conclusions

		TEP	DEP
Quantity		2 equiv	1.2 equiv
Additive		10% of PTSA	–
water		+	–
T [°C]		26	100
t		10 h	20 min
Composition [%]	BA	2	–
	imine	3	–
	AP	95	100[a]

[a]Under MW conditions.

DEP ⟺ **TEP**
∅ water, ∅ solvent, ∅ catalyst ⟺ **water, catalyst**

TEP is maldorous ⟺ **DEP**

price of TEP 18 €/2 mol > **price of DEP 12€/1.2 mol**

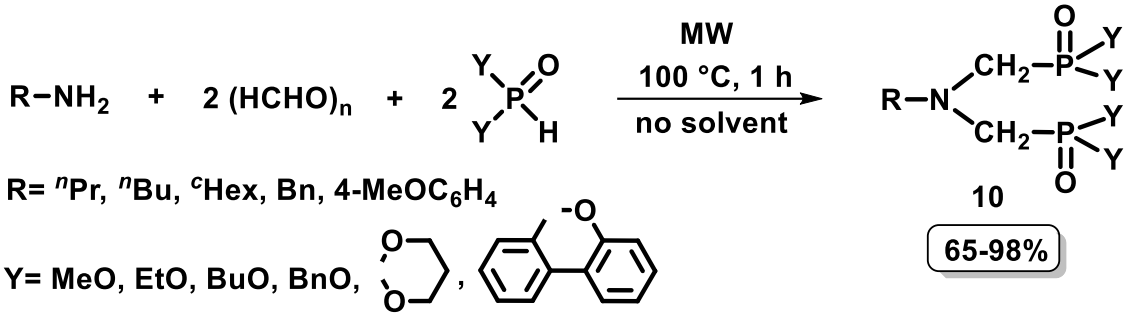
DEP is preferable to use

Keglevich, G.; Bálint, E.; Kangyal, R.; Bálint, M.; Milen, M. *Heteroatom Chem.* **2014**, *25*, 282-289.

Double Kabachnik-Fields reaction

2.1. Microwave-assisted double Kabachnik-Fields reactions with dialkyl phosphites

- **Synthesis of bis(aminophosphonates)**

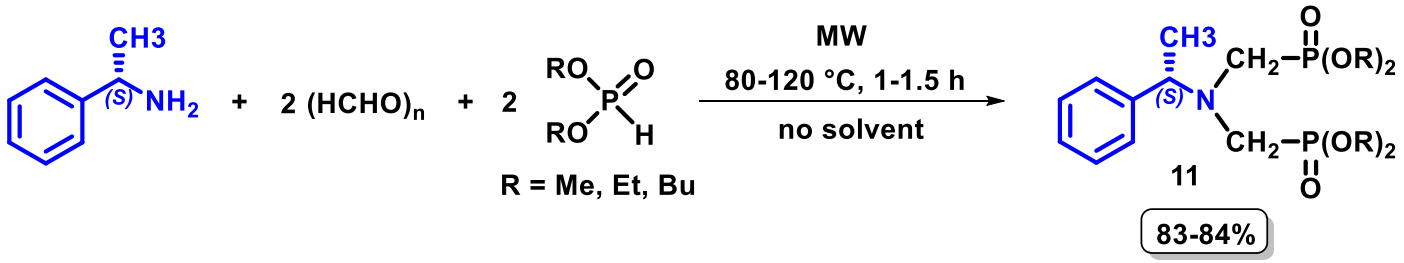


20 *N,N*-bis(phosphonylmethyl)- and *N,N*-bis(phosphinylmethyl)amine derivatives were synthesized => 19 new compounds

Keglevich, G.; Szekrényi, A.; Szöllősy, Á.; Drahos, L. *Synth. Commun.*. **2011**, *41*, 2265-2272.

Bálint, E.; Fazekas, E.; Pintér, G.; Szöllősy, Á.; Holczbauer, T.; Czugler, M.; Drahos, L.; Körtvélyesi, T.; Keglevich, G. *Curr. Org. Chem.* **2012**, *16*, 547-554.

- **Synthesis of optically active bis(aminophosphonates)**

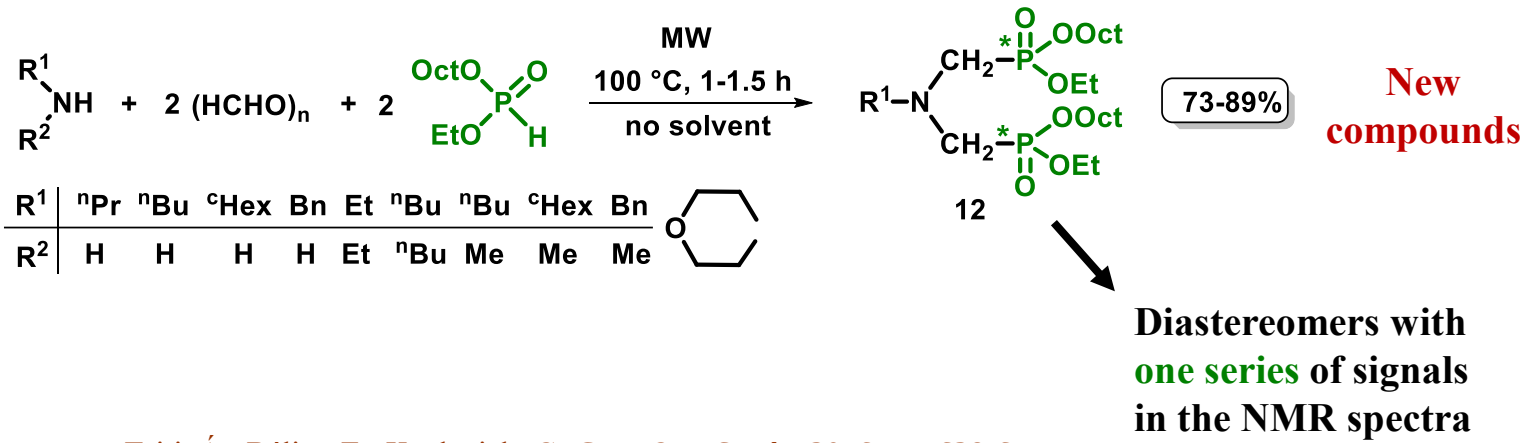


New compounds

Bálint, E.; Tajti, Á.; Kalocsai, D.; Mátravölgyi, B.; Karaghiosoff, K.; Czugler, M.; Keglevich, G. *Tetrahedron*, **2017**, *73*, 5659-5667.

Synthesis of P-chiral bis(aminophosphonates) and bis(aminophosphinates)

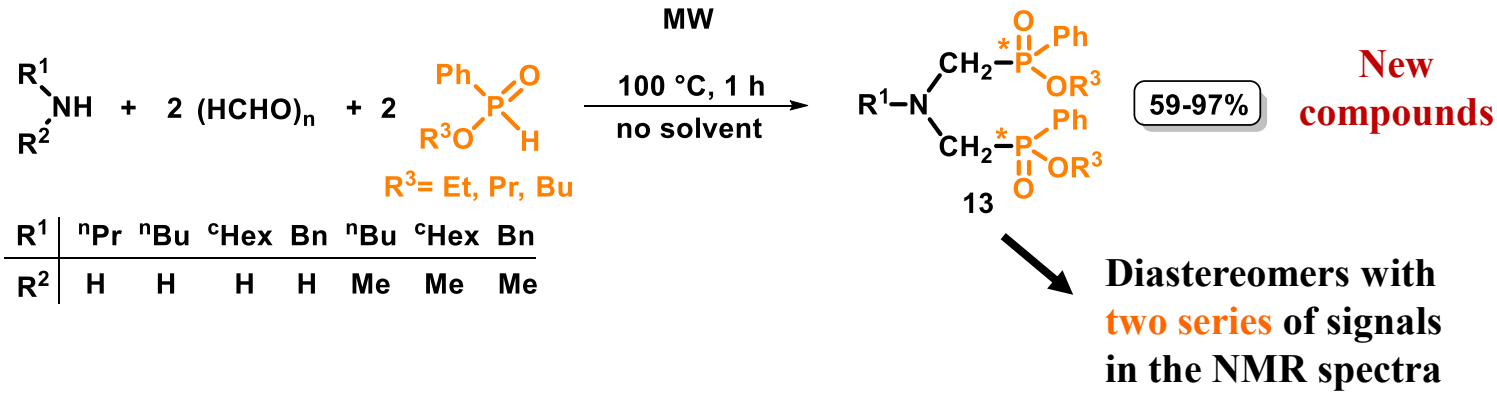
- **Kabachnik-Fileds reactions with ethyl octyl phosphite**



R^1	^{n}Pr	^{n}Bu	^{c}Hex	Bn	Et	^{n}Bu	^{n}Bu	^{c}Hex	Bn
R^2	H	H	H	H	Et	^{n}Bu	Me	Me	Me

Tajti, Á.; Bálint, E.; Keglevich, G. *Curr. Org. Synth.*, **2016**, *13*, 638-645.

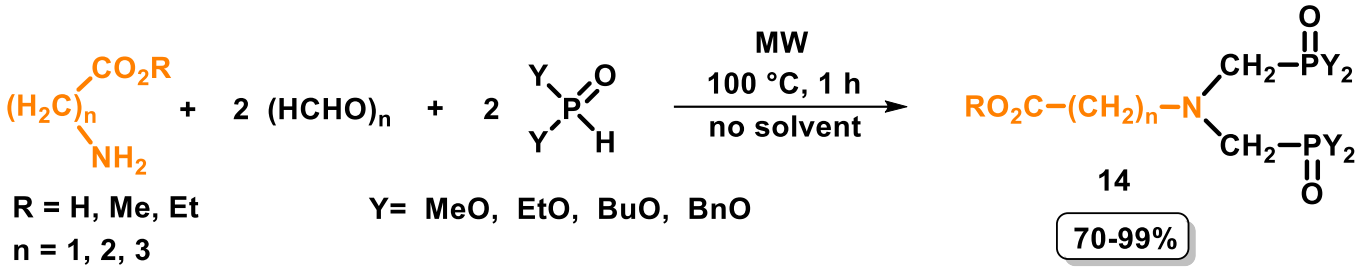
- **Kabachnik-Fileds reactions with alkyl phenyl-*H*-phosphinates**



R^1	^{n}Pr	^{n}Bu	^{c}Hex	Bn	^{n}Bu	^{c}Hex	Bn
R^2	H	H	H	H	Me	Me	Me

Bálint, E.; Tóth, R. E.; Keglevich, G. *Heteroatom Chem.*, **2016**, *27*, 323-335.

Double Kabachnik-Fields reactions of α-, β-, and γ-amino acid derivatives



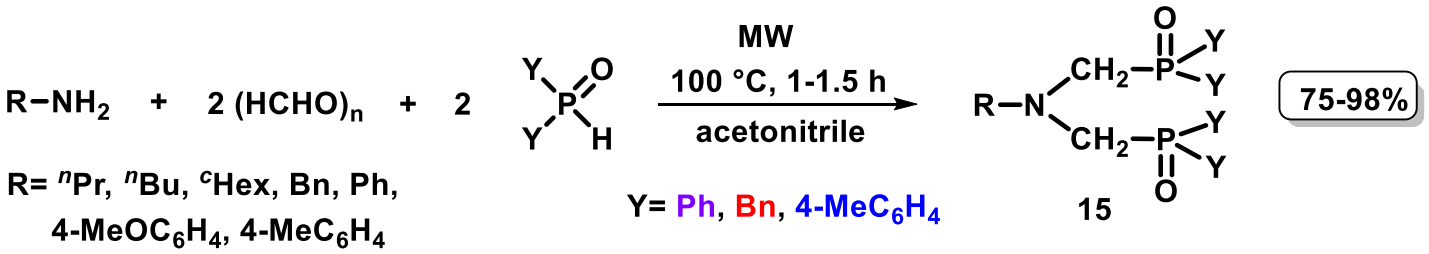
30 new bis(dialkoxyphosphonomethyl)-amino acid derivatives were synthesized

Bálint, E.; Fazekas, E.; Drahos, L.; Keglevich, G. *Heteroatom Chem.* **2013**, *24*, 510-515.

Bálint, E.; Fazekas, E.; Mucsi, Z.; Kóti, J.; Keglevich, G. *Heteroatom Chem.* **2015**, *26*, 106-115.

2.2. Double Kabachnik-Fields reactions with secondary phosphine oxides

- **Synthesis of bis(aminophosphine oxides)**



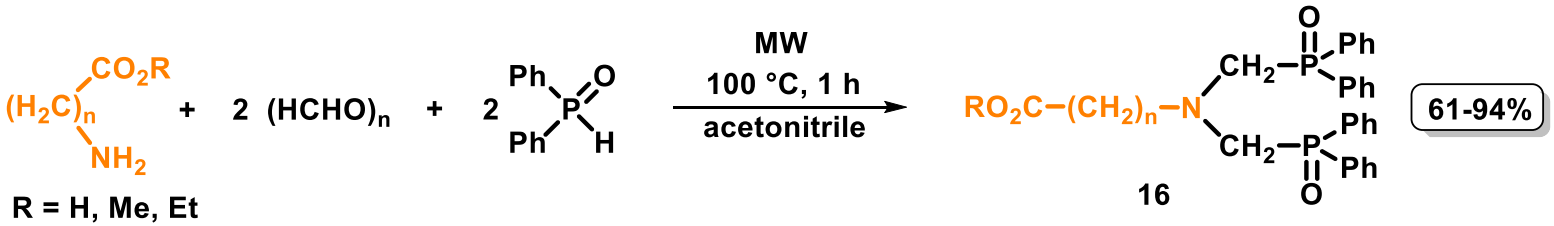
14 new *N,N*-bis(phosphinoylmethyl)amines

Keglevich, G.; Szekrényi, A.; Szöllősy, Á.; Drahos, L. *Synth. Commun.*. **2011**, *41*, 2265-2272.

Bálint, E.; Fazekas, E.; Pongrácz, P.; Kollár, L.; Drahos, L.; Holczbauer, T.; Czugler, M.; Keglevich, G. *J. Organomet. Chem.* **2012**, *717*, 75-82.

Bálint, E.; Tripolszky, A.; Jablonkai, E.; Karaghiosoff, K.; Czugler, M.; Mucsi, Z.; Kollár, L.; Pongrácz, P.; Keglevich G. *J. Organomet. Chem.* **2016**, *801*, 111-121.

- **Synthesis of bis(diphenylphosphinoylmethyl)-amino acid derivatives**



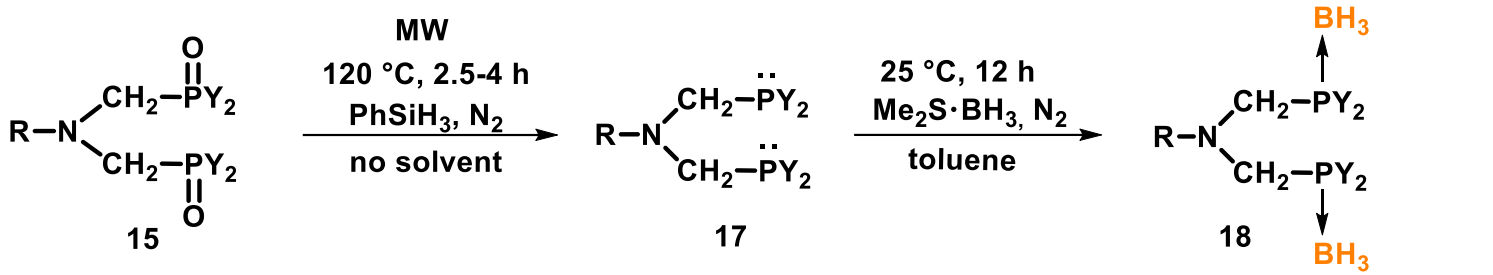
8 new compounds

Bálint, E.; Fazekas, E.; Drahos, L.; Keglevich, G. *Heteroatom Chem.* **2013**, *24*, 510-515.

Bálint, E.; Fazekas, E.; Mucsi, Z.; Kóti, J.; Keglevich, G. *Heteroatom Chem.* **2015**, *26*, 106-115.

2.3. Utilization of the bis(aminophosphine oxides)

- **Synthesis of borane complexes**

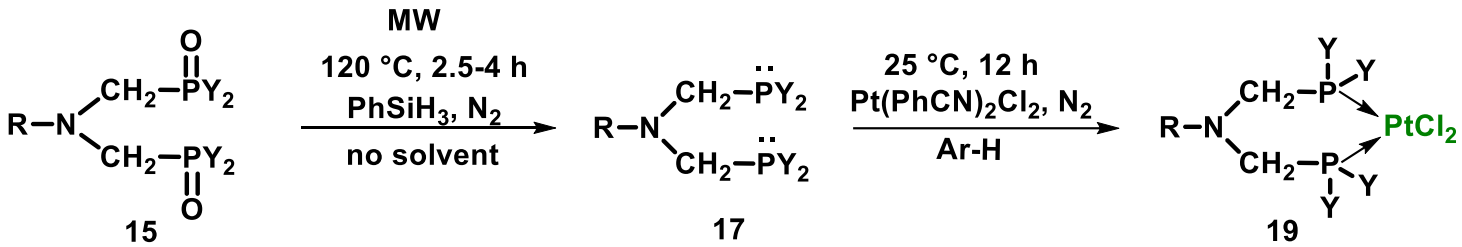


R= ^{c}Hex, Bn

Y= Ph, Bn, 4-MeC$_6$H$_4$

R	^{c}Hex	Bn	Bn
Y	Ph	Bn	4-MeC$_6$H$_4$
Yield	26%	60%	69%

- **Synthesis of platinum complexes**



R= ^{n}Pr, ^{n}Bu, ^{c}Hex, Bn, Ph, 4-MeOC$_6$H$_4$, 4-MeC$_6$H$_4$

Y= Ph, Bn, 4-MeC$_6$H$_4$

3 borane- and 13 platinum complexes => all are new

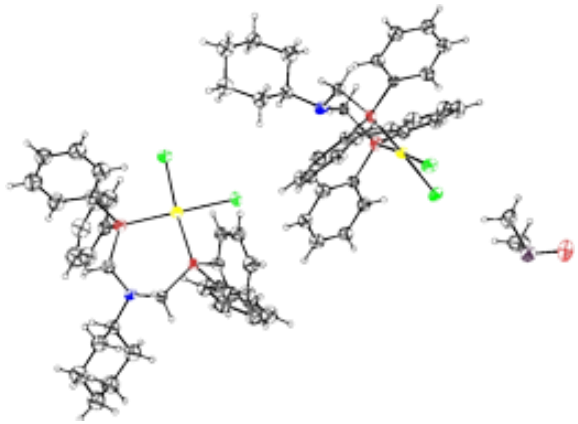
Keglevich, G.; Szekrényi, A.; Szöllősy, Á.; Drahos, L. *Synth. Commun.*. **2011**, *41*, 2265-2272.

Bálint, E.; Fazekas, E.; Pongrácz, P.; Kollár, L.; Drahos, L.; Holczbauer, T.; Czugler, M.; Keglevich, G. *J. Organomet. Chem.* **2012**, *717*, 75-82.

Bálint, E.; Tripolszky, A.; Jablonkai, E.; Karaghiosoff, K.; Czugler, M.; Mucsi, Z.; Kollár, L.; Pongrácz, P.; Keglevich G. *J. Organomet. Chem.* **2016**, *717*, 75-82.

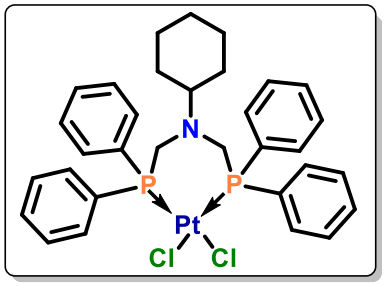
Structures of platinum complexes I.

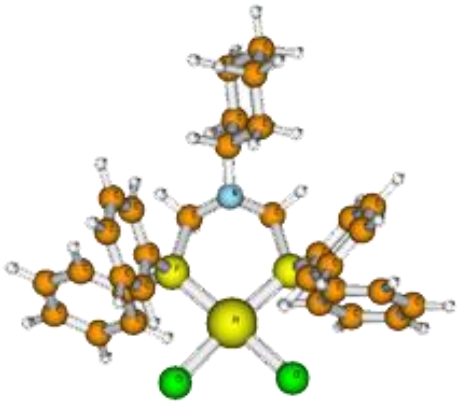
X-ray analysis



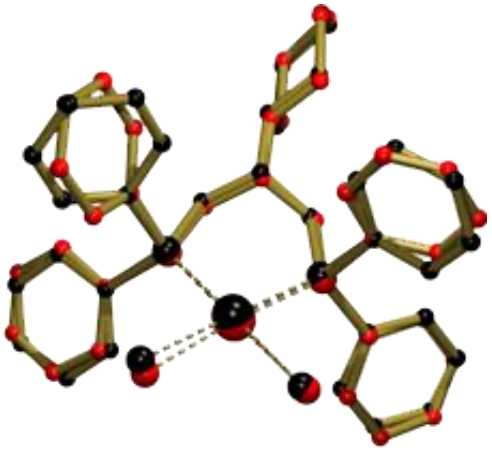
Two slightly different complex conformation and one DMSO

Quantum chemical calculations

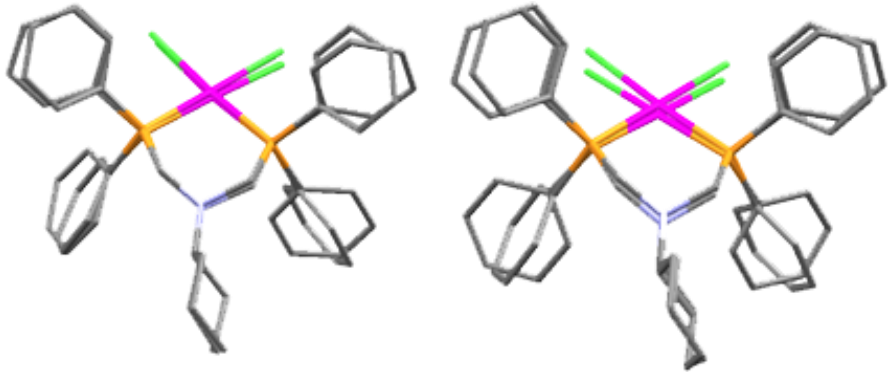




The structure determined by B3LYP/6-31G** and LANL2DZ calculations (gas phase)



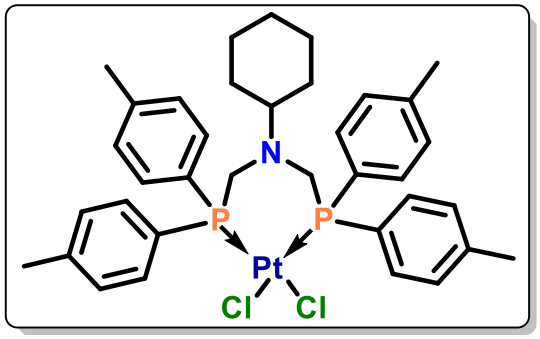
Comparison of the two conformations



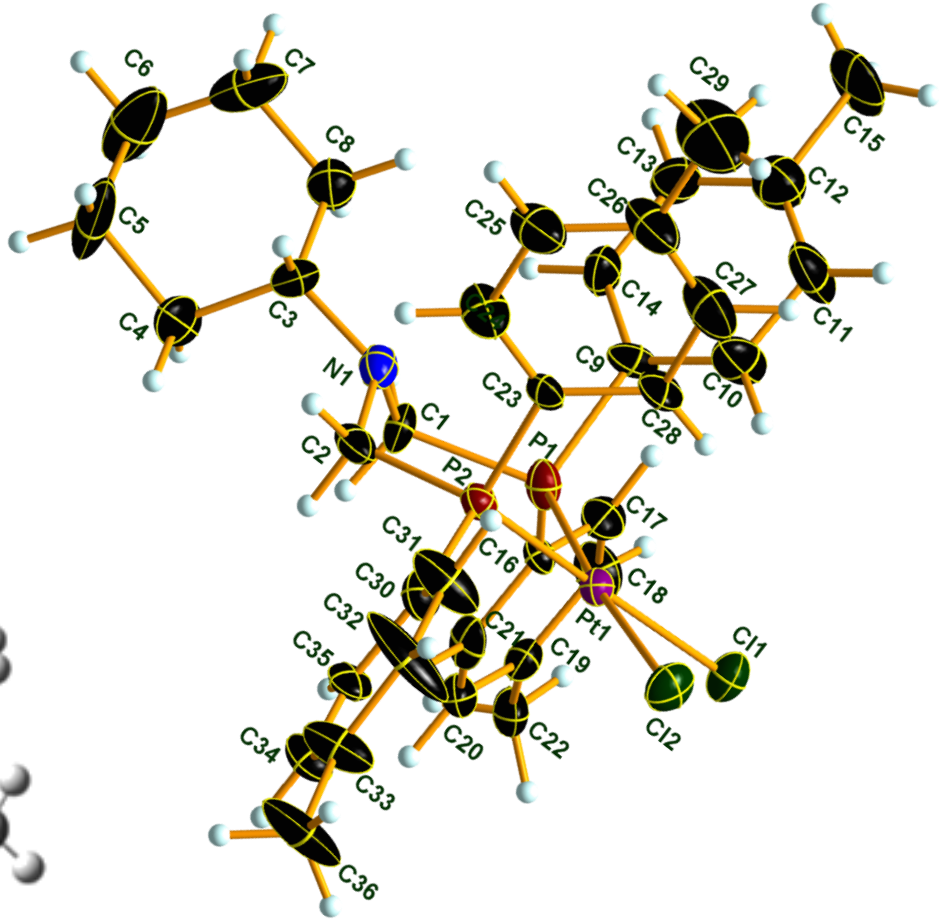
Comparison of the quantum chemical model with the two measured conformations

The fit of the central and apparently most rigid 6-ring metallo-heterocycle is seemingly acceptable

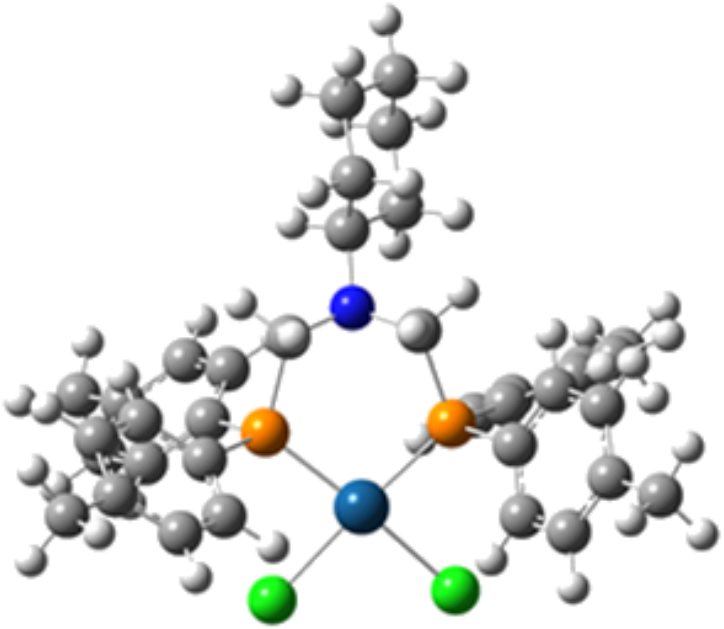
Strucrures of platinum complexes II.



X-ray analysis

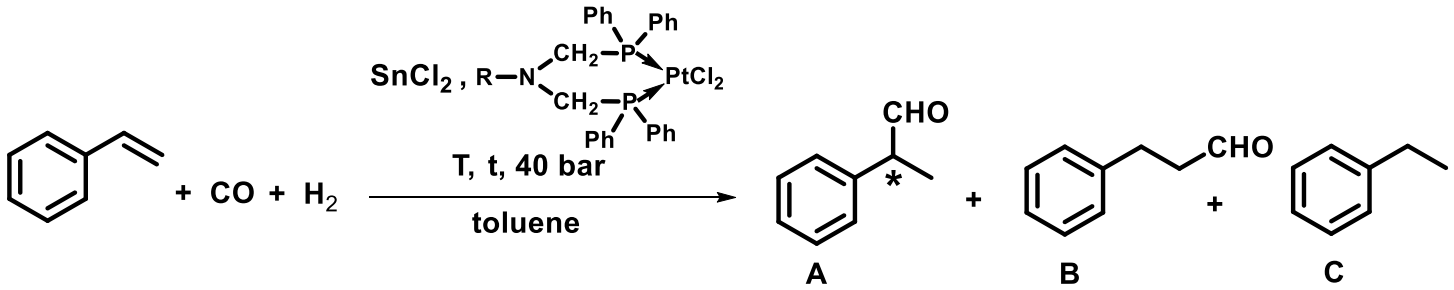


Quantum chemical calculations

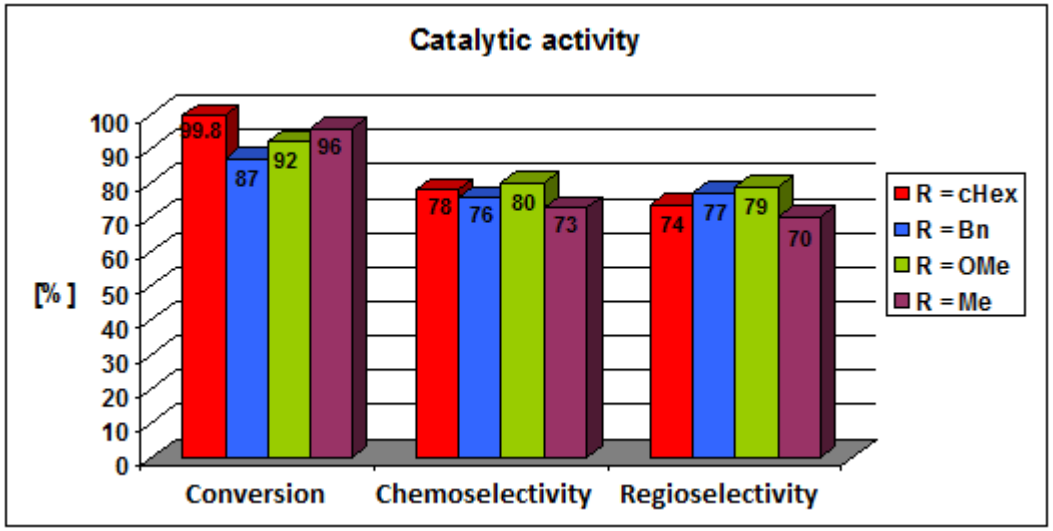


The structure determined by B3LYP/6-31G(d,p) and B3LYP/SDD(MWB60) calculations

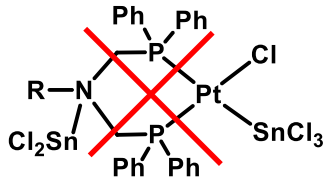
Catalytic activity of platinum complexes I.

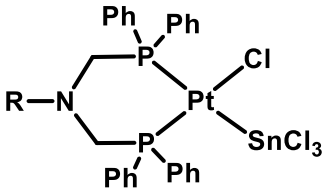


R	T [°C]	t [h]	Conv. [%]	S_{chemo} [%]	S_{regio} [%]
^{c}Hex	60	20	>99.8	78	74
Bn	60	5	87	76	77
MeO	40	20	92	80	79
Me	100	1	96	73	70



$A + B + C$ $\quad \frac{A + B}{A + B + C}$ $\quad \frac{A}{A + B}$

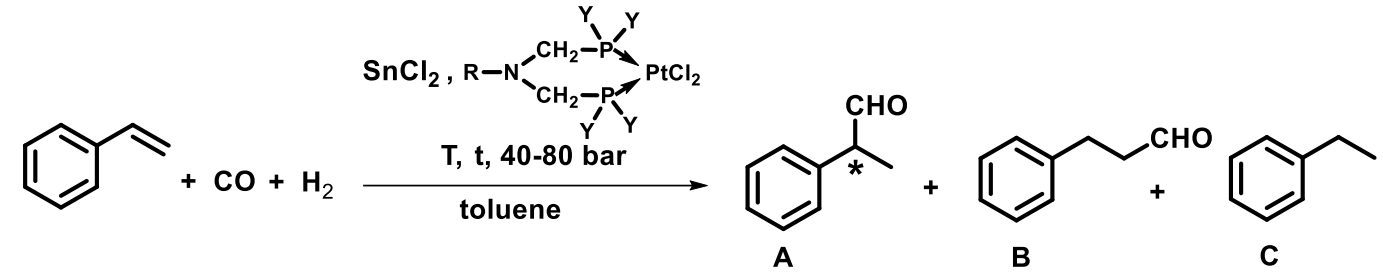




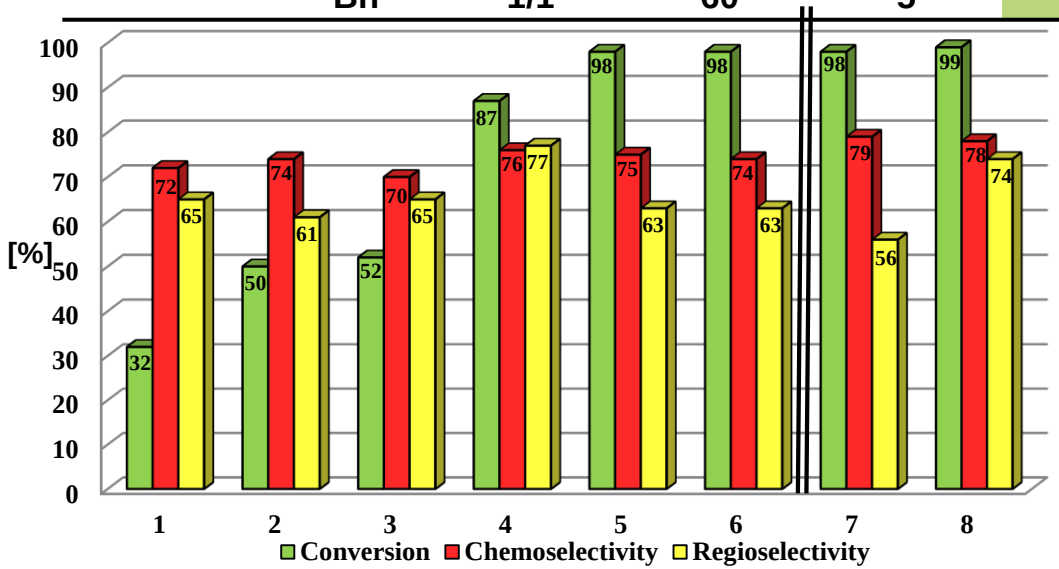
‚oxo-conditions' (p(CO) = p(H_2) = 40 bar, reaction temperature varied from 40 °C to 100 °C)

Bálint, E.; Fazekas, E.; Pongrácz, P.; Kollár, L.; Drahos, L.; Holczbauer, T.; Czugler, M.; Keglevich, G. *J. Organomet. Chem.* **2012**, *717*, 75-82.

Catalytic activity of platinum complexes II.



Y	R	Pt/$SnCl_2$	T [°C]	t [h]	Conversion [%]	S_{chemo} [%]	S_{regio} [%]
Bn	^{n}Bu	1/2	100	3	32	72	65
	^{c}Hex	1/2	100	3	50	74	61
	Bn	1/2	100	3	52	70	65
4-MeC_6H_4	^{n}Bu	1/2	100	8	98	75	63
	^{c}Hex	1/2	100	6	98	74	63
	Bn	1/2	100	3	98	79	56
Ph	^{c}Hex	1/1	60	20	99	78	74
	Bn	1/1	60	5	87	76	77



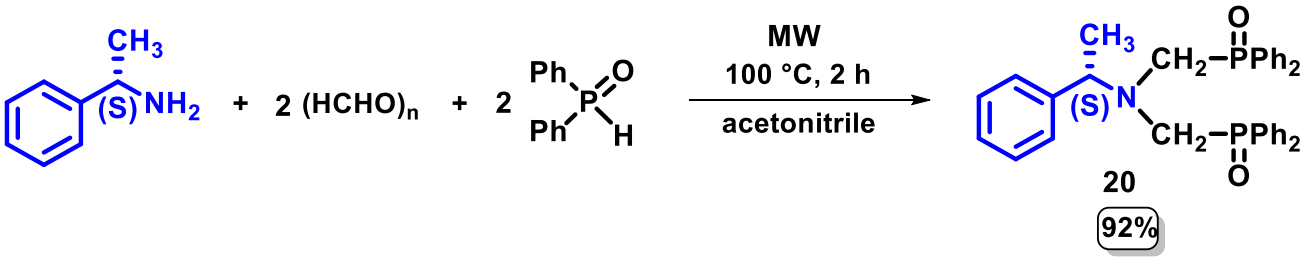
A+B+C

$$\frac{A+B}{A+B+C} \qquad \frac{A}{A+B}$$

Bálint, E.; Tripolszky, A.; Jablonkai, E.; Karaghiosoff, K.; Czugler, M.; Mucsi, Z.; Kollár, L.; Pongrácz, P.; Keglevich G. *J. Organomet. Chem.* **2016**, *717*, 75-82.

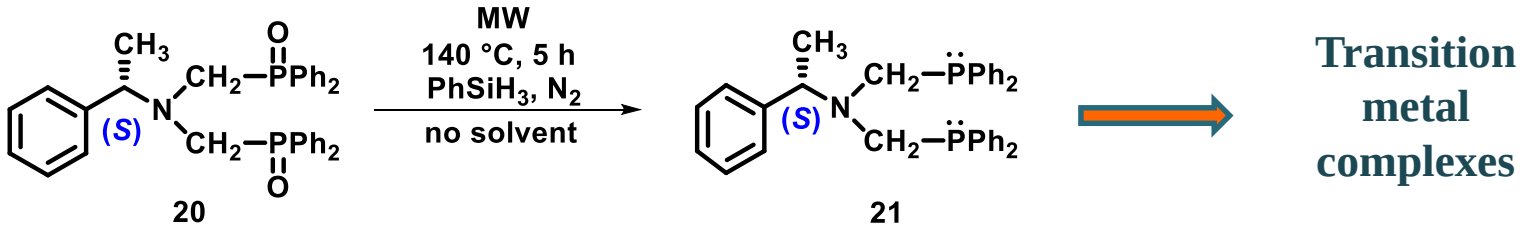
Cooperation with Prof. László Kollár and Dr. Péter Pongrácz

- **Synthesis of optically active bis(aminophosphine oxide)**



New compound

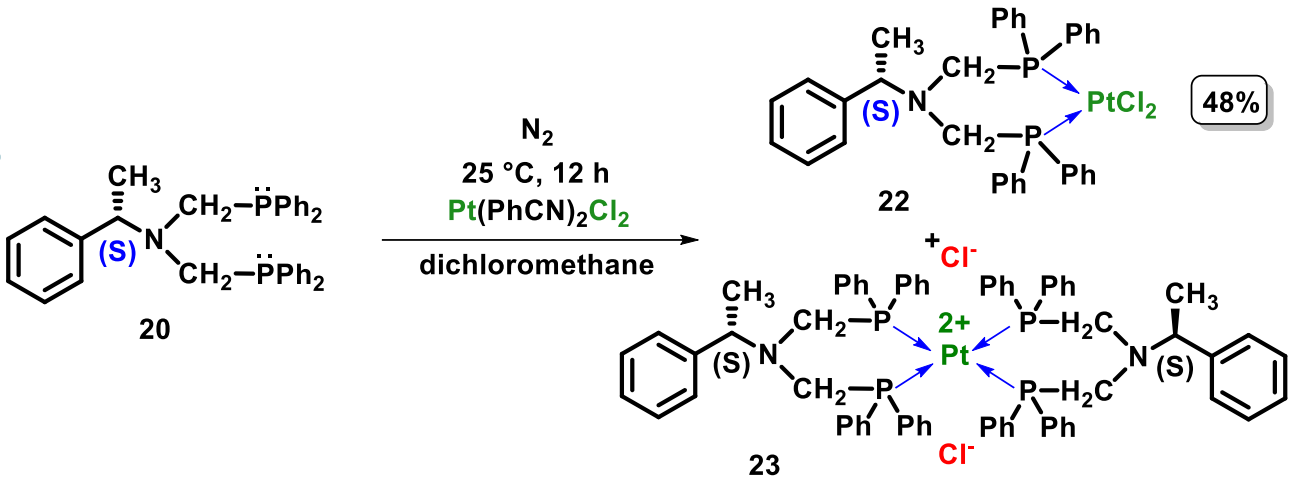
- **Utilization of the optically active bis(aminophosphine oxide)**



New chiral bidentate P-ligand

Bálint, E.; Tajti, Á.; Kalocsai, D.; Mátravölgyi, B.; Karaghiosoff, K.; Czugler, M.; Keglevich, G. *Tetrahedron*, **2017**, *73*, 5659-5667.

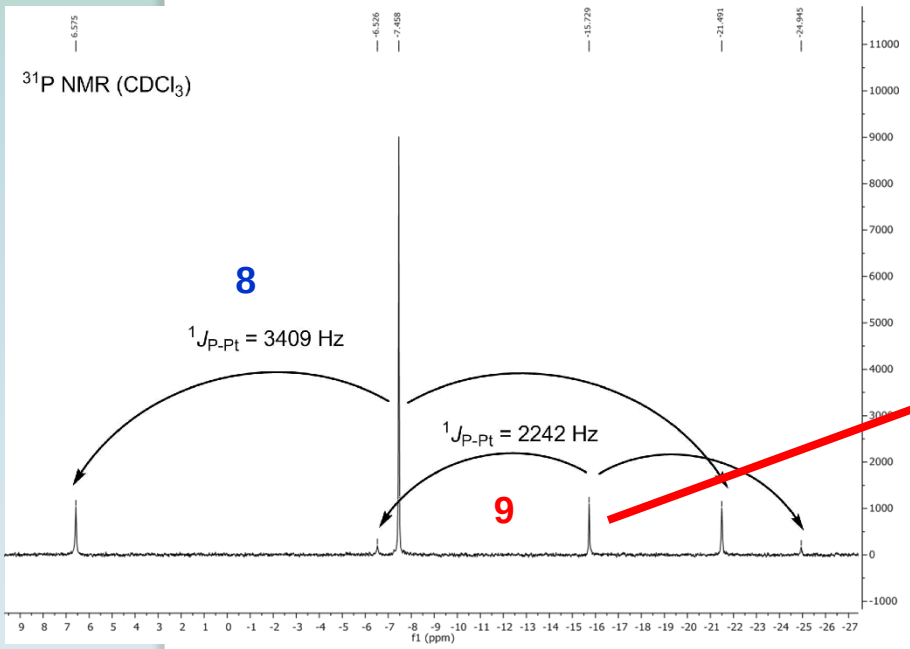
Synthesis of platinum complexes

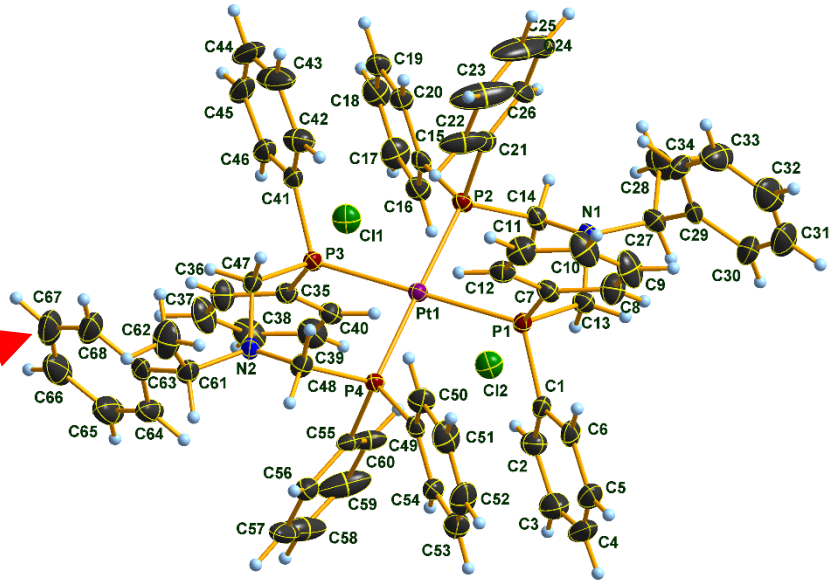


^{31}P, ^{13}C, ^{1}H NMR
HRMS

Interesting by-product

^{31}P NMR, HRMS
X-Ray



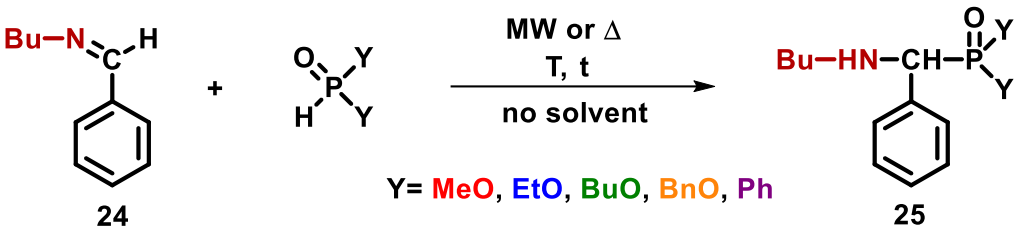


Bálint, E.; Tajti, Á.; Kalocsai, D.; Mátravölgyi, B.; Karaghiosoff, K.; Czugler, M.; Keglevich, G. *Tetrahedron*, **2017**, *73*, 5659-5667.

Pudovik reaction

3.) Pudovik reaction (addition of >P(O)H reagents to imines)

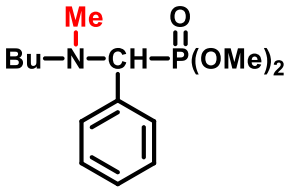
- **Reactions with (*N*-benzylidene)butylamine**



24 25

Entry	Mode of heating	Y	>P(O)H [equiv]	T [°C]	t [min]	Composition [%][a]		Yield [%]
						24	25	
1	MW	OMe	1	80	30	5	95	73
2	Δ	OMe	1	80	30	21	79	-
3	MW	OMe	1	100	30	4	90[b]	-
4	MW	OMe	1.2	100	30	0	94[b]	-
5	MW	OEt	1.2	100	30	0	100	85
6	MW	OBu	1.2	100	30	1	99	90
7	MW	OBn	1.2	100	30	0	100[c]	69
8[d]	MW	Ph	1.2	100	10	0	100[c]	89

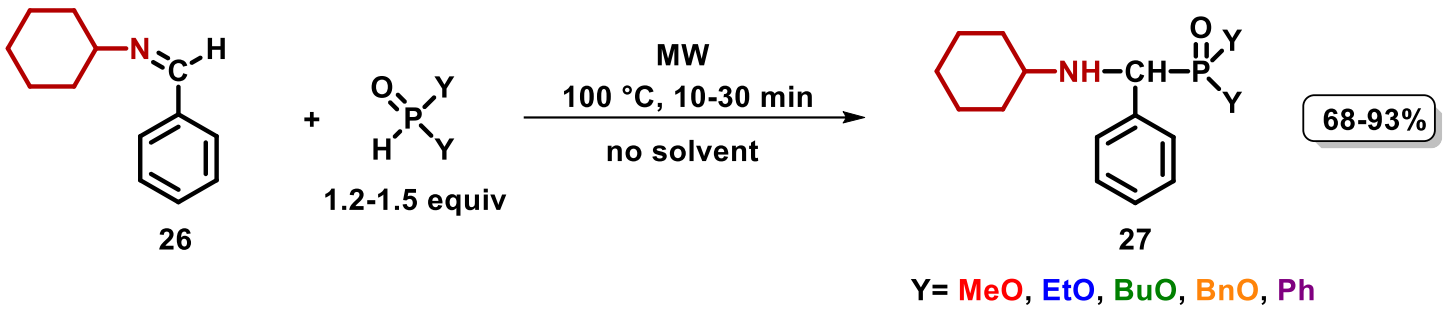
[a]Based on GC. [b]6% *N*-methylated by-product (**4**) was formed. [c]Based on HPLC. [d]Under N_2 atmosphere.



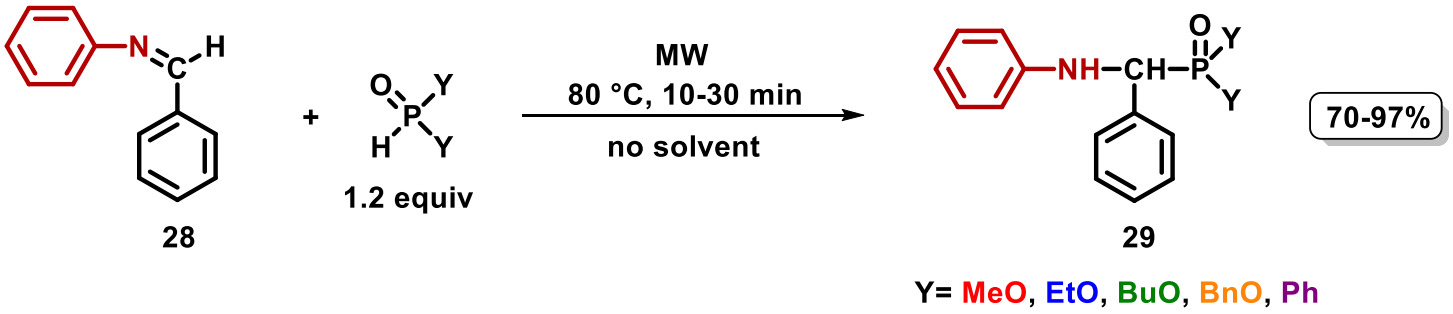
17

Optimal conditions: 1-1.2 equiv >P(O)H, 80-100 °C, 10-30 min

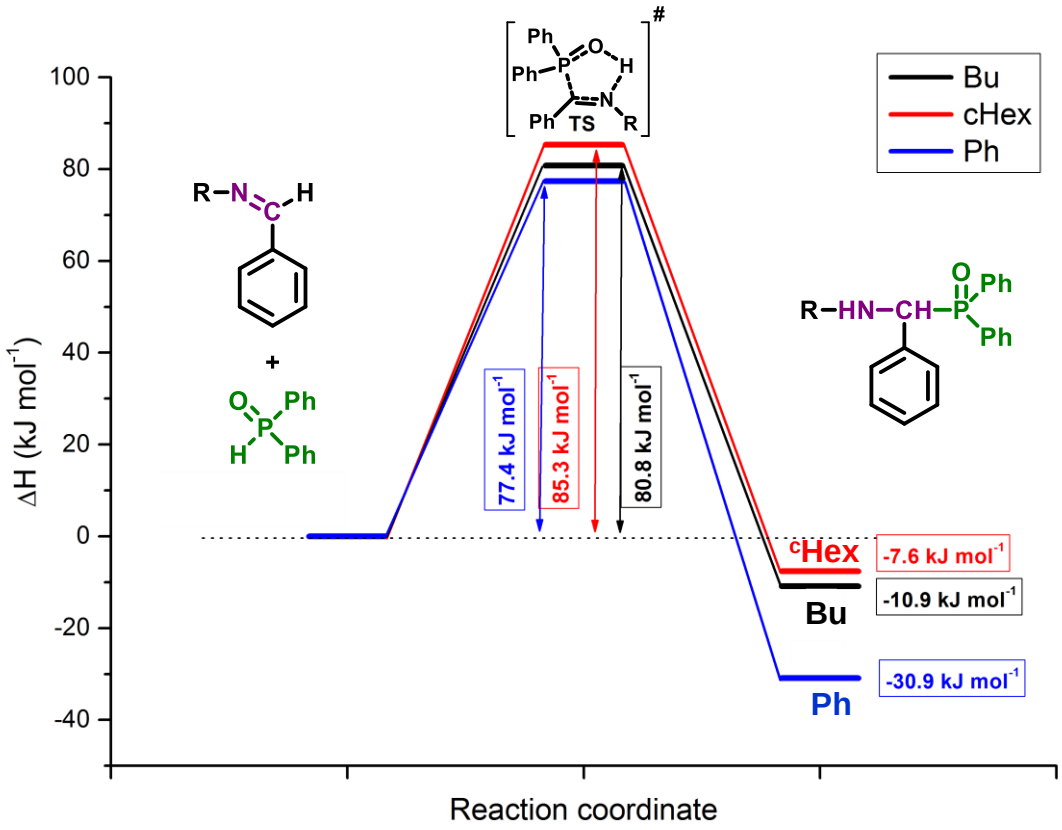
- **Reactions with (*N*-benzylidene)cyclohexylamine**

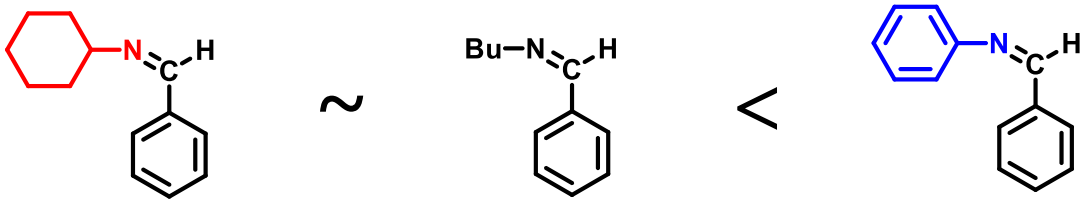


- **Reactions with (*N*-benzylidene)aniline**



Reactivity of α-aryl imines based on B3LYP/6-31G(d,p) calculations





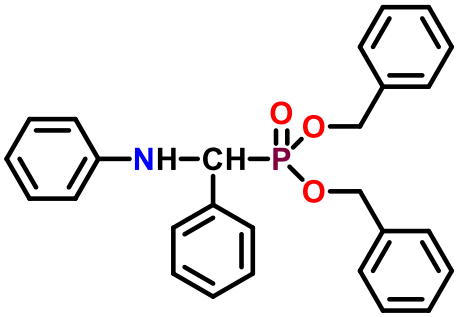
Similar results to the experiments

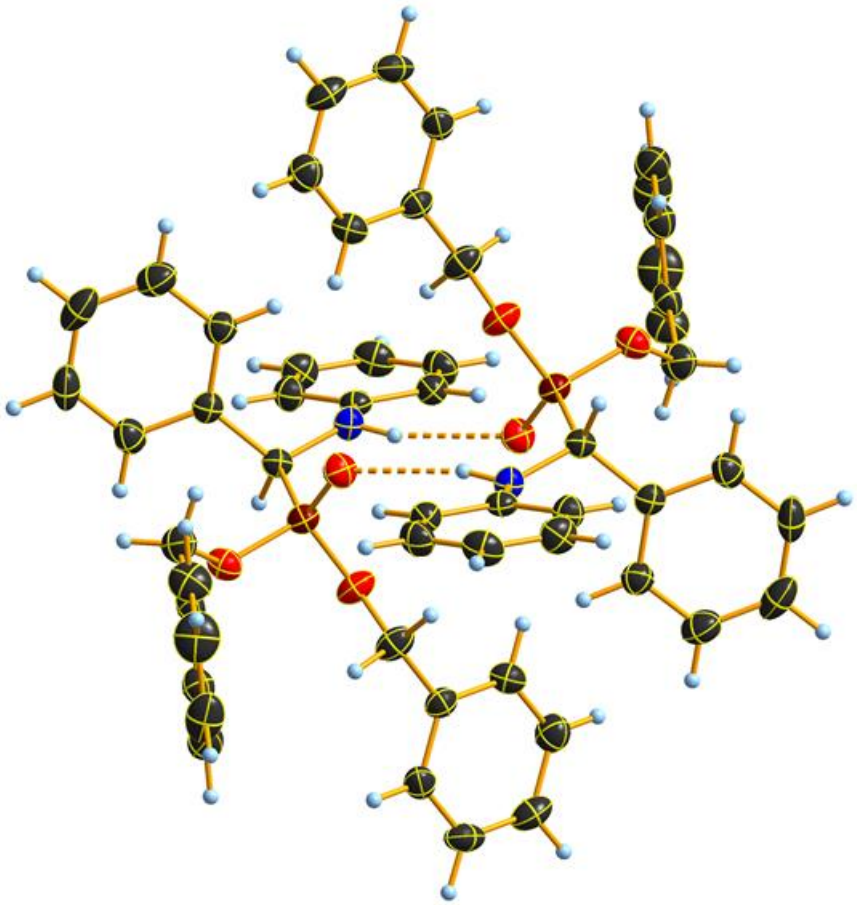
Cooperation with Dr. Péter Ábrányi-Balogh

Bálint, E.; Tajti, Á.; Ádám, A.; Csontos, I.; Karaghiosoff, K.; Czugler, M.; Ábrányi-Balogh, P.; Keglevich, G. *Beilstein J. Org. Chem.*, **2017**, *13*, 76-86.

Crystal structure of aminophosphonates by X-ray measurement

- **(R,S)-racemic dimers in the crystal structure**
- **Stabilized by two H-bridges**

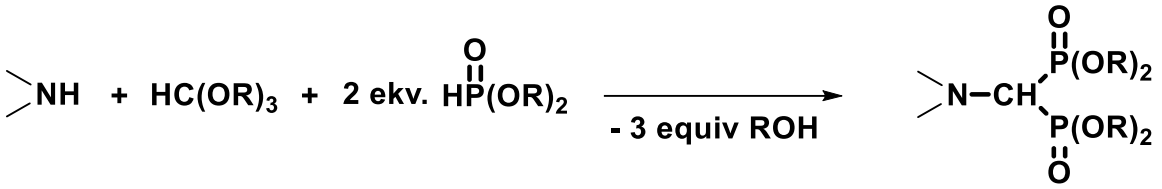




Cooperation with Dr. Mátyás Czugler and Dr. Konstantin Karaghiosoff

Bálint, E.; Tajti, Á.; Ádám, A.; Csontos, I.; Karaghiosoff, K.; Czugler, M.; Ábrányi-Balogh, P.; Keglevich, G. *Beilstein J. Org. Chem.*, **2017**, *13*, 76-86.

4.) Synthesis of (aminomethylene)bisphosphonates and (aminomethylene)-bisphosphine oxides by a three-component condensation



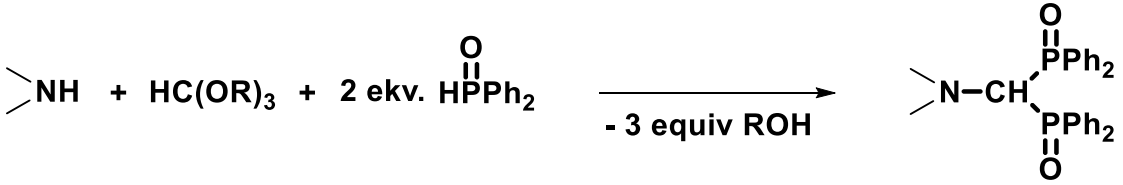
- **Unoptimized conditions**
- **Usually high temperature and long reaction time**

Romanenko, V. D.; Kukhar, V. P. *Arkivoc* **2012**, 127.

- **Few MW-assisted synthesis, mostly in kitchen MW oven***

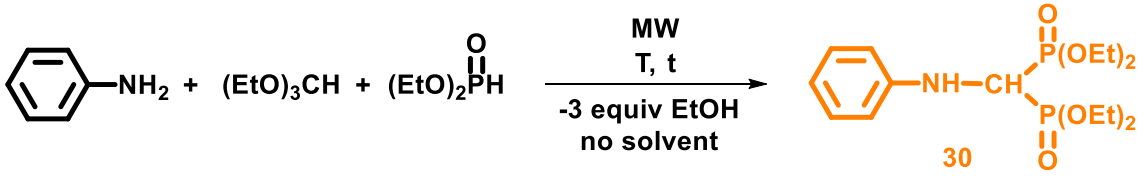
Kaboudin, B.; Alipour, S., Tetrahedron Lett., 2009, 50, 4243.
*Minaeva, L. I.; Patrikeeva, L. S.; Kabachnik, M. M.; Orlinson, B. S.; Novakov, I. A., *Heteroatom Chem.*, **2011**, *22*, 55.
*Reddy, G. C. S.; Reddy, M. V. N.; Reddy, N. B.; Reddy C. S., *Phosphorus, Sulfur, Silicon*, **2010**, *186*, 74.

- **(Aminomethylene)bisphosphine oxides have not been prepared in this way**



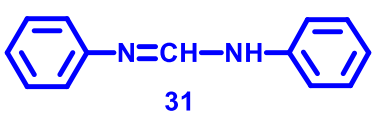
Aim: Optimized preparation of (aminomethylene)bisphosphonates and a new synthetic route for the (aminomethylene)bisphosphine oxides by the MW-assisted catalyst and solvent-free three-component condensation

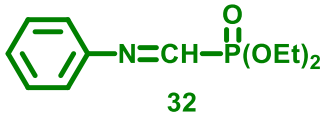
4.1. Reactions with primary amines



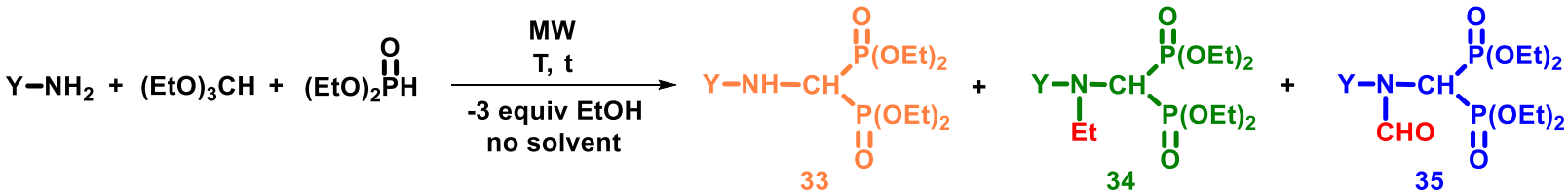
Entry	DEP [equiv]	T [°C]	T [h]	Conversion [%][a]	Product composition [%][a]			Yield [%][b]
					30	31[c]	32[c]	
1	2	125	2	68	56	29	15	36
2	2	150	1	90	70	18	12	52
3	3	125	1	100	100	0	0	82

[a]Based on LC.
[b]After column chromatography.
[c]Intermediates identified based on LC-MS:





^{31}P NMR
HRMS



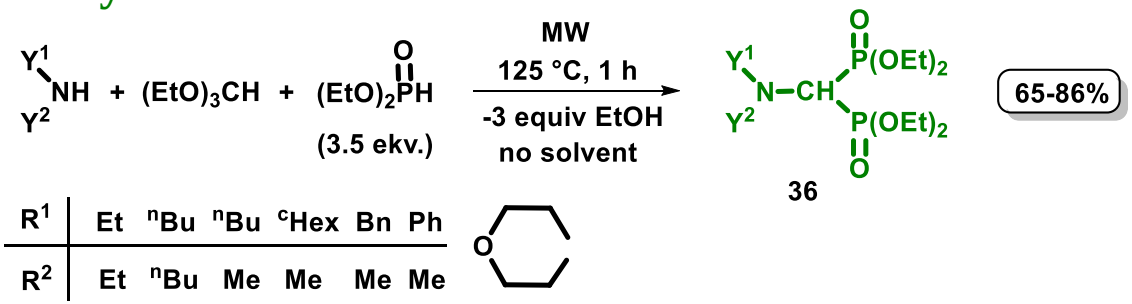
Entry	Y	DEP [equiv]	T [°C]	T [h]	Conversion [%][a]	Product composition [%][a]			Yield [%][b]
						33	34[c]	35[c]	
1	Bu	2	125	2	91	81	19	0	–
2	Bu	2	150	0.5	100	78	15	7	61
3	Bu	3.5	125	1.5	90	78	22	0	–
4	[c]Hex	2	150	0.5	100	88	10	2	68

[a]Based on GC. [b]After column chromatography.

6 new compounds

4.2. Reactions with secondary amines

- **Synthesis of ethyl esters**

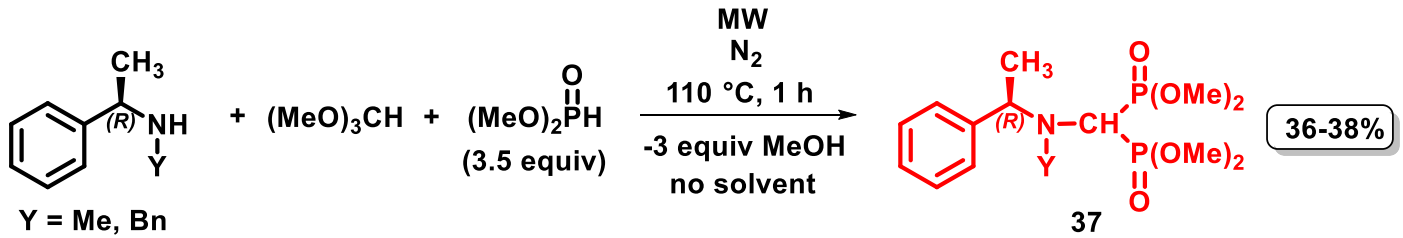


R^1	Et	^{n}Bu	^{n}Bu	^{c}Hex	Bn	Ph
R^2	Et	^{n}Bu	Me	Me	Me	Me

Bálint E.; Tajti, Á.; Dzielak, A.; Hägele, G.; Keglevich, G. *Beilstein J. Org. Chem.*, **2016**, *12*, 1493-1502.

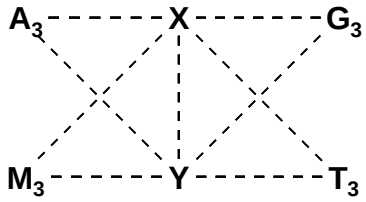
- **Synthesis of chiral methyl esters***

9 new compounds

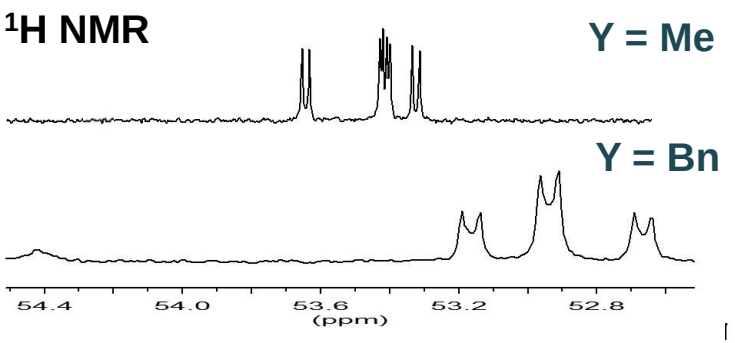


Special NMR properties

eg. in the OMe region



$A_3G_3M_3T_3XY$

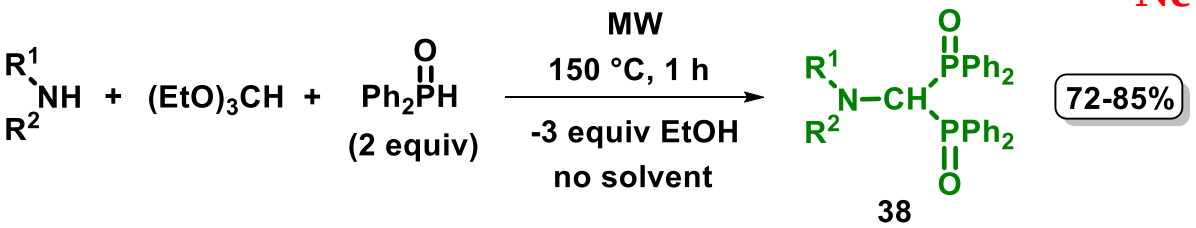


*Cooperation with Dr. Gerhard Hägele, Düsseldorf

Amadeu, N.; Bálint, E.; Boenigk, W.; Tajti, Á.; Hägele, G.; Janiak, C.; Keglevich, G. *Phosphorus, Sulfur, Silicone* **2017**, 192, 643-650.

4.3. Synthesis of (aminomethylene)bisphosphine oxides

New synthetic route



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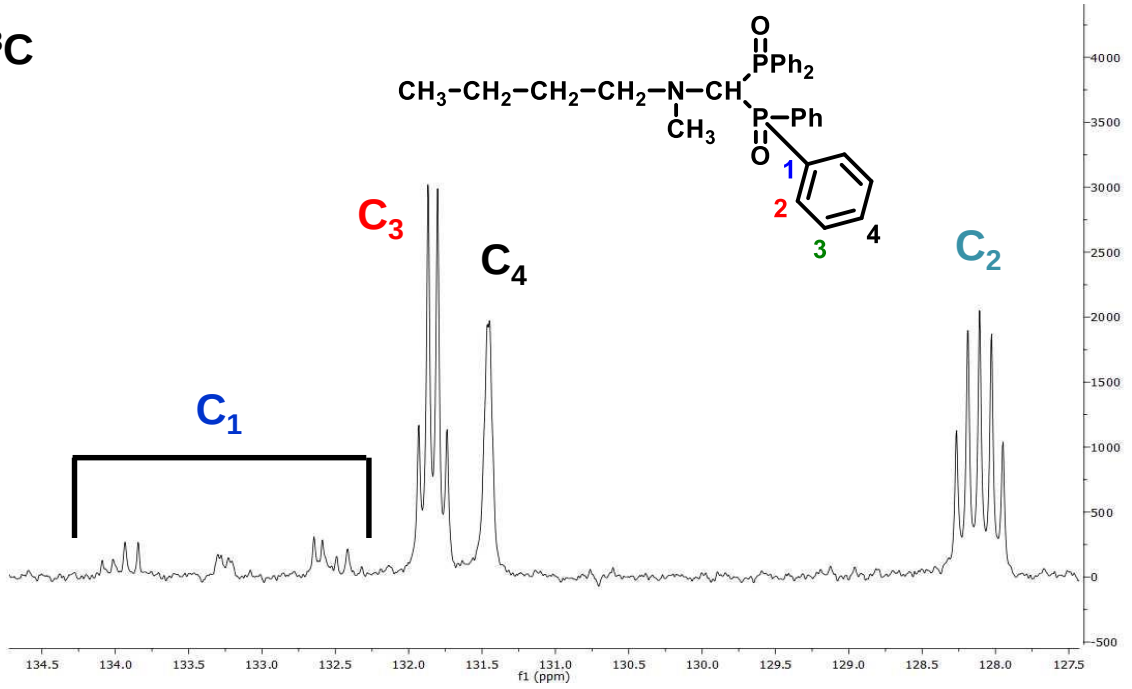
R^1	^{n}Bu	^{c}Hex	Bn	Ph	Et	^{n}Bu	^{n}Bu	^{c}Hex	Bn	Ph
R^2	H	H	H	H	Et	^{n}Bu	Me	Me	Me	Me

10 new compounds

^{31}P, ^{13}C, ^{1}H NMR, HRMS characterization

^{13}C

Complex aromatic signals in the ^{13}C spectrum*



*Cooperation with Dr. Gerhard Hägele

Bálint E.; Tajti, Á.; Dzielak, A.; Hägele, G.; Keglevich, G. *Beilstein J. Org. Chem.*, **2016**, *12*, 1493-1502.

Conclusions

„Green" syntheses of α-aminophosphonate and α-aminophosphine oxide derivatives

MW-assisted Kabachnik-Fields condensations

MW-assisted Pudovik reactions

Catalyst- and in most cases solvent-free conditions

Utilization of the bis(aminophospine oxides) as precursors of P-ligands in platinum complexes

Structures characterization: ^{31}P, ^{13}C, ^{1}H NMR, IR, HRMS, X-ray and quantum chemical calculations

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Thank you for your kind attention!