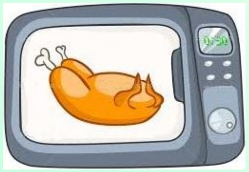

The potential and scope of the MW tool; A case study on the synthesis of phosphinates

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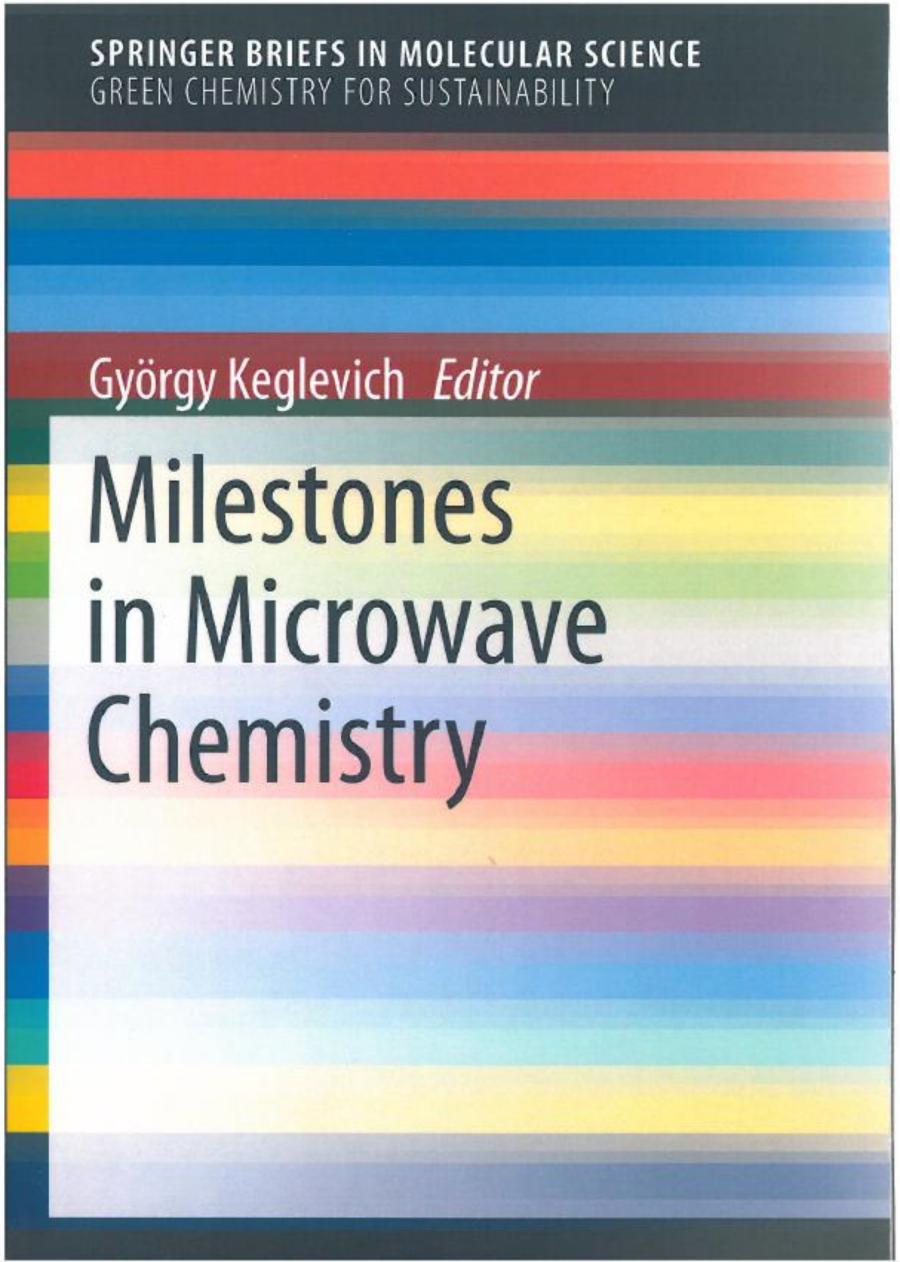
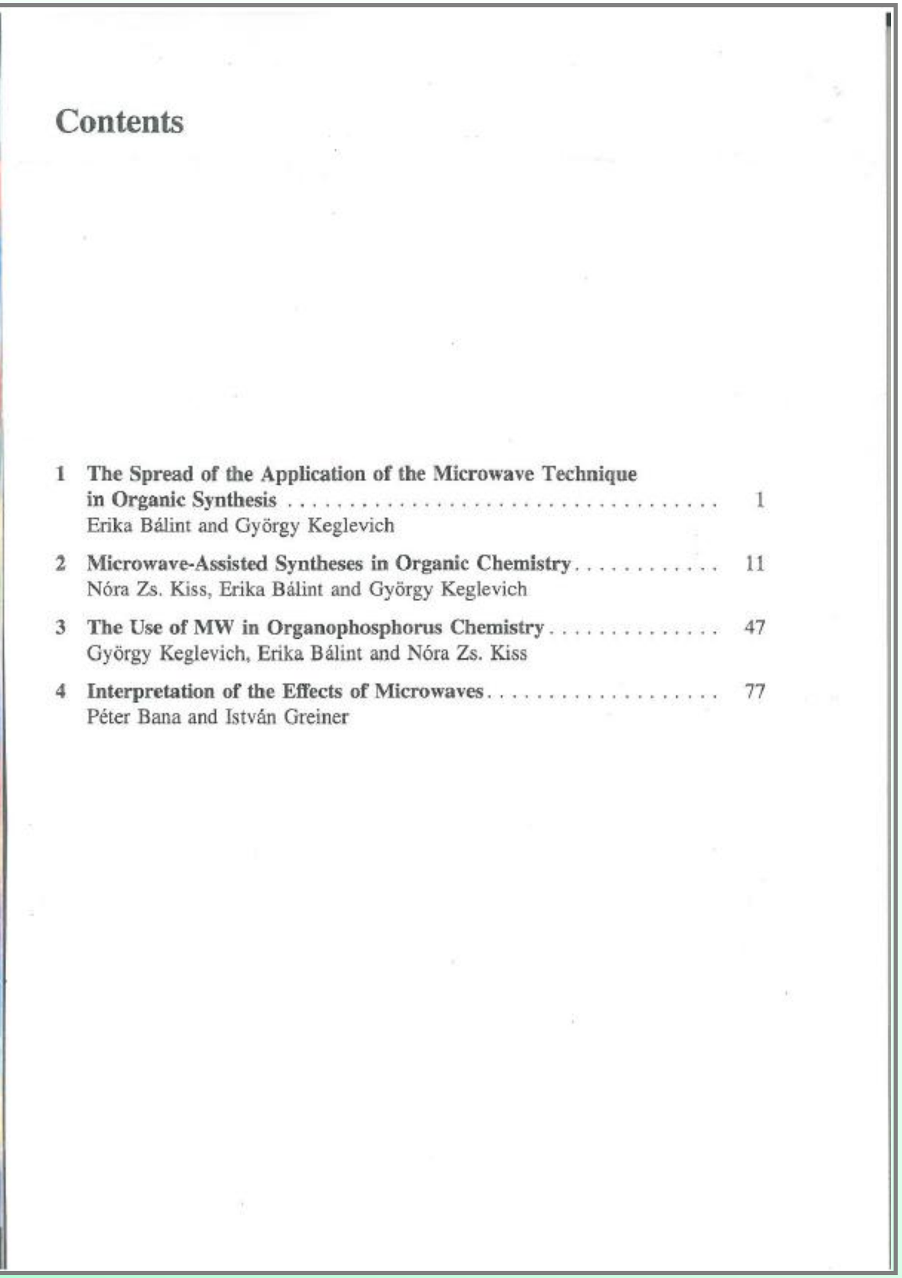
21st International Electronic Conference on Synthetic Organic Chemistry (ECSOC-21),
1–30 November, 2017



SPRINGER BRIEFS IN MOLECULAR SCIENCE
GREEN CHEMISTRY FOR SUSTAINABILITY

György Keglevich *Editor*

Milestones in Microwave Chemistry



Contents

1 **The Spread of the Application of the Microwave Technique in Organic Synthesis** 1
Erika Bálint and György Keglevich

2 **Microwave-Assisted Syntheses in Organic Chemistry** 11
Nóra Zs. Kiss, Erika Bálint and György Keglevich

3 **The Use of MW in Organophosphorus Chemistry** 47
György Keglevich, Erika Bálint and Nóra Zs. Kiss

4 **Interpretation of the Effects of Microwaves** 77
Péter Bana and István Greiner

Contents

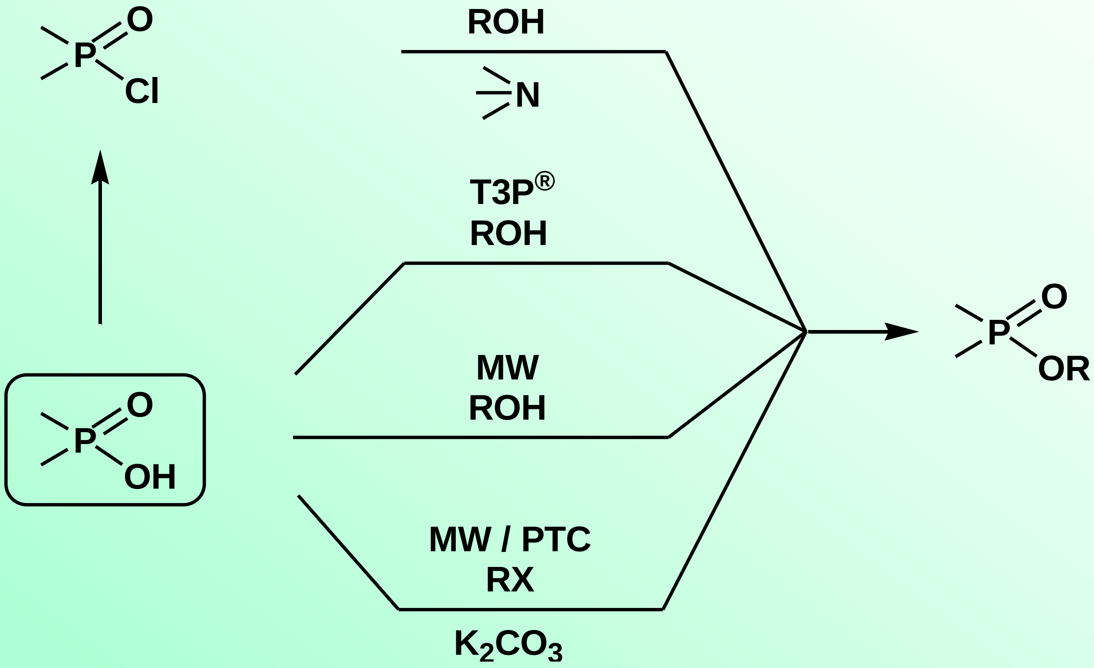
1. Introduction
Possible synthetic routes to phosphinates
2. The synthesis of ring phosphinates and related derivatives
2.1. Ring phosphinates via the corresponding phosphinic chlorides
2.2. The esterification of ring phosphinic acids in the presence of the T3P® reagent
2.3. Alkylating esterification of ring phosphinic acids
2.4. MW-assisted direct esterification of ring phosphinic acids – Reactions that are reluctant on conventional heating
3. Improvement and extension of the MW-assisted direct esterifications
3.1. Direct esterification in the presence of an ionic liquid
3.2. Direct esterification of 1-hydroxy-3-methyl-3-phospholene 1-oxide with phenol derivatives in the presence of [bmim][PF$_6$]
3.3. Extension to phosphonic acids: direct esterification of phenyl-phosphonic acid
4.1. Summary of the esterification of phosphinic acids
4.2. A case study on the preparation of butyl methyl-phenylphosphinate
5. Theoretical aspects: mechanism, energetics, scope and limitation of the application of MWs
5.1. Possible mechanisms for the direct esterification of phosphinic acids
5.2. Energetics of selected phosphinic acid derivatizations
5.2.1. MW-assisted direct esterification of 1-hydroxy-3-methyl-3-phospholene oxide
5.2.1.1. Energy profile evaluated on the basis of B3LYP/6-31++G(d,p) calculations
5.2.1.2. Mechanism for the esterification calculated by the explicit-implicit solvent model
5.2.2. MW-assisted esterification; Energetics calculated by the B3LYP/6-31++G(d,p) method
5.2.3. MW-assisted amidation; Energetics calculated by the B3LYP/6-31++G(d,p) method
5.2.4. Explanation for the effect of MWs – Scope and limitations for the use of MWs
6. Modelling and calculating of the effect of local overheatings
6.1. Principles
6.2. Modelling
6.3. The accelerating effect of local overheatings
6.4. Calculation of the experimental rate enhancement
7. A study on the conformation of cyclic phosphinic acids and their esters (that were starting materials and products in the previous study.
7.1. Conformational equilibrium and relative energies for 1-substituted-3,4-dimethyl-phospholane oxides
7.2. Conformational situation for 1-substituted 3-methyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxides
8. Summary / Conclusions

Recent papers:

- G. Keglevich, N. Z. Kiss, A. Grün, E. Bálint, T. Kovács, *Synthesis* **49**, 3069-3083 (2017).
- G. Keglevich, N. Z. Kiss, Z. Mucsi, *Pure Appl. Chem.* **88**, 931-939 (2016).

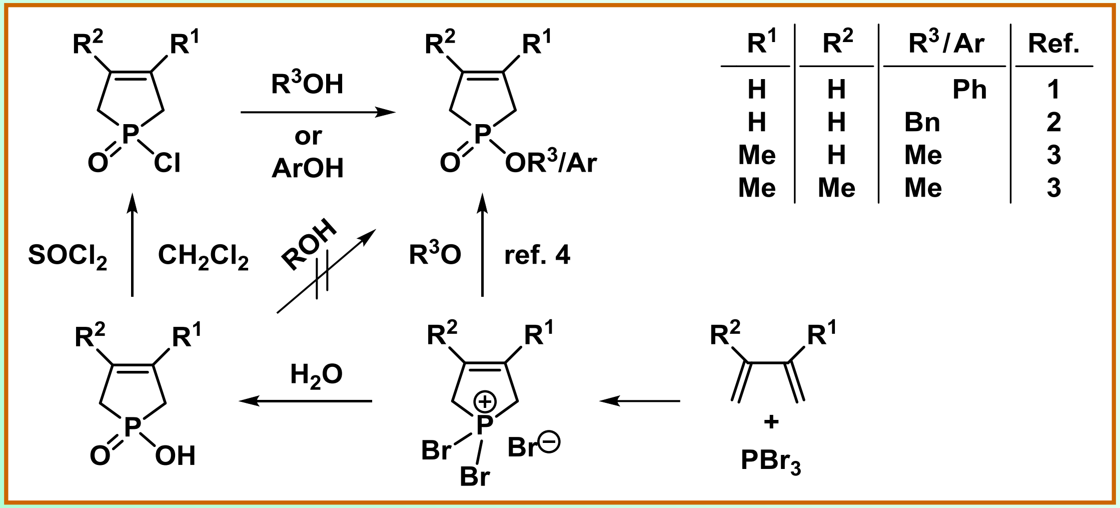
1. Introduction

Possible synthetic routes to phosphinates



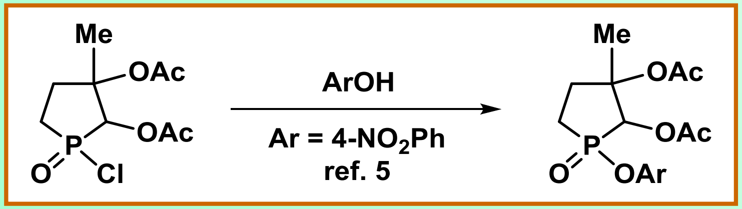
2. The synthesis of ring phosphinates and related derivatives

2.1. Ring phosphinates via the corresponding phosphinic chlorides

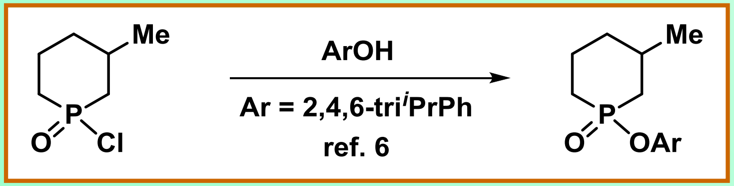


R^1	R^2	R^3/Ar	Ref.
H	H	Ph	1
H	H	Bn	2
Me	H	Me	3
Me	Me	Me	3

1. K. Moedritzer et al. *Phosphorus, Sulfur.* **9**, 293 (1981).
2. M. G. Mulkerrica et al. *US Pat. Appl.* 20050084488 (2005).
3. G. Keglevich et al. *J. Org. Chem.* **52**, 3983 (1987).
4. G. Keglevich et al. *Heteroat. Chem.* **1**, 419 (1990).

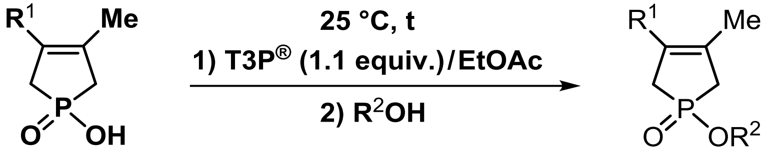


5. M. Yumashita et al. *Heterocycl. Commun.* **6**, 291 (2000).



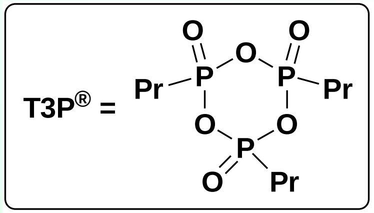
6. G. Keglevich et al. *Synth. Commun.* **34**, 4159 (2004).

2.2. The esterification of ring phosphinic acids in the presence of the T3P® reagent



R^1 = H, Me

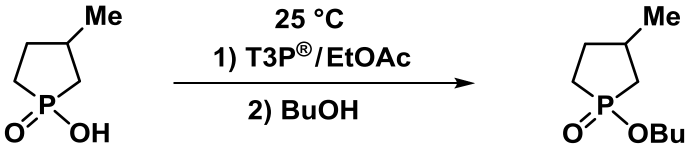
R^2 = Me, Et, Pr, *ⁱ*Pr, Bu, *ⁱ*Bu, *ˢ*Bu, Pent, *ⁱ*Pent, 3-pentyl, *ᶜ*Hexyl, Bn, menthyl



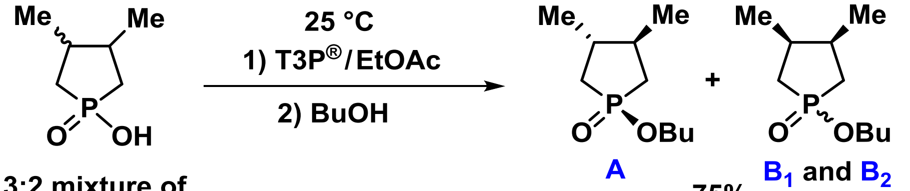
R^1 = H	t (h)	Yield (%)
with primary alcohols	0.5	77 – 95
with secondary alcohols	2 – 3	76 – 91

Rationalization:

using primary alcohols, 0.67 equiv. of the T3P® is enough if the reaction is carried out at 80 °C on MW irradiation.



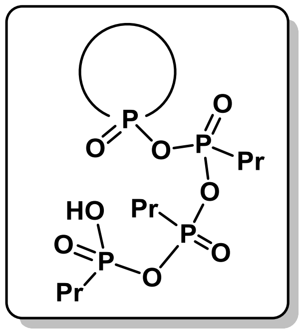
70%
1:1 mixture of two isomers



3:2 mixture of two isomers

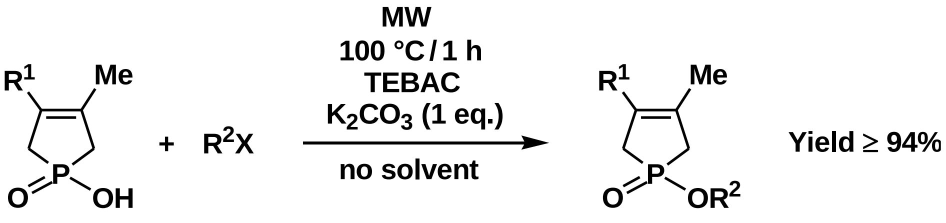
75%
3:1:1 mixture of three isomers

Active intermediate:



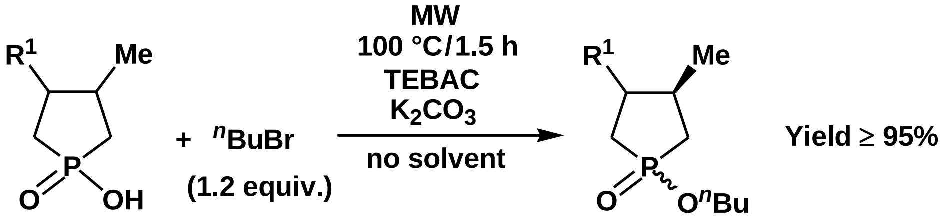
- E. Jablonkai, M. Milen, L. Drahos, G. Keglevich, *Tetrahedron Lett.* **54**, 5873 (2013).
- E. Jablonkai, R. Henyecz, M. Milen, J. Kóti, L. Drahos, G. Keglevich, *Tetrahedron* **70**, 8280 (2014).
- P. Ábrányi-Balogh, E. Jablonkai, R. Henyecz, M. Milen, G. Keglevich, *Curr. Org. Chem.* **20**, 1135 (2016).

2.3. Alkylating esterification of ring phosphinic acids



Yield ≥ 94%

R^1 = H, Me R^{2}X = EtI, ^{n}PrBr, ^{i}PrBr, ^{n}BuBr, BnBr



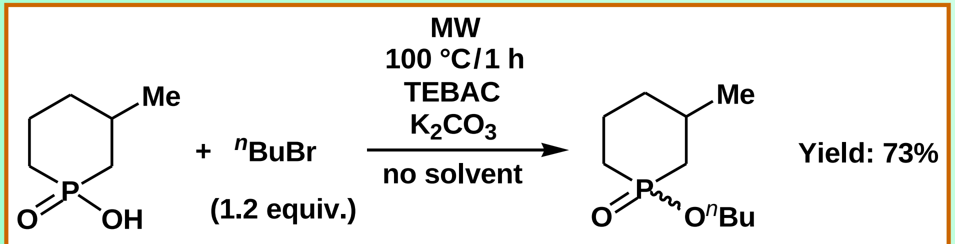
Yield ≥ 95%

R^1 = H, Me

R^1	Composition
H	1:1 mixture of two isomers
Me	3:1:1 mixture of three isomers

in case of alkyl halides with normal reactivity the combined use of PTC and MW is advantageous

synergic effect!



1:1 mixture of two isomers

Yield: 73%

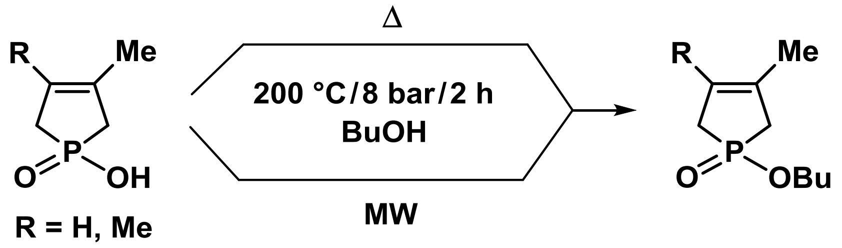
in case of alkyl halides with increased reactivity MW is enough

- E. Bálint, E. Jablonkai, M. Bálint, G. Keglevich, *Heteroatom Chem.* **21**, 211 (2010).
- G. Keglevich, E. Bálint, N. Z. Kiss, E. Jablonkai, L. Hegedűs, A. Grün, I. Greiner, *Curr. Org. Chem.* **15**, 1802 (2011).
- G. Keglevich, A. Grün, E. Bálint, *Curr. Org. Synth.* **10**, 751 (2013).

2.4. MW-assisted direct esterification of ring phosphinic acids – Reactions that are reluctant on conventional heating

2.4.1. Esterification of 1-hydroxy-3-phospholene 1-oxides

A) with BuOH

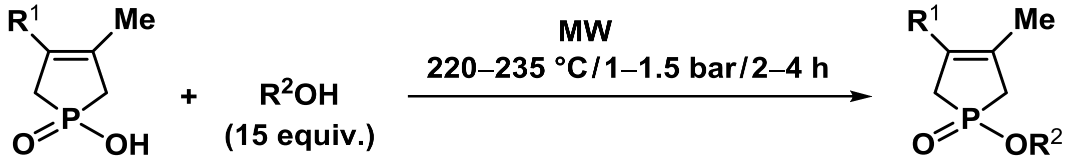


Conversion in %

R	Δ	MW
H	17	58
Me	11	29

Special MW effect!

B) with longer carbon atom chain alcohols



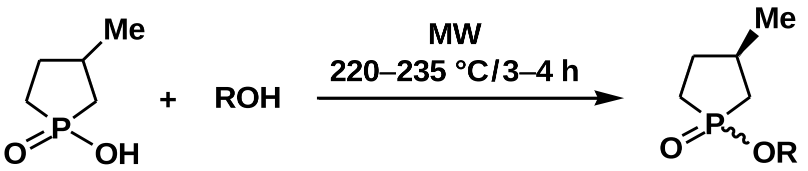
conversion: 80–100%

yield: 57–95%

R^1 = H, Me R^2 = $^n C_5H_{11}$, $^i C_5H_{11}$, $^n C_8H_{17}$, $^i C_8H_{17}$, $C_{12}H_{25}$

- N. Z. Kiss, K. Ludányi, L. Drahos, G. Keglevich, *Synthetic Commun.* **39**, 2392 (2009).
- G. Keglevich, E. Bálint, N. Z. Kiss, E. Jablonkai, L. Hegedűs, A. Grün, I. Greiner, *Curr. Org. Chem.* **15**, 1802 (2011).
- G. Keglevich, N. Z. Kiss, Z. Mucsi, T. Körtvélyesi, *Org. Biomol. Chem.* **10**, 2011 (2012).
- N. Z. Kiss, É. Böttger, L. Drahos, G. Keglevich, *Heteroatom Chem.* **24**, 283 (2013).

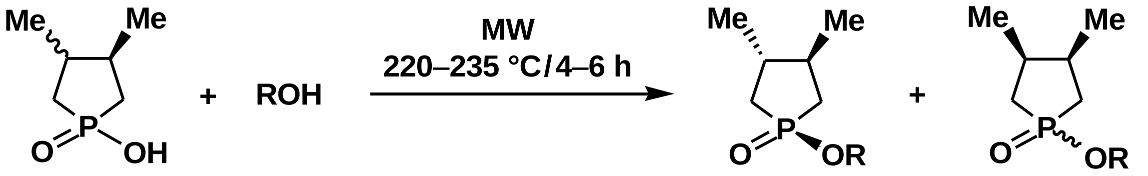
2.4.2. Extension: Direct esterification of hydroxy-phospholane oxides and a hydroxy-1,2,3,4,5,6-hexahydrophosphinine oxide



yield: 59–86%

1:1 mixture of 2 diastereomers

R = $^{n}C_5H_{11}$, $^{i}C_5H_{11}$, $^{n}C_8H_{17}$, $^{i}C_8H_{17}$



yield: 50–72%

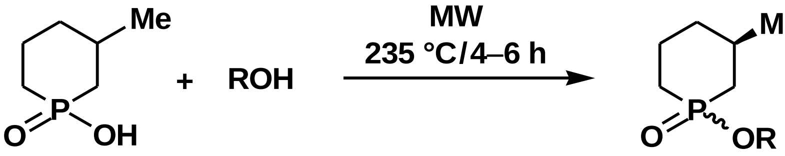
2:1 mixture of 2 isomers

a racemate

2 diastereomers

R = as above

68:17:15 mixture of 3 isomers

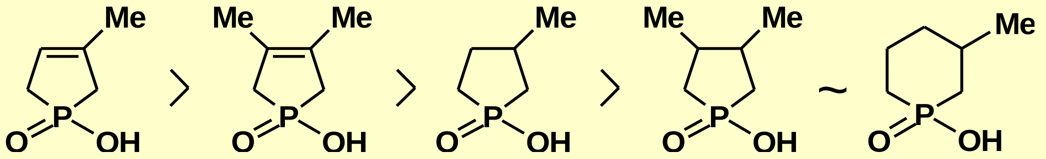


yield: 54/62%

R = $^{n}C_8H_{17}$, $^{i}C_8H_{17}$

68:32 mixture of 2 diastereomers

Order of reactivity:

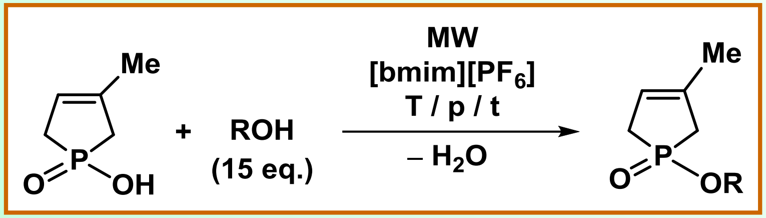


- G. Keglevich, N. Z. Kiss, Z. Mucsi, T. Körtvélyesi, *Org. Biomol. Chem.* **10**, 2011 (2012).
- N. Z. Kiss, É. Böttger, L. Drahos, G. Keglevich, *Heteroatom Chem.* **24**, 283 (2013).

3. Improvement and extension of the MW-assisted direct esterifications

3.1. Direct esterification in the presence of an ionic liquid

3.1.1. Esterification of 1-hydroxy-3-methyl-3-phospholene 1-oxide in the presence of 10% of [bmim][PF_6] as a catalyst



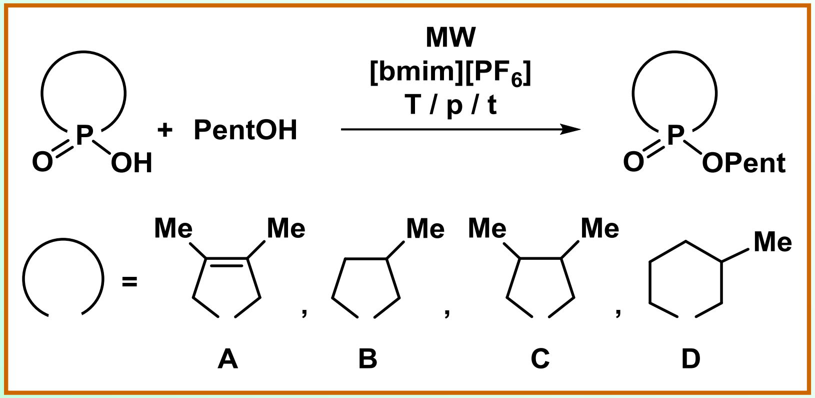
The IL exerts a pronounced enhancing effect on the courage of the esterification.

R	[bmim][PF_6]	T (°C)	p (bar)	t (h)	Conversion (%) MW (Δ*)	Yield (%)
Et	–	160	17	4	38	30
Et	10%	160	17	3	86	60
^{n}Pr	–	180	15.5	4	40	30
^{n}Pr	10%	180	15.5	3	98	68
^{n}Bu	–	200	16	2	62 (11)	58
^{n}Bu	10%	180	14	0.5	90 (19)	83
^{n}Pent	–	220	9	2.5	100	82
^{n}Pent	10%	180	5	0.5	100 (52)	94
^{i}Oct	–	220	3	1	100 (28)	76
^{i}Oct	10%	180	2	0.33	100 (75)	84

*Comparative thermal experiment.

N. Z. Kiss, G. Keglevich, *Tetrahedron Lett.* **57**, 971 (2016).

3.1.2. Extension: Direct esterification of cyclic phosphinic acids A–D in the presence of [bmim][PF$_6$] using *n*-pentanol

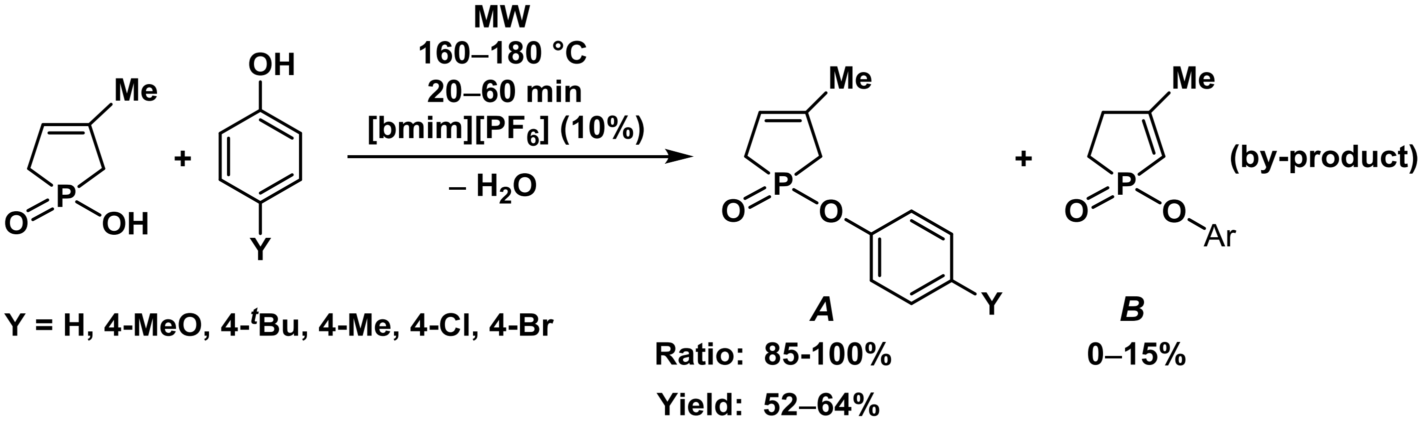


Ring substituent	[bmim][PF$_6$]	T (°C)	p (bar)	t (h)	Conversion (%)	Ratio of diastereomers (%)	Yield (%)
A	–	235	11	3	90		67
A	10%	200	6	1	95		72
B	–	235	11	3	~85	50 – 50	79
B	10%	220	9	1	~100	52 – 48	89
C	–	235	11	5	~72	70 – 15 – 15	60
C	10%	220	9	2	~95	65 – 18 – 17	84
D	–	220	9	4	~45	50 – 50	31
D	10%	200	9	2	~60	50 – 50	42

N. Z. Kiss, G. Keglevich, *Tetrahedron Lett.* **57**, 971 (2016).

3.2. Direct esterification of 1-hydroxy-3-methyl-3-phospholene 1-oxide with phenol derivatives in the presence of [bmim][PF$_6$]

In general, the direct esterification of phosphinic acids with substituted phenols is impossible. We could elaborate a method under MW irradiation in the presence of ILs.



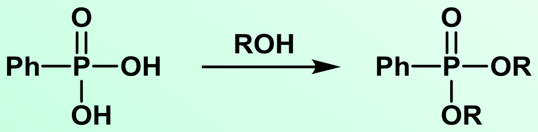
Y = H, 4-MeO, 4-^{t}Bu, 4-Me, 4-Cl, 4-Br

Ratio: 85-100% **0–15%**

Yield: 52–64%

- G. Keglevich, N. Z. Kiss, E. Bálint, E. Jablonkai, A. Grün, M. Milen, D. Frigyes, I. Greiner, *Phosphorus, Sulfur, Silicon* **186**, 802 (2011).
- N. Z. Kiss, Z. Rádai, I. Tihanyi, T. Szabó, G. Keglevich, submitted for publication.

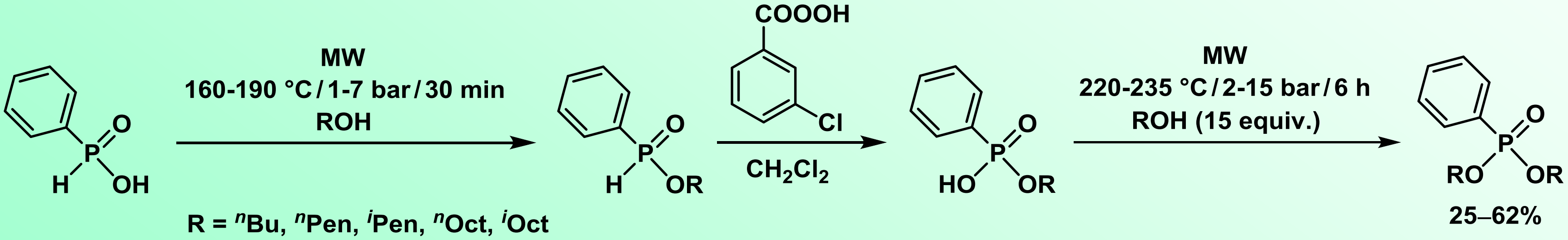
3.3. Extension to phosphonic acids: direct esterification of phenylphosphonic acid



$$\mathrm{Ph{-}P(=O)(OH){-}OH} \xrightarrow{\mathrm{ROH}} \mathrm{Ph{-}P(=O)(OR){-}OR}$$

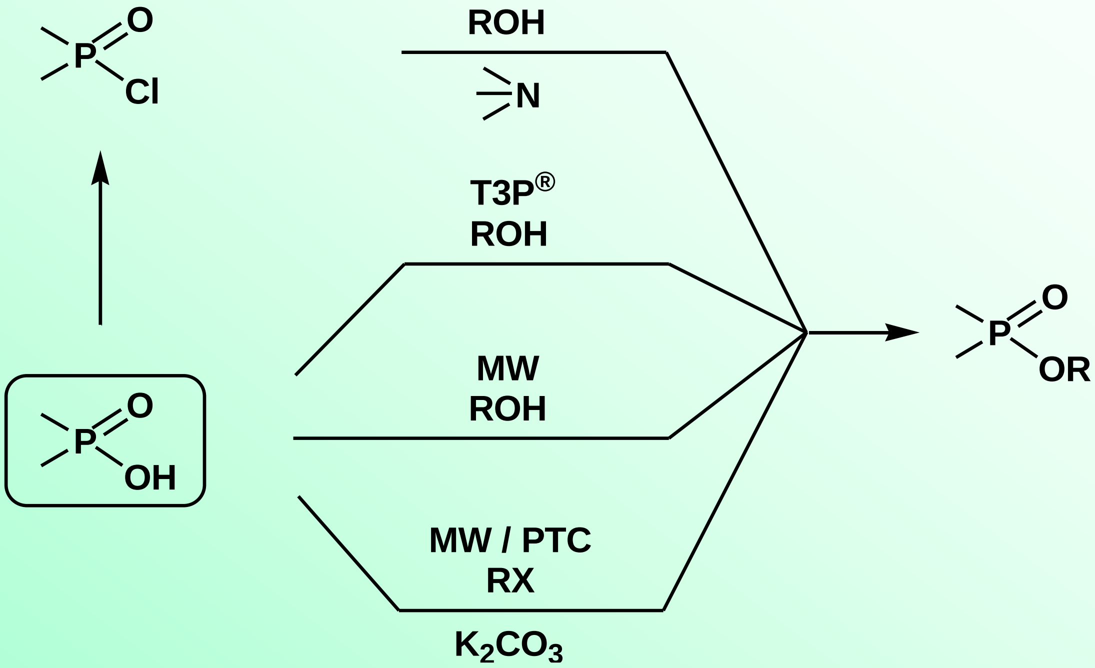
The efficiency is very low!
Efforts for a better accomplishment is in process.

Preparing dialkyl phenylphosphonates according to another protocol:



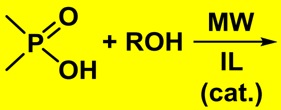
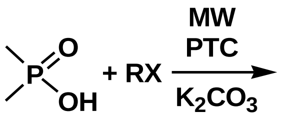
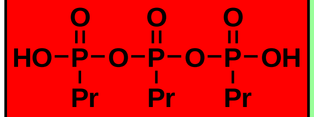
N. Z. Kiss, Z. Mucsi, É. Böttger, L. Drahos, G. Keglevich, *Curr. Org. Synth.* **11**, 767 (2014).

4. Summary of the esterification of phosphinic acids

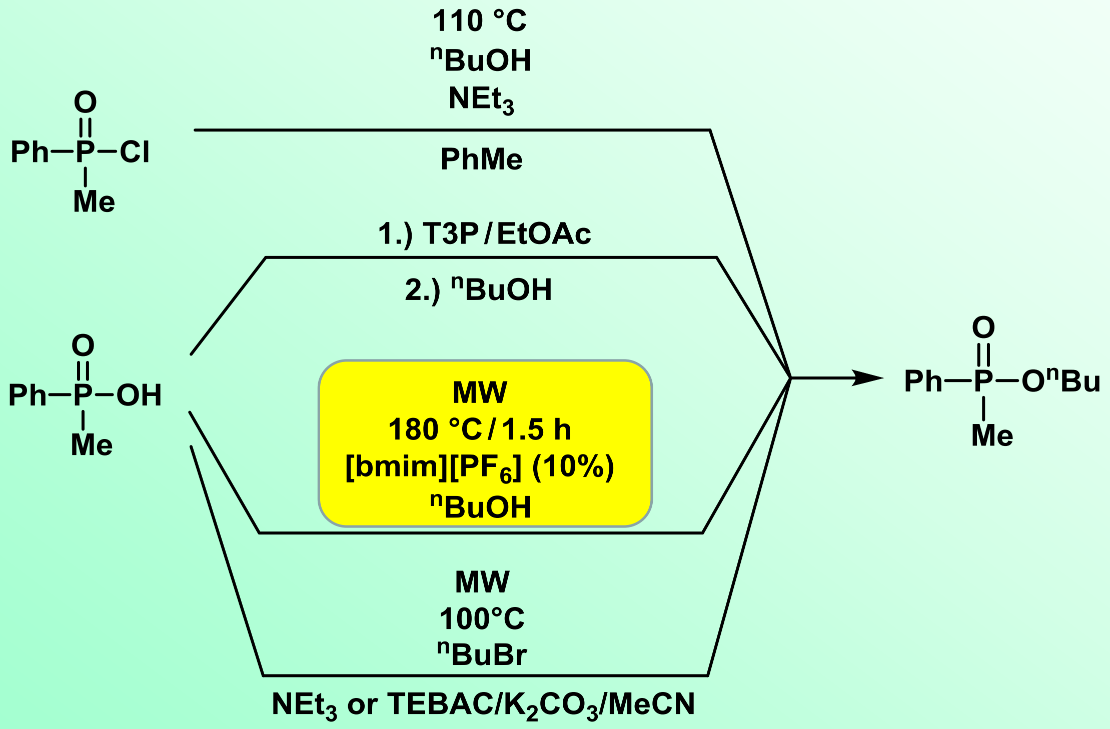


- G. Keglevich, N. Z. Kiss, Z. Mucsi, E. Jablonkai, E. Bálint, *Green Process. Synth*. **3**, 103 (2014).
- N. Z. Kiss, G. Keglevich, *Current Org. Chem.* **18**, 2673 (2014).
- G. Keglevich, N. Z. Kiss, Z. Mucsi, *Chem. Sci. J.* **5**, 1000088 (2014). doi: 10.4172/2150-3494.1000088.
- N. Z. Kiss, R. Henyecz, E. Jablonkai, G. Keglevich, *Synth. Commun*. **46**,766 (2016).

Comparison of the synthesis of phosphinates from "green" chemical point of view

		A	B	C	D	best
		A 	B 	C 	D 	best
Starting materials		>P(O)Cl means cost	a good combination	a good combination	RX means cost	C, B
Additional reagent			T3P	–	K_2CO_3	C
By-product		HCl/  · HCl	 $\mathrm{HO{-}\overset{O}{\underset{Pr}{P}}{-}O{-}\overset{O}{\underset{Pr}{P}}{-}O{-}\overset{O}{\underset{Pr}{P}}{-}OH}$	H_2O	KX, H_2O, CO_2	C
Atomic efficiency		medium	low	good	medium	C
Reaction temperature (°C)		≥ RT	RT	160–180	100–120	B, A
Reaction time (t)		~ 1–4	0.5–3	0.5–3	1–3	not relevant
Yield (%)		~ 90	76–95	60–94	73–96	not really relevant
Advantage		– low reaction temperature – industrial relevance	low reaction temperature	– best choice of reagents – no by-product (beyond water) – good atomic efficiency	– catalytic method	
Disadvantage		chloro-containing reagent	special reactant low atomic economy	high reaction temperature possible only in laboratory	halogen containing reagent	
Overall order of preference	**laboratory**	4	1/2	1/2	3	
	industry	1	2	3/4	3/4	

A case study on the preparation of butyl methyl-phenylphosphinate



$Ph-\overset{O}{\underset{Me}{P}}-Cl$

$Ph-\overset{O}{\underset{Me}{P}}-OH$

$Ph-\overset{O}{\underset{Me}{P}}-O^nBu$

110 °C
^{n}BuOH
NEt_3
PhMe

1.) T3P / EtOAc
2.) ^{n}BuOH

MW
180 °C / 1.5 h
[bmim][PF_6] (10%)
^{n}BuOH

MW
100°C
^{n}BuBr
NEt_3 or TEBAC/K_2CO_3/MeCN

Yield

93%

T3P®	T	t	
1.1 equiv.	25 °C	1 h	81%
0.66 equiv.	85 °C - MW	0.5 h	80%

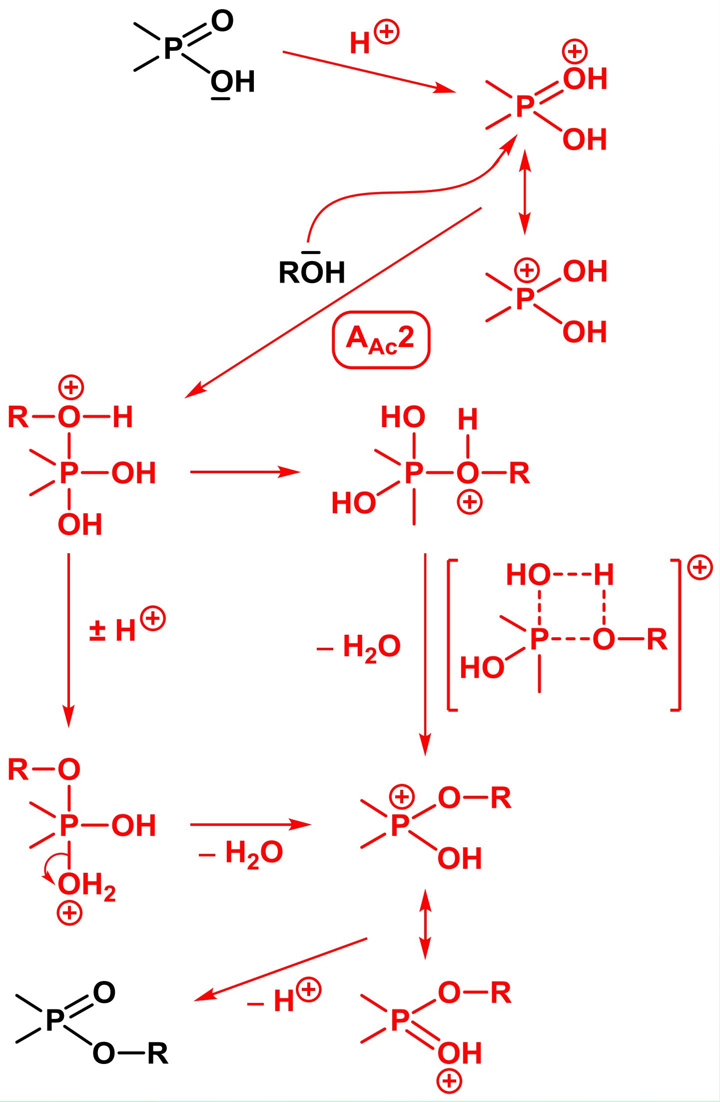
73%

Base	TEBAC	Solvent	t	
K_2CO_3	5%	MeCN	2 h	89%
Et_3N	–	–	0.5 h	89%

N. Z. Kiss, R. Henyecz, E. Jablonkai, G. Keglevich, *Synth. Commun*. **46**, 766 (2016).

5. Theoretical aspects: mechanism, energetics, scope and limitation of the application of MWs

5.1. Possible mechanisms for the direct esterification of phosphinic acids



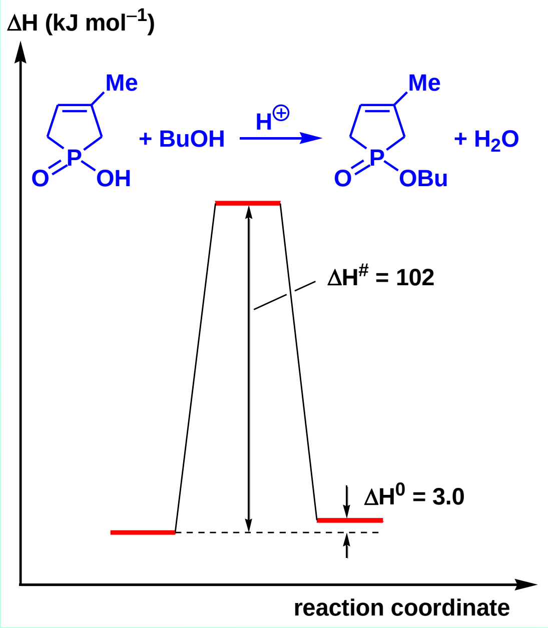
- N. Z. Kiss, G. Keglevich, *Curr. Org. Chem.* **18**, 2673 (2014).
- G. Keglevich, N. Z. Kiss, Z. Mucsi, *Chem. Sci. J.* **5**, 1000088 (2014). doi: 10.4172/2150-3494.1000088.

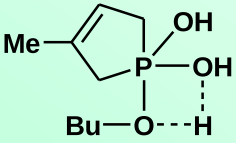
5.2. Energetics of selected phosphinic acid derivatizations

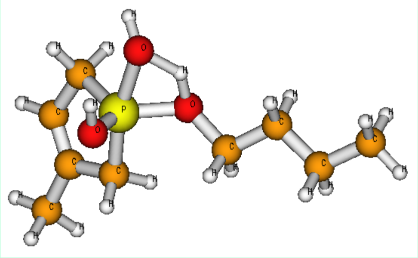
5.2.1. MW-assisted direct esterification of 1-hydroxy-3-methyl-3-phospholene oxide

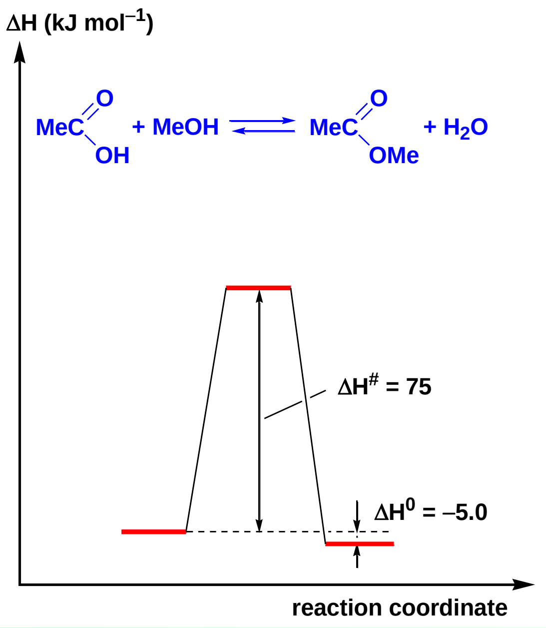
5.2.1.1. Energy profile evaluated on the basis (B3LYP/6-31++G(d,p)) calculations

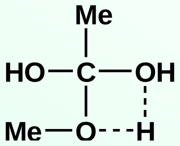
The esterification of acetic acid as a comparison

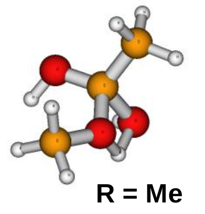








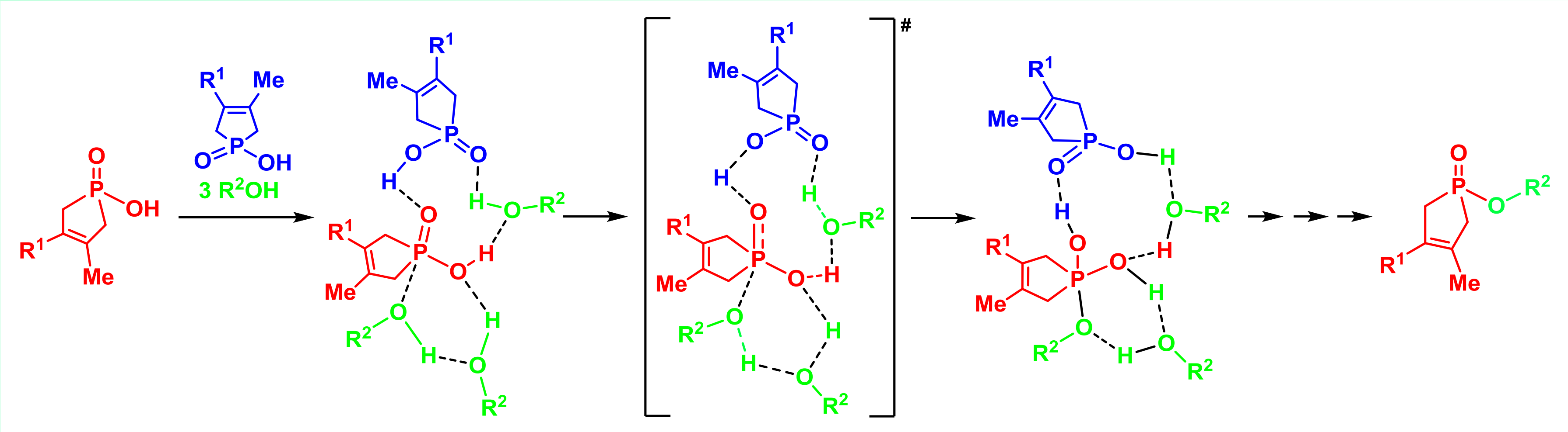




G. Keglevich, N. Z. Kiss, Z. Mucsi, T. Körtvélyesi, *Org. Biomol. Chem.* **10**, 2011 (2012).

5.2.1.2. Mechanism for the esterification of 1-hydroxy-3-phospholene oxide calculated by the explicit-implicit solvent model using the B3LYP/6-31G(d,p) method

Dependence of the enthalpy of activation values on the substituents

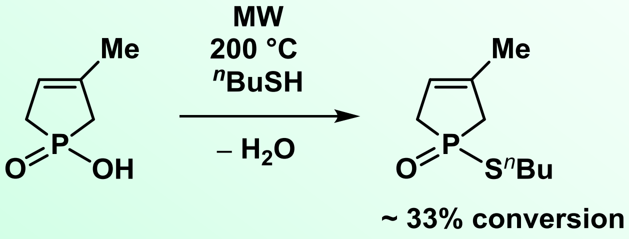


R^1	R^2	$\Delta H^{\#}$ (kJ mol^{-1})	ΔH^0 (kJ mol^{-1})
H	**Bu**	**135.0**	**0.8**
Me	**Bu**	**138.8**	**0.8**
H	**^{i}Oct**	**130.2**	**0.8**
Me	**^{i}Oct**	**134.4**	**0.9**

B3LYP/6-31G(d,p)//PCM(MeOH)

Z. Mucsi, N. Z. Kiss, G. Keglevich, *RSC Adv.* **4**, 11948 (2014).

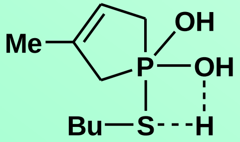
5.2.2. MW-assisted esterification of 1-hydroxy-3-methyl-3-phospholene 1-oxide with a thioalcohol; Energetics calculated by the B3LYP/6-31++G(d,p) method

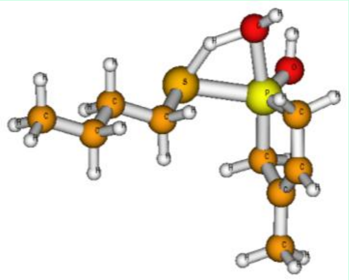


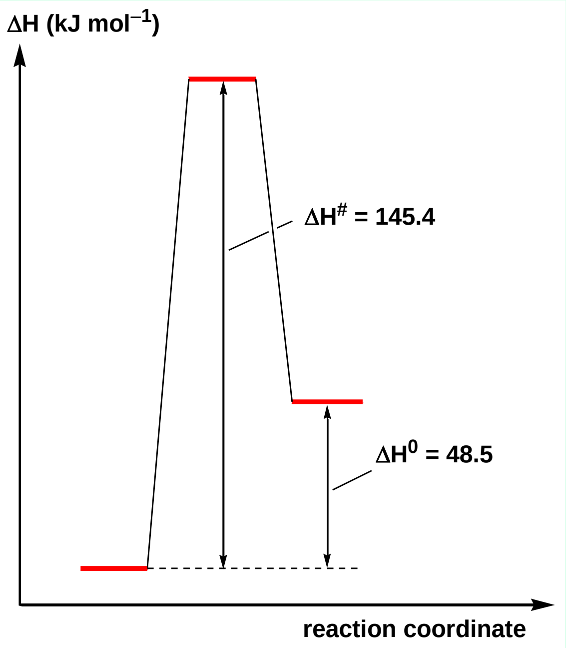
Enthalpy profile for the esterification with thiobutanol

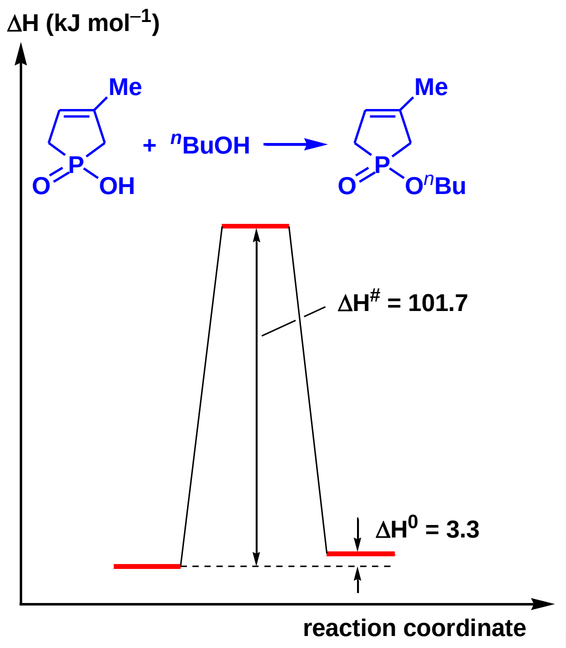
Comparison esterification with butanol

Transition state



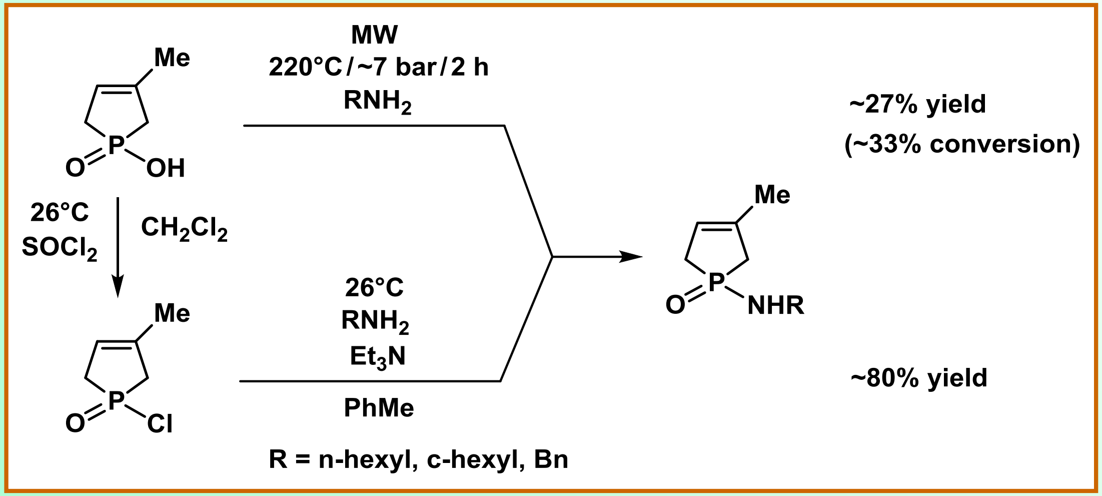


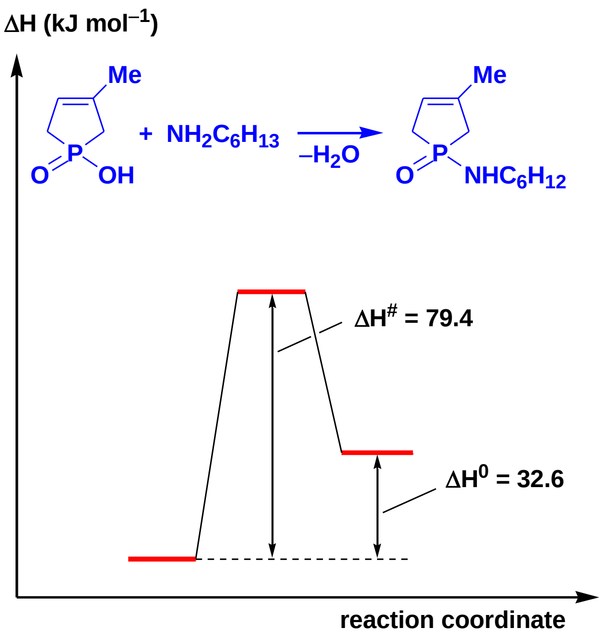




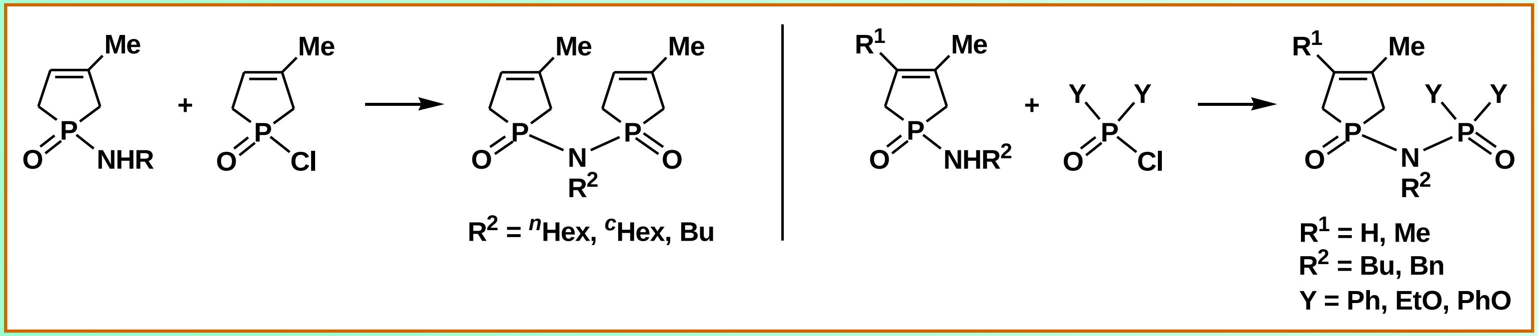
G. Keglevich, N. Z. Kiss, L. Drahos, T. Körtvélyesi, *Tetrahedron Lett.* **54**, 466 (2013).

5.2.3. MW-assisted amidation of cyclic phosphinic acids; Energetics calculated by the B3LYP/6-31++G(d,p) method





”Phosphimides” as by-products or as exclusive products – Variation of the imide formation



N. Z. Kiss, A. Simon, L. Drahos, K. Huben, S. Jankovski, G. Keglevich, *Synthesis* **45**, 199 (2013).
N. Z. Kiss, Z. Rádai, Z. Mucsi, G. Keglevich, *Heteroatom Chem.* **26**, 134 (2015).

5.2.4. Explanation for the effect of MWs – Scope and limitations for the use of MWs

- **The role of microwave is to enhance reactions with higher (≥100 kJ mol^{-1}) enthalpy of activation. The MW assistance is optimal for thermoneutral reactions. Endothermicity works against the beneficial effect of MWs.**
- **This is possible due to the statistically occurring local overheating effect (that may be in the range of 1–60 °C) in the bulk of the reaction mixture. Assuming an overheated segment of 5–40%, the effect is significant!**

- G. Keglevich, N. Z. Kiss, A. Grün, E. Bálint, T. Kovács, *Synthesis* **49**, 3069 (2017).
- G. Keglevich, Z. Mucsi, In: *Microwave Chemistry*; Cravotto, G.; Carnaroglio, D., Eds.; De Gruyter: Berlin, 2017, Ch. 4, in press.

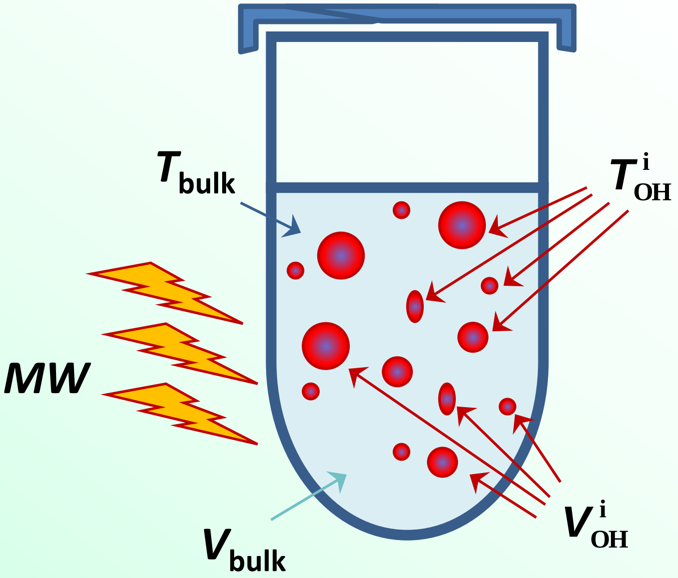
6. Modelling and calculating of the effect of local overheatings

6.1. Principles

Arrhenius equation:

$$k = A \cdot e^{-\frac{\Delta H^{\#}}{RT}}$$

$\Delta H^{\#}$: activation enthalpy (kJ mol^{-1})
T: reaction temperature
R: universal gas constant



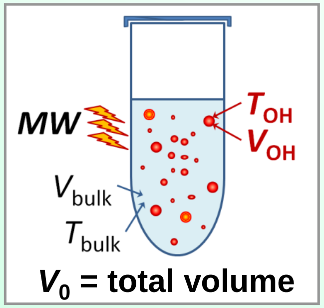
V_0 = total volume

$$\left.\begin{aligned} k_{\text{bulk}} &= A \cdot e^{-\frac{\Delta H^{\#}}{RT_{\text{bulk}}}} \\ k^{i}_{\text{OH}} &= A \cdot e^{-\frac{\Delta H^{\#}}{RT^{i}_{\text{OH}}}} \end{aligned}\right] \Rightarrow k_{\text{overall}} = \frac{V_{\text{bulk}}}{V_0} \cdot k_{\text{bulk}} + \sum_{i=1}^{n} \frac{V^{i}_{\text{OH}}}{V_0} \cdot k^{i}_{\text{OH}}$$

$$\Downarrow$$

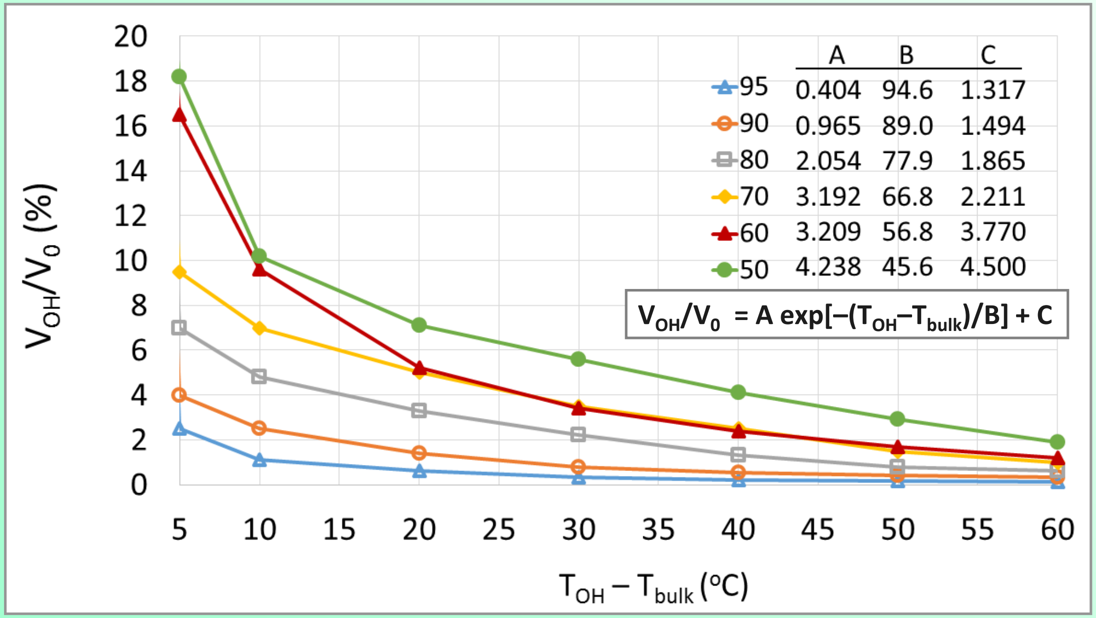
the increase may be characterized by $k_{\text{rel}} = \dfrac{k_{\text{overall}}}{k_{\text{bulk}}}$

Modelling the thermal effect of MWs by assuming an exponential relationship between (V_{OH} / V_0) and (T_{OH}–T_{bulk}) and calculating the rate enhancing effect



6.2. Modelling

The volume percentage (V_{OH} /V_0) – *overheating* (T_{OH}–T_{bulk}) relationships assumed in the overheated segments of 5–50%

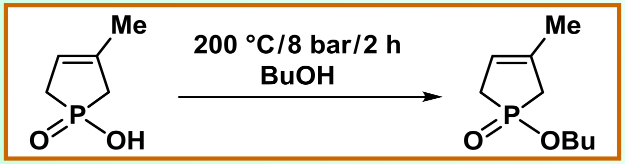


	A	B	C
95	0.404	94.6	1.317
90	0.965	89.0	1.494
80	2.054	77.9	1.865
70	3.192	66.8	2.211
60	3.209	56.8	3.770
50	4.238	45.6	4.500

$$V_{OH}/V_0 = A \exp[-(T_{OH}-T_{bulk})/B] + C$$

- G. Keglevich, I. Greiner, Z. Mucsi, *Curr. Org. Chem.* **19**, 1436 (2015).
- G. Keglevich, N. Z. Kiss, Z. Mucsi, *Pure Appl. Chem.* **88**, 931 (2016).
- G. Keglevich, N. Z. Kiss, Z. Mucsi, *Curr. Phys. Chem.* **6**, 307 (2016).

6.3 The accelerating effect of local overheatings



T_{bulk} = 200 °C; $\Delta H^{\#}$ = 135.0 kJ mol^{-1}

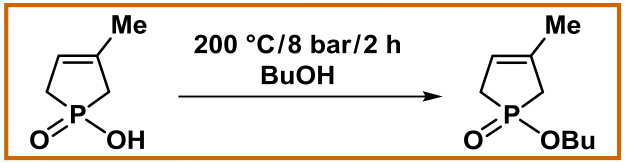
$$k = A \cdot e^{-\frac{\Delta H^{\#}}{RT}}$$

Dependence of the relative rate enhancement (k_{rel}) on the overheated segment (V_{OH}/V_0) assuming an exponential distribution of the $T_{OH} - T_{bulk}$

Model (V_{bulk}/V_0)		Reference	A (bulk)	B	C	D	E	F	G	H	Overall effect (k_{rel})
I (95%)	T_{OH}–T_{bulk} (°C)	0	0	5	10	20	30	40	50	60	
	V_{OH}/V_0 (%)	0	0	2.5	1.1	0.6	0.32	0.2	0.155	0.125	
	k_{rel}	1.00	0.95	0.04	0.02	0.03	0.03	0.03	0.05	0.07	Σ = 1.20
II (90%)	T_{OH}–T_{bulk} (°C)	0	0	5	10	20	30	40	50	60	
	V_{OH}/V_0 (%)	0	0	4	2.5	1.4	0.8	0.55	0.4	0.35	
	k_{rel}	1.00	0.90	0.06	0.05	0.06	0.07	0.09	0.12	0.19	Σ = 1.53
III (80%)	T_{OH}–T_{bulk} (°C)	0	0	5	10	20	30	40	50	60	
	V_{OH}/V_0 (%)	0	0	7	4.8	3.3	2.2	1.3	0.8	0.6	
	k_{rel}	1.00	0.80	0.10	0.10	0.14	0.18	0.20	0.24	0.32	Σ = 2.08
IV (70%)	T_{OH}–T_{bulk} (°C)	0	0	5	10	20	30	40	50	60	
	V_{OH}/V_0 (%)	0	0	9.5	7	5	3.5	2.5	1.5	1	
	k_{rel}	1.00	0.70	0.14	0.15	0.21	0.29	0.39	0.44	0.54	Σ = 2.85
V (60%)	T_{OH}–T_{bulk} (°C)	0	0	5	10	20	30	40	50	60	
	V_{OH}/V_0 (%)	0	0	16.5	9.6	5.2	3.4	2.4	1.70	1.2	
	k_{rel}	1.00	0.60	0.24	0.20	0.22	0.28	0.38	0.50	0.64	Σ = 3.06
VI (50%)	T_{OH}–T_{bulk} (°C)	0	0	5	10	20	30	40	50	60	
	V_{OH}/V_0 (%)	0	0	18.2	10.2	7.1	5.6	4.1	2.9	1.9	
	k_{rel}	1.00	0.50	0.26	0.21	0.30	0.46	0.65	0.85	1.02	Σ = 4.26

G. Keglevich, I. Greiner, Z. Mucsi, *Curr. Org. Chem.* **19**, 1436 (2015).

6.4. Calculation of the experimental rate enhancement



the relationships utilized

the data used

the calculated parameters

1.) pseudo first order kinetic equation

$$k' = B \cdot \frac{\ln[(100 - x)/100]}{t}$$

where k': pseudo first order rate constant
X: conversion
t: time

T_{set} = 200 °C	t (h)	x (%)
Δ reaction	2	17
MW reaction	3	58

$$k_{rel}^{exp} = \frac{k^{MW}}{k^{\Delta}} = 3.10$$

2.) Arrhenius equation

$$k = A \cdot e^{-\frac{\Delta H^{\#}}{R \cdot T}}$$

where k: rate constant
$\Delta H^{\#}$: enthalpy of activation
T: temperature
R: universal gas constant

$\Delta H^{\#}$ = 135.0 kJ mol^{-1}
(obtained by quantum chemical calculation)
T^{Δ} = 200 °C

T^{MW} = 215.2 °C
A = 2.32

k^{Δ} = $2.59 \cdot 10^{5}$ s^{-1}
k^{MW} = $8.03 \cdot 10^{5}$ s^{-1}

7. A study on the conformation of cyclic phosphinic acids and their esters (that were starting materials and products in the previous study.)

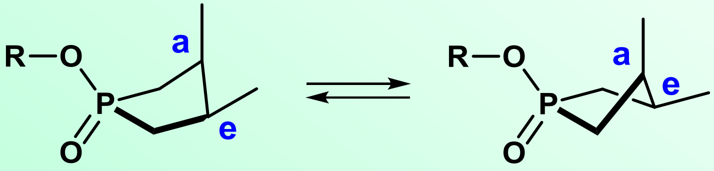
7.1. Conformational equilibrium and relative energies for 1-substituted-3,4-dimethyl-phospholane oxides

B3LYP/6-311g++(2d,2p)

ΔH (kJ mol^{-1})

The P-center remains unchanged!

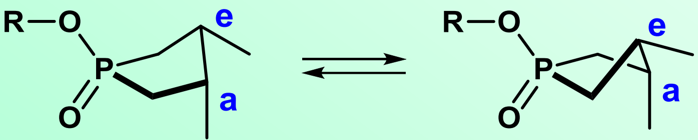
cis



A-a **A-b**

R	A-a	A-b
H	0	0
Me	0	–1.1

conformational equilibrium

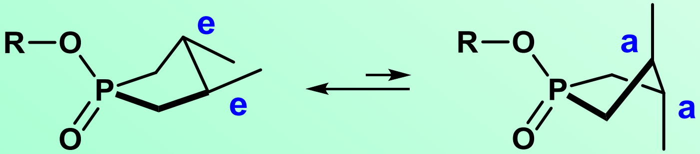


B-a **B-b**

R	B-a	B-b
H	–0.46	–0.46
Me	–0.3	–1.6

conformational equilibrium

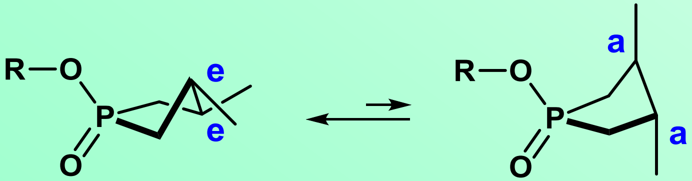
trans



C-a **C-b**

R	C-a	C-b
H	–8.1	0.9
Me	–8.1	0.0

a shifted equilibrium

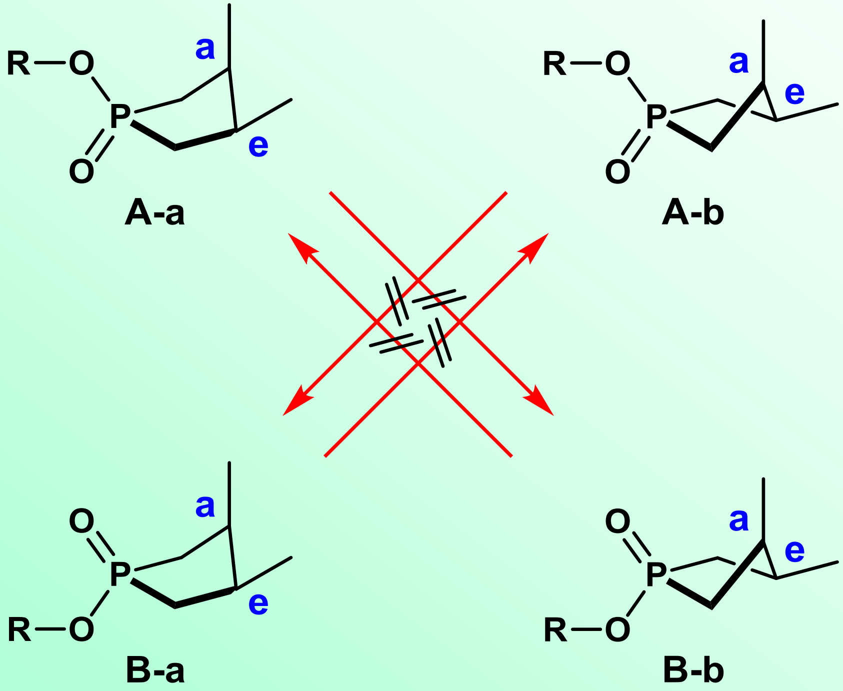


D-a **D-b**

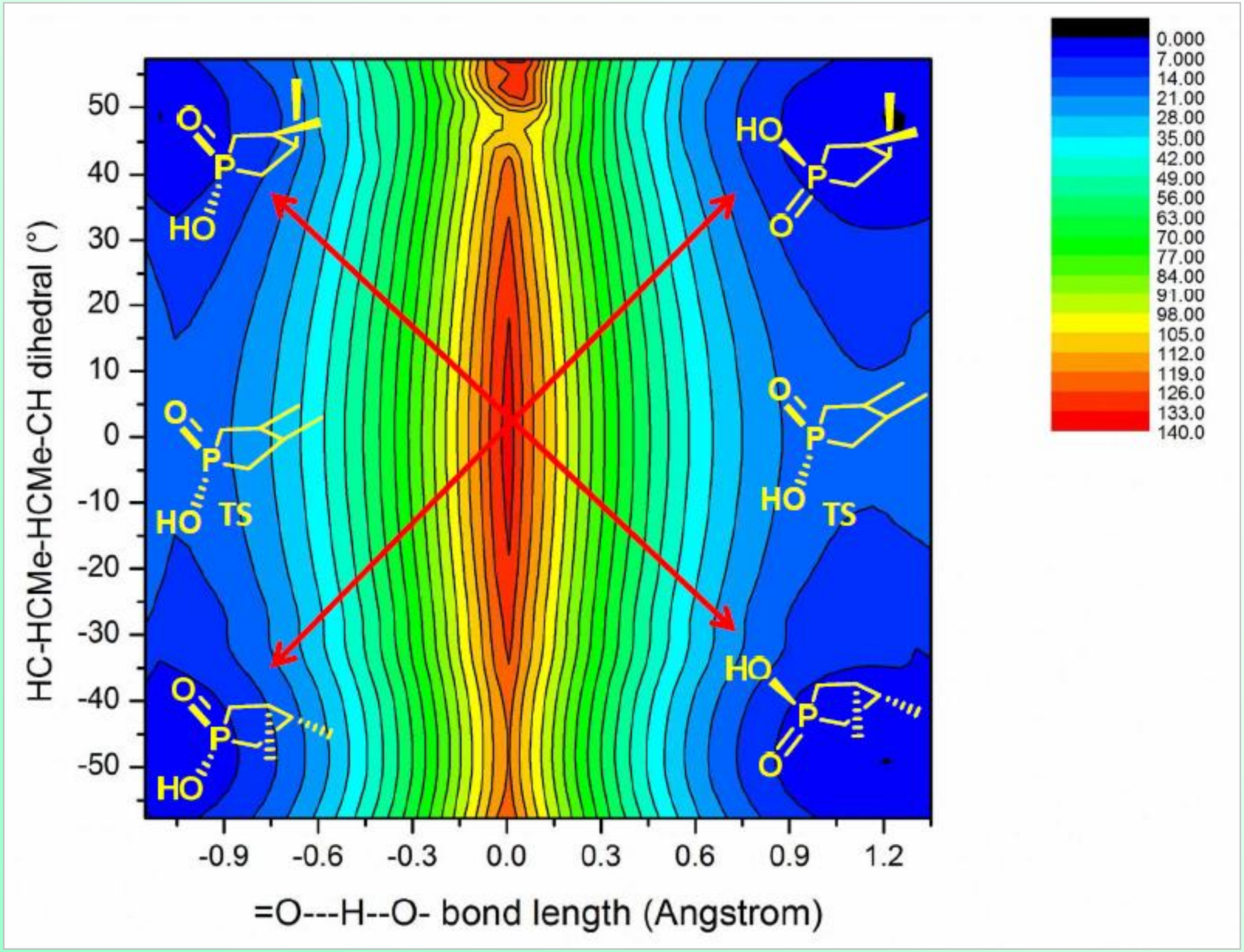
R	D-a	D-b
H	–8.1	0.9
Me	–9.3	1.2

a shifted equilibrium

Forbidden conformational/configurational changes for the *cis* forms of 1-hydroxy-3,4-dimethyl-phospholane oxide

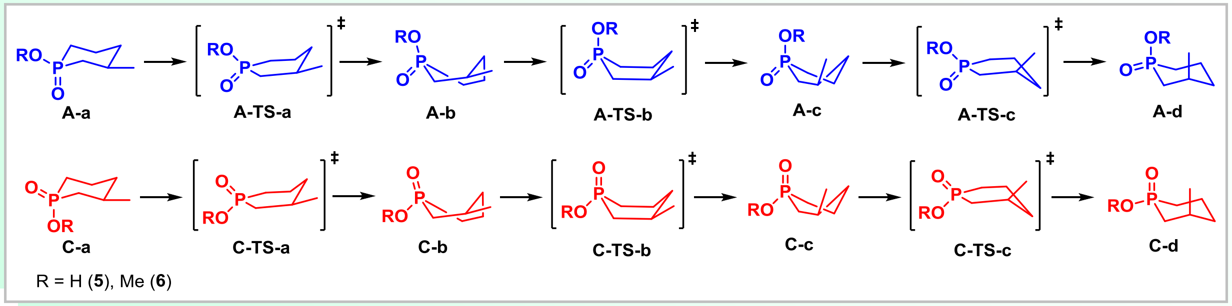


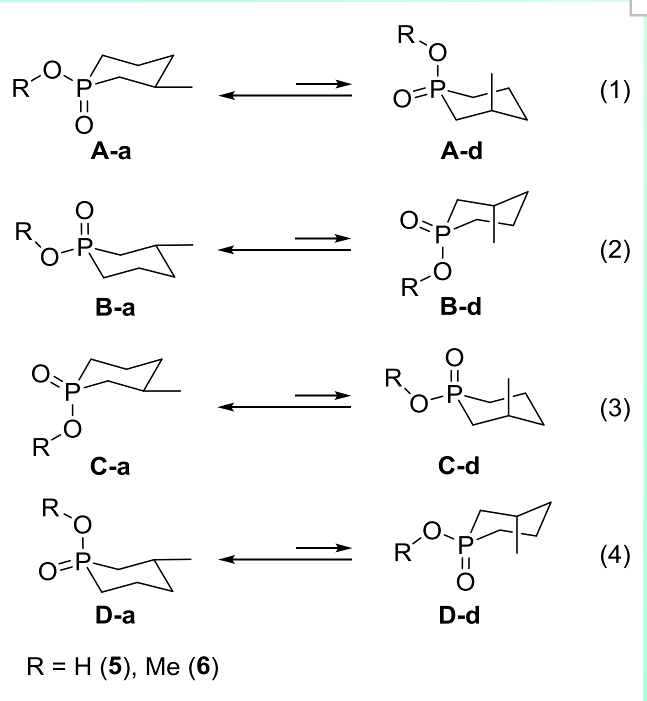
The P-centers may not undergo a configurational change



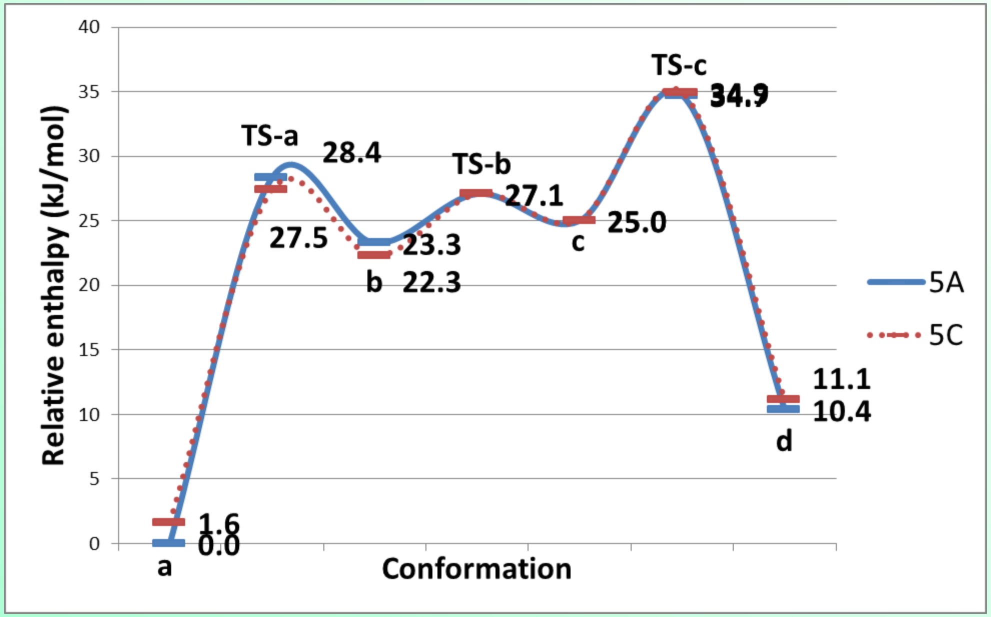
HC-HCMe-HCMe-CH dihedral (°)
50
40
30
20
10
0
-10
-20
-30
-40
-50
-0.9
-0.6
-0.3
0.0
0.3
0.6
0.9
1.2
=O---H--O- bond length (Angstrom)
0.000
7.000
14.00
21.00
28.00
35.00
42.00
49.00
56.00
63.00
70.00
77.00
84.00
91.00
98.00
105.0
112.0
119.0
126.0
133.0
140.0
O
P
HO
HO
P
O
O
P
HO
TS
O
P
HO
TS
O
P
HO
HO
P
O

7.2. Conformational situation for 1-substituted 3-methyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxides





For isomers A and C of compound 5:



8. Summary / Conclusions

- **From among the possible methods for the synthesis of phosphinates, the MW-assisted direct esterification of phosphinic acids is the most favourable. A suitable ionic liquid catalyst allows lower temperatures, shorter reaction times, and higher yields.**
- **Our experiences suggest that MW irradiation may be useful for thermoneutral reactions with high enthalpy of activation. Endothermicity works against complete conversion.**
- **The distribution of the beneficial local overheatings was modeled by an exponential function, and the extent of the rate enhancement was predicted by the Arrhenius equation.**