Received: 12 July 2017 | Revised: 18 August 2017

DOI: 10.1002/hc.21394

RESEARCH ARTICLE

WILEY Heteroatom Chemistry

A study on the acidic hydrolysis of cyclic phosphinates: 1-Alkoxy-3-phospholene 1-oxides, 1-ethoxy-3-methylphospholane 1-oxide, and 1-ethoxy-3-methyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxide

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Funding information
National Research Development and Innovation Fund, Grant/Award Number: HK119202

Abstract

The hydrochloric acid-catalyzed hydrolysis of phosphinates was studied on 1-alkoxy-3-phospholene 1-oxides, 1-ethoxy-3-methylphospholane 1-oxide, and 1-ethoxy-3-methyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxide as the model compounds. Under the conditions applied, the isomerization of the 3-phospholene moiety to the 2-phospholene ring also occurred leading to mixtures of the corresponding 1-hydroxy-3-phospholene oxide and 1-hydroxy-2-phospholene oxide. According to our optimized method, using 3 equivalents (0.5 mL) of concentrated hydrochloric acid in 1 mL of water per ca. 2 mmol of the substrate at reflux, the completion required 3-10 hour. The hydrolyses were characterized by pseudo-first-order rate constants and the isomerizations by rate constants. The application of *p*-toluenesulfonic acid under microwave irradiation at 140°C in the hydrolysis of 1-alkoxy-3-methyl-3-phospholene oxides associated with reaction times of 1-3 hour. The reactivity order of the 5- and 6-ring phosphinates in hydrolysis was set up.

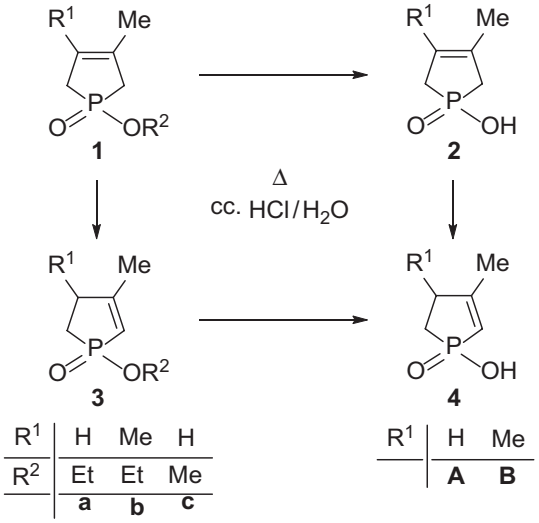
KEYWORDS

Cyclic phosphinates, 1-alkoxy-3-phospholene and phospholane oxide, 1-ethoxy-1,2,3,4,5,6-hexahydrophosphinine 1-oxide, acidic hydrolysis, phosphinic acids, rate constants.

1 | INTRODUCTION

The hydrolysis of P-esters, such as phosphinic-, phosphonic-, and phosphoric-acid esters is an important synthetic protocol; however, its realization is more difficult than that of carboxylic acid esters.[1,2] In most cases, the acid-catalyzed hydrolysis is preferred, carried out by boiling the mixture of the P-ester in aqueous hydrochloric acid. Most of the hydrolyses have not been optimized, and hence, the quantity of the hydrochloric acid and the conditions including the reaction time are excessive.[3,4] This is well demonstrated by the hydrolysis of diethyl arylphosphonates performed in 6 equivalents of concentrated (cc.) hydrochloric acid at the boiling point for 12 hour. After simple filtration, the arylphosphonic acids were obtained in 71%-93% yields.[5] 1-Alkoxyphospholane oxides were hydrolyzed in 3 mol L^{-1} hydrochloric acid at reflux for 5-8 hour to give the corresponding phosphonic acids in yields of 60%-68%.[6] Occasionally, dioxane was also used as a cosolvent or as the sole solvent.[7] Instead of HCl, HBr may also be used.[7-9] Trifluoroacetic acid-catalyzed hydrolysis of phosphinates was also reported.[10] It is also possible to carry out hydrolyses under basic conditions using aqueous NaOH or KOH.[11-17] Amine-catalyzed hydrolyses were also described.[18-21] A special protocol for the

Contract grant sponsor: National Research Development and Innovation Fund.
Contract grant number: K119202.



SCHEME 1 Acid-catalyzed hydrolysis of 3-methyl- and 3,4-dimethyl-1-alkoxy-3-phospholene 1-oxides (**1**)

>P(O) OR → >P(O)OH transformation involves a fission by the effect of trimethylsilyl bromide.[22-24] Enzymatic hydrolysis is also a good option.[25] According to an indirect approach, the phosphinate is converted to the corresponding phosphinic chloride by reaction with phosphorus pentachloride, and the P-chloride so formed is hydrolyzed.[26] It is worth noting that a microwave (MW)-assisted protocol was elaborated for the hydrochloric acid-catalyzed hydrolysis of phosphinate diesters.[27]

In this article, we investigate the hydrolysis of a series of cyclic phosphinates under acidic conditions. We wished to explore the optimum conditions for the acidic hydrolysis of a few 1-alkoxy-3-phospholene 1-oxides, 1-ethoxy-3-methylphospholane 1-oxide, and 1-ethoxy-3-methyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxide using hydrochloric acid on conventional heating, or in a few cases, para-toluenesulfonic acid under MW conditions.

2 | RESULTS AND DISCUSSION

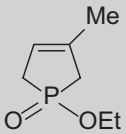
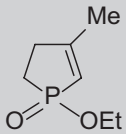
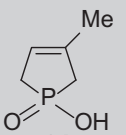
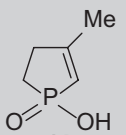
2.1 | Hydrolysis of the ring phosphinates in the presence of hydrochloric acid catalyst on conventional heating

1-Ethoxy-3-methyl-3-phospholene 1-oxide (**1a**), 1-ethoxy-3,4-dimethyl-3-phospholene 1-oxide (**1b**), and 1-methoxy-3-methyl-3-phospholene 1-oxide (**1c**) were chosen as the starting phosphinates. In the first approach, cc. hydrochloric acid and water were measured in different quantities and ratios. After the different periods of boiling the mixtures, they were extracted with dichloromethane, and the residues obtained after evaporating the solvent were analyzed by ^{31}P NMR spectroscopy.

The results on the hydrolysis of 1-ethoxy-3-methyl-3-phospholene oxide **1a** are shown in Scheme 1 and in Table 1. It can be seen that in the absence of hydrochloric acid, there was no hydrolysis (Table 1, entry 1). It is also obvious that under the conditions applied, the starting 1-ethoxy-3-phospholene oxide **1a** may have undergone partial isomerization to the 2-phospholene derivative **3a**, and hydrolysis of the two phosphinates (**1a** and **3a**) furnished the corresponding phosphinic acids (**2a** and **4a**, respectively). Boiling 1.9 mmol phosphinate **1a** with 0.5 mL of cc. hydrochloric acid in 2 mL of water, the conversion was 61% after a reaction time of 6 hour. All possible components were present in the reaction mixture (Table 1, entry 2). Working in a more concentrated solution, the conversion was 47% after 3 hour, and the completion required 6 hour. The ratio of the 1-hydroxy-3-phospholene oxide (**2a**) and its 2-phospholene isomer (**4a**) was 1:9 (Table 1, entries 3 and 4). Decreasing the quantity of water and hydrochloric acid to the half amount, the conversion remained incomplete (92%) (Table 1, entry 5).

Adding 0.1 mL of [emim][HSO_4] ionic liquid to the reaction mixtures, somewhat lower conversions were obtained. This was surprising, as in other kind of reactions, the use of ionic liquid additives was highly beneficial.[28-32]

TABLE 1 Hydrolysis of 1-ethoxy-3-methyl-3-phospholene 1-oxide (**1a**)[a] in the presence of hydrochloric acid

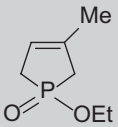
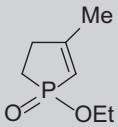
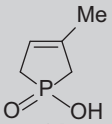
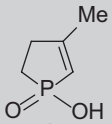
		cc. HCl				Composition[b] (%)			
									
Entry	**H_2O (mL)**	**(mL)**	**(equiv.)**	***t* (h)**	**Conversion (%)**	**1a**	**3a**	**2A**	**4A**
1	1	0	-	6	0	100			
2	2	0.5	3	6	61	18	21	27	34
3	1	0.5	3	3	47	25	28	16	31
4	*1*	*0.5*	*3*	*6*	*100*			*10*	*90*
5	0.5	0.25	1.5	6	92	2	6	19	73

Values in Italics stand for the optimum conditions of the hydrolysis.

[a]The quantity of phosphinate **1a** was 1.9 mmol.

[b]On the basis of relative ^{31}P NMR integrals.

TABLE 2 Time dependence of the hydrolysis of 1-ethoxy-3-methyl-3-phospholene oxide (**1a**) under the optimum conditions

	Composition[a] (%)					
t (h)	 **1a**	 **3a**	 **2A**	 **4A**	Conversion (%)	1a + 3a (%)
0.25	81	3	16	0	16	84
0.5	74	6	18	2	20	80
1	51	16	24	9	33	67
2	25	19	24	32	56	44
4	11	16	11	62	73	27
6	0	0	10	90	100	0
7[b]	0	0	8	92		

[a]On the basis of relative ^{31}P NMR intensities.
[b]Further heating after complete hydrolysis.

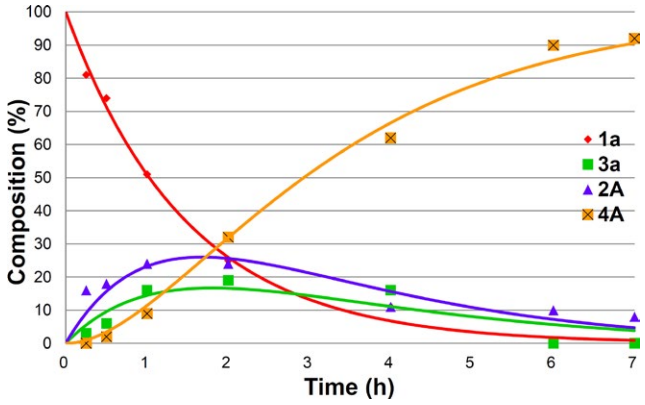
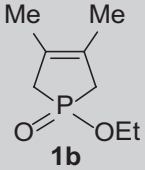
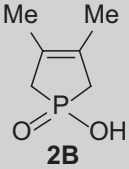
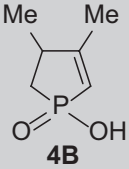


FIGURE 1 Concentration profile for the components during the hydrolysis of 1-ethoxy-3-methyl-3-phospholene oxide (**1a**) under optimum conditions. The R^2 measure of goodness of fit is .983

The hydrolysis of cyclic phosphinate **1a** performed under optimal conditions (1.9 mmol of **1a**, 1 mL of H_2O, 0.5 mL of cc. HCl/6 hour, Δ) was monitored by ^{31}P NMR spectroscopy. The data can be seen in Table 2 and Figure 1. The curves on the data points were fitted using the nonlinear generalized reduced gradient method of Microsoft Excel Solver (see Section 3). The pseudo-first-order rate constants for the hydrolysis of phosphinates **1a** and **3a** obtained by the program package were 0.42 and 0.45 hour^{-1}, respectively. The rate constants for the **1a** → **3a** and **2A** → **4A** isomerizations were found 0.25 and 0.52 hour^{-1}, respectively. The rate constants determined should be regarded approximate values that are good indicators of the reactivity.

It was proved by a separate experiment that 1-hydroxy-3-methyl-3-phospholene 1-oxide (**2A**) may be isomerized to the 2-phospholene 1-oxide (**4A**) under the conditions of the

TABLE 3 Time dependence of the hydrolysis of 1-ethoxy-3,4-dimethyl-3-phospholene 1-oxide (**1b**) under the optimum conditions

	Composition[a] (%)			
t (h)	 **1b**	 **2B**	 **4B**	Conversion (%)
1	68	31	1	32
2	39	54	7	61
3	23	67	11	78
4	16	69	15	84
6	6	73	21	94

[a]On the basis of relative ^{31}P NMR intensities.

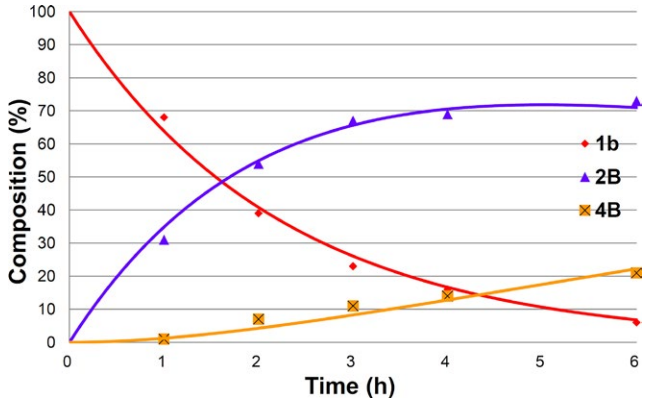


FIGURE 2 Concentration profile for the components during the hydrolysis of 1-ethoxy-3,4-dimethyl-3-phospholene oxide (**1b**) under optimum conditions. The R^2 measure of goodness of fit is .981

hydrolysis (3 mL H_2O, 1.5 mL cc. HCl/6 hour, Δ). Under these conditions, 90% of **2A** was isomerized to **4A**.

The hydrolysis of 1-ethoxy-3,4-dimethyl-3-phospholene 1-oxide (**1b**) under the optimum conditions (1.9 mmol of **1b**/0.50 mL of cc. HCl/1 mL of H_2O/Δ, 6 hour) mentioned above led to similar results ($t_{completion}$ ~ 6 hour), but phosphinate **3b** (the isomer of starting **1b**) was not an intermediate, suggesting a simple **1b** → **2B** → **4B** protocol (Table 3; Scheme 1; Figure 2). The pseudo-first-order rate constant for the hydrolysis **1b** → **2B** and the rate constant for the isomerization **2B** → **4B** obtained on the basis of the fitted curves with the help of the program mentioned above were 0.45 and 0.07 $hour^{-1}$, respectively.

The inclination of 3-phospholene oxide **2B** for isomerization to 2-phospholene derivative **4B** is significantly lower than the ability of monomethylphospholene oxide **2A** to undergo the double-bond rearrangement. This is demonstrated well by the rate constants for **2B** → **4B** and **2A** → **4A** isomerizations that were found to be 0.07 and 0.52 $hour^{-1}$, respectively, and is the consequence of the different number of the Me groups in the skeleton.

As the third model, the 1-methoxy-3-methyl-3-phospholene oxide (**1c**) was also subjected to hydrolysis under the conditions applied in the previous cases. Both intermediates (**3c** and **2A**) appeared, and the series of transformations was already complete after 3 hour (Table 4; Scheme 1; Figure 3). Similarly the case of the hydrolysis of 1-ethoxy-3-phospholene oxide **1a**, the phosphinic acid formed by isomerization (**4A**) dominated in the final mixture.

The pseudo-first-order rate constants for hydrolyses **1c** → **2A** and **3c** → **4A** were 1.77 and 2.95 $hour^{-1}$, respectively, while the rate constants for isomerizations **1c** → **3c** and **2A** → **4A** were 0.71 and 0.49 $hour^{-1}$, respectively. One can see that the hydrolysis of the methyl ester **1c** is significantly faster ($k_{\mathbf{1c}\rightarrow\mathbf{2A}} = 1.77\ hour^{-1}$) than that of the ethyl ester **1a** ($k_{\mathbf{1a}\rightarrow\mathbf{2A}} = 0.42\ hour^{-1}$).

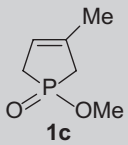
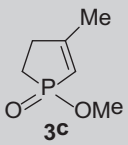
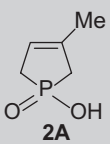
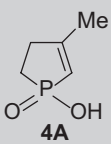
We then wished to investigate the hydrolysis of a saturated five-ring species. The model compound was 1-ethoxy-3-methylphospholane 1-oxide (**5**), and the hydrolysis was performed under the optimum conditions explored above (Scheme 2).

The hydrolysis under discussion was monitored by ^{31}P NMR spectroscopy, and it was found that the hydrolysis of 1-ethoxyphospholane oxide **5** was slower, as compared to the unsaturated cases. It is noted that although 1-ethoxy- and 1-hydroxy-3-methylphospholane oxides **5** and **6** comprise two diastereomers in a comparable quantity, only broader signals could be seen in their ^{31}P NMR spectra. The hydrolysis was complete after a reflux of 8 hour (Table 5; Figure 4). The pseudo-first-order rate constant for the hydrolysis obtained on the basis of the fitted curves with the help of a suitable program was 0.39 $hour^{-1}$.

Finally, 1-ethoxy-3-methyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxide (**7**) was also subjected to hydrolysis under the optimized conditions (Scheme 3).

The conversion-time data (Table 6; Figure 5) revealed that the rate of the hydrolysis of phosphinate **7** is somewhat slower

TABLE 4 Time dependence of the hydrolysis of 1-methoxy-3-methyl-3-phospholene oxide (**1c**) under the optimum conditions

	Composition[a] (%)					
						
t (h)	**1c**	**3c**	**2A**	**4A**	Conversion (%)	**1c** + **3c** (%)
0.25	45	8	38	9	47	53
0.5	32	11	41	16	57	43
1	17	0	43	40	83	17
2	7	6	28	59	87	13
3	0	0	21	79	100	0

[a]On the basis of relative ^{31}P NMR intensities.

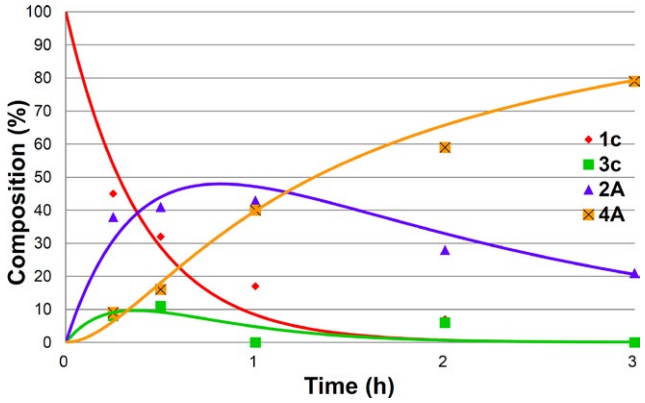
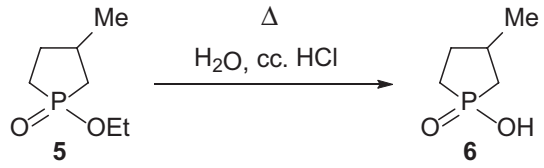


FIGURE 3 Concentration profile for the components during the hydrolysis of 1-methoxy-3-methyl-3-phospholene oxide (**1c**) under optimum conditions. The R^2 measure of goodness of fit is .921

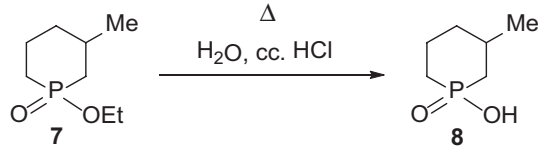


SCHEME 2 Acid-catalyzed hydrolysis of 1-ethoxy-3-methylphospholane 1-oxide (**5**)

TABLE 5 Time dependence of the hydrolysis of 1-ethoxy-3-methylphospholane oxide (**5**) under the optimum conditions

t (h)	Conversion[a] (%)
1	29
2	56
4	84
6	88
8	96

[a]On the basis of relative ^{31}P NMR intensities.



SCHEME 3 Acid-catalyzed hydrolysis of 1-ethoxy-3-methyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxide (**7**)

than that of the 5-ring analogue (**5**). Completion of the hydrolysis of phosphinate **7** required ca. 10 hour. In this instance, the fate of the two diastereomers of the starting phosphinate (**7**) could be monitored separately. The pseudo-first-order rate constant for the hydrolysis obtained on the basis of the fitted curves with the help of the program was 0.35 hour^{-1}. This rate constant is based on the average reactivity of the diastereomers.

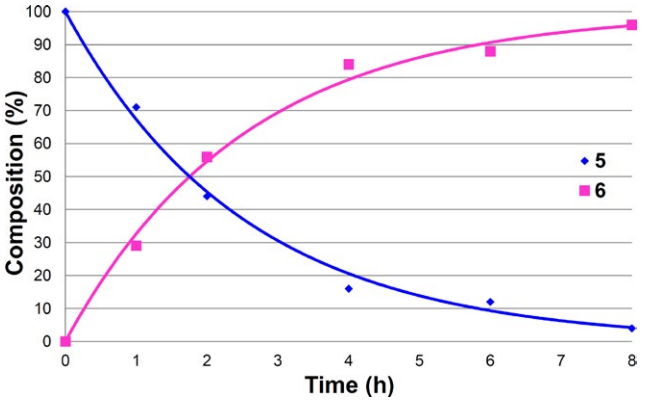


FIGURE 4 Concentration profile for the 1-ethoxy-3-methylphospholane oxide (**5**) and the corresponding phosphinic acid (**6**) during the acidic hydrolysis investigated. The R^2 measure of goodness of fit is .994

TABLE 6 Time dependence of the hydrolysis of 1-ethoxy-3-methyl-1,2,3,4,5,6-hexahydrophosphinine oxide (**7**) under the optimum conditions

	Composition[a] (%)			
t (h)	7a	7b	8	Conversion[a] (%)
1	32	40	28	28
2	19	25	56	56
4	6	21	73	73
6	1	20	79	79
8	1	8	91	91
10	0	0	100	100

[a]On the basis of relative ^{31}P NMR intensities.

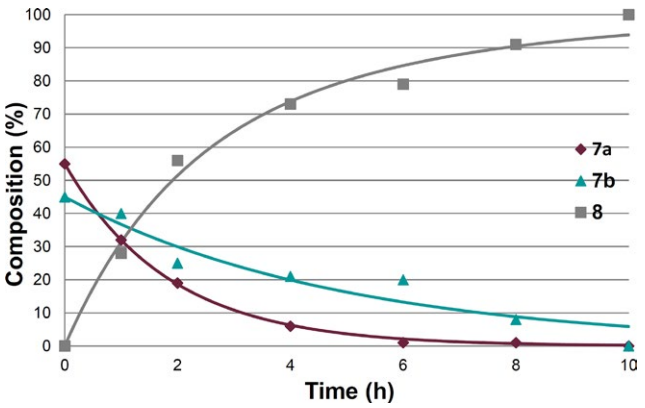
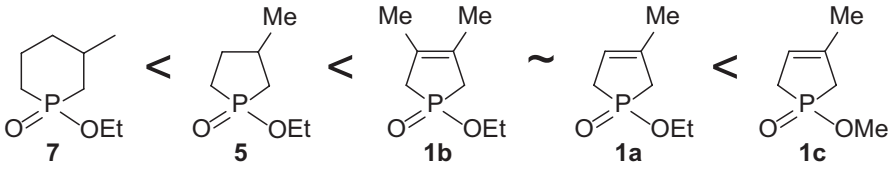


FIGURE 5 Concentration profile for the diastereomers of 1-ethoxy-hexahydrophosphinine oxide (**7a** and **7b**) and the corresponding phosphinic acid (**8**) during the acidic hydrolysis investigated. The R^2 measure of goodness of fit is .981

It can be seen that the reactivity of the P-alkoxy ring phosphinates (**1a-c**, **5** and **7**) in hydrolysis is the following:



It means that the phosphinates with saturated ring **5** and **7** are less reactive than the 3-phospholene derivatives (**1a-c**). An additional skeletal Me group decreases the reactivity (regard **1a** vs **1b**), and the methyl ester (**1c**) is more reactive than the ethyl derivative (**1a**).

We saw that the inclination for the double-bond rearrangement was at the lowest level in case of the dimethylphospholene oxide derivatives (eg **2B**).

2.2 | Microwave-assisted hydrolysis in the presence of *p*-toluenesulfonic acid catalyst

The MW-assisted variation of the hydrolysis of 1-ethoxy-3-methyl-3-phospholene 1-oxide (**1a**) in the presence of hydrochloric acid did not show any advantage, as there was no acceleration. The hydrolysis was also attempted in the presence of *p*-toluenesulfonic acid (PTSA) as the catalyst. PTSA is more attractive than aqueous HCl, due to the problem of corrosivity with HCl. The data obtained are listed in Table 7.

The first experiment was carried out using 1 equivalent of PTSA at 120°C. After an irradiation of 4.5 hour, the conversion was 89% in respect of the hydrolyzed products **2A** (43%) and **4A** (46%). The proportion of the unreacted starting material (**1c**) and the isomerized variation (**3c**) was 6% and 5%, respectively (Table 7, entry 1). Applying 3 equivalents of the catalyst, and allowing a reaction time of 2 hour, again all the four possible components **1c**, **3c**, **2A**, and **4A** were present, on this occasion, in quantities of 11%, 18%, 23%, and 48%, respectively (Table 7, entry 2). After a somewhat longer reaction time (2.5 hour), the conversion was 94%, with predominating presence of isomerized hydroxyphospholene oxide **4a** (78%) (Table 7, entry 3). The role of MW irradiation is significant, as can be seen from the comparison of the outcome of the experiments marked by entries 4 and 2. To achieve more complete conversions, the next hydrolyses were performed at 140°C. 0.33 Equivalents of the PTSA were not enough, as after a 2-hour irradiation, the conversion was incomplete (81%), and all possible components (**1c**, **3c**, **2A** and **4A**) were present (Table 7, entry 5). Increasing the quantity of the catalyst to 1 equivalent, the 1-hydroxy-2-phospholene oxide **4A** became the predominant product (69%), but some (12%) unreacted phosphinate (**3c**) also remained in the mixture (Table 7, entry 6). The best result could be obtained in the presence of 3 equivalents of the catalyst. After a 1-hour irradiation, the conversion was complete, and the ratio of the 1-hydroxy-3-phospholene and 1-hydroxy-2-phospholene derivatives (**2A** and **4A**) was 12-88 (Table 7, entry 7).

The results of the experiments with the 1-ethoxy-3-methyl-3-phospholene oxide (**1a**) revealed the lower reactivity of this phosphinate in hydrolysis. At 120°C or at 140°C in the presence of 3 equivalents of PTSA, the completion of the hydrolysis required 5.5 and 3 hour, respectively (Table 7, entries 8 and 9). Under similar conditions, complete hydrolysis of the 1-methoxy analogue **1c** required irradiation times of ca. 2.75 and 1 hour, respectively (Table 7, entries 3 and 7). The isomerized hydroxyphospholene oxide (**4A**) predominated in both cases.

In conclusion, the MW-assisted hydrolyses at 120°C in the presence of PTSA require similar reaction times as the thermal versions in the presence of hydrochloric acid (6 and 3 hour) for the two models **1a** → **4A** and **1c** → **4A** studied. At the same time, the MW variations at 140°C may be competitive, as the hydrolyses are significantly faster. (The reaction times are 3 and 1 hour for the two models investigated).

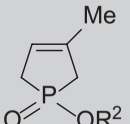
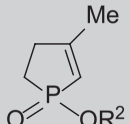
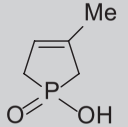
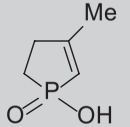
In summary, the hydrochloric acid-catalyzed hydrolysis of cyclic phosphinates, such as 1-alkoxy-3-phospholene 1-oxides, 1-ethoxy-3-methylphospholane 1-oxide, and 1-ethoxy-3-methyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxide, was optimized and characterized by rate constants. The best method involves the use of three equivalents of cc. hydrochloric acid in 1 mL of water for 2 mmol of the substrate and requires a 3-10 hour reflux. The microwave-assisted hydrolysis at 140°C in the presence of *p*-toluenesulfonic acid may be another option. The reactivity of the cyclic phosphinates was mapped as follows: The 1-alkoxy-3-phospholene 1-oxides were found more reactive than the saturated derivatives.

3 | EXPERIMENTAL

3.1 | General

The ^{31}P, ^{13}C, ^{1}H NMR spectra were taken on a Bruker DRX-500 spectrometer operating at 202.4, 125.7, and 500 MHz, respectively. The couplings are given in Hz. LC-MS experiments were performed with an Agilent 1200 liquid chromatography system coupled with a 6130 quadrupole mass spectrometer equipped with an ESI ion source (Agilent Technologies, Palo Alto, CA, USA). High-resolution mass spectrometric measurements were

TABLE 7 Microwave-assisted hydrolysis of 1-alkoxy-3-methyl-3-phospholene 1-oxides (**1c** and **1a**)[a] in the presence of *p*-toluenesulfonic acid

							Composition[b] (%)			
							 **1**	 **3**	 **2A**	 **4A**
Entry	R^2	**Heating**	**PTSA (equiv.)**	***T*** **(°C)**	***t*** **(h)**	**Conversion (%)**				
1	Me	MW	1	120	4.5	89	6 (**1c**)	5 (**3c**)	43	46
2	Me	MW	3	120	2	71	11 (**1c**)	18 (**3c**)	23	48
3	Me	MW	3	120	2.5[c]	94	-	6 (**3c**)	16	78
4	Me	Δ	3	120	2	13	78 (**1c**)	9 (**3c**)	11	2
5	Me	MW	0.33	140	2[d]	81	12 (**1c**)	7 (**3c**)	49	32
6	Me	MW	1	140	2	88	-	12 (**3c**)	19	69
7	*Me*	*MW*	*3*	*140*	*1*	*100*	-	-	*12*	*88*
8	Et	MW	3	120	5.5	100	-	-	21	79
9	*Et*	*MW*	*3*	*140*	*3*	*100*	-	-	*12*	*88*

Values in Italics stand for the optimum conditions of the hydrolysis.

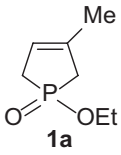
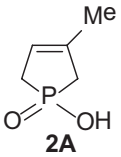
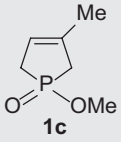
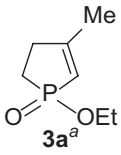
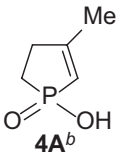
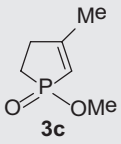
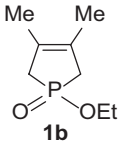
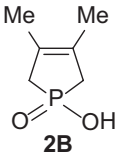
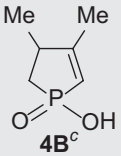
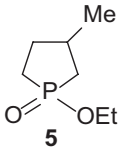
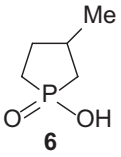
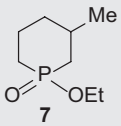
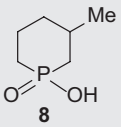
[a]The quantity of phosphinates **1c** and **1a** was 1.9 mmol; 1 mL of H_2O served as the medium.

[b]On the basis of relative ^{31}P NMR intensities.

[c]$t_{extrap} \approx 2.75$ h.

[d]$t_{extrap} \approx 2.5$ h.

TABLE 8 ^{31}P NMR characterization of the cyclic phosphinates and phosphinic acids involved in our study

Cyclic phosphinates	δ ^{31}P NMR Found	δ ^{31}P NMR Literature	$M + H$	Phosphinic acids	δ ^{31}P NMR Found	δ ^{31}P NMR Literature	$M + H$
 **1a**	76.0	74.7[35]	161.2	 **2A**	74.6 (bs)		133.2
 **1c**	77.6	76.8[36]	147.2				
 **3a**[a]	77.2		161.2	 **4A**[b]	79.7 (bs)		133.2
 **3c**	78.2	76.4[37]	147.2				
 **1b**	67.6	68.3[38]	175.2	 **2B**	69.7 (bs)		147.2
				 **4B**[c]	70.8 (bs)		147.2
 **5**	80.8 (bs)[d]	79.4[39]	163.2	 **6**	79.4 (bs)[d]	80.2 (bs)[38]	135.2
 **7**	50.4 (45%) 51.5 (55%)	51.8[40]	177.2	 **8**	52.4 (bs)[d]	51.8 (bs)[38]	149.2

[a] $[M + H]^+_{found}$ = 161.0742, $C_7H_{14}O_2P$ requires 161.0726.
[b] $[M + H]^+_{found}$ = 133.0418, $C_5H_{10}O_2P$ requires 133.0413.
[c] $[M + H]^+_{found}$ = 147.0578, $C_6H_{12}O_2P$ requires 147.0569.
[d] The two isomers cannot be distinguished.

performed using a Q-TOF Premier mass spectrometer in positive electrospray mode. The MW-assisted hydrolyses were carried out in a CEM Discover microwave reactor equipped with a stirrer and a pressure controller using 30-50 W irradiation.

3.2 | Evaluation of the ^{31}P NMR spectra

The composition of the reaction mixture was determined by the integration of the corresponding peaks in the ^{31}P NMR

spectra, or by peak deconvolution using ACD/Spectrus Processor software package.[33]

3.3 | Curve fitting on the time—relative quantity data pairs

The acidic hydrolysis and isomerization reactions were modeled assuming pseudo-first-order kinetics. The concentration of water and hydrochloric acid was constant during the reaction. The calculated time—composition curves were fitted to the experimental data using nonlinear least-squares method. The pseudo-first-order rate constants were optimized that the sum of squares of the residuals (ie the difference of the experimental and the calculated composition) to be the minimal. The approximate values of the rate constants were found iteratively, using the nonlinear generalized reduced gradient method[34] of Microsoft Excel Solver.

3.4 | General procedure for the hydrolysis of 1-alkoxy-3-phospholene 1-oxides (1a-c), 1-ethoxy-3-methylphospholane 1-oxide (5), and 1-ethoxy-3-methyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxide (7) under conventional conditions

A mixture of 1.9 mmol of cyclic phosphinate (**1a**: 0.30 g, **1b**: 0.33 g, **1c**: 0.28 g, **5**: 0.31 g, **7**: 0.33 g), 0.50 mL (6.0 mmol) of cc. hydrochloric acid, and 1.0 mL of water was stirred at reflux for 3-10 hour. The reaction mixture was extracted with 3 × 10 mL of dichloromethane, and the organic phase was dried (Na_2SO_4). Concentration of the organic phase afforded an oil that was analyzed by LC-MS and ^{31}P NMR spectroscopy.

3.4.1 | 1-Hydroxy-3-methyl-3-phospholene 1-oxide (2A)

^{31}P NMR ($CDCl_3$) δ: 74.6 (bs); ^{13}C NMR ($CDCl_3$) δ: 20.6 (d, J = 13.1, CH_3), 31.8 (d, J = 90.1, C_5), 34.4 (d, J = 94.0, C_2), 120.2 (d, J = 11.0, C_3), 136.2 (d, J = 17.1, C_4); ^{1}H NMR ($CDCl_3$) δ: 1.75 (s, 3H, CH_3), 2.35 (d, J = 12.5, 2H, CH_2), 2.45 (d, J = 13.3, 2H, CH_2), 5.47 (d, J = 35.8, 2H, C=CH), 11.13 (bs, 1H, OH).

3.4.2 | 1-Hydroxy-3,4-dimethyl-3-phospholene 1-oxide (2B)

^{31}P NMR ($CDCl_3$) δ: 69.7 (bs); ^{13}C NMR ($CDCl_3$) δ: 16.5 (d, J = 16.1, CH_3), 36.7 (d, J = 92.8, C_2), 127.4 (d, J = 13.0, C_3); ^{1}H NMR ($CDCl_3$) δ: 1.71 (s, 6H, 2× CH_3), 2.47 (d, J = 13.3, 4H, 2× CH_2), 11.74 (bs, 1H, OH).

3.5 | General procedure for the hydrolysis of 1-alkoxy-3-phospholene 1-oxides (1a-c) under MW conditions

A mixture of 1.9 mmol of 1-alkoxy-3-phospholene 1-oxide (**1a**: 0.30 g, **1c**: 0.28 g) and 0.33 g (1.9 mmol) of para-toluenesulfonic acid in 1.0 mL of water was irradiated in a sealed tube placed in a CEM MW reactor (equipped with a pressure controller) at 120-140°C (50 W) for 1.5-4 hour. The reaction mixture was extracted with 3 × 10 mL of dichloromethane, and the organic phase was dried (Na_2SO_4). Evaporation of organic solvent gave an oil that was analyzed by LC-MS and ^{31}P NMR spectroscopy.

^{31}P NMR and mass spectral data for cyclic phosphinates **1a-c**, **3a**, **3c**, **5**, and **7** together with those of the phosphinic acids (**2A**, **4A**, **2B**, **4B**, **6**, and **8**) are summarized in Table 8.

ACKNOWLEDGMENTS

This project was supported by the National Research Development and Innovation Fund (K119202). Zita Rádai is grateful for the fellowship provided by Chinoin-Sanofi Pharmaceuticals.

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How to cite this article: Keglevich G, Rádai Z, Harsági N, Szigetvári Á, Kiss NZ. A study on the acidic hydrolysis of cyclic phosphinates: 1-Alkoxy-3-phospholene 1-oxides, 1-ethoxy-3-methylphospholane 1-oxide, and 1-ethoxy-3-methyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxide. *Heteroatom Chem*. 2017;28:e21394. https://doi.org/10.1002/hc.21394