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Photolysis of the cycloadduct of a 1,2-dihydrophosphinine oxide with *N*-phenylmaleimide in the presence of protic species: new aspects on the mechanism of the fragmentation of a 2-phosphabicyclo[2.2.2]octene

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Abstract

Phosphabicyclo[2.2.2]octene **2** is useful in the UV light mediated phosphorylation of protic species. Experiments suggest that the fragmentation takes place according to concurrent EA and AE mechanisms. © 1998 Elsevier Science S.A. All rights reserved.

Keywords: 2-Phosphabicyclo[2.2.2]octene 2-oxide; Fragmentation; Mechanism; Phosphorylation

1. Introduction

The fragmentation of bridged heterocyclic systems is an attractive approach for the generation of low-coordinate fragments, especially those with 3-coordinate pentavalent phosphorus atom [1]. In this context not too much is known on methylene phosphine oxides and sulfides, the representative class of low-coordinate intermediates with pentavalent phosphorus atom. Quin, with one of the above authors, showed that on irradiation (254 nm), 2-phosphabicyclo[2.2.2]octa-5,7-diene 2-oxides are readily fragmented to methylene phosphine oxides that phosphorylate the nucleophiles added to the reaction mixture prior to irradiation [2,3]. Thermolysis of the above cycloadducts in the presence of hydroxy compounds was not too efficient in the preparation of phosphorylated species due to the forcing conditions required [4]. Mathey found, however, that the P-sulfide derivative of a similar phosphabicyclooctadiene was fragmented already at 110°C [5].

In this paper it is examined if 2-phosphabicyclo[2.2.2]octene 2-oxides can also be utilized in the UV light mediated phosphorylation of alcohols. Possible mechanistic pathways of the fragmentation are considered too.

2. Results and discussion

2.1. Synthesis of phosphabicyclo[2.2.2]octene **2** and its utilization in phosphorylations

Diels–Alder cycloaddition reaction of the double-bond isomers (**A** and **B**) of dihydrophosphinine oxide **1** with *N*-phenylmaleimide afforded phosphabicyclooctenes **2A** and **2B** in good yield after column chromatography (Scheme 1). The major isomer (**2A**) could be prepared in a pure form by fractional crystallization. Cycloadducts **2A** and **2B** were characterized by ^{31}P-, ^{13}C- and ^{1}H-NMR, as well as MS data. The ^{13}C-NMR spectral parameters are listed in Table 1. The $^{3}J_{PC}$ couplings of ca. 15 Hz detected on C_{10} of **2A** and **2B** stand for a dihedral angle of close to 180° [6]. Inspect-

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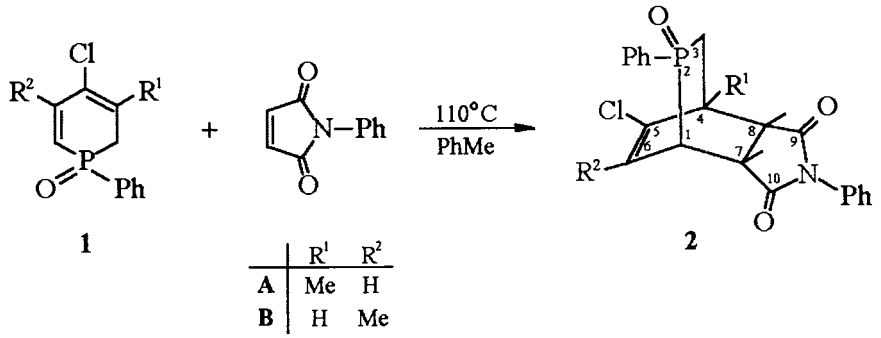


Scheme 1.

ing the Dreiding model, this angle is consistent with the endo structure (**2A** and **2B**) of the cycloadducts. 5,6-Oxaphosphabicyclo[2.2.2]octene 6-oxides are known to have a similar stereostructure. In these cases $^3J_{PC} \sim 18$ Hz was detected on the corresponding carbon atom [7].

Thermal examinations, such as differential thermal analysis (DTA) and differential scanning calorimetry (DSC) revealed that phosphabicyclooctene **2** is more thermostable than the earlier described phosphabicyclooctadienes. Bicyclooctene **2** loses the bridging moiety ($PhP(O)(CH_2)$) in the range of 330–430°C, while the bicyclooctadienes are fragmented in the range of 190–290°C [4]. Both types of fragmentations are exothermic. Due to the thermostability of cycloadduct **2**, the UV light (254 nm) mediated fragmentation seemed to be more attracting. Irradiation of the acetonitrile solution of the isomeric mixture (**A** and **B**) of precursor **2** in the presence of simple alcohols, such as methanol, ethanol, *n*-propanol, i-propanol and *n*-butanol led to the corresponding phosphinates (**4a–e**) (Scheme 2). No phosphorylated product was formed when *tert*-butanol was the protic species. Photolysis of **2** in the presence of water resulted in phosphinic acid **4f**. Small-scale preparative experiments afforded phosphinic derivatives **4a–f** in good yields after flash chromatography (Table 2). The products (**4a–f**) mostly known compounds [2,8–10], were identified by ^{31}P-NMR and mass spectroscopy including EI, FAB, HRMS and HRFAB (Table 2).

GC-MS of the crude reaction mixtures revealed the presence of dihydrophthalimide **3** ($M^+ = 273$).

It was observed that interrupting the photolyses before complete conversion, intermediates $\mathbf{5}_1$ and $\mathbf{5}_2$ formed by the reaction of cycloadduct **2** with an alcohol were also present in the mixture beside starting material **2** and product **4**. Transient species $\mathbf{5}_1$ and $\mathbf{5}_2$ were pointed out by ^{31}P-NMR and GC-MS that disappeared on further irradiation. (For **5Aa**, $\delta_P = 43.2$ and 43.5 ($CDCl_3$), $M^+ = 443$ (1Cl); for **5Ab**, $\delta_P = 41.2$ and 41.7 ($CDCl_3$), $M^+ = 457$ (1Cl).)

The above method is a good choice for the phosphorylation of primary and secondary alcohols. Attempts to extend the sphere of nucleophiles to be phosphorylated and to vary the P-function introduced are in progress.

*2.2. Mechanism for the photochemical fragmentation of phosphabicyclo[2.2.2]octene **2***

In the photolysis of phosphabicyclo[2.2.2]octadienes, rate of the fragmentation was found to be semiquantitavely the same in the presence, or in the absence of ethanol [2]. For this, an elimination–addition reaction path involving the formation of a methylene phosphine oxide in the rate-determining step followed by fast reaction with the alcohol present was suggested. The role of the alcohol, in this case, is to trap the reactive intermediate [2,3,11].

A similar mechanism seemed to be valid also for the fragmentation of phosphabicyclooctene **2** (mechanism A in Scheme 3). Of course, intermediate **5** can also be the starting compound of this mechanism. Existence of the elimination–addition mechanism involving methylene phosphine oxide **6** was confirmed by the fact that fragmentation of cycloadduct **2** also took place in

Table 1
^{13}C-NMR data for the isomers (**A** and **B**) of phosphabicyclooctene **2** in $CDCl_3$ solution

	δ_C (J_{PC} in Hz)									
	C_1	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	CH_3
2A	39.3 (62.8)	37.2 (75.8)	44.5 (6.6)	140.3 (10.7)	122.6 (5.9)	40.4 (2.9)	49.5 (10.8)	174.0	175.6 (14.8)	23.6 (10.7)
2B	44.7 (60.1)	28.1 (77.3)	42.8 (7.2)	[a]	[a]	39.4 —	45.4 (12.2)	175.2	176.0 (15.4)	18.9 —

[a] Overlapped in the region of 126–133 ppm.

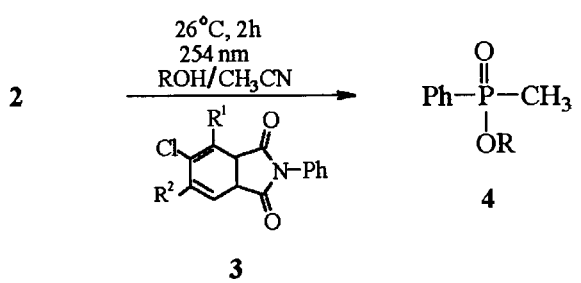
Table 2
Phosphinic esters (**4a–f**) prepared by the photolysis of phosphabicyclooctene **2** in alcohols

Product	Yield (%)	δ_p^a	(δ_p^{lit})	M^+_{found}	(M^+_{calc})	$[M+H]^{+b}_{found}$	($[M+H]^+_{calc}$)
4a[c]	90	44.8	(45.0[9])	170.0523	(170.0497)		
4b	85	42.7	(42.0[2])	184.0678	(184.0653)		
4c	84	42.8				199.0859	(199.0888)
4d	66	41.3				199.0862	(199.0888)
4e	86	42.8				213.1019	(213.1044)
4f	77	50.1		156.0326	(156.0340)		

[a] $CDCl_3$ solution.
[b] FAB measurements.
[c] bp 80–85°C/0.4 mmHg (lit[8]: 106–110°C/0.6 mmHg).

the absence of an alcohol. The result of this photolysis was a polimeric precipitate, presumably $[PhP(O)(CH_2)]_n$. We observed, however, that the fragmentation was faster in the presence of an alcohol; moreover, the rate was dependent on the molar excess of the protic species. A summary of the experiments with methanol is listed in Table 3. The nature of the alcohol also had an impact on the reaction time. The fragmentation in the presence of ethanol, *n*-propanol or *n*-butanol was slower than in methanol (Table 4). This order of reactivity corresponds to the pK_a values of the alcohols [12]. No phosphorylated product was formed when *tert*-butanol was the protic species. The above observations suggest the involvement of the alcohol in the rate-determining step of the fragmentation. According to this, the protic species is added on the phosphoryl group of the phosphabicyclooctene (either **2** or **5**) to form intermediate **7** with a pentacoordinated phosphorus atom. Adduct **7** is then fragmented in a fast step to afford phosphinate **4** (mechanism B in Scheme 3).

It can be concluded that the photochemical fragmentation of phosphabicyclooctene **2** takes place according to concurrent E–A and A–E mechanisms. Proportions of the two pathways seem to be comparable. It can be imagined that mechanism B may also play a role in the fragmentation of 2-phosphabicyclo[2.2.2]octa-5,7-dienes having a bigger ring strain (α_{C-P-C} is 99.5° [13]) than cycloadduct **2**. The above results encourage us to study further the mechanism of the photolysis of bridged P-heterocycles and to reexamine the mechanism of the fragmentation of phosphabicyclooctadienes by means of kinetic methods.



Scheme 2.

3. Experimental

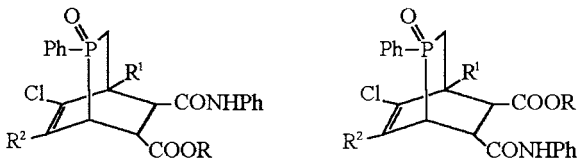
The ^{31}P-, ^{13}C- and ^1H-NMR spectra were taken on a Bruker DRX-500 spectrometer operating at 202.4, 125.7 and 500 MHz, respectively. Chemical shifts are downfield relative to 85% H_3PO_4 or TMS. Mass spectra were obtained on a MS-902 spectrometer or on a ZAB-2SEQ instrument at 70 eV. Photolyses were conducted in a photochemical reactor equipped by a quartz, water-cooled immersion well with a high-pressure mercury lamp (125 W).

3.1. Preparation of the isomers (A and B) of dihydrophosphinine-N-phenylmaleimide cycloadduct 2

A solution of 2.1 g (8.81 mmol) of dihydrophosphinine oxide **1** consisting of 75% of the **A** isomer and 25% of the **B** isomer [14] and 1.8 g (10.41 mol) of *N*-phenylmaleimide in 40 ml of toluene was stirred at boiling point for 6 days. Solvent was evaporated and the residue so obtained purified by column chromatography (silica gel, 3% methanol in chloroform) to give 2.7 g (75%) of **2** as the mixture of isomer **A** (61%) and isomer **B** (39%). Fractional crystallization from ethyl acetate-*n*-pentane led to 0.45 g (21%) of pure **2A**; mp. 211–214°C. Found: C, 64.37%, H, 4.75%. $C_{22}H_{19}ClNO_3P$ requires C, 64.16%, H, 4.62%.

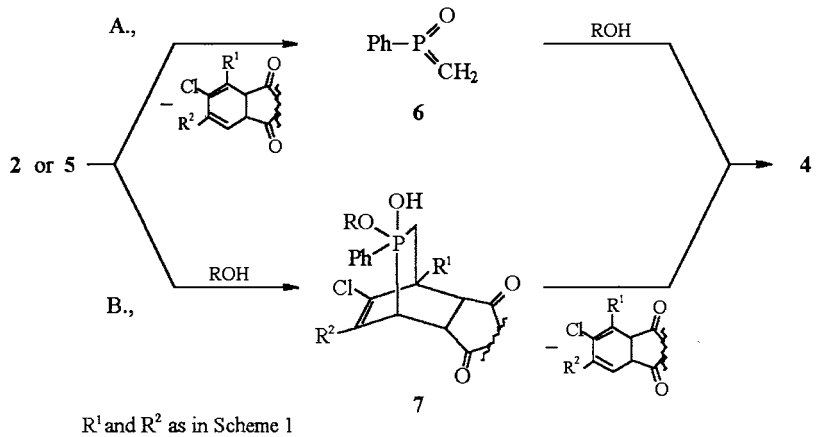
2A: ^{31}P-NMR ($CDCl_3$) δ 37.3; ^{13}C-NMR, Table 1; ^1H-NMR ($CDCl_3$) δ 1.80 (s, 3H, Me), 2.03–2.58 (m), 3.38–4.13 (m), total int. 5H, skeletal protons, 6.05 (dd, $^3J_{PH} = {}^3J_{HH} = 7.9$, 1H, CH=), 7.14–7.69 (m, 10H, Ar); MS, *m/z* (rel. int.) 411 (M^+, 28), 376 (M-35, 63), 91 (100).

2B: ^{31}P-NMR ($CDCl_3$) δ 37.1; ^{13}C-NMR, Table 1; ^1H-NMR ($CDCl_3$) δ 1.49 (s, 3H, Me); MS, *m/z* 411 (M^+).



5_1 5_2

R^1, R^2 and R as in Scheme 1



R^1 and R^2 as in Scheme 1

Scheme 3.

Table 3
Photolysis of cycloadduct **2A** carried out in the presence of different excess of methanol[a]

Molar excess of methanol ($n_{MeOH}\backslash n_{2A}$)	Approximate reaction time (min)
75	60
150	40
254	30
Without MeOH	48% Of **2A** was regenerated after 30 min of irradiation

[a] The photolyses were carried out with 0.1 g of **2A** in 45 ml of MeCN.

*3.2. General procedure for the synthesis of phenyl-methylphosphinates **4a–e***

The solution of 0.2 g (0.486 mmol) of phosphabicyclo[2.2.2]octene **2** consisting of 61% of the **A** isomer and 39% of the **B** isomer in 45 ml of acetonitrile and 4 ml of the corresponding alcohol was irradiated in a photochemical reactor with a mercury lamp (125 W) for 2 h. Volatile components were removed and the residue so obtained purified by flash column chromatography (silica gel, 3% methanol in chloroform) to give the corresponding phosphinates (**4a–e**). (The use of water instead of alcohols led to product **4f**.)

Table 4
Photolysis of cycloadduct **2A** carried out in the presence of different alcohols (ROH)[a]

R of the alcohol	Product composition (%)[b] after an irradiation time of 30 min			Estimated reaction time (min)
	2A	**4**	Other[c]	
Me (**a**)	14	67	19	40
Et (**b**)	17	63	20	45
n-Pr (**c**)	18	61	21	50
n-Bu (**e**)	23	57	20	50

[a] The photolyses were carried out with 0.1 g of **2A** in 45 ml of MeCN and 1.5 ml of ROH.
[b] Established on the basis of relative ^{31}P-NMR intensities.
[c] Including **4f** from hydrolysis.

^{31}P-NMR and MS data of the products are listed in Table 2.

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