J. Chem. Research (S), 1999, 580–581†

Phosphorylation of Amines by the UV-light Mediated Fragmentation of a 2-Phosphabicyclo[2.2.2]octene 2-Oxide†

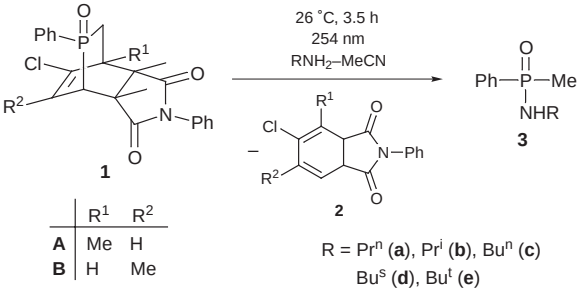
György Keglevich,*[a] Helga Szelke,[a] Zoltán Nagy,[b] András Dobó,[c] Tibor Novák[a] and László Tőke[a]

[a] *Department of Organic Chemical Technology, Technical University of Budapest, 1521 Budapest, Hungary*
[b] *Gedeon Richter Ltd., 1475 Budapest, Hungary*
[c] *Research Institute for the Hungarian Academy Sciences, 1525 Budapest, Hungary*

Irradiation of the title compound **1** at 254 nm in the presence of alkylamines or dialkylamines leads to the formation of phosphinic amides **3** and **4**, respectively.

The fragmentation of bridged heterocyclic systems[1–4] is an attractive approach for the generation of methylenephosphine oxides, a representative class of low-coordinate intermediates. On irradiation at 254 nm, the 2-phosphabicyclo[2.2.2]octene derivatives are readily fragmented to methylenephosphine oxides that phosphorylate the alcohols added to the reaction mixture prior to the irradiation.[3] Here, we report the use of phosphabicyclooctenes in the UV-light mediated phosphorylation of primary and secondary amines

.

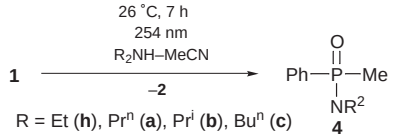


	R^1	R^2
A	Me	H
B	H	Me

Scheme 1

Irradiation of the acetonitrile solution of an isomeric mixture (**A** and **B**) of phosphabicyclooctene **1** at 254 nm in the presence of primary amines, such as alkylamines for 3.5 h led to the corresponding phosphinic amides **3a–e** (Scheme 1). Small-scale preparative experiments afforded amides **3a–e** in acceptable yields, in a purity of 88–95% after flash column chromatography (Table 1). The amides **3a–e**, mostly new compounds, were identified by ^{31}P and ^{1}H NMR, as well as GC–MS methods (Table 1).

The above method for the synthesis of phosphinic amides of type PhMeP(O)NHR may be a good alternative to previous procedures applying methyl(phenyl)phosphinic chloride[6] obtained from phosphoryl chloride. The introduction of three different substituents to a pentavalent tetracoordinated phosphorus atom is not without difficulties. Selectivity problems mean the yields are usually not high.[7]

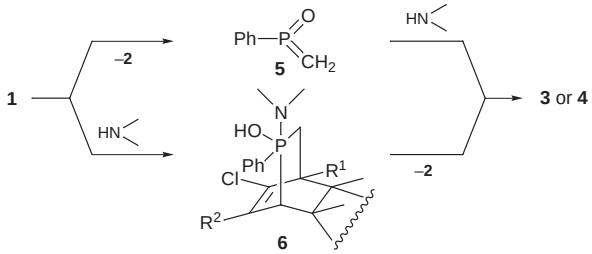


Scheme 2

The phosphorylation of secondary amines, such as dialkylamines was also attempted under the above conditions. A 7 h-irradiation of phosphabicyclooctene **1** in the presence of dialkylamines furnished complex mixtures containing the expected phosphinic amides **4a–c**,**h** in only low yields (*ca.* 6–11%) (Scheme 2). Products **4a–c**,**h** were identified by GC–MS and ^{31}P NMR (Table 2).

The low yields of dialkylamides **4** may be the consequence of steric effects. We recall that the UV-light mediated phosphorylation of alcohols by phosphabicyclooctene was also found to be sensitive to steric effects.[3]

Recently, it was substantiated that the UV-light mediated phosphorylation of alcohols by phosphabicyclooctene **1** may take place according to concurrent elimination–addition (EA) and addition–elimination (AE) mechanisms.[3] The EA reaction path involves the formation of methylenephosphine oxide in the rate-determining step followed by fast reaction with the alcohol present, while according to the AE mechanism, the nucleophile is added on the phosphoryl group of bicyclooctene **1** to form an intermediate with a pentacoordinate phosphorus atom that is then fragmented to give the phosphorylated product.



Scheme 3

As compound **1** is known to undergo fragmentation in the absence of any nucleophile,[3] there is little doubt that the EA reaction component must be effective in any case. The result of this photolysis is a polymeric material, presumably $[PhP(O)(CH_2)]_n$.[3] Irradiation of an acetonitrile solution of **1** (0.243 mmol) in the presence of equimolar *n*-propylamine (25.4 mmol) and *n*-propyl alcohol (25.4 mmol) led to a mixture of 71% phosphinic amide **3a** (δ_P 31.7) and 29% of PhP(O)(OPr^n)Me [δ_P 41.5 (lit.,[3] 42.8)] according to

* To receive any correspondence (*e-mail*: keglevich@oct.bme.hu).
† This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 Phosphinic amides **3a–e** prepared by the photolysis of phosphabicyclooctene **1** with primary amines

Product	Yield(%)	Purity (%)	δ_P ($CDCl_3$)	MS, *m/z* (rel. int. %)	HRFAB $(M+H)_{found}$	HRFAB $(M+H)_{calc}$
3a[a]	69	95	31.7	197 (M^+, 8), 168 (M − 29, 82) 139 (M − NHPr, 100), 77 (19)	198.1041	198.1048
3b[b]	65	90	29.8	197 (M^+, 1), 182 (M − Me, 100) 139 (M − NHPr, 95), 77 (Ph, 17)	198.1039	198.1048
3c[c]	82	94	31.6	211 (M^+, 8), 168 (M − Pr, 82), 139 (M − NHBu, 100), 77 (Ph, 15)	212.1199	212.1204
3d[d]	76	88	29.7	211 (M^+, <1), 196 (M − Me, 8), 182 (M − Et, 100), 139 (M − NHBu, 75), 77 (13)	212.1199	212.1204
3e[e]	81	93	27.2	211 (M^+, < 1), 196 (M − Me, 100), 139 (M–NHBu, 54), 77 (12)	212.1195	212.1204

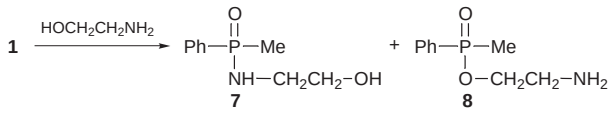
[a] δ_H($CDCl_3$), 0.92 [*t*, $J = 7.5$, $(CH_2)_2CH_3$], 1.47–1.57 (m, CH_2), 1.65 (d, $J = 14.0$, PCH_3), 3.09–3.14 (m, NCH_2), 7.36–7.86 (m, Ar); [b] δ_H($CDCl_3$), 1.15 [d, $J = 6.0$, $CH(CH_3)_2$], 1.65 (d, $J = 14.0$, PCH_3), 7.37–7.88 (m, Ar); [c] δ_H($CDCl_3$), 0.93 [*t*, $J = 7.3$, $(CH_2)_3CH_3$], 1.38–1.57 [m, $(CH_2)_2$], 1.66 (d, $J = 14.0$, PCH_3), 2.80–3.0 (m, CH_2), 7.40–7.86 (m, Ar); lit.[5] δ_H0.81 [*t*, $J = 7$, $(CH_2)_3CH_3$], 1.15–1.60 [m, $(CH_2)_2$], 1.70 (d, $J = 14$, PCH_3), 2.73–3.10 (m, CH_2), 7.35–8.0 (m, Ar); [d] δ_H($CDCl_3$), 0.92 (*t*, $J = 7.5$, CH_2CH_3), 1.12 (d, $J = 6.5$, $CHCH_3$), 1.66 (d, $J = 13.8$, PCH_3), 7.37–7.88 (m, Ar); [e] δ_H($CDCl_3$) 1.32 [s, $C(CH_3)_3$], 1.63 (d, $J = 13.5$, PCH_3), 7.40–7.89 (m, Ar).

Table 2 Phosphinic amides **4a–c**,**h** prepared by the photolysis of phosphabicyclooctene **1** with secondary amines

Product	δ_P($CDCl_3$)	MS, *m/z* (rel. int.%)
5h	36.2	211 (M^+, 4), 196 (M − 15, 35), 139 (M − NEt_2, 100), 77 (Ph, 15), 72 (NEt_2, 71)
5a	36.3	239 (M^+, 3), 210 (M − Et, 87), 139 (M − NPr_2, 100), 100 (NPr_2, 13) 77 (Ph, 13)
5b[a]	34.6	239 (M^+, < 1), 182 (M − Me − Pr + H, 100), 139 (M − NPr_2, 98), 77 (Ph, 18)
5c	36.4	267 (M^+, 3), 224 (M − Pr, 80), 182 (224 − Pr + H, 46), 139 (M − NBu_2, 100), 128 (NBu_2, 23), 77 (Ph, 10)

[a] M + H = 240 was confirmed by CI-MS.

^{31}P NMR. The significant impact of the nucleophilic character of the reagent on the product ratio may suggest at least the partial involvement of pentacoordinated intermediate **6** and hence concurrent AE mechanism (Scheme 3). The methylene phosphine oxide **5** formed in the EA mechanism should not differentiate between the amine and the alcohol to the high extent observed. The photolysis of **1** in the presence of ethanolamine was also carried out (Scheme 4). ^{31}P NMR analysis of the reaction mixture suggested the formation of phosphinic amide **7** (δ_P 34.6, 66%) and phosphinic ester **8** (δ_P 41.1, 34%) in a clean reaction. The 66 : 34 product ratio found for amide **7** and ester **8** also seems to confirm the involvement of the AE mechanism, otherwise there should not be so significant selection between the two nucleophilic centers of the ethanolamine molecule.



Scheme 4

It can be concluded that using primary amines as nucleophiles, both the EA and the AE reaction paths may be involved in the fragmentation of cycloadduct **1** to give phosphinic amides **3**.

Experimental

The ^{31}P NMR spectra were taken on a Bruker DRX-500 spectrometer operating at 202.4 MHz. Chemical shifts are downfield relative to 85% H_3PO_4. GC–MS was performed on a Fisons GC 8000/MD 800 apparatus.

General Procedure for the Synthesis of Phenyl(methyl)phosphinic Amides **3a–e**.—A solution of 0.10 g (0.243 mmol) of precursor **1** consisting of 61% of isomer **A** and 39% of isomer **B** in 45 ml of dry acetonitrile and 4 ml of the corresponding primary amine was irradiated in a photochemical reactor with a mercury lamp (125 W) for 3.5 h. Volatile components were removed and the residue obtained purified by flash column chromatography (silica gel, 3% methanol in chloroform) to give the corresponding phosphinic amides **3a–e** (Table 1). The dialkylamines were phosphorylated under similar conditions but applying an irradiation time of 7 h (Table 2).

The phosphorylation of ethanolamine was carried out similarly to give a 66–34% mixture of amide **7** and ester **8** (δ 34.6 and 41.1, respectively) in 85% yield after flash column chromatography (silica gel, 3% methanol in chloroform). The integrity of the sample was confirmed by TLC. $(M+H)^+_{found} = 200.0832$ $C_9H_{15}NO_2P$ requires 200.0840.

We thank the Ministry of Higher Education for financing this project (Grant No. FKFP 0363/1999). The OTKA support is also acknowledged (Grant No. T029039).

Received, 14th May 1999; Accepted, 14th June 1999
Paper E/9/03858B

References

1 L. D. Quin, S. Jankowski, G. S. Quin, A. Sommese, J-S. Tang and X.-P. Wu, in *ACS Symposium Series 486: Phosphorus Chemistry, Developments in American Science*, ed. E. N. Walsh, E. J. Griffith, R. W. Parry and L. D. Quin, ACS, Washington, DC, 1992, p. 115.
2 L. D. Quin, J-S, Tang, G. S. Quin and Gy. Keglevich, *Heteroatom. Chem.,* 1993, **4**, 189.
3 Gy. Keglevich, K. Steinhauser, K. Ludányi and L. Tőke, *J. Organomet. Chem.,* 1998, **570**, 49.
4 Gy. Keglevich, K. Steinhauser, Gy. M. Keserű, Zs. Böcskei, K. Újszászy, Gy. Marosi, I. Ravadits and L. Tőke, *J. Organomet. Chem.,* 1999, **579**, 182.
5 L. Horner and R. Gehring, *Phosphorus, Sulfur,* 1982, **12**, 295.
6 O. Korpiun, R. A. Lewis, J. Chickos and K. Mislow, *J. Am. Chem. Soc.*, 1968, **90**, 4842.
7 R. S. Edmundson, in *Comprehensive Organic Chemistry*, ed. D. Barton and W. D. Ollis, 1979, vol. 2, ch. 10.5 (vol. ed. I. O. Sutherland), Pergamon, Oxford, p. 1291.