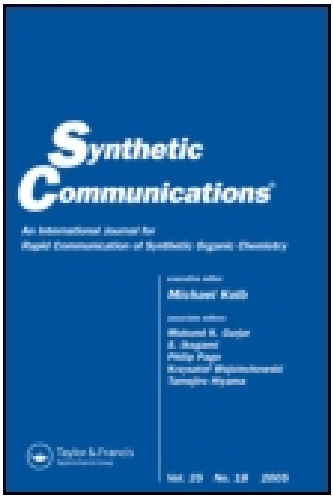

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Synthesis of H-Phosphinates by the UV Light-Mediated Fragmentation-Related Phosphorylation Using Simple P-Heterocycles

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Synthesis of H-Phosphinates by the UV Light–Mediated Fragmentation-Related Phosphorylation Using Simple P-Heterocycles

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Abstract: Photolysis of aryl-substituted 2,5-dihydrophosphole oxides (**5a–e** and **8**) in the presence of methanol afforded methyl aryl-H-phosphinates (**2a–e**) in good yields. In the case of 1-ethyl-, cyclohexyl-, or ethoxy-2,5-dihydrophosphole oxides, the reaction was much slower (**5f** and **5h**) or did not take place at all (**5g**). In such instances, the presence of an additional skeletal methyl group (**7**) or the use of the more strained 7-phosphanorbornene derivatives (**6**) promoted the fragmentation-related phosphorylations. Furthermore, the effect of the ring saturation in **8** and the possible extensions to 2-phosphabicyclo[3.1.0]hexanes (**10a** and **10f**), a 1,2-dihydrophosphinine oxide (**11**), and a 1,2,3,4,5,6-hexahydrophosphinine oxide (**12**) were also investigated. Model compounds with P-phenyl substituent that are of sufficient ring strain (**8**, **10a**, and **11**) could be utilized well.

Keywords: Photolysis, fragmentation, P-heterocycles, H-phosphinates

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INTRODUCTION

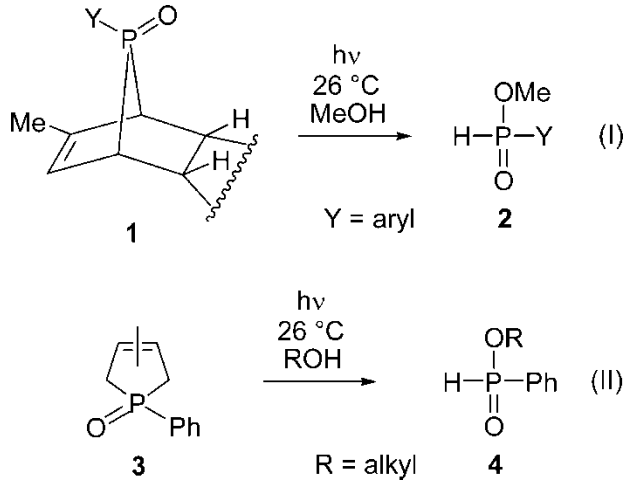
7-Phosphanorbornene derivatives, such as 7-oxides and 7-sulfides, are useful in the synthesis of H-phosphinates and H-thiophosphinates. Irradiation of the bridged precursors in the presence of an alcohol led to the formation of the corresponding phosphorylated products [Scheme 1(I)].[1–4] The early methods made available mainly phenyl-H-(thio)phosphinates; later the method was extended to aryl-H-phosphinates.[5,6]

It is noteworthy that simple 1-phenyl-2,5-dihydrophosphole oxides could also be used in the UV light–induced fragmentation-related phosphorylation of alcohols [Scheme 1(II)].[7,8] Although this is an excellent way for the synthesis of phenyl-H-phosphinates, the scope of the method is rather limited. We wished to study the possible extensions in detail.

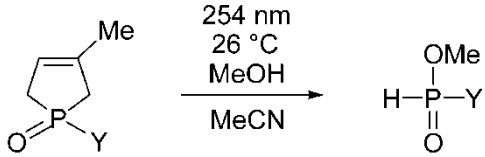
Tomioka et al. suggested an elimination–addition mechanism involving a phosphenite/phosphinidene oxide [PhP(O)] intermediate.[7,8] Quin et al. later proved that the real intermediate is, as a matter of fact, an adduct formed by the addition of the alcohol on the P═O group.[9]

RESULTS AND DISCUSSION

We aimed to synthesize aryl-H-phosphinates; a few aryl-2,5-dihydro-1H-phosphole oxides (**5b**–**e**)[10–12] were irradiated at 254 nm in acetonitrile, in the presence of methanol. As a comparison, the reaction of the phenyl-dihydro-1*H*-phosphole oxide (**5a**) was also carried out. The corresponding H-phosphinates (**2a**–**e**) were obtained in good (68–93%) yields after flash column chromatography (Scheme 2).



Scheme 1. Refs. [1–4,7,8]



5 **2**

Y	Reaction time [h]	Yield [%]
C_6H_5 (**a**)	1	93
4-MeC_6H_4 (**b**)	1	90
2-MeC_6H_4 (**c**)	1	88
2,4,6-triMeC_6H_2 (**d**)	1.5	72[a]
2,4,6-tri^{i}PrC_6H_2 (**e**)	1.5	68[b]

[a] as a 7-2-1 mixture of three isomers
[b] as a 6-2-1-1 mixture of four isomers

Scheme 2.

The products (**2a**–**e**) were identified by ^{31}P NMR chemical shifts, $^1J_{PH}$ couplings, and FAB-MS (Table 1).

The 2,4,6-trialkylphenyl products (**2d** and **2e**) were obtained as the mixture of a major and minor isomers that was confirmed by GC-MS. The formation of isomers may be the consequence of the migration of the alkyl groups in the aromatic ring under photochemical conditions.

Aryl-H-phosphinates **2a**, **2b**, and **2e** were described earlier in the literature.[5,9,13] The new products **2c** and **2d** were fully characterized (see Table 1).

We tried to extend this method to the photolysis of the 1-cyclohexyl- and the 1-ethyl-dihydro-1*H*-phosphole oxides (**5f**[14] and **5g**[15]) in the presence of methanol. In the first case, the reaction was rather slow (Scheme 3), whereas in the second instance, **5g** was regenerated unchanged. Consequently, ethyl-H-phosphinate **2g** had to be prepared by the irradiation of the mixture of 7-phosphanorbornene **6** and methanol (Scheme 4).

Both H-phosphinates (**2f** and **2g**) are known compounds.[16,17] The δ_P chemical shifts around 45 ppm confirm their structure.[18] Unreactivity of **5g** was in accord with earlier observations on 1-alkyl-dihydro-1*H*-phosphole oxides.[19] For the characterization of products **2f** and **2g**, see Table 1.

An extension for the preparation of the ethyl methyl-H-phosphonate (**2h**) by the photolysis of the 1-ethoxy-dihydrophosphole oxide (**5h**) was not successful because the reaction was reluctant and hence rather slow. It was observed, however, that the model compound with an extra methyl group (**7**)[20] was more reactive in fragmentation-related phosphorylation leading to H-phosphonate **2h** within a reasonable reaction time (Scheme 5,

Table 1. Identification/characterization of the H-phosphinates prepared

Starting product	P-cycle	^{31}P NMR ($CDCl_3$) δ_P (lit.)	^{31}P NMR ($CDCl_3$) $^1J_{PH}$ (lit.) in Hz	FAB-MS $[M+H]^+$	Ref.
5a (**8**, **10a**, **11**)	**2a**	27.7 (26.8)	566.0 (568)	157	[9]
5b	**2b**[a]	28.0	565.5	171	[13]
5c	**2c**[b]	28.5	560.2	171	
5d	**2d**[c]	27.4	555.4	199	
5e	**2e**[d]	27.3 (26.9)	539.5 (551.0)	283	[5]
5f	**2f**	46.0 (46.7)	524.9 (521)	163	[16]
6 (**10g**)	**2g**	44.3	534.1	109	[17]
7	**2h**	9.0	697.1	125	[21]

[a] ^{13}C NMR δ ($CDCl_3$) 21.7 ($C_{4'}$–Me), 52.0 ($J = 6.6$, OCH_3), 125.9 ($J = 134.4$, $C_{1'}$), 129.5 ($J = 14.3$, $C_{3'}$)*, 131.0 ($J = 12.3$, $C_{2'}$)*, 144.0 ($C_{4'}$), [lit.,[13] 21.8 ($C_{4'}$–Me), 51.5 ($J = 7.1$, OCH_3), 126.1 ($J = 134.0$, $C_{1'}$), 129.5 ($J = 14.2$, $C_{3'}$)*, 131.0 ($J = 12.0$, $C_{2'}$)*, 143.9 ($C_{4'}$)]. *May be reversed.

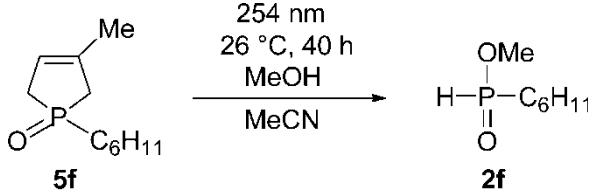
[b] ^{13}C NMR δ ($CDCl_3$) 20.1 ($J = 5.4$, $C_{2'}$–Me), 52.4 ($J = 6.9$, OCH_3), 125.0 ($J = 14.5$, $C_{5'}$)*, 127.2 ($J = 130.7$, $C_{1'}$), 131.1 ($J = 10.8$, $C_{3'}$)*, 131.9 ($J = 12.1$, $C_{6'}$)*, 133.0 ($C_{4'}$), 141.0 ($J = 11.5$, $C_{2'}$); ^{1}H NMR δ ($CDCl_3$) 2.56 (s, 3H, $C_{2'}$–CH_3), 3.80 (d, $J_{PH} = 10.5$, 3H, OCH_3), 7.30–7.85 (m, 4H, Ar–H), 7.60 (d, $J_{PH} = 559.7$, P–H); HR-FAB: $(M+H)^+_{found} = 171.0553$; $C_8H_{12}PO_2$ requires 171.0575. *May be reversed.

[c] As the mixture of a major (67%, see above) and two minor isomers [δ_P 30.7 (20%) and 28.8 (13%)]. For the major isomer ^{13}C NMR δ ($CDCl_3$) 19.8 ($C_{4'}$–Me), 20.9 ($J = 8.3$, $C_{2'}$–Me) 52.4 ($J = 6.4$, OCH_3), 128.3 ($J = 131.0$, $C_{1'}$), 130.2 ($J = 12.3$, $C_{3'}$), 142.0 ($J = 11.5$, $C_{2'}$), 142.9 ($C_{4'}$); HR-FAB: $(M+H)^+_{found} = 199.0870$; $C_{10}H_{16}PO_2$ requires 199.0888.

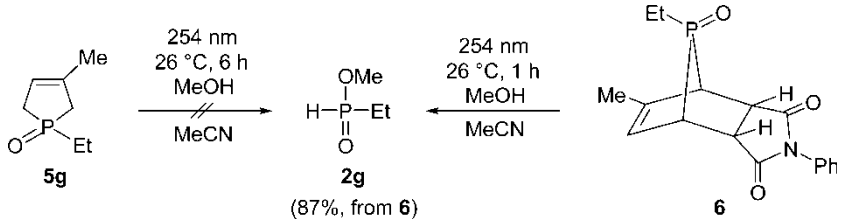
[d] As the mixture of a major (51%, see above) and three minor isomers [δ_P 34.2 (23%) and 30.6 (15%) and 26.4 (11%)].

Table 1). H-Phosphonate **2h** was described in the literature.[21] Its δ_P chemical shift and $^1J_{PH}$ coupling (see Table 1) fit the data (δ_P 5–9 and $^1J_{PH}$ 682–696 Hz) reported for analogous derivatives.[18]

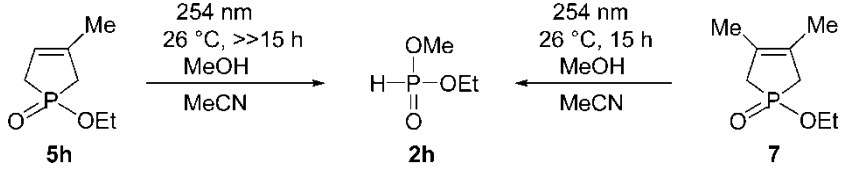
Although 2-methyl-1-phenyl-dihydro-1*H*-phosphole oxide **8**[22] was as efficient in the synthesis of H-phosphinate **2a** as the 3-methyl isomer (**5a**),



Scheme 3.



Scheme 4.



Scheme 5.

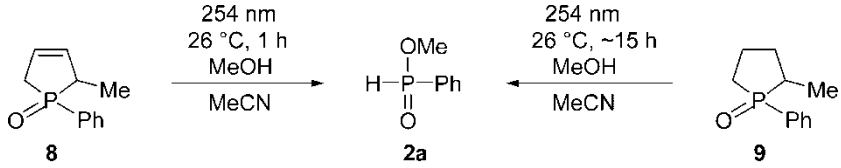
photolysis of the 1,2,3,4-tetrahydro derivative (**9**)[22] in the presence of methanol was much slower (Scheme 6).

It was interesting to find that P-phenyl 2-phosphabicyclo[3.1.0]hexane oxide (**10a**)[23] could be used as well as dihydrophosphole oxide **5a** for the preparation of H-phoshinate **2a**. At the same time, reaction of the P-ethyl phosphabicyclohexane (**10g**)[15] was reluctant (Scheme 7).

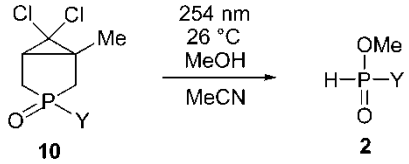
From this experiment it followed that the compound of type **10** is of significant ring strain, as was also observed earlier.[24]

Finally, we found that 1,2-dihydrophosphinine oxide **11**[25] was also a suitable precursor in the preparation of H-phosphinate **2a** (Scheme 8). At the same time, 1,2,3,4,5,6-hexahydrophosphinine oxide **12**[26] resisted undergoing photolysis in the presence of methanol. This is obviously due to the lack of ring strain. No fragmentation of the suitable P-cycles (e.g., **5**, **7**, **8**, **10**, and **11**) could be observed in the absence of methanol, confirming the addition–elimination mechanism involving intermediate **14** with a pentavalent pentacoordinated phosphorus atom (Scheme 9).

To summarize our results, the fragmentation-related phosphorylations were extended to simple precursors, such as aryl-2,5-dihydrophosphole



Scheme 6.



10 2

Y	Reaction time [h]	Yield [%]
Ph (**a**)	1	73
Et (**g**)	~20	not determined

Scheme 7.

oxides, 2-phosphabicyclo[3.1.0]hexane 2-oxides, and a 1,2-dihydrophosphinine oxide. The roles of structure and substitution pattern were evaluated.

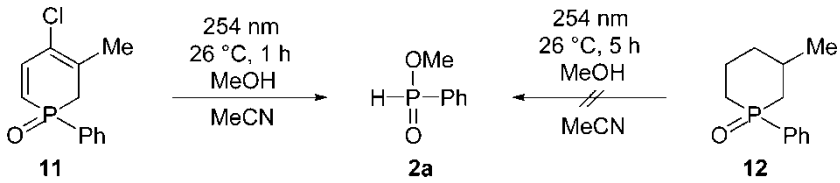
EXPERIMENTAL

General

The ^{31}P, ^{13}C, and ^{1}H NMR spectra were obtained 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. The couplings are given in Hz. Mass spectrometry was performed on a ZAB-2SEQ instrument. The starting P-heterocycles (**5a–h**, **6–12**) were synthesized as described earlier.[10–12,14,15,20,22–26]

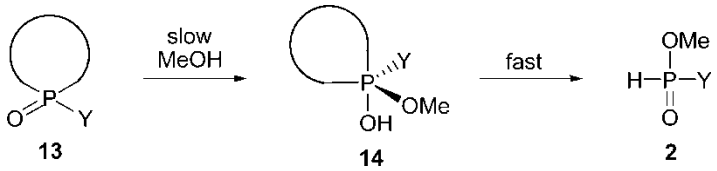
General Procedure for the Fragmentation-Related Phosphorylation of Methanol using a Variety of P-Heterocycles (5–11)

A solution of 0.52 mmol of the P-hetrocycle (**5–11**) in 45 ml of acetonitrile and 4.0 ml of methanol was irradiated by a mercury lamp (125 W) in a quartz reactor for the time shown in Schemes 2–8. Solvent was evaporated and the obtained crude product was purified by flash column chromatography



11 2a 12

Scheme 8.



Scheme 9.

(silica gel, 3% methanol in chloroform) to afford H-phosphinates **2a–h** (Table 1).

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