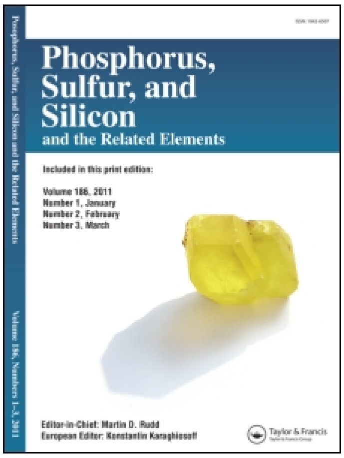

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PHOTODEPHOSPHORYLATION OF [(1-BENZYLPYRIDINO)METHYL]PHOSPHONIC ACIDS

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PHOTODEPHOSPHORYLATION OF [(1-BENZYLPYRIDINO)METHYL]PHOSPHONIC ACIDS

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Photolysis of [(1-benzylpyridino)methyl)]phosphonic acids in an alkaline aqueous solution gave 1-benzyl-methylpyridnium phosphates by the photocleavage of the C-P bond.

Key words: Photolysis; photodephosphorylation; [(1-benzylpyridino)methyl]phosphonic acids; diethyl (pyridylmethyl)phosphonate; 1-benzyl-methylpyridnium phosphates; *p*-nitrobenzylphosphonic acid.

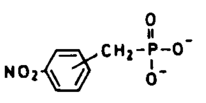
INTRODUCTION

The C—P bond of alkylphosphonic acids is generally inert to vigorously acidic and basic hydrolysis conditions.[1] Recently, the dephosphorylation of alkylphosphonic acids attracted much interest in connection with metabolism of naturally occurring alkylphosphonic acids and detoxification of herbicides, insecticides, and antibiotics that contain the phosphonic acid moiety.[2]

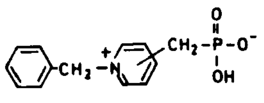
Previously, we have reported on photo-dephosphorylation of *p*-nitrobenzylphosphonic acid (**1**) in alkaline alcohol solution.[3] This mechanism has been offered: the radical anion produced by photo-intramolecular electron-transfer from the phosphono group to the nitrophenyl moiety undergoes homolytic C—P bond cleavage to give *p*-nitrobenzyl anion and monomeric metaphosphate anion,[4] followed by the reaction with alcohol to afford *p*-nitrotoluene and alkyl phosphate, respectively. The mechanism has received much attention owing to the similarity to that of photo-decarboxylation of *p*-nitrophenylacetate.[5]

In the course of these studies, we have discovered that upon irradiation in alkaline media, [(1-benzylpyridino)methyl-]phosphonic acid (**2**) also undergoes C-P bond cleavage to give 1-benzylpyridinium phosphate. It is of interest to learn if the similarities observed between pyridyl and nitrophenyl reactivities in some chemical reactions could be extended to a photo-dephosphorylation.[6]

The similar photodecarboxylation of pyridylacetic acid has been reported; irradiation of the 2-, 3-, and 4-pyridylacetic acids in aqueous solutions did indeed yield the corresponding 2-, 3-, 4-methylpyridines and CO_2.[7] In this case, electron transfer from the carboxylate to pyridinium salt chromophores is postulated.



(1a) o -
(1b) m -
(1c) p -



(2a) 2 -
(2b) 3 -
(2c) 4 -

RESULTS AND DISCUSSION

Irradiation of **2a**, **2b**, and **2c** in alkaline aqueous solutions did indeed yield the corresponding 1-benzyl-methylpyridinium phosphates [**3a**, **3b**, and **3c**], respectively.

At lower pH values than about 7, the photoreaction slowed considerably. The quantum yield of dephosphorylation of each acid increased at or near the second dissociation point of **2** (pK_a^2 8.2–8.9) and reached a maximum yield near pH 9. At this point, the maximum quantum yields for the production of orthophosphate were: **2b**, 0.16; **2a**, 0.10; **2c**, 0.05, respectively (Figure 1).

This order of the reactivity differs from that found for **1** [**1c** > **1b** > **1a**[3]], although an intramolecular charge-transfer process similar to that of **1** can be written for the photochemical reaction of **2** (Scheme 1).[3,4]

The compound (**2c**) was much more difficult to dephosphorylate than was **2a** or **2b**. A large difference in the quantum yields between **2c** and **2b** could be accounted for by the following concept: in alkaline media, the equilibrium reaction (equation 1) might be expected to lie to the right a little and some part of

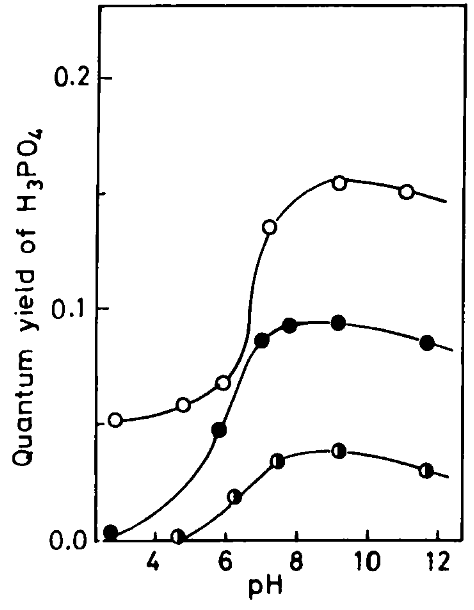
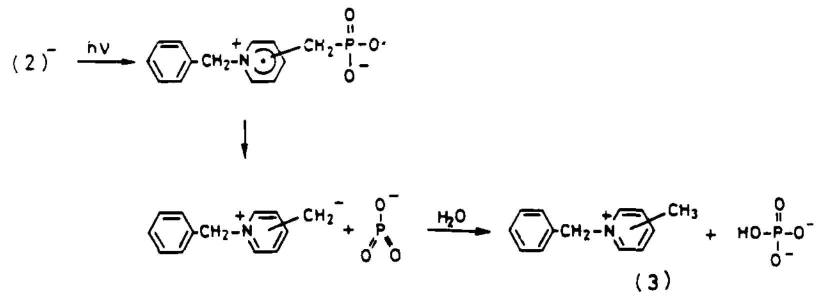


FIGURE 1 Effect of pH on quantum yield of **2**. pH's of the aqueous solutions of **2** (1.0×10^{-2} mol dm^{-3}) were adjusted with a NaOH aqueous solution (0.1 mol dm^{-3}). ● **2a**, ○ **2b**, ◑ **2c**.

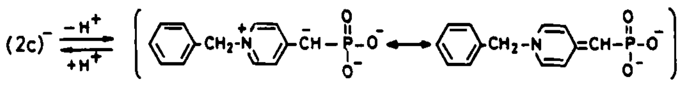


SCHEME 1

2c$^-$ can probably exist in a form $(\mathbf{2c})^{2-}$, which is the results of loss of positive charge density through the dissociation of a proton from the methylene group.

The presence of the structure $(\mathbf{2c})^{2-}$ as a ground-state species involved in the photo-reaction might reduce the efficiency of the C—P bond cleavage.

The compound (**2b**) appears not to form to such a deprotonated resonance structure.



$(2c)^{2-}$

These acids [**2a**, **2b**, and **2c**] showed absorbance peaks with maxima at 274, 269, and 237 nm at pH 5.0, in water, respectively. On going from acidic or neutral to alkaline media, **2c** displayed a color change with the appearance of a new absorption band at longer wavelength (257 nm, ε 13,000 dm^{-3} mol^{-1} cm^{-1}). This would indicate that in alkaline media a different intermolecular charge transfer process operates. The spectra of **2b** and **2a** did not display such a change. A fast proton/deuterium (H/D) exchange in the methylene group [CH_2—$PO(OH)_2$] and the slow exchange on the pyridine ring (position 3 and 5) of **2c** in alkaline deuterium oxide were observed. Such proton exchanges could not be observed on **2b**. The fast proton exchange is compatible with the structure $(\mathbf{2c})^{2-}$ drawn on the basis of UV absorption spectra change.

EXPERIMENTAL

Mp and bp were obtained with a Yanagimoto Micro Melting Point Apparatus and uncorrected. UV-visible spectra were recorded with a Hitachi 150-20 spectrometer with MeOH as solvent. ^{1}H NMR spectra were determined on a solution in D_2O with sodium 3-trimethylsilylpropanesulfonate (DSS) as an internal standard on a Bruker-AM360 spectrometer.

Preparation of [(1-Benzylpyridino)methyl]phosphonic acids (**2a**, **2b**, and **2c**). An ice-cooled benzene solution of chloromethylpyridine [from chloromethylpyridinium chloride (32.8 g, 0.20 mol) and 40% aqueous sodium hydroxide solution (13.3 ml)] was added dropwise to a benzene suspension of sodium diethyl phosphonate (0.22 mol) [from diethyl phosphite (30.3 g, 0.22 mol) and sodium (2.5 g, 0.22 mol)]. The mixture was refluxed for 2 h. The precipitate was removed by filtration, and after evaporation of the solvent, the residue was distilled *in vacuo* to give diethyl(pyridylmethyl)phosphonate (**3**, 33.0 g, 72%). A mixture of **3** (6.9 g, 30 mmol) and benzyl bromide (5.6 g, 33 mmol) in acetonitrile (50 ml) was stirred at ambient temperature. The reaction was complete after overnight stirring (monitored by ^{1}H NMR spectrometry), and then a mixture of lithium bromide (5.7 g, 66 mmol) of trimethylsilyl chloride (7.2 g, 66 mmol) was added to the mixture, which was refluxed for 4 h. After the precipitated lithium chloride was filtered, the solvent and ethyl bromide were distilled off by means of an aspirator. The residue was hydrolyzed with water. The crude product was purified with HPLC using Dowex 1X4 (200–400 mesh, OH form). Aqueous acetic acid (0.1 N) was used as an eluent. A pure product was obtained by recrystallization from water.

[(1-Benzylpyridino)-2-methyl]phosphonic acid (**2a**), 5.4 g (68%), m.p. (d.p.) 142–145°C, pK_a^1 4.6, pK_a^2 8.2, UV/λ max(H_2O) 274 nm (ε 6200 dm^{-3} mol^{-1} cm^{-1}), ^1H NMR (D_2O, DSS) $\delta_H = 3.46$ (2H, d, J_{HP} 18.9 Hz, CH_2P), 5.89 (2H, s, CH_2Ph), 7.1–7.4 (5H, m, Ph), 7.6–8.7 (4H, m, Py) (Found: C, 59.11; H, 5.41; N, 5.18; P, 11.70. $C_{13}H_{14}NPO_3$ requires C, 59.32; H, 5.36; N, 5.32; P, 11.77%).

[(1-Benzylpyridino)-3-methyl]phosphonic acid (**2b**), 4.4 g (56%), m.p. (d.p.) 265–267°C, pK_a^1 4.6, pK_a^2 8.7, UV/λ max(H_2O) 269 nm (ε 4500 dm^{-3} mol^{-1} cm^{-1}), ^1H NMR (D_2O, DSS) $\delta_H = 3.12$ (2H, d, J_{HP} 18.9 Hz, CH_2P), 5.70 (2H, s, CH_2Ph), 7.40 (5H, s, Ph), 7.8–8.7 (4H, m, Py) (Found: C, 59.27; H, 5.51; N, 5.29; P, 11.68. $C_{13}H_{14}NPO_3$ requires C, 59.32; H, 5.36; N, 5.32; P, 11.77%).

[(1-Benzylpyridino)-4-methyl]phosphonic acid (**2c**), 5.6 g (71%), m.p. (d.p.) 166–167°C, pK_a^1 4.3, pK_a^2 8.9, UV/λ_{max}(H_2O) 237 nm(ε 12,000 dm^{-3} mol^{-1} cm^{-1}), ^1H NMR (D_2O, DSS) $\delta_H = 3.03$(2H, d, J_{HP} 18.9 Hz, CH_2P), 5.55(2H, s, CH_2Ph), 7.33(5H, s, Ph), 7.52[2H, d, $J_{HH} = 7.0$ Hz, Py(3-, 5-)], 8.40[2H, d, $J_{HH} = 7.0$ Hz, Py(2-, 6-)] (Found: C, 59.42; H, 5.31; N, 5.26; P, 11.62. $C_{13}H_{14}NPO_3$ requires C, 59.32; H, 5.36; N, 5.32; P, 11.77%).

General Procedure for Photolysis of **2** A 3-ml sample of an aqueous solution of **2** (1.0×10^{-2} mol dm^{-3}) was added to a quartz tube ($\phi = 10$ mm) (if in alkaline media, the solution was adjusted at prescribed pH with 10% aqueous NaOH) and purged of dissolved air by bubbling with argon gas. It was irradiated with a merry-go-round apparatus using a high pressure mercury lamp (300 W) at ambient temperature for 8 h. After irradiation the mixture was sampled for analysis of ^1H and ^{31}P NMR. The products were analyzed by comparison with data of authentic samples prepared by an usual method. 1-Benzylmethyl-pyridinium phosphate (**3**) formed. The compounds **2a**, **2b**, and **2c** gave 1-benzyl-2-methylpyridinium phosphate [**3a**, 68%, ^1H NMR (D_2O, DSS, pH 4.5) $\delta_H = 2.66$(3H, s, Me), 5.71(2H, s, CH_2), 7.37(5H, s, Ph), 7.80–8.69(4H, m, Py), ^{31}P NMR (H_2O, PPh_3, pH 10) $\delta_P = 4.8$(s)], 1-benzyl-3-methylpyridinium phosphate [**3b**, 92%, ^1H NMR (D_2O, DSS, pH 4.5) $\delta_H = 2.38$(3H, s, Me), 5.65(2H, s, CH_2), 7.38(5H, s, Ph), 7.83–8.61(4H, m, Py), ^{31}P NMR (H_2O, PPh_3, pH 10) $\delta_P = 4.7$(s)], and 1-benzyl-4-methylpyridinium phosphate [**3c**, 87%, ^1H NMR (D_2O, DSS, pH 4.5) $\delta_H = 2.64$(3H, s, Me), 5.70(2H, s, CH_2), 7.43(5H, s, Ph), 7.86[2H, d, $J_{HH} = 6.0$ Hz, Py(3-, 5-)], 8.73[2H, d, $J_{HH} = 7.0$ Hz, Py(2-, 6-)], ^{31}P NMR (H_2O, PPh_3, pH 10) $\delta_P = 4.8$(s)] were obtained, respectively. the other photolysis product could not be detected by TLC analysis.

Measurement of the quantum yield The quantum yield was on the basis of generated orthophosphate. A 3-ml aqueous solution of **2** (1.0×10^{-2} mol dm^{-3}) in a quartz cell (10 mm × 10 mm) was irradiated (the pH of the solution was adjusted to 12 with 10% NaOH aqueous solution). A low-pressure mercury lamp (60 W) with a Vycor glass filter was used as the 254-nm radiation source. The yields of orthophosphate were measured by heteropoly blue method.[8] A ferric oxalate solution was used for actinometry.[9] The photolyses were carried out at the conversions less than 5%.

D/H-Exchange of **2** A 0.3-ml NaOD/D_2O solution (1.0 mol dm^{-3}) was added to a 0.5-ml D_2O solution of **2** (15 mg) at 15°C, (pH 12–13) and the H/D ratios were measured by ^1H NMR spectromtery. In the case of **2c**, the methylene signal of (CH_2-P) disappeared immediately. Further H/D exchange on the pyridine ring occurred after 1 h. Such a D/H exchange could not be observed on **2b**.

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