Photolysis of Pyridylmethyl- and Pyridiniomethylphosphonic Acids

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Synopsis. Upon UV-irradiation, the C-P bond of (4-pyridylmethyl)phosphonic acid cleaved only near the isoelectronic point to give 4-methylpyridinium phosphate, while (1-benzyl-4-pyridiniomethyl)phosphonic acid underwent C-P bond cleavage above pH 4 to give 1-benzyl-4-methylpyridinium phosphate. On the other hand, the C-P bond of (2-pyridylmethyl)phosphonic acid cleaved under pH region of about 1 to 2, while (1-benzyl-2-pyridiniomethyl)phosphonic acid underwent C-P bond cleavage above pH 4.

Recently, the dephosphorylation of alkylphosphonic acids attracted much interest.[1] Photo-dephosphorylation of *p*-nitrobenzylphosphonic acid was recently thoroughly studied.[2] The similar reaction has been observed in photolysis of (1-alkyl-4-pyridiniomethyl)phosphonic acid.[3] In these cases, the C-P bond cleavage occurred only at the state of complete dissociation of acid group under alkaline conditions, because of increasing of electron-donating ability of the acid group.[4] We found that the C-P bond cleavage of (4-pyridylmethyl)phosphonic acid (**1a**) did not occur under alkaline conditions but occurred near its isoelectronic point. The photochemical behaviors of other positional isomers of (3-pyridylmethyl)- (**1b**) and (2-pyridylmethyl)phosphonic acid (**1c**), were found to be different from that of **1a**.

In this report we wish to describe the photolysis of pyridylmethyl- (**1**) and (1-benzylpyridiniomethyl)-phosphonic acids (**2**).

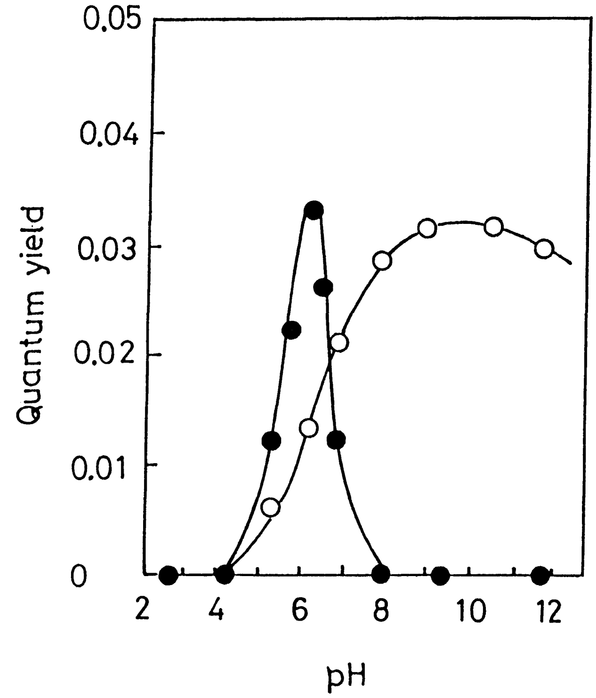
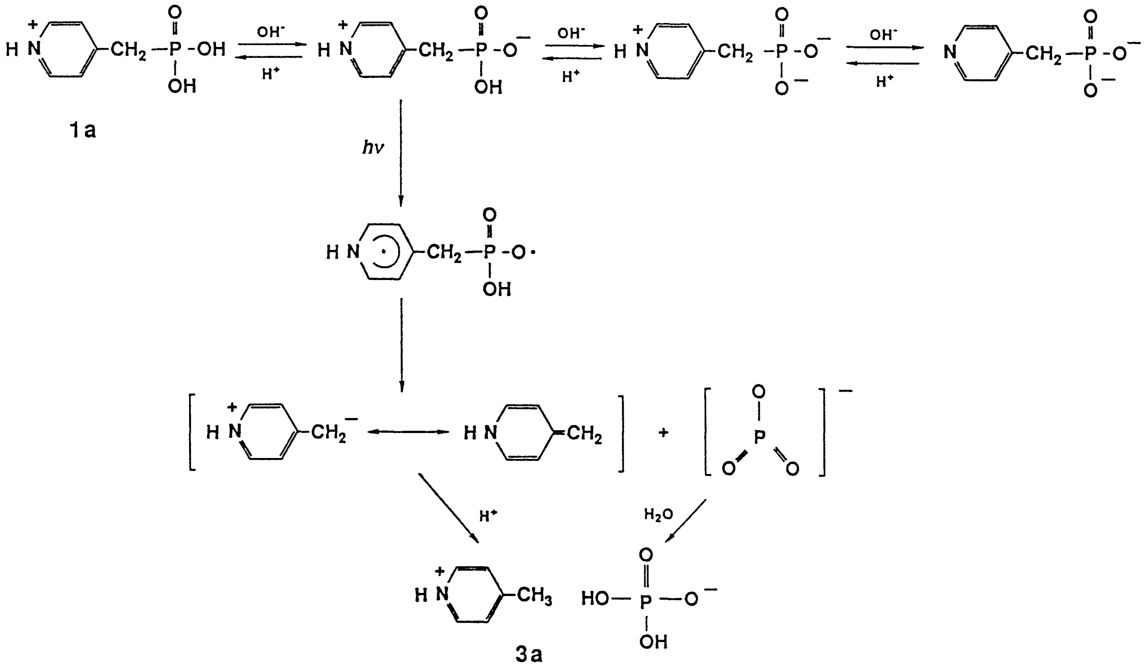


Fig. 1. Effect of pH on quantum yields for production of orthophosphate from **1a** and **2a**. pH's of the aqueous solutions of **1a** and **2a** (1.0×10^{-2} mol dm^{-3}) were adjusted with a NaOH aqueous solution (0.1 mol dm^{-3}). **1a**; ●, **2a**; ○.



Scheme 1.

Results and Discussion

Upon UV-irradiation, (4-pyridylmethyl)phosphonic acid (**1a**) underwent the C-P bond cleavage to give 4-methylpyridinium phosphate (**3a**) only near the isoelectric point (pH 6.0—6.2) with a maximum quantum yield of 3.4×10^{-2} at pH 6.0, while the C-P bond cleavage of (1-benzyl-4-pyridiniomethyl)-phosphonic acid (**2a**) occurred to give 1-benzyl-4-pyridinium phosphate (**4a**) above pH 4 and reached at a maximum quantum yield of 3.3×10^{-2} at pH 9, as shown in Fig. 1.

In the case of **1a**, the donor ability of phosphonic acid moiety increased with an increase of pH. While electron acceptability of the pyridine moiety much increased by the protonation of the nitrogen atom. Therefore, at the isoelectronic point photo-intramolecular electron transfer may be facilitated. Similar photodecarboxylation of pyridylacetic acids has been reported,[5,6] in which the rates of decarboxylation of the acids were maxima at or near the isoelectric point (pH 4.0—4.2).

The C-P bond of (2-pyridylmethyl)phosphonic acid (**1c**) began to cleave to give 2-methylpyridine and orthophosphate at pH 11, and the quantum yield of the bond cleavage gradually increased with lowering pH of the solution and reached at a maximum value of 0.16 under pH 3. This is a first example of photochemical C-P bond cleavage of alkylphosphonic acid under acidic conditions, to the best of our knowledge. On the other hand, (1-benzyl-2-pyridiniomethyl)-phosphonic acid (**2c**) underwent C-P bond cleavage above pH 3 to give the corresponding 1-benzyl-2-methylpyridinium phosphates (**4c**) and its quantum yield increased with an increase of pH and reached to 0.10 (Fig. 2).[4]

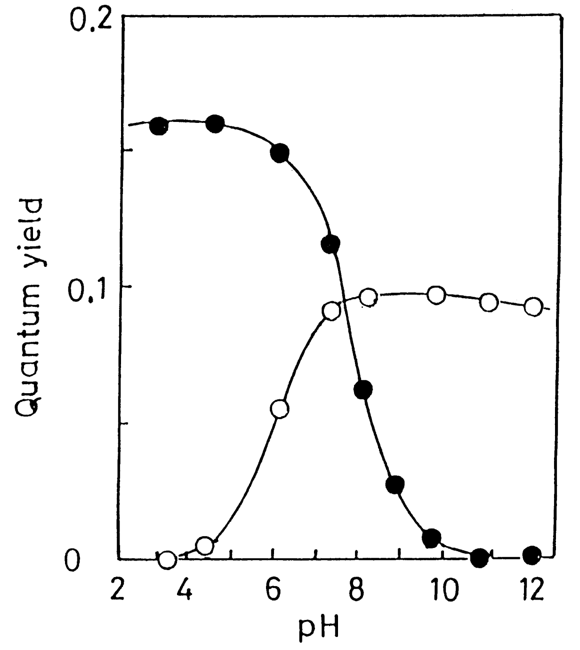
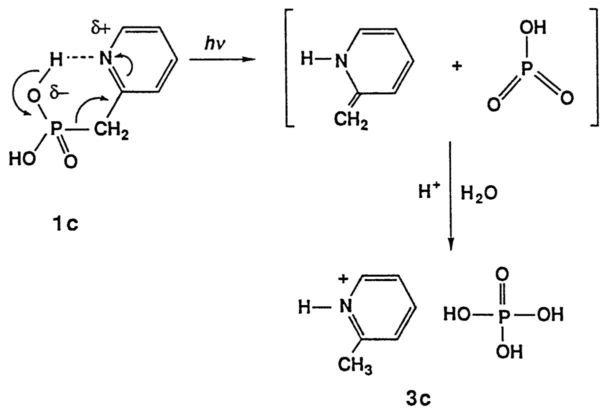


Fig. 2. Effect of pH on quantum yields for production of orthophosphate from **1c** and **2c**. pH's of the aqueous solutions of **1c** and **2c** (1.0×10^{-2} mol dm^{-3}) were adjusted with a NaOH aqueous solution (0.1 mol dm^{-3}). **1c**; ●, **2c**; ○.



Scheme 2.

A large difference of behavior of dephosphorylation between **1a** and **1c** might point to an importance of Scheme 2, in which the unusually high reactivity of the 2-isomer can be postulated with photo-migration of proton (or photo-electron transfer as shown with arrows) in the cyclic intermediate illustrated.

A similar mechanism to that speculated for the photolysis of **1c** was proposed for enhanced C-C bond photocleavage of 2-(2-pyridyl)ethanol.[5]

Upon UV-irradiation under alkaline conditions (3-pyridylmethyl)phosphonic acid (**1b**) was also stable, although in acidic media, it decomposed to give orthophosphoric acid in high quantum yield of 0.23, but 3-methylpyridinium phosphate was not detected, but a very complex mixture was obtained, which can not be confirmed yet. The photolysis of **1b** may proceed by a different route from that in photolysis of **1a** or **1c**. (1-Benzyl-3-pyridiniomethyl)phosphonic acid (**2b**) underwent photochemical C-P bond cleavage under alkaline conditions (pH>7) at high quantum yield of 0.26 to give 1-benzyl-3-methylpyridinium phosphate (**4b**). The photolysis of **2b** may proceed in the similar route as that in photolysis of **2a** or **2c**.

Experimental

^{1}H NMR spectra were determined on a solution in D_2O with sodium 3-trimethylsilyl-1-propanesulfonate (DSS) as an internal standard on a Bruker-AM360 spectrometer.

Preparation of Pyridylmethylphosphonic Acids (1a, 1b, and 1c). Typical Precedure: An ice-cooled benzene solution of 4-(chloromethyl)pyridine [from 4-(chloromethyl)-pyridinium chloride (32.8 g, 0.20 mol) and 40% aqueous sodium hydroxide solution (13.3 ml)] was added dropwise to suspension of sodium diethyl phosphonate (0.22 mol) [from diethyl phosphonate (30.3 g, 0.22 mol) and sodium (2.5 g, 0.22 mol)] in benzene. 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 (4-pyridylmethyl)phosphonate (**5a**), bp 120—125 °C (0.1 mmHg, 1 mmHg≈133.322 Pa), yield 33.0 g (72%). A mixture of lithium bromide (5.7 g, 66 mmol) and trimethylsilyl chloride(7.2 g, 66 mmol) was added to **5a** [6.9 g, 30 mmol in acetonitrile (50 ml)]. The mixture was refluxed for 4 h. After the precipitated lithium chloride was filtered off, 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 1×4 (200—400 mesh, OH form). Aqueous acetic acid (0.1 M, M=mol dm^{-3}) was used as an eluent. A pure product of **1a** was obtained by recrystallization from water.

(4-Pyridylmethyl)phosphonic Acid (1a). Mp (dp) 195—198 °C, UV max (H_2O) 230 nm (ε 4,800 dm^{-3} mol^{-1} cm^{-1}); ^{1}H NMR (D_2O, DSS) δ=2.73 (2H, d, J_{HP}=21.6 Hz, CH_2), 7.2—8.2 (4H, m), pK_a^1 4.0, pK_a^2 6.8, pK_a^3 8.9. Found: C, 41.90; H, 4.53; N, 8.24; P, 17.98%. Calcd for $C_6H_8NPO_3$: C, 41.63; H, 4.66; N, 8.09; P, 17.89%.

(3-Pyridylmethyl)phosphonic Acid (1b). Mp (dp) 225—227 °C, UV max (H_2O) 264 nm (ε 6,200 dm^{-3} mol^{-1} cm^{-1}); ^{1}H NMR (D_2O, DSS) δ=2.66 (2H, d, J_{HP}=18.9 Hz, CH_2), 7.1—8.3 (4H, m), pK_a^1 4.1, pK_a^2 6.8, pK_a^3 9.3. Found: C, 41.76; H, 4.73; N, 7.87; P, 17.75%. Calcd for $C_6H_8NPO_3$: C, 41.63; H, 4.66; N, 8.09; P, 17.89%.

(2-Pyridylmethyl)phosphonic Acid (1c). Mp (dp) 285—287 °C, UV max (H_2O) 267 nm (ε 8,300 dm^{-3} mol^{-1} cm^{-1}); ^{1}H NMR (D_2O, DSS) δ=3.37 (2H, d, J_{HP}=21.6 Hz, CH_2), 7.7—8.6 (4H, m), pK_a^1 4.2, pK_a^2 6.8, pK_a^3 9.2. Found: C, 41.58; H, 5.72; N, 8.23; P, 18.04%. Calcd for $C_6H_8NPO_3$: C, 41.63; H, 4.66; N, 8.09; P, 17.89%.

Preparation of (1-Benzylpyridiniomethyl)phosphonic Acids (2a. 2b, and 2c). Typical Procedure: A mixture of **5a** (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 an overnight stirring (monitored by ^{1}H NMR spectrometry), and then lithium bromide (5.7 g, 66 mmol) and trimethylsilyl chloride (7.2 g, 66 mmol) were added to the mixture. The mixture was refluxed for 4 h. After the precipitated lithium chloride was filtered off, the solvent and ethyl bromide were distilled off by means of an aspirator. The residue was hydrolyzed with water. The crude product was purified as described above.

(1-Benzyl-4-pyridiniomethyl)phosphonic Acid (2a). 5.6 g (71%), mp (dp) 166—167 °C, pK_a^1 4.3, pK_a^2 8.9, UV max(H_2O) 237 nm (ε 12000 dm^{-3} mol^{-1} cm^{-1}); ^{1}H NMR (D_2O, DSS) δ=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_{HP}=7.0 Hz, Py (2-, 6-)]. Found: C, 59.42; H, 5.31; N, 5.26; P, 11.62%. Calcd for $C_{13}H_{14}NPO_3$: C, 59.32; H, 5.36; N, 5.32; P, 11.77%.

(1-Benzyl-3-pyridiniomethyl)phosphonic Acid (2b). 4.4 g (56%), mp (dp) 265—267 °C, pK_a^1 4.6, pK_a^2 8.7, UV max(H_2O) 269 nm (ε 4500 dm^{-3} mol^{-1} cm^{-1}); ^{1}H NMR (D_2O, DSS) δ=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%. Calcd for $C_{13}H_{14}NPO_3$: C, 59.32; H, 5.36; N, 5.32; P, 11.77%.

(1-Benzyl-2-pyridiniomethyl)phosphonic Acid (2c). 5.4 g (68%), mp(dp) 142—145 °C, pK_a^1 4.6, pK_a^2 8.2, UV max (H_2O) 274 nm (ε 6200 dm^{-3} mol^{-1} cm^{-1}); ^{1}H NMR (D_2O, DSS) δ=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%. Calcd for $C_{13}H_{14}NPO_3$: C, 59.32; H, 5.36; N, 5.32; P, 11.77%.

General Procedure for Photolysis of 1. A 3-ml of an aqueous solution of **1** (1.0×10^{-2} M) was placed in a quartz tube (ϕ=10 mm) (pH of the solution was adjusted with 1 M NaOH or 1 M HCl aqueous solution) and purged off 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 acidified with HCl aqueous solution, and water was evaporated in vacuo. The residue was identified by ^{1}H and ^{31}P NMR spectrometry by comparison with the data of an authentic sample which was commercially available.

The compounds **1a** and **1c** gave 4-methylpyridinium phosphate (**3a**) and 2-methylpyridinium phosphate (**3c**) in 86 and 82% yield, respectively. But **1b** gave orthophosphoric acid [yield 91%, ^{31}P NMR (H_2O, PPh_3, pH 10) δ=4.9 (s)] and the complex products, which could not be identified.

General Procedure for Photolysis of 2. Irradiation of an aqueous solution of **2** was carried out in the manner similar to that described above. The products were identified by comparison with data of authentic samples prepared by an usual method. The photolysis of compounds **2a**, **2b**, and **2c** gave 1-benzyl-4-methylpyridinium phosphate (**4a**, 87%), 1-benzyl-3-methylpyridinium phosphate (**4b**, 92%), and 1-benzyl-2-methylpyridinium phosphate (**4c**, 68%), respectively.

Measurement of the Quantum Yield. The quantum yields were determined on the basis of generated orthophosphate. A 3 ml aqueous solution of **2** (1.0×10^{-2} M) in a quartz cell (10 mm×10 mm) was irradiated. A low-pressure mercury lamp (60 W) with a Vycor glass filter was used as a 254 nm radiation source. The yields of orthophosphate were measured by heteropoly blue method.[7] A potassium trioxalatoferrate solution was used for actinometry.[8] The photolyses were carried out at the conversions less than 5%.

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