ALKYL AND ALKENYL-PYRIDINES. XIX.*

DIETHYL-2 AND 4-PYRIDYLMETHYLPHOSPHONATE 1-OXIDES AND THEIR APPLICATION TO SYNTHESIS OF 2- AND 4-ALKENYLPYRIDINE 1-OXIDES

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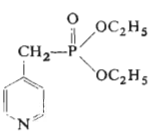
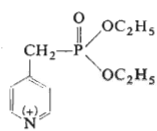
Alkenylpyridine 1-oxides can be used as convenient starting materials in the synthesis of compounds containing the pyridyl 1-oxido group including polymers and copolymers[1]. Known methods of preparation, such as direct oxidation of alkenylpyridines[2], dehydration of alkylpyridine alcohol 1-oxides[3] and condensation of picoline 1-oxides with aldehydes[4], suffer from limited application and often give low yields. Recently we outlined a simple approach to 2-, 3-, and 4-alkenylpyridines by a Wittig-Horner reaction of diethyl 2, 3 and 4-pyridylmethylphosphonates with aldehydes and ketones[5,6]. Now we wish to report some observations on the preparation of diethyl 2- and 4-pyridylmethylphosphonate 1-oxides *V* and *I* and their use in the synthesis of 2- and 4-alkenylpyridine 1-oxides *VI*.

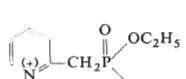
Diethyl 4-pyridylmethylphosphonate 1-oxide (*I*) can be prepared by oxidation of diethyl 4-pyridylmethylphosphonate[7] (*II*) with aqueous hydrogen peroxide in acetic acid to give a product of suffficient purity to be used directly for further transformations. This is important since the oxide *I* is thermally unstable and cannot be purified by distillation.



II

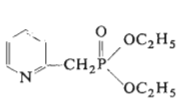


I

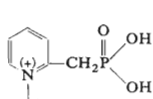


V

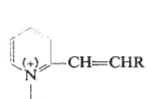
It is worthwhile to emphasize that oxidation of diethyl 2-pyridylmethylphosphonate[8] (*III*) under the same conditions results in the formation of 2-pyridylmethylphosphonic acid 1-oxide (*IV*).



III



IV



VI

* Part XVIII: Bull. Acad. Polon. Sci., Ser. Chim. *18*, 343 (1970).

The difference in behaviour of the two phosphonates *II* and *III* towards hydrolysis is most probably due to the fact that neighbouring group participation is possible for *III* but not for *II*. The proximity of nucleophilic oxygen to the phosphonyl centre in *III* allows formation of a pentacovalent intermediate and assists hydrolysis. A similar example of neighbouring group participation was recently reported[9].

The preparation of diethyl 2-pyridylmethylphosphonate 1-oxide (*V*) under the standard conditions of peracetic acid oxidation failed, but we successfully prepared *V* by an alternative synthetic route[10] using a Michaelis–Becker reaction between 2-chloromethylpyridine 1-oxide and sodium diethyl phosphite. The yield is almost quantitative and the product does not need purification. It is thermally unstable and, like its isomer *I*, decomposes violently at elevated temperatures.

Both oxides *I* and *V* readily give carbanions which undergo the Wittig-Horner reaction with aldehydes. To form 4- and 2-alkenylpyridine 1-oxides *VI* respectively addition of the substrates to a suspension of sodium hydride in boiling benzene appeared to be the best way of obtaining satisfactory yields. These reactions, like most other phosphonate modifications of the Wittig synthesis[11], are stereospecific. All the alkenyl pyridine 1-oxides obtained in this way were found to show IR absorption at 965–995 cm^{-1} which is characteristic of *trans*-configuration about the olefin bond.

EXPERIMENTAL

Diethyl 4-Pyridylmethylphosphonate 1-Oxide (*I*)

A mixture of the ester *II*, (40 g, 0·17 mol), hydrogen peroxide (17·6ml; 30% solution) and of glacial acetic acid (106 ml) was heated for 3·5 h at 75–80°C. Then additional hydrogen peroxide (12·5 ml; 30% solution) was added and heating was continued for 9 h. The acetic acid and water were evaporated off under reduced pressure, the residue was dissolved in water (80 ml), neutralized with sodium carbonate and extracted with chloroform (8 × 50 ml). The extract was dried over magnesium sulphate. Evaporation of the solvent gave 42 g (98%) of the crude oxide *I*; IR (film) 1 250 cm^{-1} (N—O); NMR δ_{CH_2} 3·22 (2 H, d, J_{PH} 22·5 Hz). For $C_{10}H_{16}NO_4P$ (245·1) calculated: 12·6% P; found: 12·2% P.

2-Pyridylmethylphosphonic Acid 1-Oxide (*IV*)

Ester *III* (5 g; 0·22 mol) was oxidized in the same way as described above. Exaporation of the acetic acid and water afforded 4·8 g (90%) of the oxide (*IV*); m.p. 224–228°C (dec.) (ethanol); IR (nujol): 1 250 cm^{-1} (N—O); NMR δ_{CH_2} 3·61 (2 H, d, J_{PH} = 21 Hz). For $C_6H_8NO_4P$ (188·0) calculated: 38·1% C, 4·2% H, 7·4% N, 16·4% P; found: 38·0% C, 4·3% H, 7·0% N, 16·2% P.

Diethyl 2-Pyridylmethylphosphonate 1-Oxide (*V*)

A solution of 2-chloromethylpyridine 1-oxide (13·5 g; 0·093 mol) in benzene was added dropwise to a suspension of sodium diethyl phosphite (16·1 g; 0·1 mol) in boiling benzene (50 ml). Heating was continued for 2 h. Then the solvent was evaporated under reduced pressure and water (50 ml) was added. The solution was extracted with chloroform (8 × 50 ml) and the extract was dried over magnesium sulphate. Evaporation of the solvent gave 17·5 g (77%) of the crude oxide *V*; IR 1 250 cm^{-1} (N—O); NMR δ_{CH_2} 3·74 (2 H, d, J_{PH} = 22·5 Hz). For $C_{10}H_{16}NO_4P$ (245·1) calculated: 12·6% P; found: 12·4% P.

2 and 4-Alkenylpyridine 1-Oxides *VI*

A solution of diethyl pyridylmethylphosphonate 1-oxide (0·02 mol) and the respective aldehyde (0·02 mol) in benzene (80 ml) was added dropwise to a suspension of sodium hydride (0·02 mol) in boiling benzene. Heating was continued for 3 h. Then hydrochloric acid (100 ml, 5% solution) was added and the water layer was separated, neutralized with sodium carbonate and extracted with chloroform (5 × 50 ml). The extract was dried over magnesium sulphate. Evaporation of the solvent gave the product which was purified either by distillation or by crystallization. The results are shown in Table I.

TABLE I

4- and 2-Alkenylpyridine 1-Oxides *VI*

Locant[a] R	Yield, % IR, cm^{-1}	M.p., °C (solvent)	Formula (m.w.)	Calculated/Found % C	% H	% N
2 —CH_3	48·5 973	[b]	C_8H_9NO (135·0)	71·1 71·0	6·7 6·4	10·3 10·2
4 CH_3	83·8 970	148—149 (benzene)	C_8H_9NO (135·0)	71·1 70·8	6·7 6·4	10·3 10·1
2 —CH=CHC_6H_5	76·0 995	170—171 (acetone)	$C_{15}H_{13}NO$ (223·2)	81·4 81·3	5·9 6·0	6·3 6·2
4 —CH=CHC_6H_5	65·5 990	196—198 (hexane–acetone)	$C_{15}H_{13}NO$ (223·2)	81·4 81·2	5·9 6·0	6·3 5·9
2 —C_6H_5	70·5 970	161—161·5[c] (benzene)	$C_{13}H_{11}NO$ (186·1)	79·3 78·9	5·6 5·6	7·1 6·8
4 —C_6H_5	72·5 968	171—172[d]	$C_{13}H_{11}NO$ (186·1)	79·3 78·9	5·6 5·8	7·1 6·9
2 4-Pyridyl	73·0 979	154—155 (benzene)	$C_{12}H_{11}N_2O$ (199·2)	72·7 72·5	5·1 5·1	14·1 14·0
4 4-Pyridyl	53·0 970	218—220 (benzene)	$C_{12}H_{11}N_2O$ (199·2)	72·7 72·3	5·1 5·0	14·1 13·9

[a] Position on the pyridine 1-oxide ring; [b] b.p. 98—100°C/0·04 Torr, ref.[3]; [c] ref.[2–4]; [d] from acetone-light petroleum ref.[2,4].

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EXPERIMENTS IN THE FURAN SERIES. XIII.*

INTERACTION OF SUBSTITUENTS ON THE FURAN NUCLEUS CAUSED BY ELECTRON IMPACT

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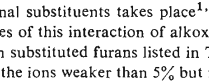
Systematic studies of furan derivatives[1,3] have shown that on fragmentation caused by electron impact mutual interaction of vicinal substituents takes place[1,2] (*ortho*-effect[4]). The aim of this paper is to point to certain features of this interaction of alkoxymethyl and carboxyl groups not yet observed. The spectra of seven substituted furans listed in Table I comprise all ions stronger than 5% of the base peak (100%); the ions weaker than 5% but relevant to the discussion are also given in Table I.



I, $R^1 = CH_3$; $R^2 = CH_3$; $R^3 = H$ *III*, $R^1 = CH_3$; $R^2 = C_2H_5$; $R^3 = CH_3$
II, $R^1 = CH_3$; $R^2 = CH_3$; $R^3 = CH_3$ *IV*, $R^1 = H$; $R^2 = C_2H_5$; $R^3 = CH_3$

* Part XII: This Journal *35*, 3478 (1970).