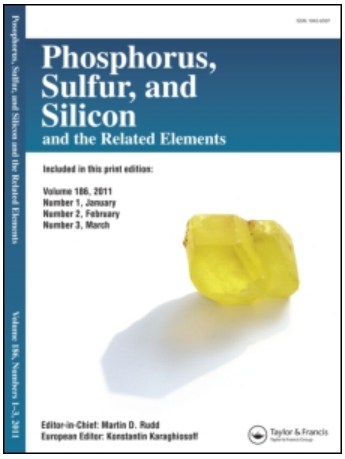

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ADDITION OF HYPOPHOSPHOROUS ACID TO α,β-UNSATURATED AMIDES

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ADDITION OF HYPOPHOSPHOROUS ACID TO α,β-UNSATURATED AMIDES

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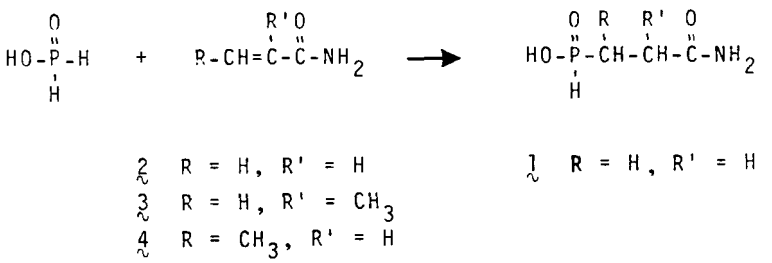
The reaction between hypophosphorous acid and acrylamide gave 2-carbamylethylphosphinic acid. Similar reactions involving methacrylamide and crotonylamide were not successful.

Hypophosphorous acid (phosphinic acid) adds to various compounds containing double bonds and these studies have been reviewed.[1-3] Up to the present the addition of hypophosphorous acid to α,β-unsaturated amides has not been investigated and no phosphinic acid containing an amido group in a side chain has been prepared. In this paper we report the synthesis of 2-carbamylethylphosphinic acid (**1**) by the addition of hypophosphorous acid to acrylamide (**2**) and the attempted preparation of its homologs using methacrylamide (**3**), with and without ethanol, and crotonylamide (**4**).



2 R = H, R' = H
3 R = H, R' = CH_3
4 R = CH_3, R' = H

1 R = H, R' = H

RESULTS AND DISCUSSION

The condensation reaction between hypophosphorous acid and acrylamide proceeded smoothly and was favored over acrylamide polymerization at the temperature employed. Since the free acid is utilized in this procedure the reaction temperature is limited to below 100°C. When higher melting **3** and **4** were heated with the acid at 100°C the mixtures vigorously evolved heat and fumes, assumedly due to the decomposition of hypophosphorous acid to flammable phosphine at this temperature. The reaction between hypophosphorous acid and methacrylamide using the described experimental conditions but with ethanol solvent gave only methacrylamide polymer as the product. Compound **1** was obtained in good yield and represents the sole example of a phosphinic acid possessing an amido side chain. This agent is a potential intermediate in the synthesis of the phosphinic acid

derivative of γ-aminobutyric acid which represents the closest phosphorus analogue of this inhibitory neurotransmitter. The product is very hygroscopic and decomposes at a relatively low temperature. Its structure was confirmed by IR and ^{1}H-NMR spectrometry and elemental analysis.

EXPERIMENTAL

The ^{1}H-NMR spectrum was measured on a Varian Associates FT-80A spectrometer using tetramethylsilane as the internal standard and deuterated dimethylsulfoxide as the solvent with chemical shifts reported in δ units and coupling constants in Hz. The IR (KBr) spectrum was obtained with a Perkin-Elmer 283 spectrophotometer and absorbances are reported in cm^{-1}. The elemental analysis was performed by Atlantic Microlab Inc., Atlanta, GA. The melting point was taken on a Thomas-Hoover apparatus whose reading was corrected to reference standards.

Acrylamide (12.6 g, 0.172 mole) and hypophosphorous acid (12.5 g, 0.189 mole) were heated at 70°C for 16 h under N_2. The resulting white, waxy solid was triturated three times with absolute EtOH and twice with anhydrous Et_2O. 2-Carbamylethylphosphinic acid (**1**) was obtained in 73% yield (12.1 g): mp 85°C (dec.); IR: 3450 (OH), 3370, 3200 (NH_2), 2390 (P—H), 1670, 1630 (C=O amide), 1235, 1200 (P=O); ^{1}H-NMR: 1.65–2.39 (m, 4 H, $2CH_2$), 6.87–7.44 (bd, 2 H, NH_2), 7.86 (s, 1 H, P—OH), 3.64, 10.29 (1: 1d, 1 H, J_{P-H} = 528). Anal. Calc. for $C_3H_8NO_3P.H_2O$: C, 21.06; H, 5.89. Found C, 21.06; H, 5.85.

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