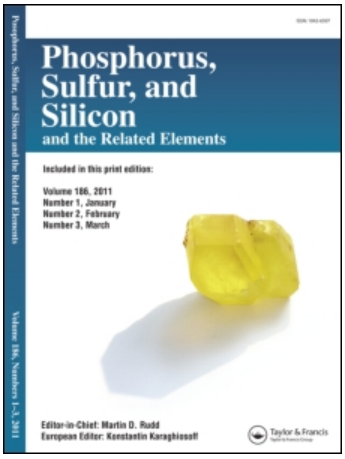

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Acylphosphonic Derivatives - New Precursors for Low Coordination Phosphorus Species

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ACYLPHOSPHONIC DERIVATIVES - NEW PRECURSORS FOR LOW COORDINATION PHOSPHORUS SPECIES

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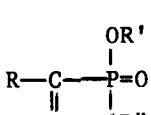
Although dialkyl acylphosphonates (**1**) have been known for over four decades,[1] their dealkylated derivatives, namely acylphosphonic acids (**2**) and alkyl hydrogen acylphosphonates (**3**), have only been isolated as salts. Characterization of compounds of type **2** and **3** have not been previously reported, neither have

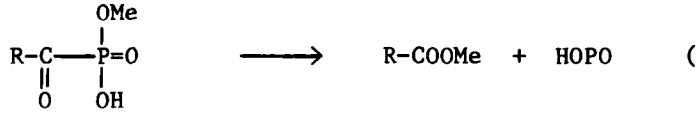


1; $R' = R'' =$ alkyl
2; $R' = R'' = H$
3; $R' =$ alkyl, $R'' = H$

their chemical and physical properties been described. In this paper we wish to describe some new chemical properties of these types of compounds.

Methods for mono-[2] and didealkylation[3] of dialkyl acylphosphonates have been described by several groups. We found that salts obtained by these methods can be converted to the free acids of type **2** and **3**, which can be characterized by spectral methods.

Thermal and acid catalyzed fragmentation of acylphosphonates. Methyl hydrogen acylphosphonates (**3**, R' = Me) are stable compounds at ambient temperature, however upon heating they are converted, in nearly quantitative yield, to the corresponding methyl carboxylates (equation 1). Similarly

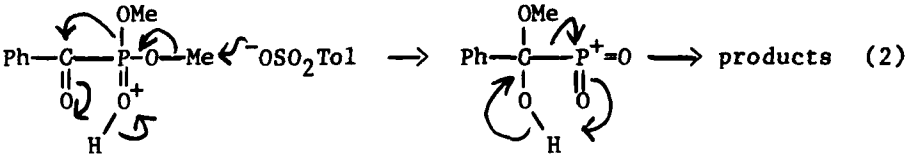


R-COOMe + HOPO (1)

R = phenyl or n-hexyl

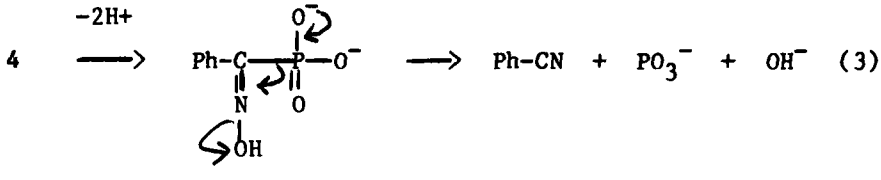
acylphosphonic acids yield carboxylic acids upon heating.

As this behavior is different from that shown by acylphosphonate esters (**1**), that are thermally stable, it was assumed that the fragmentation is acid catalyzed. Indeed it was found that dimethyl acylphosphonates (**1**, R' = R" = Me) also give methyl carboxylates, under the influence of protic or Lewis acids, in neat form, or in aprotic solvents. Furthermore we discovered, that heating a benzene solution of equimolar amounts of acylphosphonate and p-toluenesulfonic acid, results in the formation, in high yield, of the methyl carboxylate and methyl p-toluenesulfonate. This reaction is visualized as shown in equation 2.



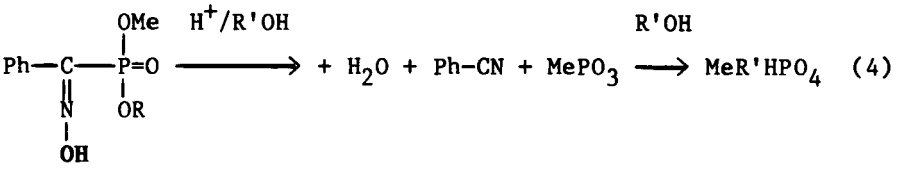
The stoichiometry of these reactions requires the formation of phosphenous acid (HOPO) or its ester. Indeed the formation of this species, in the thermal decomposition of methyl hydrogen benzoylphosphonate (**3**, R = Ph, R' = Me), could be demonstrated recently by high resolution mass spectrometry.[4]

Base catalyzed C-P bond cleavage in acylphosphonic derivatives. Dialkyl acylphosphonates (**1**) suffer fast hydrolytic cleavage of the C-P bond, which can be catalyzed either by base[5] or by acid.[6] We found that methyl hydrogen benzoylphosphonate (**3**, R = Ph, R' = Me) is stable at pH 8.5 at room temperature, but it hydrolyses to benzoic acid at higher pH. In comparison, benzoylphosphonic acid (**2**, R = Ph), though stable at pH 7.4, hydrolyses rapidly at pH 8.5 to a hitherto unidentified, phosphorus containing product. A similar trend is exhibited by oximino derivatives. Methyl hydrogen oximinobenzylphosphonate (**5a**) is stable at room temperature for 24 hours at pH 14; in contrast, oximinobenzylphosphonic acid (**4**) is rapidly converted to benzonitrile, in high yield, at pH 7.4, with the putative formation of monomeric metaphosphate anion (equation 3).



Acid catalyzed and thermal fragmentation of mono- and

dimethyl oximinophosphonates. Dialkyl acylphosphonates (1) react with hydroxylamine, as ketones do, to yield oximes.[7] When the application of this reaction was attempted with alkyl hydrogen acylphosphonates (3), the formation of nitriles, in high yields was observed. Furthermore it was found that dissolution of methyl hydrogen oximinobenzylphosphonate (**5a**) in alcoholic hydrogen chloride solution results in the formation of benzonitrile and methyl alkyl phosphate, (equation 4) both in high yields. This novel phosphorylation reaction can be



(4)

5a (R' = Me, Et, i-Pr, or t-Bu)

(**5a**, R = H ; **5b**, R = Me)

rationalized by assuming, that compound **5a** first undergoes fragmentation to monomeric methyl metaphosphate, which is captured subsequently by the solvent. Moreover, while the oxime methyl ether of **5a** behaves similarly to **5a**, the related dimethyl ester, **5b**, is inert under these conditions. However, we found that heating **5b** with equimolar amounts of p-toluenesulfonic acid in benzene, results in the formation of benzonitrile and methyl p-toluenesulfonate in high yields. This reaction can be rationalized by assuming that the fragmentation of **5b** is promoted both by protonation of the N-OH group and by nucleophilic attack of the tosylate anion upon the O-Me group, again with the putative formation of monomeric methyl metaphosphate.

Finally, it is worthy of note that oximinophosphonates undergo also thermal fragmentation, in the absence of acids. Thus refluxing **5b** in benzene, or heating it in the neat form, leads to the formation of benzonitrile and dimethyl phosphate in high yields. The fragmentation of the corresponding oxime methyl ether: dimethyl methoximinobenzylphosphonate proceeds considerably slower, also yielding benzonitrile and,in this case, trimethyl phosphate.

Quantum mechanical calculations of the benzoylphosphonates and of the products of their protonation were carried out with semiempirical MNDO[8] with hydrogen bonding correction,[9] which was recently improved to account for multiple hydrogen bonding.[10] The preferred conformation of the parent derivatives is one in which the C=O and the P=O groups are

trans oriented, with the cisoid conformer being about 1.8 Kcal higher in energy. According to the calculations, protonation occurs at the most negative P=O oxygen, leading to C-P bond breaking to dimethyl phosphite and benzoyl cation. Protonation on the carbonyl oxygen gives a stable species with intramolecular hydrogen bonding between the C=O and the oxygen of the P-OMe group. This product is higher in energy than the sum of the products' energy in the P=O protonation by ca. 80 Kcal.

Initial calculations on the oximino derivatives show a preference for a cis arrangement with internal hydrogen bonding between the N-O-H and O=P groups. The preferred site of protonation in these compounds is also the phosphoryl oxygen atom.

Reaction mechanisms, that can accomodate the results of the quantum mechanical calculations, along with the rate differences between the various derivatives, and in particular, between the pairs of syn and anti isomers, will be presented.

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