Pergamon

Tetrahedron Letters, Vol. 38, No. 35, pp. 6245-6246, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)01383-X

Aminoalkylation of Organophosphorus Compounds with P-H Bond by Using Vilsmeier Reagents

Ding Quan Qian, Xiao Dong Shi, Xing Zhong Zeng
Ru Zhen Cao and Lun Zu Liu*

Institute of Elemento-Organic Chemistry, Nankai University
Tianjin 300071, People's Republic of China

Abstract: Iminium salts derived from amides and phosphoryl chloride or oxalyl chloride are demonstrated to be excellent reagents for the aminoalkylation of organophosphorus compounds containing a P-H bond. © 1997 Elsevier Science Ltd.

The aminoalkylation of organophosphorus compounds containing P-H bond is generally performed by the Mannich reaction, and is of considerable importance for the synthesis of pesticides and other fine chemical products.[1,2] However, the conventional Mannich procedure only affords aminomethylene phosphates, and is only suitable for the aminoalkylation of dialkyl phosphites. In contrast to this, aminoalkylation of hydridophosphorane and dialkyl phosphite using the Vilsmeier reagents provides a novel aminomethylene diphosphoranes and diphosphonates. Since these compounds belong to importmant members of 1-aminoalkylphosphonic acid derivatives, we may expect that they should possess some potential biological activities. As the area continues to develop, the novel species will be received with a great deal of interest.

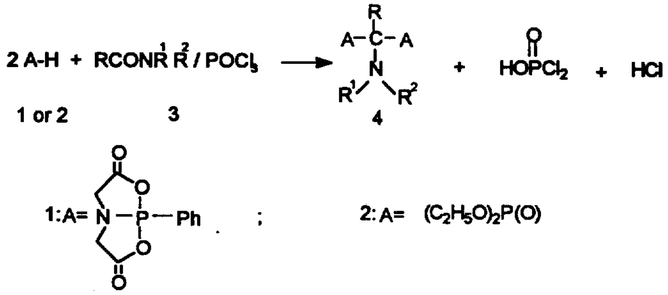
The Vilsmeier reagents are an equilibrium mixture of two iminium salts, the more reactive being the beta-phosphoryliminium chloride rather than the beta-chloroiminium phosphate.[3,4]

In principle, the Vilsmeier reagents as electrophiles can attack suitable carbon, oxygen and nitrogen nucleophiles. However, to our knowledge, the action of the Vilsmeier reagents on a phosphorus nucleophile is much less well-understood. Since phosphorus atoms in the hydridophosphorane 1 and diethyl phosphite 2 are relatively nucleophilic, it is conceivable that the penta-, tetra- coordinate phosphorus atoms could attack the carbon atom of the iminium salts giving, after loss of dichlorophosphorous acid and hydrogen chloride, the corresponding diphosphoranes or diphosphonates. We were pleased to find that the following reaction provides an efficient and convenient access to the desired products (Scheme 1). Our results also indicate that the Vilsmeier reagents derived from amides and oxalyl chloride were also used successfully for the reaction.

The reaction was carried out under a one pot procedure. Phosphoryl chloride or oxalyl chloride (10 mmol) was added dropwise to excess amides(24 ml) at 0 - -5 °C. One hour later the compounds 1 or 2 (20 mmol) were added in situ at 0°C. The reaction mixture was stirred at room temperature for 8-12 hours. After removal of excess amides in vacuum, the residue was washed with water. The compounds were purified by recrystallization or with layer chromatographic technology in acceptable yields(40-70%). The structures of these compounds were confirmed by ^{1}H NMR, ^{31}P NMR , ^{13}C NMR, MS and quantitative elemental analyses.

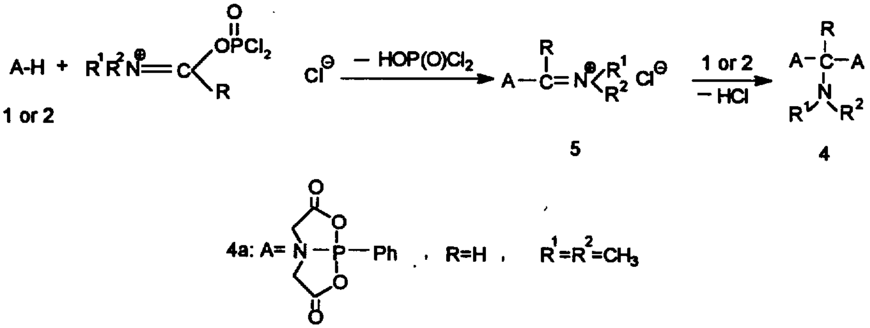
Our investigation has shown that this reaction might consist of two steps. In the first step, the nucleophilic phosphorus center apparently attacks the electrophilic central carbon of iminium salts with elimination of $HOP(O)Cl_2$ to give the intermediate 5, which then reacts further with another mole of 1 or 2 in this manner that phosphorus atom attacks the carbon of 5 with elimination of HCl (Scheme 2).

Scheme 1



3,4: R=H, CH_3, C_6H_5 ; R^1,R^2 = CH_3, C_2H_5, C_3H_7, C_6H_5, $(CH_2)_5$, $(CH_2CH_2)_2O$

Scheme 2



To further ascertain the configuration of 4, we have performed an X-ray single-crystal diffraction study on compound 4a. Crystallographic analysis has shown that the geometry about the two phosphorus atoms was distorted trigonal bipyramidal. The dihedral angle formed by two equatorial planes is 58.4 °.

In summary, we report a new synthetic procedure for the preparation of substituted aminomethylene diphosphoranes and diphosphonates using Vilsmeier reagents. Work is under way to establish the generality of this methodology for the preparation of various other compounds 4, and will be reported in forthcoming publications.

Acknowledgments: This research has been supported by National Natural Science Foundation of China (29672019).

Reference:

[1] Tramontini, M. ; Angiolini, L. *Tetrahedron* 1990, 46, 1791

[2] Krutikov, V. I. ; Lavrentev , A. N. *Zh. Obshch. Khim.* 1993, 63(1), 102: *Chem. Abstr.*, 119, 95638.

[3] Meth-Cohn, O. ; Stanforth, S.P. In Comprehensive Organic Synthesis, Trost, B. M. , Ed. ; Pergamon : Oxford 1991, Vol. 2. p777

[4] Tebby, J. C. ; Willetts, S.E. *Phosphorus and Sulfur*, 1987, 30, 293

(*Received in China* 29 *January* 1997; *revised* 31 *March* 1997; *accepted* 7 *May* 1997)