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A Convenient Method for the Synthesis of 1,3,2-Oxazaphospholidin-[3,2-a]-8-oxo-10-thio(or seleno)-[1,3,2]-benzodiazaphosphorines

Sheng Lou DENG, Jun Min HUANG, Ru Yu CHEN*

Institute of Elemento-Organic Chemistry, National Key Laboratory of Elemento-Organic Chemistry, NanKai University, Tianjin 300071

Abstrat: A Convenient method for the synthesis of fused phosphorusheterocycle 1,3,2-oxazaphosphorin-[3,2-a]-8-oxo-10-thio(or seleno)-[1,3,2]-benzodiazaphosphorines was carried out in one pot by the reaction of Tris(diethylamino)phosphine with multifunctional compounds 2-(N-(β or γ-hydroxyl) alkylene) amino-benzamides **1**. When PCL_3 was used, only chlorinated product was obtained.

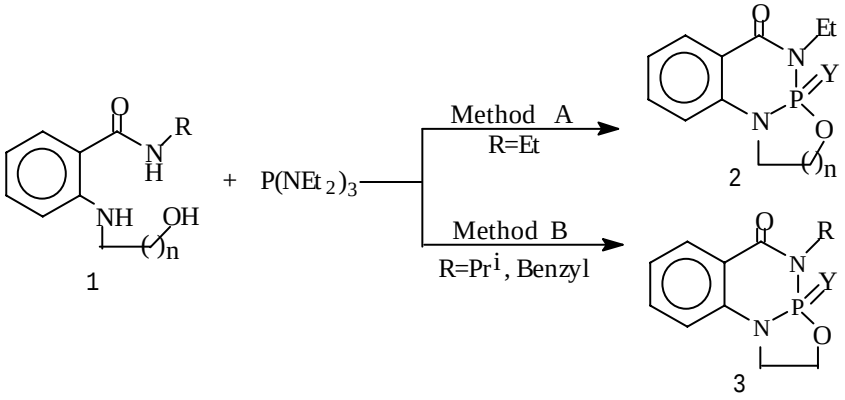
Keywords: Convenient method, synthesis, multifunctional compounds, fused phosphorus heterocycle, one-pot.

Tris(diethylamino)phosphine was widely used as a cyclizing reagent in the synthesis of different phosphorusheterocycles[1,2,3,4], however, it was seldom reported that $P(NEt_2)_3$ acted as a cyclocondensation reagent for compounds with groups of which one being quite different from the others in reactivity. Usually, the fused phosphorusheterocycles were prepared step by step in the ring closure [5,6], while this paper focused on the utilization of $P(NEt_2)_3$ for the synthesis of the fused heterocycles **2** and **3** conveniently in one pot. In contrast, PCL_3 only gave the corresponding chlorinated product. The suggested mechanism involved Arbuzov reaction **(Scheme 2)**.

Experimental

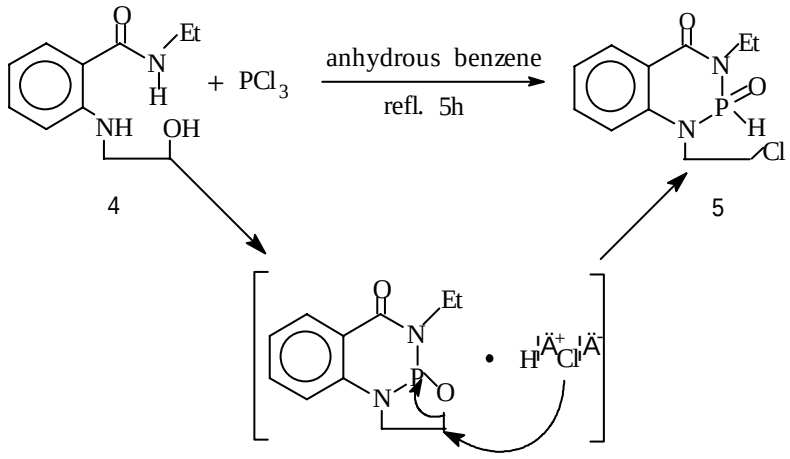
^1H NMR and ^{31}P NMR spectra were recorded with a BRUKER AC-P 200 Spectrometer ($CDCl_3$ as solvent, TMS as internal, 85%H_3PO_4 as outside standard) Melting Points were determined by Thomashoover melting point apparatus and the thermometer was uncorrected, the elemental analysis was carried out with Yanaco CHN CORDER MT-3 autoanalysis apparatus. The intermediates **1** were prepared by the reaction of corres- ponding amines with 2-bromoethanol or 3-bromopropanol in the presence of triethylamine in refluxing toluene for 15 h or so in good yields.

Scheme 1



2a: n=1 Y=S, **2b:** n=1 Y=Se, **2c:** n=2 Y=S, **2d:** n=2 Y=Se
3a: R=Pr^i Y=S, **3b:** R=Pr^i Y=Se, **3c:** R=Benzyl Y=S, **3d:** R=Benzyl Y=Se

Scheme 2



*Synthesis of **2a** (Method A)*

0.55g (2.2mmol) of $P(NEt_2)_3$ was dropped into 30 mL anhydrous benzene at room temperature, and then 0.051g (0.2mmol) of iodine was added at 70℃. After stirring for 15 min, 0.42g (2mmol) of **1** was added, the solution was heated at 75℃ for 2.5 h, After the addition of an equivalent amount of S_8 or Se, and refluxing for another 1.5 h, the product was isolated and purified by flash chromatography with ethyl acetate- petroleum ether (1:1 by vol.) as the eluent and recrystallization from a mixture of chloroform and petroleum ether. 0.25g of **2a** was obtained. yield: 46.6%, m.p. 130-132℃.

*Synthesis of **3a** (Method B)*

The intermediate **1** (0.44g, 2mmol) was heated directly with equal molar $P(NEt_2)_3$ under N_2 atmosphere at 110-120℃ for 2.5-3 h, followed by oxidation with a slight excess of sulfur or selenium and refluxing in anhydrous benzene. The product was purified according to method A. 0.23g of **3a** was obtained. yield: 41.2%, m.p. 186-188℃.

*Synthesis of **5***

A suspention of 2.08g (0.01mole) **4** in 100 mL anhydrous benzene was heated until the mixture became transparent , Then equimolar PCL_3 was dropped in within 30 min, After refluxing for 5h, the mixture was concentrated, and the product was isolated by flash chromatography. 1.67g of **5** was obtained. yield: 61.5%, m.p. 99-101℃.

^{1}H NMR, ^{31}P NMR,Elemental Analysis or MS of selected compounds

2a: ^{1}HNMR: δ 8.13-7.03 (m,4H,Ar-H), 4.64-4.16 (m,3H), 3.98-3.64 (m,3H), 1.36-1.29 (t, 3H, $^3J_{H-H}$=7.07Hz); ^{31}P NMR: 71.94 ppm; Elememtal Analysis: Calcd (%) C: 49.25, H: 4.85, N: 10.44; Found (%) C: 49.12, H: 4.95, N: 10.36
2c: ^{1}HNMR: δ 8.14-6.88 (m,4H,Ar-H), 4.84-4.68 (m,1H), 4.44-4.28 (m,1H), 3.94-3.72 (m,4H), 2.4-2.02 (m,2H), 1.38-1.31 (t,3H); ^{31}P NMR: 65.44 ppm; Elememtal Analysis: Calcd (%) C: 51.06, H: 5.32, N: 9.93; Found (%) C: 51.06, H: 5.42, N: 9.65
5: ^{1}HNMR: δ 8.2-6.9 (m,4H), 7.87 (d,1H), 3.60-4.10 (m,6H), 1.32 (t,3H); MS: 272 (M^+, 22.7%) 274 (M^++2,7.6%)

Results and Discussion

It is facile to use Tris(diethylamino)phosphine instead of PCL_3 as cyclization reagent for the synthesis of the title compounds. PCL_3 only gives the chlorinated product. The suggested mechanism involves fused heterocycle which then undergoes Arbuzov reaction.

It seems that the synthetic method depends on the bulky groups of the substrates. In the presence of ethyl, the reaction can be carried out under mild condition when the iodine was employed as catalyst, while method B resulted in complicated products (unisolable). It must be initiated under strong conditions such as high temperature and vigorously stirring when bulky substitutents appeared in the substrates (method B), however, higher temperature (>150℃) usually led to the formation of a polymer. Lower temperature (<80℃) gave poor yields of desired products. In addition, a slight excess of Tris(diethylamino)phosphine would favor for good yield both for method A and method B.

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