Graduate School of Pure and Applied Science

Studies on the preparation of organophosphines via sodium organophosphides
(ナトリウムオルガノホスファイドを用いる有機ホスフィン類の合成に関する研究)

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Abstract

Organophosphines are important reagents which widely used in organic synthesis as catalysts and ligands. For example, tertiary phosphines are widely used in many famous synthetic reactions as reagents in preparing vitamins, pharmaceuticals and agrochemicals. They are also organocatalysts that can trig a variety of organic reactions. Moreover, they are excellent ligands for transition metal in catalysis reactions, especially, chiral phosphines that play a pivotal role in a number of asymmetric transition-metal-catalyzed reactions. Despite the importance, general and efficient methods for their synthesis are limited. In the industry, tertiary phosphines R_3P are generally produced either by the addition of PH_3 to olefins or by the nucleophilic substitution reactions of RM with phosphorus trichloride. In the laboratory, organophosphines are prepared by metal-catalyzed couplings of ArX with diarylphosphines Ar_2PH or nucleophilic substitution reactions of lithium phosphides Ar_2PLi with alkyl halides RX. However, these methods lack efficiency. Moreover, the starting materials used are toxic, bad-smelling or difficult to prepare or handle. To precisely and efficiently generate organophosphines, I have developed new methods for the generation of tertiary phosphines, a polymeric phosphine and BINAP derivatives by using sodium phosphides efficiently generated using SD.

In my first work, I found that sodium reacts more accurately and selectively than other alkali metals (Li and K) to generate R_2PNa via the cleavage of the P-Ph bond of R_2PPh. For example, by adding SD (sodium finely dispersed in mineral oil) to a THF solution of Ph_3P at room temperature, the solution turned to brown instantly, and after 0.5 h, Ph_2PNa was generated nearly quantitatively. This sodium phosphide generated was stable for several weeks under nitrogen at room temperature. A series of sodium phosphides could be

conveniently and accurately prepared similarly by using SD. Thus, chlorophosphines (Ph_2PCl, (-)MenPhPCl and *n*-Bu_2PCl) and diphenylphosphinites (Ph_2POPh and Ph_2POEt) all readily reacted with SD to generate the corresponding sodium phosphides in quantitative yields. Triorganyl phosphines R_2PPh could also be employed as the substrates to efficiently produce R_2PNa via the selective cleavage of the Ph−P bonds by SD. The cleavage of Ar-P bonds by SD is substituent-depending, and that with an electron-withdrawing group was easier to be cleft. As to the selectivity of the cleavage of an aryl Ar-P bond vs. an alkyl R-P bond, it was found that the selectivity could be explained by considering the stability of the radical anion intermediates involved. The cleavage of the C-P bonds by an alkali metal was proposed to take place via a SET mechanism.

In my second work, I developed a new method to efficiently produce organophosphines by using aryl chlorides. First, the coupling reactions of phenyl halides PhX with Ph_2PNa generating Ph_3P were studied. It was found that both phenyl bromide and phenyl iodide gave low yields of the coupling product Ph_3P, while phenyl chloride gave high yield of Ph_3P. Therefore, the generally recognized inert PhCl, not the more reactive PhBr and PhI, was the chemical of choice for this reaction. The reaction was general and practicable. A series of aryl chlorides, with electron-donating groups or electron-withdrawing groups at the *para*-position of the chlorobenzene rings, all were readily phosphinated by Ph_2PNa, affording the corresponding organophosphines in high to excellent yields. In addition, chloronaphthalenes, heteroaryl chlorides, chloropyridines, chlorothiophenes and multi-chloroarenes were tolerable under similar conditions to give the expected phosphines in good to high yields. The couplings of ArCl with Ph_2PNa generating Ph_2PAr in high yields took place via a unique $S_{RN}1$ mechanism. Dichloroethene and aliphatic chlorides could be used directly in the coupling reactions with Ph_2PNa. Similarly, the chiral menthyl chlorides reacted with Ph_2PNa to give the corresponding chiral phosphines via S_N2 mechanism. To further elucidate the generality of the present method for the preparation of organophosphines, the reactions of other sodium phosphides (PhMePNa, Ph*n*-BuPNa, etc.) with aryl chlorides were also studied. The reactivity of R_2PNa was strongly affected by the R substituent.

In my third work, a novel poly(vinyldiphenylphosphine), that is soluble in common solvents, was prepared from the reactions of Ph_2PNa with the cheap poly(vinyl chloride) as an application of our new method for the preparation of organophosphines using Ph_2PNa. By using the newly generated poly(vinyldiphenylphosphine)

in Wittig reactions, the corresponding aromatic and aliphatic olefins were readily synthesized in good yields. The use of poly(vinyldiphenylphosphine) in Wittig reactions could overcome the shortcomings of the classical Wittig reactions using R_3P. Because the corresponding by-products tertiary phosphines oxides $R_3P(O)$ were soluble in organic solvents, they were difficult to remove from the products. On the other hand, because poly(vinyldiphenylphosphine oxide) was insoluble in common solvents, it could be easily removed by simple filtration. Moreover, comparing to the insoluble polymer-supported phosphines used in Wittig reactions, the newly prepared poly(vinyldiphenylphosphine) was more reactive and economic.

Finally, I also studied the modification of BINAP using SD. By controlling the reaction conditions, both the corresponding cyclic binaphthylphospholes and binaphthyl-based phosphines BINAPs could be generated, respectively. Early literatures reported that under similar conditions, lithium only generated cyclic binaphthylphospholes. Therefore, sodium was superior to lithium because sodium could not only cleave BINAP to generate the corresponding cyclic sodium phosphide, but also give binaphthyl-based disodium phosphides via the selective cleavage of P–C bonds.

Key words: Organophosphine, SD (sodium dispersion), sodium phosphide, aryl chloride, soluble polymeric phosphine, poly(vinyl chloride), Wittig reaction, BINAP, one-pot reaction, BINAP derivatives.