INSECTICIDAL CYCLIC PHOSPHORUS COMPOUNDS

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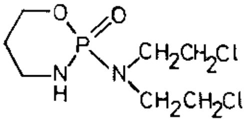
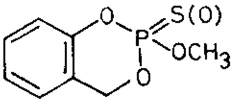
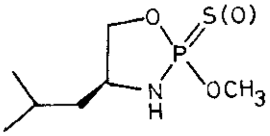
Although numerous kinds of cyclic phosphorus compounds have been synthesized by many reseachers, only a few compounds have been found, that highly effect biological activities; e.g., cyclophosphamide(I) and salithion(II). Recently, we reported the stereoselective syntheses of insecticidal five-membered cyclic phosphoramides(III) and six-membered cyclic enol phosphates(IV). The cyclic phosphoramides(III) were stereoselectively synthesized from optically active α-aminoalcohols with methyl phosphorodichloridothionate. The cyclic enol phosphates(IV) have been prepared through two general procedures. 1) Treatment of 2-alkylketophenols with PCl_3 and triethylamine followed by an addition of alcohol and triethylamine, yielded the cyclic phosphates, which could be oxidized to the analogous phosphates with peracid. 2) The more convenient method to prepare (IV) was the treatment of the appropriate 2-alkylketophenyl phosphonates or phosphates with K_2CO_3 in acetonitrile for 30 min at 70°C. Also a trace amount of this cyclization was observed by using bovine serum albumin at 40°C in a phosphate buffer of pH 7.4. The cyclic enol phosphates(IV) with R = Me or Et might exist in E or Z forms, yet these derivatives were each a single isomer based on ^{1}H, ^{13}C and ^{31}P NMR and a single HPLC peak. Thus, the (IV) were formed exclusively with the Z-configuration; proton H_a is coupled to the phosphorus via the ^{4}J-^{31}P-^{1}H trans effect. The potency of phosphates (IV) in inhibiting fly head and electric eel acetylcholinesterase was similar to that of the phosphate analogue of salithion(II). The phosphorothionate derivatives of (IV) with lower 2-alkoxy or 2-alkylamino and 4-alkylidene substituents were potent insecticides. An acid and a base hydrolyses, alcoholyses, chemical and physical properties, and the reactions with α-chymotrypsin of (III) and (IV) will be discussed. We also will compare the conformations and the structure-activity relationships of these compounds.



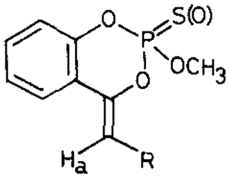
(I)



(II)



(III)



(IV)