

SYNTHESES OF PHOSPHORUS CONTAINING HETEROCYCLES  
BY THE OZONOLYSES OF ALKENYL PHOSPHORAMIDATES

Akira Takamizawa, Saichi Matsumoto, Tsuyoshi Iwata,

Shoji Sakai, and Itsuo Makino

Shionogi Research Laboratory,

Fukushima-ku, Osaka 553

Ozonolysis of O-(3-butenyl)-N,N-bis(2-chloroethyl)phosphorodiamidate afforded 2-[bis(2-chloroethyl)amino]-4-hydroperoxytetrahydro-2H-1,3,2-oxazaphosphorine-2-oxide which on deoxygenation yielded 4-hydroxycyclophosphamide, an active species of the antitumor agent cyclophosphamide. By the ozonolyses of O-alkenyl phosphoramidates bearing a nitrogen mustard residue, various phosphorus containing heterocycles (A ~ F) related to the cyclophosphamide active species were synthesized.



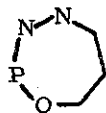
( A )



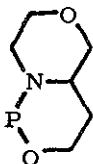
( B )



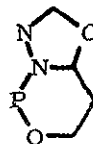
( C )



( D )



( E )



( F )