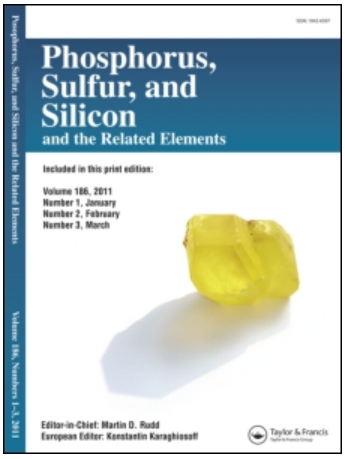


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# N-(Diethoxyphosphoryl)Aldimines as Synthetic Equivalents of $A^1$ Type Synthons

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Novel organophosphorus reagents useful for convergent synthesis of primary amines are presented.

*Keywords:* Nucleophilic addition; organometallic compounds; amino acid esters; deprotection of P-N bond



## INTRODUCTION

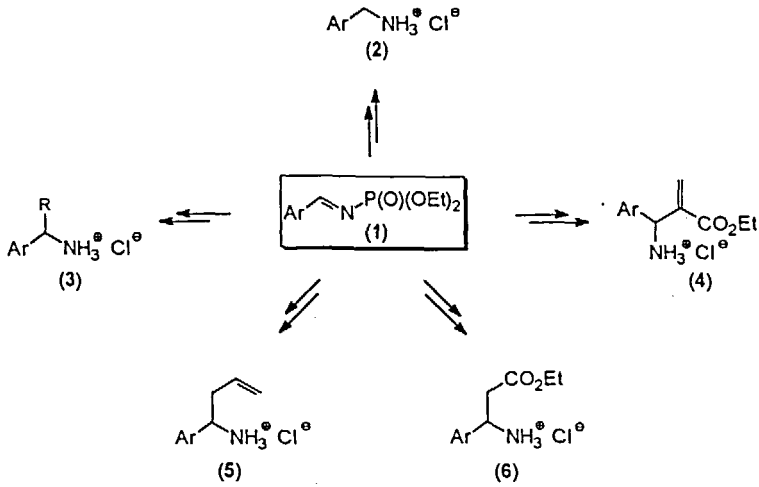
The tremendous importance of primary amines due primarily to their key position as synthetic intermediates continues to provide the impetus to evolve new and effective methods for their synthesis.N-Phosphorylated imines are natural precursors of primary amines owing to their enhanced electrophilicity and easy P-N bond cleavage under relatively mild conditions. The reported single nucleophilic additions to N-(diphenylphosphinyl) imines [1] which are neither conveniently nor inexpensively available [2] cannot be, however, considered as reliable and recommended synthetic procedures. Recently we have discovered a simple and economic method for the synthesis of N-(diethoxyphosphoryl)aldimines [3]. As potential equivalents of $a^1$ type synthons they proved very useful for convergent synthesis of primary amines with α-branched carbon skeletons.

## APPLICATION OF N-(DIETHOXYPHOSPHORYL)ALDIMINES FOR THE SYNTHESIS OF AMINES AND THEIR DERIVATIVES.

Deprotection of N-substituted phosphoramidates obtained on nucleophilic addition to N-(diethoxyphosphoryl)aldimines (**1**) was accomplished using three different procedures:

(A) - refluxing with 20% hydrochloric acid for 1 h.

Scheme






(B) - treatment with 1:1 (v/v) mixture of 20% hydrochloric acid and tetrahydrofuran at room temperature for 24h.

(C) – refluxing with ethanolic or methanolic hydrogen chloride for 2h. Amine hydrochlorides obtained according to (A) and (B) were transformed into free amines (solid NaOH) and then again into hydrochlorides by means of gaseous HCl in ether.

Reduction of C=N double bond in (diethoxyphosphoryl)aldimines (1) with sodium borohydride (2 moles) in THF at room temperature for 0.5 h followed by aqueous ammonium chloride quenching and dephosphorylation (procedure B) afforded arylmethylamines in high yields.

TABLE. Amine and amino acid esters hydrochlorides (2 – 6)

| Comp. No | Ar (R) | Dephospho-rylation procedure[a] | Overall yield (%)[b] | M.p.[c] |
|---|---|---|---|---|
| 2a | Ph | B (24h) | 74% | 243-245° |
| 2b | Ph-CH=CH | B (24h) | 65% | 198-200°(dec.) |
| 2c | 2-furyl | B (24h) | 73% | 142-144 °(dec.) |
| 2d | p-Me-$C_6H_4$ | B (24h) | 77% | 203-207° |
| 3a | Ph, Et | A (1h) | 66% | 190-191° |
| 3b | Ph, i-Pr | A (1h) | 49% | 286-288° |
| 3c | p-Br-$C_6H_4$, $CH_2$=CH | B (7d) | 61% | 225-228°(dec.) |
| 3d | p-MeO.$C_6H_4$, Bu | B (2d) | 63% | 204-206° |
| 3e | p-Br-$C_6H_4$, $C_6H_{11}$ | A (1h) | 56% | 320°(dec.) |
| 4a | Ph, Et | C (in EtOH) | 71% | 135-136° |
| 4b | Ph, Me | C (in MeOH) | 63% | 150-152° |
| 4c | p-Br-$C_6H_4$, Et | C (in EtOH) | 66% | 161-163° |
| 4d | p-Br-$C_6H_4$, Me | C (in MeOH) | 60% | 164-166° |
| 5a | Ph | B (3d) | 65% | 223-225 (dec.). |
| 5b | p-$CH_3$-$C_6H_4$ | B (4d) | 63% | 212-214 (dec.). |
| 5c | 1-naphthyl | C (in EtOH) | 59% | 204-205° |
| 5d | Ph-CH=CH | B (30h) | 47% | 163-165° |
| 6a | Ph | C (in EtOH) | 79% | 134-136° |
| 6b | m-Cl-$C_6H_4$ | C (in EtOH) | 42% | 103-105° |
| 6c | 1-naphthyl | C (in EtOH) | 78% | 165-167° |

[a] Reaction time is given in parentheses.

[b] Yield of spectroscopially pure compounds (2-6).

[c] Crystallized from EtOH-$Et_2O$. Methyl esters were crystallized from MeOH-$Et_2O$.

Addition of Grignard reagents (2 moles) to the C=N double bond in (1) (1 mole) performed in THF solution at room temperature for 2 h followed by aqueous ammonium chloride quenching at 5-10° and deprotection (procedure A or B) (see Table) gave α-arylalkylamines. In the case of allylmagnesium bromide the Barbier version involving addition of allyl bromide to the suspension of magnesium in THF containing (1) at 0-10° was applied.

Addition of ethyl bromoacetate to the suspension of activated zinc dust in THF solution of imine (1) followed by refluxing for 2 h, quenching ($NH_4Cl$aq.), and dephosphorylation (procedure C) resulted in the formation of β-arylamino acid ester hydrochlorides in moderate to good yields.

α-Methylene-β-arylamino acid esters were prepared by Baylis-Hillman reaction [4] of imines (1) with an excess of methyl or ethyl acrylate in the presence of 20 mol-% DABCO at room temperature for 3-5 days (monitoring by $^{31}$P-NMR). After removal of DABCO (5% $H_2SO_4$aq) crude amides were subjected to dephosphorylation (procedure C in MeOH or EtOH).

Yields and m.p.'s of all compounds (2-6) (see Scheme) prepared are compiled in the Table.



**Acknowledgments**

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