[2,3] SIGMATROPIC REARRANGEMENT OF N-SUBSTITUTED QUARTERNARY SALTS OF DIETHYL PYRROLIDINOMETHYLPHOSPHONATE

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The base-catalyzed rearrangement of N-benzyl-N-diethylphosphonomethylpyrrolidinium bromide (2) was investigated to afford the diethyl pyrrolidinobenzylphosphonate (3). In a similar fassion, the quarternary salts (4) and (6) were converted to the corresponding substituted diethyl pyrrolidinomethylphosphonates (5) and (7), respectively. Condensation of 3 with anisaldehyde, followed by hydrolysis of the resulting enamine (8) yielded 4-methoxybenzyl 2-methylphenyl ketone (9).

Dialkylaminomethylphosphonic acid esters have been proposed as efficient aldehyde generators through condensation of ketones and concomitant hydrolysis[1,2] and diethyl pyrrolidinomethylphosphonate was used for providing an efficacious synthesis of α-substituted aldehydes[3] (See Chart 1).

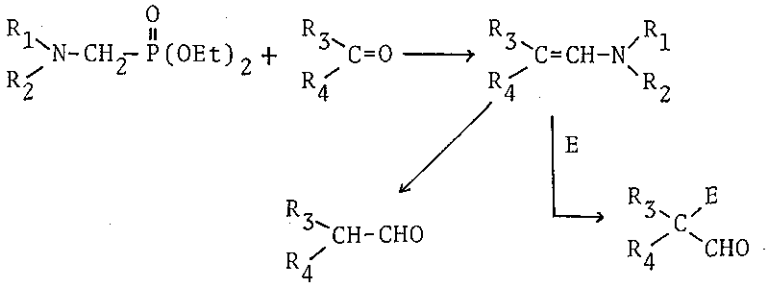


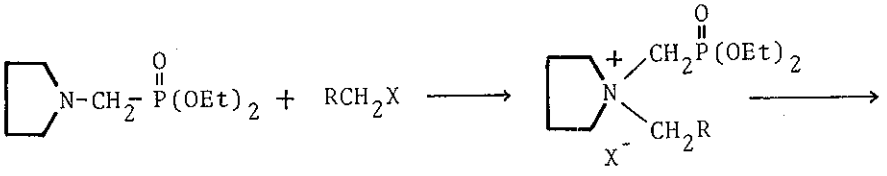
Chart 1

We have investigated the [2,3] sigmatropic rearrangement of N-substituted pyrrolidinium salts of diethyl pyrrolidinomethylphosphonate (1), easily obtained by alkylation of 1, in order to obtain a new enamine precursor, which would be a useful intermediate leading to ketones. These results were described in this paper.

N-Benzylation of 1 with benzyl bromide in dimethyl sulfoxide at 50-55 °C for 3 hr, followed by treatment of the N-benzylpyrrolidinium bromide (2) with potassium t-butoxide in a mixture of dimethyl sulfoxide-tetrahydrofuran (1:4)[4] at -10-0 °C for 3 hr to give the diethyl pyrrolidinobenzylphosphonate (3) in 68.3 % yield, bp_1 159-161 °C, δ ($CDCl_3$) 1.05, 1.31 (6H, each t, J= 7 Hz, CH_3CH_2), 1.5-2.1 (4H, m, 2x NCH_2CH_2), 2.40 (3H, s, Ar-CH_3), 2.5-2.9 (4H, m, 2x NCH_2CH_2), 3.4-4.4 (5H, m, 2x $POCH_2$ and ArCHPO), 6.9-7.9 (4H, m, Ar-H), m/e 311 (M^+). In a similar fassion, the quarternary pyrrolidinium salts (4) and (6), obtained as in the formation of 2, were converted to the corresponding substituted

diethyl pyrrolidinomethylphosphonates (5) [5.2 % yield, δ ($CDCl_3$) 1.07, 1.33 (6H, each t, J=7 Hz, CH_3CH_2), 1.5-2.0 (4H, m, 2x NCH_2CH_2), 2.2-3.0 (7H, m, 2x NCH_2 and Ar-CH_3), 3.6-4.8 (5H, m, 2x $POCH_2$ and NCHPO), 7.0-8.6 (3H, m, Ar-H), m/e 312 (M^+)] and (7) [15.2 % yield, δ ($CDCl_3$) 1.03, 1.18 (6H, each t, CH_3CH_2), 1.5-2.0 (4H, m, 2x NCH_2CH_2), 2.6-3.3 (4H, m, 2x NCH_2), 3.3-4.1 (5H, m, 2x $POCH_2$ and NCHPO), 4.7-5.2 (2H, m, $CH=CH_2$), 5.8-6.6 (1H, m, $CH=CH_2$), 7.25 (5H, s, Ar-H), m/e 337 (M^+)].

Finally, the Wittig reaction of 3 with anisaldehyde was examined. Hexane solution of n-butyllithium (1.1 equimol) was added to a solution of 3 in dry tetrahydrofuran under nitrogen atmosphere at -78 °C, and then to this solution was added anisaldehyde at the same temperature. After being allowed to stand at room temperature under stirring for 1 hr, the mixture was worked up as usual to give the enamine (8) [m/e 293 (M^+)]. Hydrolysis of 8, without purification, in a mixture of 10 % HCl-ethanol (1:1) under reflux gave 4-methoxybenzyl 2-methylphenyl ketone (9) in 95 % yield, mp 60-62 °C (ether-n-hexane); δ ($CDCl_3$) 2.37 (3H, s, Ar-CH_3), 3.65 (3H, s, OCH_3), 4.02 (2H, s, Ar-CH_2CO). Thus, 3 was found to be effective o-methylphenyl ketone precursor.

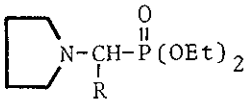


(1)

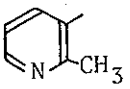
(2) R=C_6H_5-, X=Br

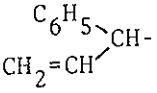
(4) R=  , X=Cl

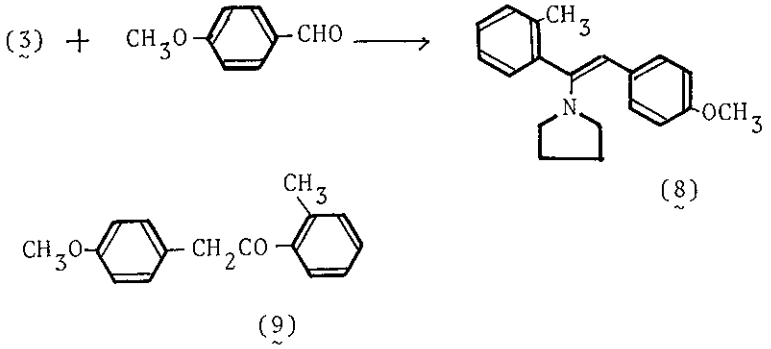
(6) R=C_6H_5CH=CH-, X=Cl



(3) R=o-CH_3-C_6H_4-

(5) R= 

(7) R= 



(8)

(9)

Chart 2

References and Foot Note

1. H. Zimmer and J. P. Bercz, Annalen, 686, 107.(1965).
2. H. Bohme, M. Haake, and G. Auterhoff, Arch. Pharm., 305, 88 (1972).
3. S. F. Martin and R. Gompper, J. Org. Chem., 39, 2814 (1974).
4. After benzylation, the reaction mixture was diluted with dry tetrahydrofuran and then this solution was used for the following reaction.

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