Tetrahedron Letters,Vol.26,No.7,pp 945-948,1985
Printed in Great Britain

0040-4039/85 $3.00 + .00

# NEIGHBOURING GROUP PARTICIPATION IN PHOSPHATE ESTERS. FRAGMENTATION OF {2-ARYLETHYL} PHOSPHOROCHLORIDATES

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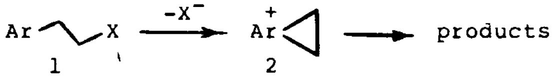
Abstract: (β-Arylethyl)phosphorochloridates decompose easily yielding 1-chloro-2-arylethanes and/or arylethylenes, presumably via the concerted P-Cl fission and the expulsion of metaphosphate-like species.

Nucleophilic assistance by the β-aryl group is a well known example of neighbouring group participation in the nucleophilic displacement at carbon:[1]



1 2 (1)

Reaction (1) which was the object of detailed kinetic, mechanistic and stereochemical investigations,[2] usually involved organic sulfonates or halides as substrates (1, X = $RSO_3$, halogen) and was usually carried out under solvolytic conditions, i.e. the arenium ion 2 was trapped by a molecule of nucleophilic solvent. Although interest in nucleophilic displacement at the α-carbon atom of organic phosphates is increasing,[3] and β-arylethyl phosphates have found application in oligonucleotide synthesis,[4] to our knowledge no work on reaction (1) involving phosphate esters (1, X = $OP(O)Y_2$) has been reported. Moreover because of the known[5] ability of $P^V$ derivatives to reduce the coordination number of phosphorus (formation of a "metaphosphate" species) the substrate molecule itself could be expected to yield a nucleophile, $Y^-$, and substitution may occur under non-solvolytic conditions. We have found that (2-arylethyl)-phosphorochloridates (1) when heated at 80°C can be easily converted into the corresponding 1-chloro-2-arylethanes (3). Reaction (2) can be considered as a

1 3 (2)

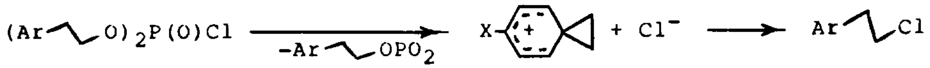
specific example of the collapse of a phosphate RO-P(O)ZY, (4), proceeding with expulsion of the metaphosphate species, $ZPO_2$ and with formation of an alkyl derivative, RY. This study shows that such a collapse is strongly facilitated by the β-aryl substituent in the ester group, and hence suggests the participation of the intermediate (2). Our results are given in Table 1.

Table I. Decomposition of phosphate derivatives, RO-P(O)ZY (4) at 80°C[a]

| | Substrate (4)[b] | | | Reaction time(h)[b] | Conversion % | Products |
|---|---|---|---|---|---|---|
| | RO | Z | Y | | | |
| 4a | EtO | Cl | Cl | 168 | 10 | EtCl[8] |
| 4b | EtO | EtO | Cl | 162 | 16 | EtCl[8] |
| 4c | $PhCH_2CH_2O$ | Cl | Cl | 20 | 100 | $PhCH_2CH_2Cl$[9] (minor)<br>$(PhCHCH_2)_n$[10] (major) |
| 4d | $PhCH_2CH_2O$ | EtO | Cl | 114 | 80 | EtCl[8], $PhCH_2CH_2Cl$[9] |
| 4e | $PhCH_2CH_2O$ | $PhCH_2CH_2O$ | Cl | 114 | 90 | $PhCH_2CH_2Cl$[9] |
| 4f | $PhCH_2CH_2O$ | EtO | PNPO[c] | 210 | 0 | d |
| 4g | $PhCH_2CH_2O$ | $PhCH_2CH_2O$ | PNPO | 114 | 0 | d |
| 4h | $PhCH_2CH_2O$ | EtO | EtO | 162 | 0 | d |
| 4i | $AnCH_2CH_2O$[e] | Cl | Cl | f | 100 | $AnCH_2CH_2Cl$[11] (minor)<br>$(AnCHCH_2)_n$[12] (major) |
| 4j | $AnCH_2CH_2O$ | $AnCH_2CH_2O$ | Cl | 1(2) | 64(86) | $AnCH_2CH_2Cl$[11] |
| 4k | $AnCH_2CH_2O$ | $AnCH_2CH_2O$ | PNPO | 321 | 0 | d |

[a] Reactions were carried out in sealed tubes which were cooled in dry ice/acetone before opening.
[b] The Table lists the final readings; in each case the reaction mixtures were analyzed at various intervals to monitor the reaction progress.
[c] PNPO = p-nitrophenoxy
[d] Substrate stable under these conditions.
[e] An = p-methoxyphenyl
[f] Substrate decomposes at rt. after a few hours & after 1 week in a refrigerator.

Ethyl esters of chlorphosphoric acid (4a,b), decompose slowly producing chloroethane in low yields. Since in this case, $S_N1$ type ionization via C-O or P-Cl cleavage is unlikely because of the instability of the possible cations formed (ethylcarbonium or phosphorylium[13]), the reaction probably involves direct phosphorus→carbon chloride transfer possibly analogous to that occuring during the collapse of organic chlorosulfites and related systems.[14] However, substitution of the two ethyl groups of 4b by β-phenylethyl (4e), or better still by β-(p-anisyl)ethyl (4j) substituents dramatically increases the reactivity of the substrates which produce the corresponding substituted chloroethanes in high yields. Undoubtedly, this rate enhancement indicates the intermediate formation of an arenium species (2).



(3)

4e, Ar = Ph
j, Ar = An

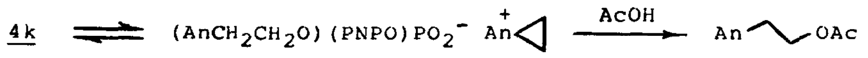
2a, X = H
b, X = MeO

Introduction of the β-aryl group into the ester function also greatly increases the reactivity of the corresponding phosphorodichloridates, (4c,i). However, for these substrates, although the substitution products were observed, the major reaction involves 1,2-elimination with formation of the corresponding styrene. Since the triesters (4f,g,h,k) are perfectly stable under the same conditions, we believe the formation of styrene does not involve elimination of a phosphoric acid species, but of HCl, presumably via the formation of the common intermediate (2). The preference for the elimination reaction over the nucleophilic displacement reaction, seems to be a function of the number of Cl atoms in the substrate molecule, while the anchimeric assistance by the β-aryl group and the intrinsic stability of the alkene formed are responsible for the increased reactivity of (4c,i) relative to (4a). We found the behaviour of the mixed diester (4d) particularly interesting. This compound has a reactivity similar to (4e), but decompositon yields both chloroalkanes, EtCl and $PhCH_2CH_2Cl$ in comparable quantities.[15] The ability of the chloride ion to displace the phosphate function at the α-carbon atom of the alkyl group is well documented.[16] Indeed, when (4b) was heated at 80°C in the presence of 23 mole% $Ph_4PCl$, the substrate was converted into EtCl within 64h. Since the yield of EtCl formed showed complete incorporation of all the chlorine initially present, both as ionic $Cl^-$ (in $Ph_4PCl$) and as covalently bonded chlorine in (4b), the external chloride acts only as a catalyst, and the reaction can be envisaged as the following sequence.

$$\underset{4b}{(EtO)_2P(O)Cl} + Cl^- \longrightarrow EtCl + {}^-O(EtO)P(O)Cl \longrightarrow EtOPO_2 + Cl^- \longrightarrow \text{etc} \qquad (4)$$

In the mixed diester 4d, the β-phenyl substituent plays the role of the "internal nucleophile", releasing chloride ion from substrate molecule via the anchimerically assisted formation of the phenonium ion. The $Cl^-$ ion released, can then attack the phenonium ion to form 2-phenylchloroethane, or dealkylate the substrate molecule to give one of the two possible chloroalkanes.

The anchimerically assisted C-O cleavage and the fission of the P-Cl bond (reacion 3) can be a synchronous or a step-wise process. We believe the former is more likely and all factors, i.e. the stability of the incipient ion (2), the departure of the chloride ion and the bonding reorganization at phosphorus, leading to the metaphosphate-type species, are responsible for the observed increase in reactivity. We found that substitution of chlorine by the PNPO group at the phosphorus atom (substrates 4f,g,k) results in thermal stability of the system.[17] This is in accord with the PNPO⁻ anion being a poorer leaving group than $Cl^-$,[18] but it does not of course preclude the ionisation of the C-O bond of the β-arylethylphosphate function, to give the arenium ion/phosphate ion pair. However, if this were true and the phosphate group as a whole were to behave just as a leaving group (like, for example, $RSO_3$), the arenium ion formed would be easily trapped by a nucleophilic solvent. We found that acetolysis of 4k at 80°C yields ca. 50% of the (β-anisylethyl)acetate[21] after



(5)

150h. This result shows that the ionization of 4k into the corresponding arenium phosphate is a slow process, and contrasts sharply with the rate of collapse of 4j (reaction 3). The solvolysis result together with the spontaneous collapse of the phosphorchloridate (4j) leads us to think that reaction (3) does not proceed via fast C-O cleavage, followed by a slow release of the chloride ion from the phosphate ion. Rather, we believe that the ($\beta$-arylethyl)phosphorochloridates represent a new type of an organophosphorus system, capable of expulsion of a metaphosphate-type species. In this case, the driving force for such expulsion is the nucleophilic assistance by the aryl group with respect to the $\alpha$-carbon atom, coupled together with the departure of the good leaving group ($Cl^-$) from the phosphoryl centre.

Acknowledgements.

Financial Assistance from the University of Cape Town and from C.S.I.R is gratefully acknowledged. S.C. thanks Beit Trust for a Scholarship.

## References and Notes

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8. Identified by $^1H$ NMR ($CDCl_3$) spectroscopy, after trapping the volatile reaction products in a dry ice/acetone cooled trap.
9. Identified by $^1H$ NMR ($CDCl_3$) spectroscopy by comparison with an authentic sample of 2-phenylchloroethane (Merck).
10. Gummy substance. IR (film) and $^1H$ NMR ($CDCl_3$) identical to those of the genuine sample of polystyrene.
11. Identified by $^1H$ NMR ($CDCl_3$) spectroscopy by comparison with the authentic $\beta$-(4-Methoxyphenyl)ethyl chloride prepared by reduction ($LiAlH_4$) of (4-Methoxyphenyl)acetic acid, treatment of the alcohol with conc. $HCl/ZnCl_2$, followed by column chromatography.
12. Amorphous solid isolated by column chromatography. $^1H$ NMR (DMSO-$d_6$, 120°C) and IR (Nujol & HBCD) spectra identical to those of the product obtained by treating p-methoxystyrene (Aldrich) with conc. $H_2SO_4$. Anal. Calcd. for $(C_9H_{10}O)_n$: C,80.60; H,7.52. Found: C,79.30; H,8.00.
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15. The molar ratio, $EtCl/PhCH_2CH_2Cl$ obtained varied in the range 1 - 2.4.
16. Ref. 7, p. 256.
17. No p-nitrophenyl($\beta$-phenylethyl) ether (possible product of 4f,g) or p-nitrophenyl $\beta$-(4-methoxyphenyl)ethyl ether (expected from 4k) were detected by means of $^1H$ NMR spectroscopy and/or TLC.
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21. Identified by $^1H$ NMR ($CDCl_3$) spectroscopy. $\delta$ 2.00 (s, 3H, $COCH_3$), 2.85 (t, 2H, J 7 Hz, $ArCH_2$), 3.77 (s, 3H, $OCH_3$), 4.21 (t, 2H, J 7 Hz, $OCH_2$), 6.76-7.26 (d of d, 4H, J 8.6 Hz, aromatic H's).

(Received in UK 6 December 1984)