Tetrahedron Letters No. 17, pp 1439 - 1442, 1975. Pergamon Press. Printed in Great Britain.

A NEW REACTION OF PHOSPHORUS YLIDS WITH ESTERS
DIRECT CONVERSION OF ESTER- INTO ISOPROPENYLGROUPS.

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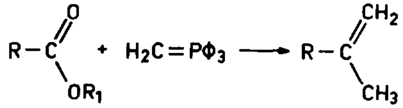
(Received in UK 3 March 1975; accepted for publication 19 March 1975)

Esters react with excess methylenetriphenylphosphorane in dimethylsulfoxide to give, after hydrolysis, the corresponding isopropenyl compounds:

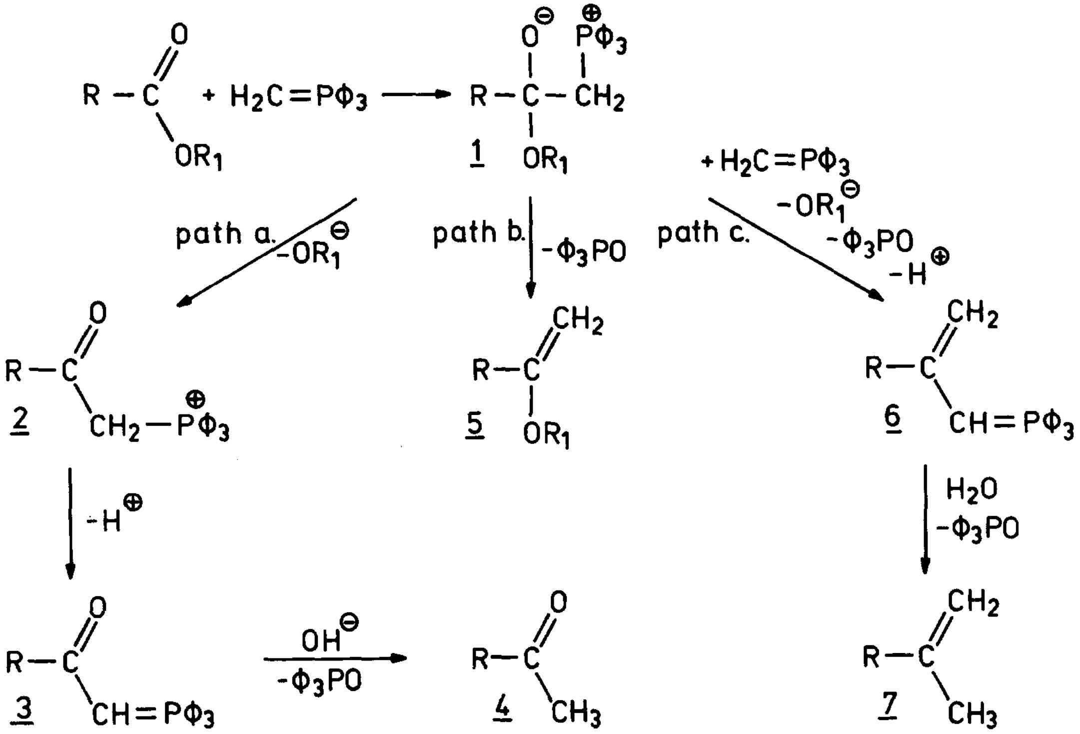


$$R-C(=O)OR_1 + H_2C=P\Phi_3 \longrightarrow R-C(=CH_2)CH_3$$

Reaction of esters with phosphoranes in ether solution normally leads to acylated phosphonium salts 2, which are converted to acylated phosphoranes 3 by a second equivalent of phosphorane (path a)[1]. These acylphosphoranes can be converted by basic hydrolysis into the corresponding methyl ketones 4 [1,2]. Recently it has been shown that with some activated esters [e.g.: R = CO_2Et or $CH(OEt)_2$] reaction in toluene with conjugated phosphoranes can give rise to the formation of vinyl ethers by loss of triphenylphosphine oxide rather than alkoxide ion from the intermediate 1 (path b) [3].

We have found that, when carried out in dimethylsulfoxide with excess methylenetriphenylphosphorane, the reaction takes a completely different course. Three equivalents of ylid are consumed per mole of ester and, upon neutral hydrolysis and solvent extraction, the isopropenyl compounds 7 are the only products isolated. The mechanism of this interesting reaction is currently being investigated.

Sofar we have shown that under the reaction conditions compounds 5 and 3 are stable to further reaction with methylenetriphenylphosphorane, while 2 is quantitatively converted into 3. Neither 2, nor 3 nor 5 are therefore intermediates in the formation of 7. These results indicate a mechanism in which compound 1, resulting from attack of the phosphorane on the ester carbonyl, is substituted at the central carbon atom by a second molecule of the ylid to give an intermediate which undergoes proton abstraction by a third molecule of ylid and looses one equivalent of triphenylphosphine oxide to give the phosphorane 6. Upon hydrolysis this phosphorane is expected to eject preferentially the hydrocarbon that gives the most stable carbanion, thus yielding the isopropenyl compound 7 [4]; (path c).



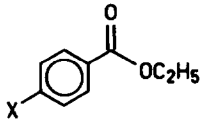
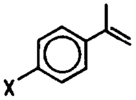
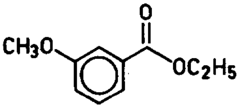
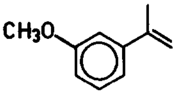
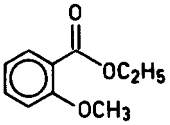
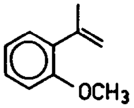
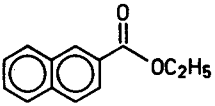
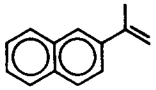
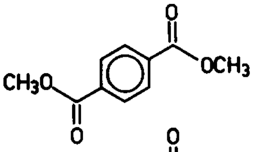
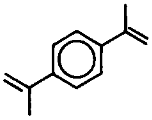
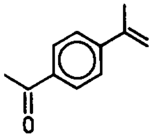
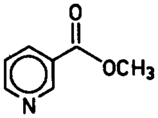
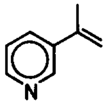
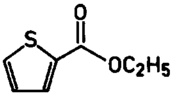
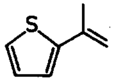
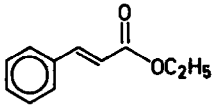
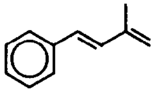
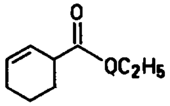
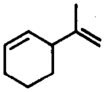
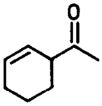
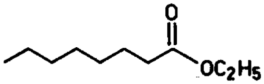
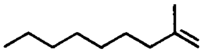
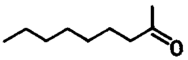
Some results that demonstrate the synthetic utility of this reaction are presented in the table. Aromatic esters give fair to good yields of the corresponding isopropenyl compounds 7. With some substrates, in particular aliphatic esters, the direct yields of 7 are lower, mainly because of concommittant formation of acetylated phosphoranes 3. These usually precipitate during workup, together with the triphenylphosphine oxide. Alkaline hydrolysis of this precipitate affords the corresponding methyl ketone, as indicated in examples 5, 9 and 10, from which an additional amount of 7 can be obtained by a normal Wittig reaction.

Although phosphoranes usually react with α,β-unsaturated carbonyl compounds by conjugate addition [5,6,7], we have found that ethyl cinnamate (example 8) under our conditions affords only 1-phenyl-3-methylbutadiene upon neutral hydrolysis.

Examples 1 indicate that the reaction is not very sensitive to substituent effects in the aromatic ring. Steric factors can be important, as shown by the observation that ethyl 2,4,6-trimethylbenzoate does not react under the conditions described. The full scope of this reaction, in particular the reactivity of the phosphorane intermediates, such as 6, is presently under investigation in these laboratories.

TABLE

Reactions of esters with methylenetriphenylphosphorane in dimethylsulfoxide

	Starting material	Product	Yield*		
1.			X = H, 56% Cl, 68% Br, 78% OCH_3, 61%		
2.			73%		
3.			65%		
4.			71%		
5.			27% +		10%**
6.			60%		
7.			71%		
8.			52%		
9.			30% +		36%
10.			40% +		17%

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* Yields refer to distilled products of at least 95% purity (glc) and are calculated on starting ester

** Prolonged hydrolysis of the residue (DMSO-H_2O-KOH) afforded 30% of p-diacetylbenzene.

General Procedure [8]

A solution of 0.02 mole of ester in 20 ml of dimethylsulfoxide was added at room temperature in a 10 min period to a stirred solution of 0.08 mole of methylenetriphenylphosphorane (from 32.5 g of methyltriphenylphosphonium iodide [9]) in 100 ml of dimethylsulfoxide in a nitrogen atmosphere. After additional stirring for 1 hr at room temperature and another hr at 50° C the reaction mixture was poured onto 200 g of crushed ice and 200 g of pentane. The mixture was stirred overnight at room temperature [10]. The precipitate was filtered and the pentane layer separated. The aquous layer was extracted twice with pentane. The combined pentane layers afforded the isopropenyl compounds in the yields, indicated in the table [11]. The filtered precipitate consists of triphenylphosphine oxide and, especially in the case of aliphatic substrates, of the acylphosphoranes <u>3</u>. Where indicated, the latter were converted into the corresponding methyl ketones by alkaline hydrolysis (12 hr reflux in a 2N solution of NaOH in 80% methanol).

References and Notes

1. H.J.Bestmann and B.Arnason, Chem. Ber. <u>95</u>, 1513 (1962)
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3. M.M. Le Corre, C.R.Acad.Sc. Serie C, <u>276</u>, 963 (1973)
4. A.W.Johnsen, Ylid Chemistry, p. 89, Academic Press (1966)
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6. J.P.Freeman, J.Org.Chem. <u>31</u>, 538 (1966)
7. P.F.Grieco and R.S.Finkelhorn, Tetrahedron Letters, 3781 (1972)
8. The reaction was usually carried out on ethyl esters. In the case of the benzoates it was found that methyl and isopropenyl esters gave very similar results. If however a better leaving group OR_1 was introduced (p-nitrophenoxide) the reaction followed exclusively path a.
9. R.Greenwald, M.Chaykovsky and E.J.Corey, J.Org.Chem. <u>28</u>, 1128 (1963)
10. This is usually beneficial for the yield, because triphenylphosphine oxide has a strong tendency to adsorb the reaction products.
11. Satisfactory analyses (glc, ir, nmr, ms) were obtained for all compounds described.