Pergamon

Tetrahedron Letters, Vol. 37, No. 22, pp. 3853-3856, 1996
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0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)00698-3

Reaction of non Stabilised Phosphonium Ylides with Lactones

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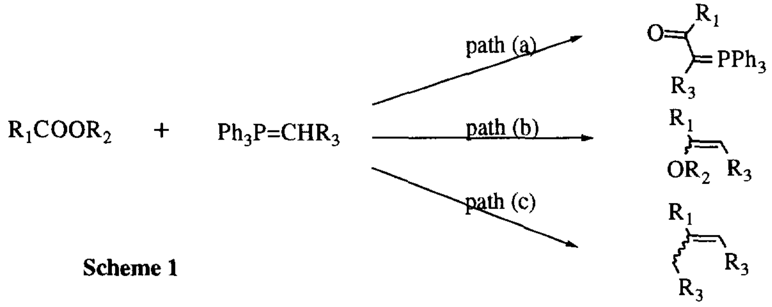
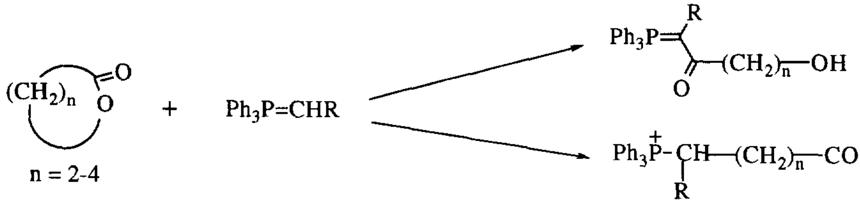
Abstract. Reaction of medium ring lactones with methylene and alkylidene triphenylphosphoranes in dimethyl sulfoxide led to unsaturated alcohols. Copyright © 1996 Elsevier Science Ltd

Reaction of esters with phosphonium ylides [1] can conduct to several types of products as reported in Scheme 1. Path (a) was mainly observed for the reaction of non stabilised phosphoranes with formates and esters having an α-electron withdrawing group.[2] Path (b) was reported with these esters in the reaction with stabilised phosphoranes.[2,3] Path (c) was shown to occur with aromatic and aliphatic esters with an excess of methylenetriphenylphosphorane ($R_3 = H$) in dimethyl sulfoxide (DMSO).[4] A complex reaction pathway was proposed to explain this formation of olefins from esters.[5]



Scheme 1

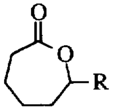
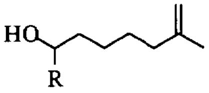
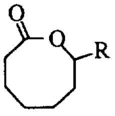
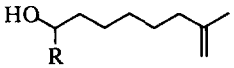
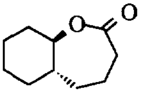
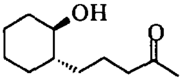
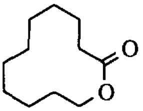
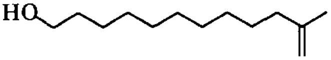
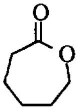
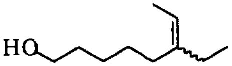
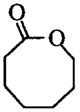
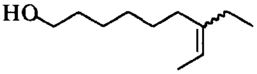
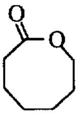
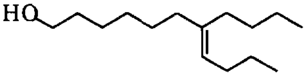
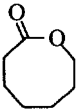
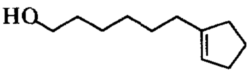
Reaction of Wittig reagents with lactones are much less known,[1] leading either to β-ketophosphoranes,[6] or to phosphonium carboxylates [7] (Scheme 2). Enol ethers can also be obtained in some cases.[8]



Scheme 2

The results reported by Van der Gen in the case of esters (Scheme 1, path c), led us to study the behavior of lactones in similar conditions. The first results were disappointing, since the reaction of γ-butyrolactone or δ-valerolactone with an excess of methylenetriphenyphosphorane in DMSO did not lead to detectable product. Our interest in the medium ring lactones, [9] led us to check their reactivity in these conditions. Our results are reported in Table 1.

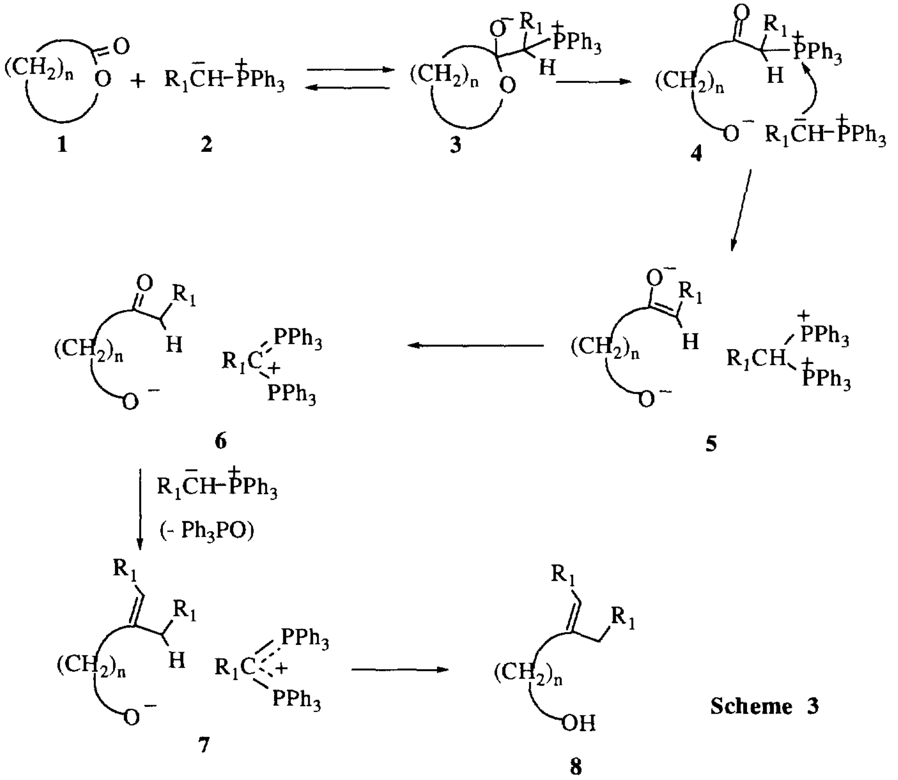
Table 1 : Reaction of ylides with lactones.

Entry	Substrate	Ylide	Product	(Yield, %)
a		$H_2C{=}PPh_3$		R = H (30)
b				R = Me (10)
c		$H_2C{=}PPh_3$		R = H (57)
d				R = Me (40)
e		$H_2C{=}PPh_3$		(24)
f		$H_2C{=}PPh_3$		(25)
g		$MeHC{=}PPh_3$		(48)[a]
h		$MeHC{=}PPh_3$		(64)[a]
i		$PrHC{=}PPh_3$		(35)[b]
j		$(CH_2HC{=}PPh_3)_2$		(24)

[a] mixture of isomers (65-35).[b] only one isomer was isolated (stereochemistry not determined).

The Wittig reaction of these lactones were carried in DMSO in the presence of four equivalents of ylide (generated by reaction of the dimsyl anion with the corresponding phosphonium salt) at 45°C for 12 h.[10] In all cases but one (entry e), unsaturated alcohols were obtained in moderate yields. The structures of these products were easily deduced from their NMR and IR spectra. The best results were observed with the eight-membered lactone. Entry f shows that this reaction is also possible with a macrolactone. Formation of a cyclopentene derivative is observed by reaction of a diylide (entry j). These reactions did not occur in solvents such as DMF or THF, or in DMSO with ylides generated by bases such as KOtBu or $NaNH_2$.

The proposed mechanism for the formation of alkenes by reaction of ylides with esters [5] *cannot* be used to explained our results. The fact that ethylenic alcohols and not alkenes were obtained suggest a specific reaction pathway. To understand how the products were formed, further experiments were carried out. If D_2O was added instead of water during the work-up, no deuterium insertion could be seen on the carbon chain; in the same way no oxidation product could be noticed if $NaIO_4$ was added before water. These results ruled out the formation of an β,γ-unsaturated phosphorane as reaction product.[4] To rationalise these results we propose the mechanism depicted in Scheme 3. The first step implies the attack of the lactone carbonyl by the ylide **2** to form the alkoxybetaine **3**. This betaine undergoes a ring opening to phosphonium **4**. The nucleophilic attack of the phosphorus atom by a second molecule of ylide **2** leads to formation of ketone enolate **5** with a carbobis-phosphonium as counterion; evidence for such a formation of carbobis-phosphonium has some precedent in the literature.[11] Acid-base equilibration gives ketone **6** possessing a 1-phosphoniumalkylidene-phosphorane [12] as counterion. A Wittig reaction of this ketone with a third molecule of ylide **2** forms the ethylenic alcoholate **7**. The structure of intermediate **7** was confirmed by ^{31}P-NMR in the case of entry h (Table 1). An AB system was observed at δ 32.9 ppm (δ = 0 for H_3PO_4 in DMSO) which can be attributed to the phosphoniumethylidene-phosphorane.[13]



Scheme 3

This mechanism is compatible with the absence of product established with the 5- and 6-membered lactones, since for these ring sizes the first intermediate **3** is probably stable. The ketone isolated in one case

(Table 1, entry e) may be explained by the formation at the ketone step (Scheme 3, intermediate **6**) of a cyclic hemiacetal which prevents the subsequent ylide reaction.[14]

The preparation of ω-isopropenyl alcohols have some precedents in the literature.[15] However, they implied multistep processes and the alcohols were generally obtained as a mixture of isomers. Even if the yields in ethylenic alcohols are modest, this reaction appears as a convenient way to prepare them.

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10. General procedure: under argon, a three-neck round-bottom flask was charged with 1.83 g (0.046 mole) of sodium hydride (used as a 60% dispersion in oil washed three times with dry hexane before use) and 20 ml of dry DMSO. The mixture was heated at 70°C until the gas evolution occurred. After cooling at 0°C a solution of 19.3 g (0.054 mole) of methyltriphenylphosphonium bromide in 70 ml of DMSO was transferred. After 10 min at rt. the lactone (0.0135 mole) was added. The mixture was heated 12 h at 45°C, then poured into a mixture of 150 ml of water and 100 ml of hexane. After separation, the aqueous phase was extracted with hexane (4x80 ml). The combined organic phases were dried (Na_2SO_4), concentrated and the residue was purified by liquid chromatography on silica gel (ether/hexane : 40/60).
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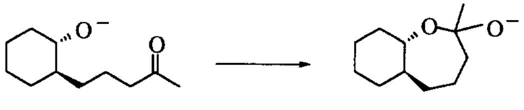
14. 

    The formation of the hydroxyketone by hydrolysis of the acylphosphorane (formed from **4** in Scheme 3) seems less propable, since acylphosphoranes are usually stable in presence of water (see ref. 1b p.131).

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(*Received in France* 2 *February* 1996; *accepted* 9 *April* 1996)