REVERSE MICROEMULSIONS MEDIATED SYNTHESIS OF VINYLPHOSPHONIUM SALTS.

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Abstract: PPh₃ reacts with activated alkynes in reverse (water-hydrocarbon) microemulsions giving specifically rise to a mixture of Z and E triphenylvinylphosphonium salts which are readily isolated in good yields.

Vinylphosphonium salts are valuable synthetic reagents used in the synthesis of heterocyclic compounds, cycloadditions and Michael additions ¹⁻⁴. They are currently prepared by reaction of allylbromides with triphenylphosphine and subsequent base catalyzed prototropic rearrangement to vinyl compound ⁵, nickel catalyzed coupling of vinylbromides with triphenylphosphine ⁶, palladium catalyzed vinylation of triphenylphosphine via vinyl triflates ⁷. Vinylphosphonium salts have also been obtained by nucleophilic addition of PPh₃ in concentrated acidic media (HCl or HBr) or of Ph₃P, HBr in organic solvents to activated alkynes ⁸. We have recently shown that reactions between water-soluble phosphines and activated alkenes or alkynes occurs readily in water because the equilibria were displaced by protonation of the carbanionic intermediates ⁹.

In this paper, we wish to describe that triphenylvinylphosphonium salts are readily obtained by nucleophilic addition of triphenylphosphine to activated alkynes in reverse microemulsions. In these thermodynamically stable liquid-liquid dispersions 10-11, water is solubilized within swollen micelles in an organic solvent (hydrocarbon) which contains the other reagents (phosphine and unsaturated compound) (scheme 1). The water microdroplets act as microreservoirs of protons which afford the necessary driving force to displace the equilibrium. Moreover, the compartimentalization of water within the reverse micelles avoids side reactions and vinylphosphonium salts are the sole reaction products 12. By using these reverse microemulsions as reaction medium, various vinylphosphonium salts bearing functionnal groups have been synthetized and isolated in a one step procedure with fairly good yields. Moreover, vinylphosphonium salts selectively deuterated at the carbon β to the phosphorus are obtained when D₂O is used.



Scheme 1

Our studies were performed in the well known microemulsions system ¹⁰ consisting of waterhydrocarbon-anionic surfactant (sodium bis-2-ethylhexyl sulphosuccinate : Aerosol OT). Thus, the reactive microemulsions were prepared by dropwise addition of as aqueous solution to a 20 % wt solution of AOT in cyclooctane or hexane containing stoechiometric amounts of α -alkynic acids 1a,b,c, esters 2a,b, ketones 3a,b or aldehyde 4 and PPh₃. The choice of the hydrocarbon depends on whether the vinylphosphonium salt has to be isolated (hexane) or not (cyclooctane). The pH of the aqueous phase depends on the nature of the electron withdrawing group : the reactions with α -alkynic acids were conducted at neutral pH (equation 1) while additions to acetylenic compounds 2, 3 and 4, unable to neutralize the hydroxide anion produced by the protonation of the carbanonic intermediate, were performed

(1)
$$PPh_3 + R - C \equiv C - CO_2H$$

 $intermediate{H_2O(D_2O) = pH = 7 \ microemulsion} = Ph_3P - C(R) = C + Z + CO_2 + H(D)$
 $intermediate{H_1D} = C + Z + Z + C(R) = C + Z + CO_2 + CO_2$

with water solutions containing stoechiometric amounts of HCl (equation 2).

(2)
$$PPh_3 + R - C \equiv C - A$$

$$\begin{array}{c} H_2O/HCl \ leq \\ (D_2O/DCl \ leq) \\ \hline microemulsion \end{array} Ph_3P - C(R) = C A + C(R) + C(R$$

The reaction rates, monitored by ³¹P NMR spectroscopy of the reactive microemulsion, were found to depend on the nature of both substituents (electron withdrawing group and R) and mainly on the location of the alkynic substrate at the interface or in the bulk organic phase (Table). For example, the reaction with lipophilic ester **2b** is much slower than the reaction with octynoic acid **2a** presumably located in the interfacial region. Vinylphosphonium salts are always the sole products detected in the reaction medium as a mixture of Z and E isomers. These two isomers are easily isolated from the reaction mixture and in most cases separated by column chromatography. They were characterized by ³¹P, ¹³C, ¹H NMR spectroscopy ¹³; the ³¹P chemical shifts and the ³J_{P-C} and ³J_{P-H} values are in agreement with previously described data ^{9,14}. For compounds **5a**, **6a** and **7a** the assignments are proved by ³J_H, ¹H values.

Highly reactive triphenylvinylphosphonium salts 6, 7 and 8 are stable and can be used for further reactions within the microemulsion but underwent side reactions with methanol on silica gel during the chromatography and were therefore isolated in lower yields (other separation methods are currently in progress).

Vinylphosphonium salts specifically deuterated at the carbon β to the phosphorus are easily obtained by using D₂O or D₂O/DCl; owing to the very small amount of incorporated aqueous phase, these reactions in microemulsions offer a cheap and efficient deuteration method. These results represent a new useful application of microemulsion as a reaction medium in organic synthesis by using water solubilized within swollen micelles as a proton source.

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Substrate	Conditions	Reaction ^(a) Time	% Vinylphosphonium salts ^(b) (δ ppm, H D-alkane)		Product isolated (c) yield (%)		
			Z	Е		Z	E
la	H ₂ O/hexane	2	77 (18.56)	23 (14.71)	5a	76	21
	D ₂ O/hexane	2	70 (18.58)	31 (15.26)	5a (D)	68	26
1b ^(e)	H ₂ O/hexane	48	46 (23.10)	29 (25.50)	5b	42	28
	D ₂ O/hexane	22	41 (22.80)	54 (24.23)	56 (D)	29	50
lc	H ₂ O/hexane	48	35 (22.38)	53 (25.85)	5c	31	35
	D ₂ O/hexane	48	41 (22.40)	56 (26.25)	5c (D)	41	54
2 a	H ₂ O/HCl/hexane	18	50 (18.66)	39 (15.94)	6a ^(d)		21
	D ₂ O/DCl/hexane	18	52 (18.73)	31 (16.02)	6a (D) ^(d)		17
2Ъ	H ₂ O/HCl/hexane	140	36 (23.86)	38 (26.57)	not isolated		
3 a	H ₂ O/HCl/hexane	18	73 (16.99)	15 (19.44)	7a ^(d)	Z + E :	9
3Ъ	H ₂ O/HCl/hexane	24	53 (24.16)	29 (25.37)	76 ^(d)	28	25 (E + Z)
	D ₂ O/DCl/hexane	22	51 (24.16)	29 (25.37)	7 b (D) ^(d)	31	7 (E + Z)
4	H ₂ O/HCl/cyclooctane	86	23 (20.83)	55 (23.47)	not isolated		

Table 15

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12 - In biphasic medium (water-organic solvent) the reaction does not occur. Moreover in water-alcohol (or THF) mixture competitive alcoholysis and hydrolysis of the phosphonium salts are observed.

13 - Representative NMR data : ¹H NMR, 90 MHz, CD₃OD, δ ppm : 5aE : 6.73 (dd, ³J_{H-H} = 17 Hz, ³J_{P-H} = 21Hz, 5aZ : 6.99 (dd, ³J_{H-H} = 11 Hz, ³J_{P-H} = 29 Hz), 6aE : 3.78 (s), 6.56 (dd, ³J_{H-H} = 17 Hz, ³J_{P-H} = 19 Hz), 8.31 (dd, ³J_{H-H} = 17 Hz, ²J_{P-H} = 19 Hz). ¹³C{¹H}NMR, 22.5 MHz, δ ppm : 5aZ : 120.2 (d, ¹J_{P-C} = 91 Hz), 157.3 (d, ²J_{P-C} = 1 Hz), 169.1 (d, ³J_{P-C} = 7 Hz); 5aE : 117.5 (d, ¹J_{P-C} = 83 Hz), 157.8 (d, ²J_{P-C} = 1Hz), 170.2 (d, ³J_{P-C} = 21 Hz); 5a(D)Z : 119.2 (d, ¹J_{P-C} = 91 Hz), 156.0 (dt, ²J_{P-C} = 2 Hz, ¹J_{C-D} = 24 Hz), 168.2 (d, ³J_{P-C} = 7 Hz); 5a(D)E : 116.5 (d, ¹J_{P-C} = 82 Hz), 156.6 (dt, ²J_{P-C} = 2 Hz, ¹J_{C-D} = 24 Hz), 169.3 (d, ³J_{P-C} = 21 Hz); 5bZ : 154.3 (d, ²J_{P-C} = 7 Hz), 169.2 (d, ³J_{P-C} = 5Hz); 5bE : 122.2 (d, ¹J_{P-C} = 75 Hz), 155.4 (d, ²J_{P-C} = 6 Hz), 170.5 (d, ³J_{P-C} = 20 Hz); 5cZ : 151.9 (d, ⁻²J_{P-C} = 5 Hz), 169.7 (d, ³J_{P-C} = 5Hz); 5cE : 124.1 (d, ¹J_{P-C} = 71 Hz), 153.9 (d, ²J_{P-C} = 6 Hz), 171.6 (d, ³J_{P-C} = 23 Hz); 6aZ : 120.7 (d, ¹J_{P-C} = 48 Hz), 146.8 (d, ²J_{P-C} = 4Hz), 172.0 (d, ³J_{P-C} = 5 Hz); 6aE : 118.4 (d, ¹J_{P-C} = 91 Hz), 146.8 (d, ²J_{P-C} = 4 Hz), 164.9 (d, ³J_{P-C} = 24 Hz); 7bZ : 119.0 (d, ¹J_{P-C} = 88 Hz), 151.4 (d, ²J_{P-C} = 4Hz), 199.7 (d, ³J_{P-C} = 5 Hz).

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15 - a) General experimental procedure : 0.5 ml of water [H₂O or D₂O or H₂O/HCl (1N) or D₂O/DCl (1N)] were added dropwise to 5.4 g of a 20 % wt AOT solution in cyclooctane or hexane containing 0.5 mmol of PPh₃ under gentle magnetic stirring. After addition of pure alkyne (0.5 mmol) the clear mixture was allowed to stand at room temperature with stirring. At the end of the reaction, determinated by ³¹P NMR spectrocopy or TLC analysis (ethylacetate-methanol 50/50), the product were separated from the crude microemulsion by column chromatography on silica gel (100 g), eluent : gradient ethylacetate-methanol . b) Determinated by ³¹P NMR study of the microemulsion, percentage relative to initial amount of PPh₃. c) Yields relative to PPh₃. d) These products have been isolated in low yields because they underwent a side reaction with methanol during the column chromatography on silica. e) 1b was introduced in n-butanol solution.

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