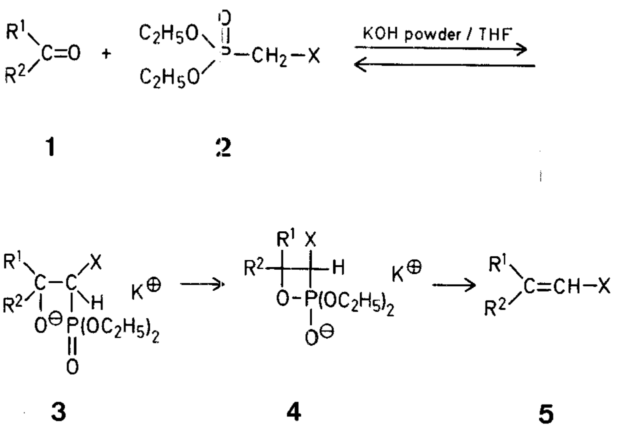
The Wittig-Horner Reaction in Solid-Liquid Two Phase Systems

Francoise Texier-Boullet, André Foucaud*

Groupe de Chimie Structurale associé au CNRS, Université de Rennes, Campus de Beaulieu, F-35042 Rennes, France

The technique of phase transfer catalysis is widely used in organic synthesis. In particular, Wittig-Horner reactions in aqueous sodium hydroxide/organic solvent two phase systems in the presence of quaternary ammonium salts[1, 4-6], of crown ethers[8,9], or in the absence of a catalyst[5] have been described. In these systems, the water which is transferred to the organic phase solvates the anions formed[6,14] and thus reduces their reactivity. Otherwise, undesired side reactions, such as hydrolysis of esters, are observed[1,4].

The system sodium (or potassium) hydroxide (or carbonate)/organic solvent has been less used[10,11,13,18]. In the present communication we report that the Wittig-Horner reaction can be carried out at room temperature using this liquid-solid two phase system (Method A). The reaction generally gives better yields and proceeds more rapidly than with liquid-liquid two phase systems (Method B). The isolation of the products is easier and hydrolysis-sensitive groups remain intact under these conditions. The role of the water in this solid-liquid system is less pronounced than in the aqueous/organic two phase liquid-liquid system[14,18]. The phosphonates **2** react with aldehydes and also with aromatic ketones in the absence of a phase transfer catalyst under the present conditions to give the alkenes **5**.



Under the present conditions, the carbanions are formed at the interface[12,15] and the ion pairs migrate in the solvent, more readily when the cation is solvated as demonstrated by the fact that the reaction proceeds more rapidly in tetrahydrofuran than in benzene. The stereoselectivity of the reaction is the same as with the aqueous hydroxide/organic solvent liquid-liquid two phase systems and in homogeneous media and is dependent on the solvent and the cation[7]. It is not affected by the presence of crown ethers.

Addition of 30% basic aluminium oxide to the potassium hydroxide results in a decrease in the rate of formation of **3**. This can be explained by adsorption of the anion of **3** on the aluminium oxide which, in turn, moderates the rate of formation of the oxaphosphetane **4**. The stereoselectivity of the reaction, which is a result of the thermodynamic control of the formation of **3**[7,17], is unchanged.

Table. Alkenes **5** from the Wittig-Horner Reaction

Carbonyl compound **1**		Phosphonate **2**	Yield [%][a] by		E-Isomer [%][b]	b.p./torr or	^{1}H-N.M.R. (100 MHz, $CDCl_3$)	Ref.
R^1	R^2	X	Method A	Method B	by Method A	m.p. (solvent)	δ (olefinic protons) [ppm]	
C_6H_5	H	$-CN$	98	(Lit. [1] 77)	82	90–92°/2 (90–92°/2)[1]	E: 5.80, 7.30 (J = 17 Hz) Z: 5.36, 7.03 (J = 12 Hz)	1, 19
$4-Cl-C_6H_4$	H	$-CN$	98	56	80	78° (C_2H_5OH)	E: 5.79, 7.26 (J = 18 Hz) Z: 5.37, 6.98 (J = 12 Hz)	7
$4-O_2N-C_6H_4$	H	$-CN$	82	45	73	204–205° (C_2H_5OH)	E: 6.01, 7.42 (J = 18 Hz) Z: 5.85, 7.37 (J = 13 Hz)	20
$2-Br-C_6H_4$	H	$-CN$	95	52	60	100°/0.03[c]	E: 5.78, 7.65 (J = 16 Hz) Z: 5.51, 7.38 (J = 13 Hz)	7
$2-Cl-C_6H_4$	H	$-CN$	98	69	60[d]	110°/0.03[c]	E: 5.79, 7.64 (J = 18 Hz) Z: 5.51, 7.41 (J = 12 Hz)	7
C_6H_5	H	$COOC_2H_5$	90	(Lit. [1] 56)	100	103–105°/8 (103–108°/8)[1]	E: 6.37, 7.63 (J = 16 Hz)	1
$4-Cl-C_6H_5$	H	$COOC_2H_5$	96	56[e]	100	115°/0.3	E: 6.29, 7.50 (J = 16 Hz)	21
$C_6H_5-CH=CH$	H	C_6H_5	76[f]	(Lit. [2] 72[f])	100	147–149° (C_2H_5OH) (147–149°)[2]	E: 6.48–7.48 (m)	2
C_6H_5	H	C_6H_5	80[f]	0	100	124° (C_2H_5OH)	E: 7.15	22
C_6H_5	CH_3	$-CN$	88	60	83	80°/0.03[c]	E: 5.55 Z: 5.34	16
C_6H_5	C_2H_5	$-CN$	90	49	80	72–73°/0.2	E: 5.49 Z: 5.37	16
C_6H_5	CH_3	$COOC_2H_5$	35	0	87	127°/10	E: 6.12 Z: 5.74	21

[a] Purity ≥98% as determined by ^{1}H-N.M.R. spectroscopy (JEOL MH 100 spectrometer); purity of **5** ($R^1 = C_6H_5$, $R^2 = H$, $X = -CN$) ≥98% by G.L.C. analysis.

[b] As determined by ^{1}H-N.M.R. spectroscopy.

[c] Bulb-to-bulb short path distillation.

[d] No change in proportion on addition of 5% 18-crown-6.

[e] Yield of p-chlorocinnamic acid: 16%.

[f] Time of reaction: 1 h (30 min under reflux).

0039-7881/79/1132-0884 $ 03.00

When the phosphonate **2** is not very acidic or when potassium carbonate is used in place of potassium hydroxide the rate of formation of the carbanion may be increased by warming. Thus, with **2** ($X=C_6H_5$), treatment with sodium hydride in tetrahydrofuran results in a carbanion which reacts exothermically with benzaldehyde at room temperature to give a 50% yield of stilbene within 1 h. In contrast, the phosphonate **2** ($X=C_6H_5$) does not react with benzaldehyde at room temperature in the potassium hydroxide/tetrahydrofuran system; at 70°, however, an 80% yield of stilbene is obtained within 1 h.

The carbanion of **2** (X= CN) reacts rapidly with benzaldehyde at room temperature in the potassium hydroxide/tetrahydrofuran system to give a 98% yield of cinnamonitrile within 15 min. With the potassium carbonate/tetrahydrofuran system, **2** (X= CN) does not react with benzaldehyde at room temperature but at 70° a 94% yield of cinnamonitrile is obtained within 1 h.

Wittig-Horner Reaction in Solid-Liquid Two-Phase System; General Procedure for Method A:

A solution of diethyl cyanomethanephosphonate (**2**, X= CN; 10 mmol) and the carbonyl compound **1** (10 mmol) in tetrahydrofuran (10 ml) is added to a suspension of powdered potassium hydroxide (1 g, 20 mmol) in tetrahydrofuran (30 ml). The suspension is stirred for 15 min at room temperature, filtered, and the filtrate evaporated under reduced pressure. The residual oil is distilled or recrystallised to give alkene **5** (see Table).

Wittig-Horner Reaction in Liquid-Liquid Two-Phase System; General Procedure for Method B:

A solution of the phosphonate **2** (10 mmol) and the carbonyl compound **1** (10 mmol) in dichloromethane (20 ml) is added at room temperature to a stirred two-phase system of dichloromethane (30 ml), 50% aqueous sodium hydroxide (20 ml), and tetrabutylammonium iodide (700 mg) during 15 min. The organic layer is separated, washed with water (20 ml), and dried with sodium sulfate. Evaporation of the solvent and recrystallisation or distillation of the residue gives the product **5** (see Table).

This work was supported by D.G.R.S.T.

Received: April 17, 1979
(Revised form: May 29, 1979)

---

[1] C. Piechucki, *Synthesis* **1974**, 869.

[2] C. Piechucki, *Synthesis* **1976**, 187.

[3] M. Mikołajczyck, S. Grzejszczyk, W. Midura, A. Zatorski, *Synthesis* **1975**, 278.

[4] E. D'Incan, J. Seyden-Penne, *Synthesis* **1975**, 516.

[5] M. Mikołajczyk, S. Grzejszczak, W. Midura, A. Zatorski, *Synthesis* **1976**, 396.

[6] E. D'Incan, *Tetrahedron* **33**, 951 (1977).

[7] B. Deschamps, G. Lefebvre, A. Redjal, J. Seyden-Penne, *Tetrahedron* **29**, 2437 (1973).

[8] C. J. Pederson, H. K. Frensdorff, *Angew. Chem.* **84**, 16 (1972); *Angew. Chem. Int. Ed. Engl.* **11**, 16 (1972).

[9] C. L. Liotta, H. P. Harris, *J. Am. Chem. Soc.* **96**, 2250 (1974).

[10] S. Julia, A. Ginebreda, *Synthesis* **1977**, 682.

[11] E. Marchand, G. Morel, A. Foucaud, *Synthesis* **1978**, 360.

[12] A. Jończyk, A. Kwast, M. Mąkosza, *J. Chem. Soc. Chem. Commun.* **1977**, 902.

[13] M. Fedorynski, K. Wojciechowski, Z. Matacz, M. Mąkosza, *J. Org. Chem.* **43**, 4682 (1978).

[14] D. Landini, A. M. Maia, F. Montanari, F. M. Pirisi, *J. Chem. Soc. Chem. Commun.* **1975**, 950.

[15] M. Mąkosza, E. Bialecka, *Tetrahedron Lett.* **1977**, 183.

[16] G. Jones, R. F. Maisey, *J. Chem. Soc. Chem. Commun.* **1968**, 543.

[17] E. Breuer, D. M. Bannet, *Tetrahedron* **34**, 997 (1978).

[18] B. Mlotkowska, A. Zwierzak, *Tetrahedron Lett.* **1978**, 4731.

[19] B. Deschamps, G. Lefebvre, J. Seyden-Penne, *Tetrahedron* **28**, 4209 (1972).

[20] N. O. Postushak, N. F. Stadniichuck, A. V. Dombrovski, *Zh. Obshch. Khim.* **33**, 2950 (1963).

[21] H. J. Bestmann, K. Rostock, H. Dornauer, *Angew. Chem.* **78**, 335 (1966); *Angew. Chem. Int. Ed. Engl.* **5**, 308 (1966).

[22] D. Y. Curtin, E. E. Harris, *J. Am. Chem. Soc.* **73**, 4519 (1951).

0039-7881/79/1132-0885 $ 03.00