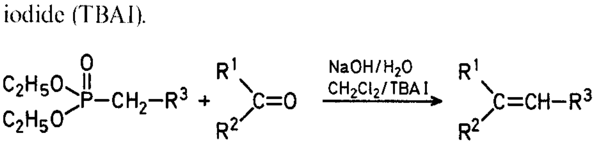
Wittig-Horner Synthesis in an Aqueous Two-Phase System using Phase-Transfer Catalysis

C. PIECHUCKI

Institute of General Chemistry, Technical University
(Politechnika), 90-924 Łódź, Poland

In phase-transfer catalyzed reactions[1,2], the anionic intermediates are generated in an aqueous sodium hydroxide/organic solvent two-phase system in the presence of alkylaminium- or phosphonium salts bearing relatively large alkyl groups. Owing to the formation of ion pairs with these aminium- or phosphonium salts, the anionic intermediates are transferred into the organic phase where they can react with suitable reagents.

The phase-transfer method was recently used for the generation of halocarbenes[3], dimethylsulfonium methylides[4] (alkylidenedimethylsulfuranes) or dimethylsulfoxonium methylides[4] and in Wittig olefin synthesis[5]. We have found that also the Horner reaction of phosphonates **1** with carbonyl compounds **2** proceeds readily in a two-phase system in the presence of catalytic amounts of tetrabutylaminium iodide (TBAI).

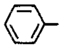
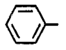
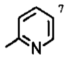
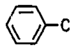
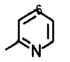


The outlined synthesis, particularly convenient on account of the simple and short preparative procedure, gives generally good yields of conjugated alkenes **3** (Table). Limitations of the synthesis result both from low reactivity and from possible hydrolysis of some substrates. For example, diethyl 2-pyridylmethanephosphonate was almost quantitatively recovered after attempted reaction with acetone and only a small amount of unidentified material was obtained from the reaction of ethyl *O*,*O*-diethylphosphonoacetate with the same ketone.

To avoid undesired reactions, especially aldolization of acetaldehyde, both substrates should be added simultaneously to the reaction mixture.

G.L.C. analyses were performed on a Giede III instrument, 1 m column, 30% silicone gum on Chromosorb W. ^{1}H-N.M.R. spectra were measured at 80 MHz on a Tesla BS 487 C spectrometer with TMS as internal reference. Concerning the deshielding of *cis* methyl protons in 3-methyl-2-butenenitrile (0.1 ppm) see Lit.[10].

Table. Horner Reactions of Phosphonates **1** in an Aqueous Two-Phase System

R^1	R^2	R^3	Products **3**	Yield[a] (%)	b.p./torr
	H	$-CN$[6]	Cinnamonitrile	77 Z/E ratio 24:76[b]	90–92°/2
CH_3	H	$-CN$	Crotonitrile	51 Z/E ratio 39/61[c]	116–118°/760
CH_3	CH_3	$-CN$	3-Methyl-2-butenenitrile	62	40–42°/20
	H	$-COOC_2H_5$[6]	Ethyl *trans*-cinnamate	56	103–105°/8
CH_3	H	$-COOC_2H_5$	Ethyl *trans*-crotonate	54	51–52°/25
	H	 [7]	*trans*-2-Styrylpyridine	71	m.p. 91–92°[8]
 $-CH=CH-$	H	 [6]	1-Phenyl-4-(2-pyridyl)-butadiene	68	m.p. 121–123°[9]

[a] Based on G.L.C.-pure product.

[b] G.L.C. conditions: 180°, $t_Z = 3.6$ min, $t_E = 5.7$ min.
^{1}H-N.M.R. (CCl_4): $\delta = 5.31$ (d, $J = 12.1$ Hz), 5.73 (d, $J = 17.3$ Hz), 7.11 ppm (m, 6H).

[c] G.L.C. conditions: 120°, $t_Z = 3.1$ min, $t_E = 4.4$ min.
^{1}H-N.M.R. (CCl_4): $\delta = 1.91$ (d, $J_1 = 8.2$ Hz, $J_2 = 2.1$ Hz), 2.02 (d, $J_1 = 8.2$ Hz, $J_2 = 2.1$ Hz), 5.38 (m, 1H), 6.68 ppm (m, 1H).

Horner Reactions of Diethyl Phosphonates 1 in an Aqueous Two-Phase System; General Procedure:

A solution of the diethyl phosphonate **1** (35 mmol) and the aldehyde or ketone **2** (35 mmol) in dichloromethane (5 ml) was added dropwise to a stirred two-phase system consisting of dichloromethane (35 ml), 50% aqueous sodium hydroxide (20 ml), and tetrabutylaminium iodide (0.7 g). The strongly exothermic reactions of the phosphonates **1** ($R^3 = -CN$ or $-COOC_2H_5$) were complete within 15 min; in the case of the 2-pyridylmethylphosphonates, refluxing for ~3 h was necessary (I.R. analysis of reaction mixtures). The organic layer was separated, washed with water (5 ml), and dried with magnesium sulfate. Evaporation of the solvent and distillation or recrystallization of the residue from petroleum ether afforded the pure products **3**.

The structure of compounds **3** was confirmed by their I.R.- and ^{1}H-N.M.R. spectra and by elemental analysis.

Dr. R. Soloniewicz is gratefully acknowledged for his interest.

Received: July 29, 1974

---

[1] J. Dockx, *Synthesis* **1973**, 441.
[2] E. V. Dehmlow, *Angew. Chem.* **86**, 187 (1974); *Angew. Chem. Internat. Edit.* **13**, 170 (1974).
[3] M. Mąkosza, M. Wawrzyniewicz, *Tetrahedron Lett.* **1969**, 4659.
[4] A. Merz, G. Märkl, *Angew. Chem.* **85**, 867 (1973); *Angew. Chem. Internat. Edit.* **12**, 845 (1973).
[5] G. Märkl, A. Merz, *Synthesis* **1973**, 295.
[6] E. C. Ladd, *U.S. Patent* 2632019 (1953), United States Rubber Co.; *C.A.* **48**, 1418 (1954).
[7] E. Maruszewska-Wieczorkowska, J. Michalski, A. Skowrońska, *Rocz. Chem.* **30**, 1197 (1957).
[8] I. L. R. Williams, et al., *J. Org. Chem.* **28**, 387 (1963).
[9] E. Späth, G. Kubiczek, E. Dubensky, *Chem. Ber.* **74**, 873 (1941).
[10] T. Hayashi, et al., *J. Org. Chem.* **30**, 696 (1965).