

Gas-Liquid Phase-transfer Catalysis: Wittig-Horner Reaction in Heterogeneous Conditions

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The Wittig-Horner synthesis of alkenes has been carried out under gas-liquid phase-transfer catalysis (g.l.-p.t.c.) conditions. With this technique the carbonyl compound and the phosphonate flow, under pressure, through solid potassium carbonate contained in a thermostatted column where the conditions (temperature and pressure) are such as to ensure that the reactants are gaseous. The alkene so produced was cooled and collected at the column outlet. Reaction yields were higher when the solid potassium carbonate was coated with poly(ethylene glycol)-Carbowax 6000. The function of the poly(ethylene glycol) is discussed. Aromatic aldehydes react successfully with triethyl phosphonoacetate and diethyl (cyanomethyl)phosphonate; ketones react only with diethyl (cyanomethyl)phosphonate. Reaction conversions (based on the purity of the recovered alkene) are always high, while yields (measured on the basis of the actual amount of pure alkene recovered, with respect to the reacting carbonyl compound) are lower.

It has been reported that the Wittig¹ and the Wittig-Horner² reactions are advantageously carried out under typical two-phase conditions.³ In particular, phosphonates, which are relatively cheap starting materials, react with a wide variety of aldehydes and ketones usually under mild conditions. Such reactions have been performed using polymer-supported reagents:⁴ the main advantage of this technique lies in the possibility of eliminating all the phosphorus-containing species with the polymer at the end of the reaction, without resorting to extraction or chromatographic procedures.

We have recently shown how displacement reactions can be performed allowing an organic gaseous reagent to flow over a solid bed made up of a salt of the nucleophile or by a stronger base able to generate it.⁵ The reaction takes place only if the solid bed is uniformly covered with a film of a thermally stable, molten phase-transfer catalyst [phosphonium salts, crown-ethers or poly(ethylene glycol)].

The term gas-liquid phase-transfer catalysis (g.l.-p.t.c.) underlines the analogy between this technique and gas chromatography: thus, the gaseous organic species flow through the liquid film, in which the substitution reaction is promoted and anion exchange between the underlying solid salt and the diffusing reagents takes place.

In a previous communication⁶ we have described that the Wittig synthesis can be performed under g.l.-p.t.c. conditions to yield alkenes in good yields. Under the reported conditions the by-product, triphenylphosphine oxide, remains adsorbed on the solid bed, so that the alkene produced is free of phosphorus-containing species.

Here we report the results obtained in the Wittig-Horner synthesis under heterogeneous conditions, *i.e.* when both the carbonyl compound and the phosphonate are gaseous and the base that generates the phosphonate anion is solid (potassium carbonate).

Results and Discussion

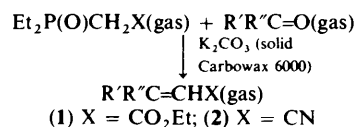
α,β -Unsaturated esters or nitriles were obtained by passing a 1:1 molar mixture of carbonyl compound and phosphonate, under pressure, through a thermostatted column (130–150 °C, depending on the reaction to be performed) containing the basic catalytic bed (see Scheme).

The reagent mixture was introduced as a liquid into the column where the pressure and temperature conditions were

Table 1. Reaction between benzaldehyde and triethyl phosphonoacetate (1) and diethylcyanomethyl phosphonate (2) as a function of the temperature

	<i>T</i> (°C)	Conversion (%) ^a	<i>Z</i> : <i>E</i> Ratio ^b
Reaction with (1) ^c	120	100	0:100
	130	100	0:100
	140	89	0:100
	150	70	0:100
Reaction with (2) ^c	120	100	33:67
	130	100	36:64
	150	80	36:64
	180	27	34:66

^a By ¹H n.m.r. spectroscopy, comparing the integration area of the aldehydic proton to that of the olefinic ones. ^b By g.l.c. and n.m.r. analysis. ^c Pressure = 5 Torr.



Scheme.

always such as to make it gaseous. The reaction product was collected by cooling at the column outlet.

During the process neither aqueous nor organic solvents were used: this allowed easier recovery of the reaction product and avoided saponification side-reactions of reagent and product, as occur in the presence of aqueous base, under liquid-liquid phase-transfer catalysis conditions.^{3,9}

The phosphonates used in this work have methylene groups acidic enough to allow the generation of the corresponding anions in the presence of a rather weak base such as potassium carbonate.

The reaction between benzaldehyde and triethyl phosphonoacetate (1) and diethyl cyanomethylphosphonate (2) was studied in order to evaluate the effect of temperature on both the conversion and the *Z*:*E* ratio of the product. The results (see Table 1), show that although the isomer ratio is unaffected by temperature, the conversion decreases with increasing temperature. This latter feature may arise because (i) phosphonates are unstable in basic media at high temperatures and (ii) an increase

Table 2. Wittig–Horner synthesis under g.l.–p.t.c. conditions^a

Carbonyl compd.	Phosphonate	Conversion ^b (%)	Yield ^c (%)	Z:E ^d Ratio
PhCHO	(EtO) ₂ P(O)CH ₂ CO ₂ Et	100 (74) ^e	50 (31) ^e	0:100
<i>p</i> -MeOC ₆ H ₄ CHO ^f		90	66	0:100
<i>trans</i> -PhCH=CHCHO ^f		100	56	0:100
PhCHO	(EtO) ₂ P(O)CH ₂ CN	100 (82) ^e	64 (34) ^e	36:64
<i>p</i> -MeOC ₆ H ₄ CHO ^f		94 (75) ^e	67 (31) ^e	34:66
PhCOMe		56	42	19:81
C ₆ H ₁₀ (=O)		61	46	

^a Carbonyl compound (25 mmol) phosphonate (25 mmol) catalytic bed (K₂CO₃ + Carbowax 6000, 5% by weight) (60 g), temperature 130 °C, unless indicated otherwise; pressure 5 Torr, unless indicated otherwise. ^b By ¹H n.m.r. spectroscopy, comparing integration area of the aldehydic proton to that of the olefinic ones. ^c Isolated product. ^d By g.l.c. and n.m.r. analysis. ^e Synthesis carried out using K₂CO₃ (60 g) without Carbowax 6000. ^f Temp. 150 °C; pressure 2.5 Torr.

in temperature lowers the contact time of the reactant species adsorbed on the liquid film and, consequently, the reaction rate decreases.

In order to optimize the conversions, the temperature and pressure were set so as to ensure that the reagents and products were gaseous without inducing thermal decomposition of the phosphonate and without minimizing the reagents contact time: Table 2 reports the results for the reaction of (1) and (2) with various carbonyl compounds under such conditions.

High conversions are always obtained with aldehydes, whereas reaction yields are lower: this is because the reaction products remain partly adsorbed on the solid bed and are not thus recovered at the column outlet.*

Because of their lower electrophilic character, ketones give rise to lower conversions and, in particular, do not react with (1). However, the yields obtained in the reactions with (2) are comparable with those reported working under typical phase-transfer catalysis conditions.

Although both Wittig⁶ and Wittig–Horner reactions also proceed in the presence of uncoated potassium carbonate (see Table 2, conversions and yields reported in brackets) the conversions and yields are lower. This result suggests that, as for similar reactions under liquid–liquid and solid–liquid phase-transfer catalysis conditions, alkyltriphenylphosphonium salts and triethylphosphonates could themselves be catalysts under g.l.–p.t.c. conditions. This behaviour is certainly possible for alkyltriphenylphosphonium salts that are effective phase-transfer catalysts. However it must be taken into account in that in the absence of any solute–solvent interaction, potassium carbonate increases its basicity and can generate the anion of the reagents adsorbed on its surface even in the absence of an activating agent such as poly(ethylene glycol). In this case, the real function of poly(ethylene glycol) would not be that of activating the ylide generation, according to a phase-transfer mechanism, but rather that of assuring the presence of a liquid film. Such a film favours the reaction between the solid base and the phosphonate and the subsequent reaction of the ylide with the carbonyl compound, by means of adsorption and diffusion phenomena that increase the contact time between the reagents, similarly to that occurring in a gas–liquid chromatographic process.

Experimental

¹H n.m.r. spectra were recorded on a Hitachi–Perkin–Elmer R-24B 60 MHz spectrometer. A Varian series Vista mod. 6000, equipped with a CDS 111L integrator was used. The pressure in the reaction column was controlled by means of an Officine

* In the reaction of entry 1 in Table 2, washing of the cooled solid bed with diethyl ether at the end of the reaction afforded 1.8 g of ethyl cinnamate, while no unchanged benzaldehyde was recovered.

Galileo vacuum gauge Sibel 90 NW 16, and a Lauda MGW ultrathermostat was used.

Phosphonates were prepared according to reported methods⁷ and used after distillation; all other reagents were ACS grade and were used without further purification.

Preparation of the Catalytic Bed.—Poly(ethylene glycol) Carbowax 6000 (5% by weight with respect to the base) was dissolved in methanol, potassium carbonate was added, and the suspension evaporated under reduced pressure to remove the solvent. The solid mass so obtained was oven-dried at 130 °C for 10 h.

G.l.–p.t.c. Synthesis of Alkenes—Typical Procedure: Ethyl Cinnamate Synthesis.—The reaction column (115 ml volume, 40 cm length) was filled with the catalytic bed (60.0 g); the temperature and pressure were 130 °C and 5 Torr respectively. A 1:1 molar mixture of triethyl phosphonoacetate (5.6 h, 25 mmol) and benzaldehyde (2.6 g, 25 mmol) was introduced by means of a dripping device within 10 min; after 20 min the reaction products began to condense at the column outlet. After 1 h the heating and vacuum were discontinued and the reaction mixture (2.5 g) was collected: this was analysed by ¹H n.m.r. spectroscopy and by g.l.c. and showed a 100% conversion and a 0:100, Z:E ratio. After distillation (b.p. 140 °C, 15 Torr) 2.2 g of pure ethyl cinnamate were recovered.

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