Barium Hydroxide as Catalyst in Organic Reactions; V. Application in the Horner Reaction under Solid-Liquid Phase-Transfer Conditions

J. V. SINISTERRA*

Organic Chemistry Department, Science Faculty, University of Córdoba, Córdoba, Spain

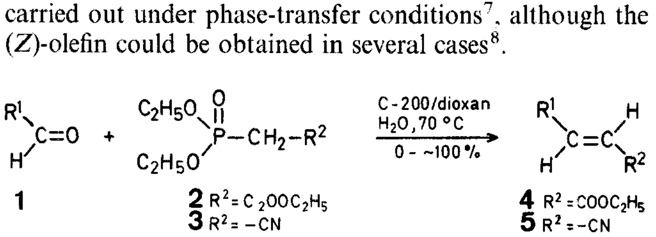
Z. MOULOUNGUI, M. DELMAS, A. GASET

Laboratoire de Chimie Organique et d'Agrochimie, Ecole Nationale Supérieure de Chimie, INPT, 118 Route de Narbonne, F-31077 Toulouse Cedex, France

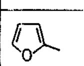
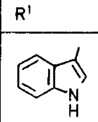
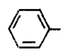
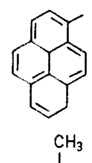
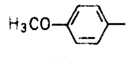
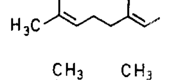
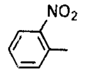
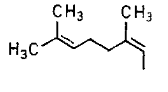
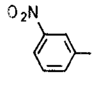
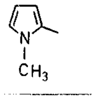
A new application of a barium hydroxide catalyst for the Horner reaction is described. The scope of the synthetic method is shown; furthermore, the yields are higher and the reaction times shorter than those previously reported for similar experimental conditions (solid-liquid). Ethyl 3-(1'-pyrenyl)-acrylate and the 3-(1'-pyrenyl)-acrylonitrile are described for the first time.

The Horner reaction (Wittig-Horner reaction) is a versatile method for the preparation of α,β-unsaturated esters **4** from aldehydes **1** and results in very good yields. This reaction avoids some of the drawbacks of classic Wittig reaction and, in addition, requires lees expensive starting materials. A great deal of work has been done on the synthetic aspects of this reaction[1]. Recently, the Horner reaction has been carried out using polymer-supported phosphonates[2], two-phase liquid-liquid[3] or solid-liquid phase-transfer conditions[4-7] and better yields were obtained than those achieved under classical conditions.

The stereochemistry of **4** is generally (*E*) when the process is carried out under phase-transfer conditions[7], although the (*Z*)-olefin could be obtained in several cases[8].



1 + **2** $R^2 = COOC_2H_5$; **3** $R^2 = -CN$ → **4** $R^2 = COOC_2H_5$; **5** $R^2 = -CN$

1	R^1	1	R^1
a		g	
b		h	
c		i	
d		j	
e		k	C_2H_5
f			

We have previously reported on the barium hydroxide catalyst (C-200) and studied its catalytic activity. Its use afforded good yields in several organic reactions in solid-liquid media: the Williamson reaction[9], Michael addition[10], the Claisen-Schmidt reaction[11], etc. The present paper describes the results obtained with this catalyst in the Horner reaction under solid-liquid phase-transfer conditions. The synthetic method has been directed to the synthesis of 3-substituted ethyl acrylates **4** due to the usefulness of these molecules as monomers in polymerization. The synthesis of acrylonitriles **5** can also be performed in this way (see Table 4) although these compounds are readily accessible by other synthetic methods.

The synthesis of ethyl 3-(2'-furyl)-acrylate (**4a**) was used to compare the catalytic activity of C-200 with that of other solids (Table 1) used under solid-liquid phase-transfer conditions. This acrylate may be used as a monomer in polymerization and the starting material furfural (**1a**; a very reactive aldehyde) can be obtained from biomass. No secondary reactions of furfural (Cannizzaro, crotonization, Knoevenagel reaction, etc.), were observed although they have been reported when aqueous bases were used as catalysts[3,12]. The synthesis was improved because the molar ratio "catalyst/aldehyde" and the reaction time were diminished (only 25 min versus 1 or 2 h). The yield and the selectivity with C-200 were 100%.

A small amount of water must be added in order to increase the reaction rate (see Table 2). This fact has been observed using other basic solids under similar solid-liquid phase-transfer conditions: potassium carbonate in the Wittig reaction[13,14] and Horner reaction[8]; potassium hydroxide in the synthesis of epoxides[15], etc. Nevertheless the role of water is not clear. Some workers say that small amounts of water are necessary to dissociate the 1,2-oxaphosphetane intermediate[13,16]. In our case, we have observed an alteration in the activity of the C-200 catalyst through elimination of the water in the active site resulting from the use of anhydrous solvents. So, the number of the active sites per unit weight of catalyst is reduced and the reaction takes place more slowly. An excess of water results in the formation of an amount of inactive barium hydroxide trihydrate and the reaction rate diminishes (Table 2). A mechanistic discussion of the process will be published later.

The dielectric constant of the solvent is not important in the Horner reaction catalyzed by C-200 in the heterogeneous phase (see Table 3). The only necessary condition seems to be

Table 1. The Horner Reaction of **1a** with **2**[a]

Catalyst	Reaction Time	Molar Ratio catalyst/**1a**	Yield [%] of **4a**
NaOH	1 h	0.66	93
KOH	1 h	0.66	83
K_2CO_3[7]	1.5 h	0.66	96
$Ba(OH)_2 \cdot 8H_2O$[b]	2.5 h	0.66	96
C-200[c]	25 min	0.52	100

[a] Reaction conditions: **1a** (0.03 mol), **2** (0.03 ml), 1,4-dioxan as solvent, water (0.5 ml), temperature: 70 °C.

[b] Commercial barium hydroxide.

[c] Molecular formula: $Ba(OH)_2 \cdot 0.8H_2O$.

Table 2. Influence of Water on the Reaction of **1a** with **2**[a]

ml of water added to 1,4-dioxan (99%; 30 ml)	Yield [%] of **4a**
0.0	20[c]
0.5	100
1.0	98
2.0	97
5.0	98

[a] Reaction conditions: **1a** (0.025 mol), **2** (0.025 mol), C-200 (2.5 g), temperature: 60 °C, time: 25 min.

[b] Molar conversion after 25 min (error ± 5%).

[c] Molar conversion after 3 h is 80%.

Table 3. Influence of Solvent on the Reaction of **1a** with **2**[a]

Solvent	Purity [% in vol]	Dielectric constant	Yield [%] of **4a**[b]
1,4-dioxan	>99%	2.2	100
ethanol	98%	24.5	97
acetonitrile	99%	30	100
tetrahydrofuran[c]	99%	2	100
benzene	100%	2.28	73[d]

[a] Reaction conditions: **1a** (0.025 mol), **2** (0.025 mol), C-200 (2.5 g), solvent (30 ml), water (0.5 ml), temperature: 70 °C, time: 25 min.

[b] Molar conversion after 25 min (error ± 5%).

[c] Reaction at 60 °C.

[d] Yield of **4a** after 60 min is 93%.

that the solvent be miscible with water: when benzene is used, the reaction takes place more slowly than with 1,4-dioxan (which has a similar dielectric constant). We therefore think that the water plays an important role in the destruction of the 1,2-oxaphosphetane intermediate and in the regeneration of the catalytic active site. That the 1,2-oxaphosphetane is produced on the solid surface is confirmed as the authors have observed characteristic signals in the I.R. spectra. Thus, the reaction takes place on the solid surface and a true phase-transfer of ylid does not take place with this catalyst, contrary to that described in the literature for other systems such as crown ethers or ammonium salts. This fact could explain why there is no observation of the influence of the dielectric constant or of the nature of the solvent.

To study the scope of the synthetic method, several aldehydes **1** with very different structures were tested using the activated barium hydroxide catalyst C-200 in the Horner reaction under the solid-liquid phase-transfer conditions. The results obtained are shown in Table 4. The yields are not optimized but they are higher than those reported under similar experimental conditions (solid-liquid).

Reaction times are dramatically reduced in some typical exemples: e.g., **1a**, 25 min versus 60 min[7]; **1b**, 25 min versus 24h[4], 3h[3], 2h[7], etc. Thus, it can be seen that the C-200 catalyst is better for the Horner reaction under solid-liquid experimental conditions than other catalysts because the reaction time is diminished. In other cases the reaction temperature is diminished, e.g. for **1b** (70 °C), 95% versus 110 °C (15 min); 91–96%[5] using potassium carbonate/toluene/Aliquat R 336. No secondary reactions are observed with very reactive aldehydes such as **1a** and **1k**.

There are no steric restrictions for the aromatic aldehydes because very favourable yields are obtained with extremely large aldehydes such as pyrene-1-carboxaldehyde (**1h**). If the planarity of the aldehyde is altered (e.g. **1d** and **1f**) lower yields are obtained than with planar aldehydes (compare **1d** with **1e**). This can be explained by a *supra-supra* reaction of the aldehyde **1** on the adsorbed ylid[17]. The aliphatic groups do not produce a great steric hindrance effect in the transition state because no difference is observed between the propanal (**1k**) and the citral isomers (**1i** and **1j**). This fact shows that in the transition state on C-200, only the CHO group participes actively while the R group is off the surface of the solid. The presence of saturated or unsaturated groups in the α position to the carbonyl group is irrelevant as far as this catalyst is concerned.

The nature of the aromatic ring substituents is important. The presence of an electron-donating group (e.g. **1c**) diminishes the electrophilicity of the C=O bond and the yield diminishes as the reaction time increases. Electron-withdrawing groups favour the process (e.g. in **1e**) if the steric hindrance does not increase. This fact is in accord with results from reactions with potassium carbonate under similar conditions[7].

The Horner process does not take place with the ketones such as acetophenone (even at 90 °C) or with aldehydes with acidic protons (e.g. **1g**) using this catalyst. This is due to the steric hindrance that prevents the C=O bond of ketone from reaching the catalytic surface. The acidity of the proton poisons the active site of the catalyst[18].

The synthesis of 3-substituted acrylonitriles **5** can be carried out with this catalyst under similar experimental conditions although increased reaction times are necessary (compare **4h** and **5h**). This could be due to the lower affinity of nitrogen than of oxygen with respect to barium(II). This could hinder the formation of the carbanion that remains adsorbed on the catalytic surface.

Ethyl 3-Substituted-acrylates 4a–k; General Procedure:

The aldehyde **1** (0.025 mol), triethyl phosphonoacetate (**2**; 5.61 g, 0.025 mol), 1,4-dioxan (30 ml), C-200 catalyst[19] (0.013 mol), and water[20] (0.5 ml) are succesively introduced into a 100 ml flask fitted with a mechanical stirrer, a thermometer, and a reflux condenser. The reaction mixture is stirred at 70 °C for the time given in Table 4. Then, the mixture is filtered and purified by chromatography on a short, broad column of silica gel Merck 40, using hexane/diethyl ether (1/1, v/v) as the eluent. The solvent is evaporated and the product recrystallized or distilled (Table 4).

3-Substituted Acrylonitriles 5a and 5h; General Procedure:

The above procedure is followed with the exception that diethyl cyanomethanephosphonate (**3**; 4.43 g, 0.025 mol) is used in place of **2** (Table 4).

Table 4. Reaction of Aldehydes **1** with **2** or **3**[a]

Product	Yield [%]		Reaction Time		m.p. [°C] or b.p. [°C]/torr		G.L.C. Retention Time [min][c] (column)
	found[b]	reported	this work	reported	found	reported	
4a	100	90[7]	25 min	60 min[d]	94–98°/5	86°/2.5[7]	2.46/5.14 (A)
4b	95	100[4]	25 min	24 h[e]	92–95°/3	95°/3[7]	1.21/8.9 (B)
4c	77	60[6]	60 min	60 min[d]	148–150°/5	125°/1[6]	2.45/5.39 (B)
4d	93	74[7]	60 min	60 min[d]	41–43°	41–42°[22]	2.99/5.86 (B)
4e	100	–	25 min	–	74–75°	75°[22]	4.27/7.95 (B)
4f	42[f]	–	120 min	–	–	–	1.74/4.58 (B)
4g	0	–	2 h	–	–	–	–
4h	84	–	25 min	–	–	–	8.25/16.8 (A)
4i	67[f,g]	–	25 min	–	–	–	2.35/4.7 (B)
4j	74[f,g,h]	–	25 min	–	–	–	2.50/5.12 (B)
4k	80[g]	92[7]	25 min	150 min[d]	30°/2	30°/2[7]	0.72/1.21 (B)
5a	100	–	40 min	–	102–105°	105°[23]	2.46/4.0 (B)
5h	91	–	90 min	–	–	–	3.25/11.5 (A)

[a] Reaction conditions: **1** (0.025 mol), **2** or **3** (0.025 mol), 1,4-dioxan (30 ml), C-200 (0.5 g, 0.013 mol), water (0.5 ml); temperature: 70 °C.
[b] Yield of recrystallized or distilled product.
[c] Retention time of aldehyde/retention time of product. Retention time of **2** = 4.49 min (column A) or 3.47 min (column B).
[d] In the presence of potassium carbonate/trace of water.
[e] In the presence of crown ether; catalyst: potassium fluoride/trace of water.
[f] Product mixture analyzed by G.L.C. and ^{1}H-N.M.R. spectrometry.
[g] No increase in yield observed after 60 min.
[h] Reaction temperature: 40 °C.
[i] In the presence of sodium hydroxide/water.

Ethyl 3-(1'-Pyrenyl)-acrylate (4h):
Prepared from 1-pyrenecarboxaldehyde (**1h**; 5.76 g, 0.025 mol; m.p. 123–126 °C, from EGA Chemie) as described above; reaction time: 25 min. The product **4h** is recrystallized from acetone; yield: 6.3 g (84%); m.p. 92 °C.

$C_{21}H_{16}O_2$	calc.	C 83.98	H 5.37
(300.3)	found	84.1	5.1

I.R. (KBr): $\nu = 1710\ cm^{-1}$ ($\underline{C}O—OC_2H_5$).

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 1.40$ (t, 3 H, $J = 7$ Hz); 4.45 (g, 2 H, $J = 7$ Hz); 6.60 (d, 1 H, $J = 16$ Hz); 7.9–8.4 (m, 9 H); 8.75 ppm (d, 1 H, $J = 16$ Hz).

^{13}C-N.M.R. (C_6D_6/TMS_{int}): $\delta = 14.5$ ($OCH_2\underline{C}H_3$); 60.5 ($O\underline{C}H_2CH_3$); 120.6, 122.4, 124.1, 125.8, 126.4, 127.3, 128.0, 128.4, 129.6, 130.4, 130.8, 131.4, 132.6 (C_{arom}); 141.2 ($=\underline{C}—COOC_2H_5$); 166.8 ppm ($\underline{C}OOC_2H_5$).

3-(1'-Pyrenyl)-acrylonitrile (5h):
Prepared as described above from **1h** (0.025 mol) and **3** (0.025 mol); reaction time: 90 min. The product is recrystallized from methanol/water (80/20, v/v); yield: 5.7 g (90%); m.p. 164–165 °C.

$C_{19}H_{11}N$	calc.	C 90.09	H 4.38	N 5.53
(253.3)	found	89.61	4.25	5.20

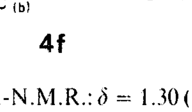
I.R. (KBr): $\nu = 2210\ cm^{-1}$ (CN).

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 6.20$ (d, 1 H, $J = 16$ Hz); 8.0–8.4 (m, 9 H); 8.6 ppm (d, 1 H, $J = 16$ Hz).

Barium Hydroxide C-200 catalyst:
Prepared as described previously[9,10]; the number of basic sites (6 ± 1.10^{-6} equiv/g solid) was described previously[21].

Analysis of the Products:
All the products were analyzed by ^{1}H-N.M.R. (Varian EM 360A). The progress evolution of the reactions as well as the purities of the end products (≥ 99% G.L.C) were deteriminated by G.L.C. (Intersmat I. G.C. 120DFL) using two columns (A ≡ 3 m × 1/8 in and B ≡ 2 m × 1/8 in) packed with 5% OV 101 on Chromosorb W-HMDS, 80–60 mesh. Carrier gas: nitrogen N_2: (1.8 bar) initial temperature: 140 °C; end temperature = 300 °C; heating rate = 20 °C min^{-1}. The microanalysis and the m.p. and b.p. of the pure reaction products agree with those in the literature.

Ethyl 3-(*N*-methyl-2-pyrrolyl)-propenoate (4f):
The reaction mixture from pyrrole-2-carboxaldehyde (**1f**) and **2** was not distilled under vacuum because decomposition was observed. The mixture was analyzed by G.L.C. (Table 4) and ^{1}H-N.M.R. [$C\underline{H}O$ of aldehyde (9.5 ppm) versus olefinic proton at 6.1 ppm] however the precision was not good. The significant signals for **4f** are given below.



4f

^{1}H-N.M.R.: $\delta = 1.30$ (t, $J = 7$ Hz, $CH_3^{(e)}$); 3.50 (s, $N—CH_3^{(a)}$); 4.10 (g, $J = 7$ Hz, $CH_2^{(d)}$); 6.10 (d, $J = 16$ Hz, $H^{(e)}$); 7.60 ppm (d, $J = 16$ Hz, $H^{(b)}$).

Received: January 21, 1985

---

[1] Becker, K.B. *Synthesis* **1983**, 341–368.
[2] Cainelli, G., Content, M., Manescalchi, F., Regnoli R. *J. Chem. Soc. Perkin Trans. 1* **1980**, 2516–2519.
[3] Piechucki, C. *Synthesis* **1974**, 869–870.
[4] Texier-Boullet, F., Foucaud, A. *Tetrahedron Lett.* **1980**, *21*, 2161–2164.
[5] Villieras, J., Rambaud, M., Kirshleger, B. *Phosphorus Sulfur* **1983**, *14*, 385–391.
[6] Villieras, J., Rambaud, M. *Synthesis* **1983**, 300–303.
[7] Mouloungui, Z., Delmas, M., Gaset, A. *Synth. Commun.* **1984**, *14*, 701–705.
[8] Still, W.C., Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405–4408.
[9] Garcia-Raso, A., Sinisterra, J.V., Marinas, J.M. *Pol. J. Chem.* **1982**, *56*, 1435–1445.
[10] Garcia-Raso, A., Garcia-Raso, J.A., Campaner, B., Mestres, R., Sinisterra, J.V. *Synthesis* **1982**, 1037–1041.
[11] Sinisterra, J.V., Garcia-Raso, A., Cabello, J.A., Marinas, J.M. *Synthesis* **1984**, 502–504.
[12] Hünig, S., Stemmler, I. *Tetrahedron Lett.* **1974**, 3151–3154.
[13] Delmas, M., Le Bigot, Y., Gaset, A. *Tetrahedron Lett.* **1980**, *21*, 4831–4833.

[14] Delmas, M., Le Bigot, Y., Gaset, A., Gorrichon, J. P. *Synth. Commun.* **1981**, *11*, 125–132.

[15] Borredon, E., Delmas, M., Gaset, A. *Tetrahedron Lett.* **1982**, *23*, 5283–5286.

[16] Artaud, I., Seyden-Penne, J., Viout, P. *Tetrahedron Lett.* **1980**, *21*, 613–616.

[17] The 1,2-oxaphosphetane intermediate remains adsorbed on the solid surface as has been observed in I. R. spectra (unpublished data).

[18] The Horner reaction was not observed with ethyl methyl ketone, *i*-propyl methyl ketone, *t*-butyl methyl ketone, and salicylic aldehyde.

[19] The molecular ratio catalyst/aldehyde is lower for C-200 than previously described for the other catalysts potassium carbonate, potassium hydroxide, and sodium hydroxide[7].

[20] The process does not take place unless water is added. The influence of water in the Horner reaction mechanism catalyzed by C-200 is under research.

[21] Sinisterra, J. V., Garcia-Blanco, F., Iglesias, M., Marinas, J. M. *React. Kinet. Catal. Lett.* **1984**, *25*, 277–282.

[22] Tanaka, S., Uekama, K., Ikeda, K. *Chem. Pharm. Bull.* **1976**, *24*, 2825–2831.

[23] Fujiwara, Y., Maruyama, O., Yushidomi, M., Taniguchi, H. *J. Org. Chem.* **1981**, *46*, 851–855.