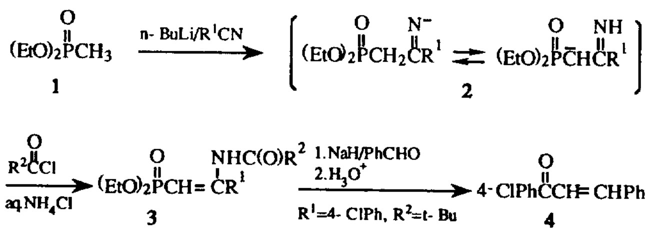

Scheme 1.

Table 1. Preparation of Enamine Phosphonates **3**

Product	R^1	R^2	Yield (%)^a	^{1}H NMR^b P(O)CH=C
3a	Ph	Ph	67(16)	5.03, d, J=11Hz
3b	Ph	4-ClPh	78(10)	4.98, d, J=12Hz
3c^c	Ph	N(Me)$_2$	36(27)	4.80, d, J=11Hz
3b	Ph	t-Bu	76(10)	5.00, d, J=12Hz
3e	4-ClPh	Ph	75(12)	5.08, d, J=11Hz
3f	4-ClPh	t-Bu	82(10)	4.95, d, J=11Hz
3g	4-MePh	Ph	60(13)	4.84, d, J=10Hz

[a] Isolated yield, the values given in parenthesis are yield of the corresponding β-keto phosphonates. [b] Obtained in $CDCl_3$ and expressed in δ (ppm) downfield from TMS, d=doublet. [c] The reaction time was 3 h at room temperature after the addition of dimethylcarbamyl chloride.

In the course of our investigations into synthetic utility of nitrile group,[1] we have further studied the nucleophilic addition of α-lithioanion of diethyl methylphosphonate to nitriles followed by subsequent acylation and isomerization to give enamine phosphonates, which is used as the basis for an efficient synthesis of α,β-unsaturated ketones and β-ketophosphonates.[2]

As shown in Scheme 1. α-lithiomethane phosphonates react with nitriles to give ketimine intermediates **2**, which react with acyl halides and subsequently isomerized in saturated NH_4Cl solution to give enamine phosphonates **3**. Our results are summarized in the Table 1. All but one of the acyl derivatives studied gave satisfactory yields along with a small amount of corresponding β-ketophosphonates (10-27%).

Among several acylating agents tested in this study, trimethylacetyl chloride gave the best results. The β-keto phosphonates are derived from the unreacted ketimine intermediates, which is proved by TLC.

Although the anion **2** is more nucleophilic at carbon than it is at nitrogen, the acylation occurs only at nitrogen. The ketimine → enamine isomerization takes place very rapidly. The driving force for this isomerization may be attributed to the conjugation of the two activating groups with the amino group[3].

As an example for the synthesis of α,β-unsaturated ketones with N-acylated enamine phosphonates obtained by our procedure, we have treated that enamine phosphonate (**3f**) successively with NaH-PhCHO-hydrolysis (**3** → **4**). As expected, 4′-chlorochalcone was obtained in nearly quantitative yield (93%). In summary, the α-lithiomethane phosphonate addition-N-acylation-isomerization of nitriles to form enamine phosphonates has been established as an attractive synthetic method.

Experimental

General procedure for 1→3. To a stirred solution of diethylmethane phosphonate (1.1 mmol) in dry THF (3 m*l*), is added n-butyllithium (1.1 mmol, 1.6 M in hexane) at −78 °C under nitrogen atmosphere. After being stirred for 1 h at −78 °C, nitrile (1 mmol) is added and the reaction mixture is warmed to −5 °C for 2 h. Acyl halide (1 mmol) is added dropwise at −78 °C and stirred for 30 min at −78 °C. Usual work up with sat. aq. NH_4Cl give the crude enamine phosphonates, which is purified by short-path column chromatography on silica gel (8/2: hexane/ethylacetate).

Procedure for 3→4. To a suspension of NaH (1 mmol) in dry THF (3 m), is added 1 mmol of enamine phosphonate (3f, R^1=4-ClPh, R^2=t-Bu) at 0° under nitrogen atmosphere. The reaction mixture is stirred for additional 5 min at 0 °C to allow completion of the H_2 evolution. Benzaldehyde (1 mmol) is added and the solution is refluxed for 10 h. Hydrolysis is accomplished directly by addition of 10% oxalic acid (1 mL) for 8 h at room temperature. Normal workup give the 4′-chlorochalcone, which is purified by short-path column chromatography on silica gel (10/1: hexane/ethylacetate). mp: 93-95 °C, ^{1}H-NMR (δ, $CDCl_3$): 7.17-8.10 (11H, m). IR (cm^{-1}, KBr): 1660 (C=O), 1590 (C=C). MS (%): 244 (M+2, 16.4), 242 (57.9), 241 (72.4), 207 (37.7), 179 (82.2), 139 (42.8), 111 (100), 77 (97.9).

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Carbonylation of Benzal Chloride to Alkyl Phenylacetates using $Co_2(CO)_8$ Catalyst

Sang Chul Shim*, Chil Hoon Doh, and Chan Sik Cho

Department of Industrial Chemistry, Kyungpook National University, Taegu 702-701

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The technology of transition metal complexes catalyzed

Table 1. Carbonylation of Benzal Chloride to Alkyl Phenylacetates using $Co_2(CO)_8$[a]

Entry	Base (5 meq.)	Alcohol ROH	Yield of[b] $C_6H_5CH_2COOR$	C_6H_5CHO
1	K_2CO_3	C_2H_5OH	92(85)	6
2	None	C_2H_5OH	11	49
3	$Ca(OH)_2$	C_2H_5OH	59	19
4	KOH	C_2H_5OH	43	39
5	NEt_3	C_2H_5OH	32	trace
6	K_2CO_3	CH_3OH	36(32)	54
7	K_2CO_3	$n-C_3H_7OH$	34(31)	10
8	K_2CO_3	$i-C_3H_7OH$	45(43)	5
9	K_2CO_3	$n-C_4H_9OH$	69(48)	6
10	K_2CO_3	$t-C_4H_9OH$	trace	4

[a] Benzal chloride (0.325g, 2 mmol) base (5 meq), alkanol (10 m*l*), and $Co_2(CO)_8$ (0.034g, 0.1 mmol) at 80 °C for 24 h under 30 atm of CO. [b] GLC yield, phenyl ether as internal standard; parentheses are isolated yields.

carbonylation reaction is being currently used for the production of large volume chemicals.[1] Many applications are reported on the carbonylation of benzyl halides with carbon monoxide using cobalt,[2] iron,[3] ruthenium,[4] rhodium,[5] and palladium.[6] However, there are few reports on the carbonylation of benzal halides as the geminal dihalide compound to give alkyl phenylacetates[7] and phenylacetic acids.[8] The alkyl phenylacetates are used as a perfume in waxes and honey.

We herein wish to report a simple method for the carbonylation of benzal chloride leads to alkyl phenylacetates in good yield.

$$C_6H_5CHCl_2 + \underset{(30\ \mathrm{atm})}{CO} + ROH \xrightarrow[80\ ^\circ C]{Co_2(CO)_8,\ K_2CO_3} C_6H_5CH_2COOR$$

A typical procedure is illustrated as follows: In a 100 m*l* stainless steel autoclave, a mixture of benzal chloride (0.325 g, 2.0 mmol), potassium carbonate (0.345g, 2.5 mmol), ethanol (10 m*l*), and dicobalt octacarbonyl (0.034 g, 0.1 mmol) is placed under an argon atmosphere. Carbon monoxide is charged up to 30 atm at room temperature, and then the mixture is stirred at 80 °C for 24 h. After cooling, the carbon monoxide is vented out in fume hood. The mixture is filtered, concentrated, and then separated by column chromatography (SiO_2, ethyl acetate-hexane). The products are analyzed by means of ^1H, ^{13}C-NMR, mass, and IR spectra.

Table 1 shows that dicobalt octacarbonyl in alkanol medium can be used for selective monocarbonylation of benzal chloride. The optimum condition is found as 80 °C and 30 atm of carbon monoxide. Potassium carbonate, calcium hydroxide, triethylamine, and potassium hydroxide are used both as acid scavenger and catalyst activator in alkanol medium. Potassium carbonate is superior for the selective monocarbonylation to others (Entry 1). In the absence of base, formation of the carbonylated product is reduced and benzaldehyde is formed in considerable amount (Entry 2). With potassium hydroxide, ethyl phenylacetate and benzaldehyde are formed almost equally (Entry 4). The use of other alcohols-potassium carbonate system leads to lower yields of carbonylated products (Entries 6-10). Application of the present procedure to other substituted benzal chlorides and elucidation of reaction mechanism are now in progress and will be reported in due time.

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Enantiospecific Synthesis of (+)-Coriolic Acid, A Self-Defensive Substance against Rice Blast Disease[1]

Suk-Ku Kang* and Kun-Soo Kim

Department of Chemistry, Sung Kyun Kwan University,
Natural Science Campus, Suwon 440-746

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Coriolic acid **1**[2] is an oxygenated unsaturated fatty acid which has the structure of 13-hydroxy-9Z,11E-octadecadienoic acid. This metabolite of linoleic acid in vegetable oils or in bovine heart mitochondria, exhibits unique calcium-specific ionophoric activity.[3] Recently (+)-**1** has been