The Conversion of Benzyl Alcohols into Phenylacetic Acid Derivatives by Cobalt Carbonyl Catalyzed Carbonylation

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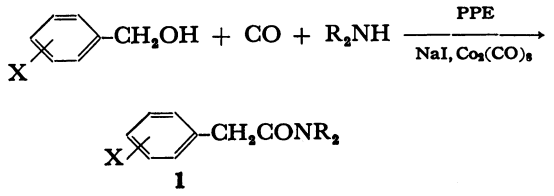
Synopsis. Benzyl alcohols were converted into the corresponding one carbon-homologated amides or esters in one pot by cobalt carbonyl catalyzed carbonylation in the presence of ethyl polyphosphate (PPE) and sodium iodide.

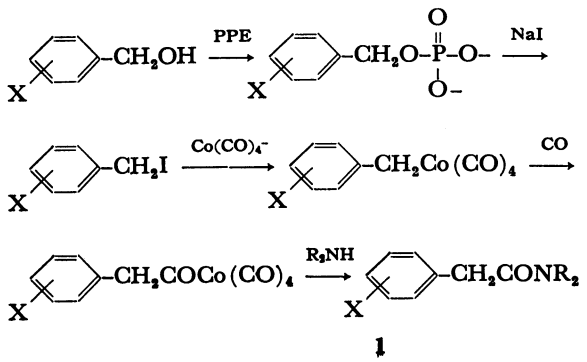
Recently, attention is focused on the catalytic carbonylation under mild conditions and many efficient methods including catalytic systems have been developed.[1-6] For example, phase transfer technique has been successfully employed for the carbonylation of benzyl, aryl, and vinyl halides to the homologous acids.[7-10] However, direct carbonylation of alcohols requires drastic conditions (high temperature and high pressure).[11] We report here a facile method for the conversion of benzyl alcohols into one carbon-homologated amides or esters by cobalt carbonyl catalyzed carbonylation under mild conditions.

In the previous papers,[12-14] we noted the synthetic utility of ethyl polyphosphate (PPE).[15,16] The reagent PPE has strong dehydration power as well as the commonly used polyphosphoric acid (PPA), but it is, different from PPA, essentially aprotic and has good solvent power at room temperature. Taking account of these characteristics of PPE, we have examined the title reaction.



Scheme 1.

Our initial work was conducted with the preparation of substituted phenylacetamides (**1**), as is shown in the Scheme 1. This work was undertaken based on the following considerations; a benzyl alcohol is activated by PPE to form a polyphosphoric acid benzyl ester which is subject to nucleophilic attack of iodide ion to generate a benzyl iodide. This intermediate readily undergoes cobalt carbonyl catalyzed carbonylation in the presence of secondary amine to afford an amide (**1**).



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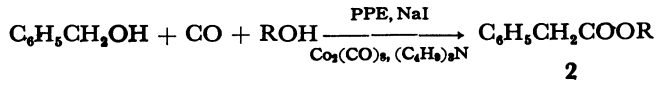
After various screenings of the reaction conditions, it was found that the reaction proceeded smoothly at room temperature under carbon monoxide atmosphere by the use of large excess of sterically hindered secondary amine. While, the use of less sterically hindered amine such as diethylamine resulted in poor yields. These results are summarized in Table 1.

Next, we tried the conversion of benzyl alcohol into phenylacetic esters (**2**) in one pot, according to the



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Scheme 2.

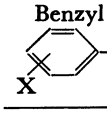
Scheme 2. In these cases, better results were obtained by initial stirring of a mixture of benzyl alcohol, sodium iodide, and PPE for 2 h, prior to the addition of a mixture of an alcohol, dicobalt octacarbonyl, and tributylamine. The results are shown in Table 2.

From these data, it may be concluded that our method is superior to those[11] reported hitherto, since the procedure is simple and the products are isolated in moderate yields.

Experimental

Spectra. Proton NMR spectra were measured on a JEOL C-60HL spectrometer. The chemical shifts are given in ppm with TMS as an internal standard. Infrared spectra

Table 1. Conversion of benzyl alcohols to substituted phenylacetamides (**1**)

Benzyl alcohol 	Secondary amine R_2NH	Product	Yield/%[a]
X=H	R=*i*-C_3H_7	**1a**	71
H	Cyclohexyl	**1b**	49
H	C_2H_5	**1c**	20
p-CH_3O	*i*-C_3H_7	**1d**	47
p-Cl	*i*-C_3H_7	**1e**	62
o-Cl	*i*-C_3H_7	**1f**	78
p-Br	*i*-C_3H_7	**1g**	82
p-NO_2	*i*-C_3H_7	**1h**	40

a) Yields after chromatography.

Table 2. Conversion of benzyl alcohol to phenylacetic esters (**2**)

Alcohol	Product	Yield/%[a]
CH_3OH	$C_6H_5CH_2COOCH_3$	77
C_2H_5OH	$C_6H_5CH_2COOC_2H_5$	47
t-C_4H_9OH	$C_6H_5CH_2COOC_4H_9$-*t*	35
C_6H_5OH	$C_6H_5CH_2COOC_6H_5$	68
—	$C_6H_5CH_2COOCH_2C_6H_5$	37

a) Yields after chromatography.

Table 3. Physical properties and analytical data of substituted phenylacetamides

Compound	Mp θ_m/°C	IR ($\tilde{\nu}_{C=O}$/cm^{-1})	^{1}H-NMR(δ)	Found (Calcd) (%)		
1a	52 Lit,[a] 51	1620	0.65—1.90(m, 12H), 2.95—4.30 (m, 2H), 3.60 (s, 2H), 7.25(s, 5H)			
1b	83—84	1620	0.65—3.75 (s, 22H), 3.60 (s, 2H), 7.25 (s, 5H)	79.85 (80.22)	9.69 (9.76)	4.65 (4.68)
1c	Oil Lit,[a] Bp 120—122 °C/0.3 Torr†	1635	1.00 (t, 3H, J=7.5 Hz), 1.05 (t, 3H, J=7.5 Hz), 3.25 (q, 2H, J=7.5 Hz), 3.30 (q, 2H, J=7.5 Hz), 3.60 (s, 2H), 7.25 (s, 5H)			
1d	63—64	1635	0.65—1.90 (m, 12H), 2.90—4.25 (m, 2H), 3.55 (s, 2H), 3.75 (s, 3H), 6.75 (d, 2H, J=9.0 Hz),7.15 (d, 2H, J=9.0 Hz)	71.99 (72.25)	9.26 (9.30)	5.55 (5.62)
1e	52—53	1640	0.65—1.85 (m, 12H), 2.95—4.30 (m, 2H), 3.55 (s, 2H), 7.25 (s, 4H)	66.01 (66.26)	7.86 (7.94)	5.42 (5.52)
1f	53—54	1640	0.65—1.90 (m, 12H), 2.90—4.35 (m, 2H), 3.65 (s, 2H), 7.25 (m, 4H)	66.03 (66.26)	7.85 (7.94)	5.41 (5.52)
1g	50—51	1630	0.80—1.70 (m, 12H), 3.00—4.25 (m, 2H), 3.65 (s, 2H), 7.15(d,2H, J=8.0 Hz),7.50 (d, 2H, J=8.0 Hz)	56.29 (56.39)	6.72 (6.76)	4.61 (4.70)
1h	77—78	1635	0.75—1.65 (m, 12H), 2.90—4.30 (m, 2H), 3.70 (s, 2H),7.45 (d,2H,J=9.0 Hz),8.15 (d, 2H, J=9 Hz)	63.48 (63.62)	7.55 (7.63)	10.48 (10.60)

a) R. Mukherjee, *J. Chem. Soc., Chem. Commun.*, **1971**, 1113. † 1 Torr ≈ 133.322 Pa.

were recorded on a Hitachi 215 spectrophotometer. Products were identified by NMR and IR spectra together with elemental analyses.

Materials. Ethyl polyphosphate was prepared according to the method described in the Ref. 15. Benzyl alcohols, secondary amines, and tributylamine were distilled or recrystallized before use. Dicobalt octacarbonyl was purchased from Strem Chemicals, Inc. and was used without purification.

General Procedure for the Preparation of Phenylacetamides (1a—h). A mixture of a benzyl alcohol (2 mmol), sodium iodide (600 mg, 4 mmol), dicobalt octacarbonyl (34 mg, 0.1 mmol), a secondary amine (20 mmol), and PPE (3 ml) was stirred at room temperature under carbon monoxide atmosphere. After 12 h, water was added and the mixture was extracted with chloroform. The combined extracts were dried over sodium sulfate and evaporated. The residual oil was chromatographed on silica gel using benzene–ethyl acetate (6 : 1) as the eluent. The product was further purified by short-path distillation under reduced pressure (Kugelrohr apparatus; *ca.* 190 °C/0.3 Torr). Pure materials thus obtained crystallized on standing at room temperature except *N,N*-diethylphenylacetamide (**1c**). The NMR, IR, and analytical data of the products are listed in Table 3.

General Procedure for the Preparation of Phenylacetic Esters (2). A mixture of benzyl alcohol (216 mg, 2 mmol), sodium iodide (400 mg, 4 mmol), and PPE (3 ml) was stirred at room temperature for 2 h. To this mixture was added a mixture of an alcohol (8 mmol), dicobalt octacarbonyl (34 mg, 0.1 mmol), and tributylamine (3.7 g, 20 mmol) under carbon monoxide atmosphere. After stirring for 12 h, water was added and the mixture was extracted with chloroform. The combined extracts were dried over sodium sulfate and evaporated. The residual oil was chromatographed on silica gel using benzene as the eluent. The product was further purified by short-path distillation under reduced pressure. The esters thus obtained were identified by comparison of their IR and NMR spectra with those of authentic samples.

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