**G. Preparation of compound 1-C.** The same procedure as employed with A was used yielding compound 1-C. 1-C: IR($\nu$(CO)) 2017, 1921 $cm^{-1}$, $^1H$ NMR($CDCl_3$) $\delta$ 2.90(dd, 1H), 3.50(m, 2H), 3.65(d, -OMe, J(p, OMe) 10 Hz), 4.06(s, -OMe), 4.99(t, 1H), 5.90(d, 1H).

**H. Reaction between compound 1-C and $^t$BuLi.** The same procedure as employed with was used yielding compound 3-D (73%). 3-D: IR($\nu$(CO)) 2013, 1921 $cm^{-1}$, $^1H$ NMR ($CDCl_3$) $\delta$ 0.58($\delta$, $^t$Bu), 2.48(t, 1H), 3.00(d, 1H), 3.20(m, 1H), 3.47(s, OMe), 4.90(t, 1H), 5.53(d, 1H).

**I. Demetallation of compound 3-D.** I-a). A little excess of $Me_3NO$ was added to compound 3-D(0.85 mmole) in benzene (30 m*l*). The reaction mixture was refluxed for 4 hrs. After cooled to room temperature, any solids were filtered off. After removal of the solvent, NMR spectrum was taken.

I-b). A solution of iodine (7-10 mg-atoms) in THF (10 m*l*) was added rapidly via syringing to the solution of compound 3-D at -78 °C. The resulting mixture was warmed to room temperature and stirred for 16 hrs. After evaporation of the solvent, extracted with ethylether. After chromatographed on silica gel, the meta-tert-butyl-anisole was obtained in 77%. The $^1H$ NMR spectrum of the meta-tert-butyl-anisole was $\delta$1.27(s, $^t$Bu), 3.70(s. OMe), 6.5-7.1 (Ph).

**Acknowledgement.** This work was supported by KAIST and the Korea Science and Engineering Foundation.

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# Clean Reduction of $\alpha,\beta$-Unsaturated Carboxylic Acid Derivatives to the Saturated Derivatives by Potassium Triphenylborohydride in the Presence of Phenol

**Soo Bong Park, Kwan Eung Kim, and Nung Min Yoon***

*Department of Chemistry, Sogang University, Seoul 121-742.* *Received June 9, 1988*

$\alpha,\beta$-Unsaturated carboxylic acid derivatives such as esters, amides, and nitriles are readily reduced to the corresponding saturated derivatives by potassium triphenylborohydride, $KPh_3BH$, in the presence of phenol, a quenching agent, in excellent yields.

## Introduction

Aside from the catalytic hydrogenation,[1] there have been reported several reducing systems which could be effectively used for the reduction of $\alpha,\beta$-unsaturated acid derivatives to the corresponding saturated ones. These are Mg/MeOH[1], Lis-$Bu_3BH$ (L-Selectride)/$t$-BuOH[2], copper(I) hydride complex[3], DIBAH with MeCu[4] and silicone hydrides with Pd[5] or

**Table 1. Reduction of Representative α,β-Unsaturated Esters to the Corresponding Saturated Esters with $KPh_3BH$ in the Presence of Phenol[a]**

| entry | substrate | phenol[b] | $KPh_3BH$[b] | temp (°C) | time (h) | yield (%)[c] | |
|---|---|---|---|---|---|---|---|
| | | | | | | product (sat. ester) | substrate (unreacted) |
| 1 | ethyl acrylate | 1.5 | 2.0 | 25 | 0.25 | 90 | 0 |
| 2 | ethyl methacrylate | 0 | 1.0 | −78 | 10.0 | 21 | 68 |
| | | 0 | 1.0 | 0 | 1.0 | 0 | 0 |
| | | 1.5 | 1.5 | 0 | 0.25 | 92 | 6 |
| | | 1.5 | 2.0 | 25 | 0.25 | 99.5 | 0 |
| 3 | ethyl crotonate | 1.5 | 2.0 | 25 | 0.25 | 94 | 0 |
| 4 | ethyl 3,3-dimethylacrylate | 1.5 | 2.0 | 65 | 1.0 | 43 | 55 |
| | | 1.5 | 4.0 | 65 | 3.0 | 85 | 12 |
| | | 1.5 | 4.0 | 65 | 6.0 | 93 | 0 |
| 5 | methyl 1-cyclohexenecarboxylate | 1.5 | 2.0 | 65 | 2.0 | 78 | 19 |
| | | 1.5 | 4.0 | 65 | 1.] | 95 | tr. |
| 6 | ethyl cinnamate | 1.5 | 2.0 | 25 | 1.0 | 99(90)[d] | 0 |

[a]A mixture of substrate and phenol was added to $KPh_3BH$ in THF. [b]Mmoles per mmole of substrate. [c]Analyzed by GLC. [d]Isolated yield.

**Table 2. Reduction of Representative α,β-Unsaturated Amides to the Corresponding Saturated Amides with $KPh_3BH$ in the Presence of Phenol[a]**

| entry | substrate | phenol[b] | $KPh_3BH$[b] | temp (°C) | time (h) | yield (%)[c] | |
|---|---|---|---|---|---|---|---|
| | | | | | | product (sat. ester) | substrate (unreacted) |
| 1 | N,N-dimethylacrylamide | 2 | 2 | 65 | 0.5 | 90 | 0 |
| 2 | N,N-dimethylmethacrylamide | 2 | 2 | 65 | 12.0 | 60 | 40 |
| | | 2 | 4 | 65 | 6.0 | 93 | 7 |
| | | 2 | 4 | 65 | 12.0 | 100 | 0 |
| 3 | N,N-dimethylcrotonamide | 0 | 2 | 25 | 24.0 | 94 | 0 |
| | | 0 | 2 | 65 | 1.0 | 42 | 0 |
| | | 2 | 2 | 65 | 0.5 | 99 | 0 |
| 4 | N,N,3,3-tetramethylacrylamide | 2 | 4 | 65 | 3.0 | 0 | 96 |
| 5 | N,N-dimethylcinnamide | 2 | 2 | 65 | 3.0 | 87[d] | 0 |

[a]A mixture of substrate and phenol was added to $KPh_3BH$ in THF. [b]Mmoles per mmole of substrate. [c]Analyzed by GLC. [d]Isolated yield.

Mo[6] catalyst. However, some of these suffer from their own difficulties; the reaction of α,β-unsaturated esters by L-Selectride sometimes provides poor yield, and cases where L-Selectride[2], the copper(I) hydride complex[3] and DIBAH with MeCu system involved require low temperature (−78 °C and −50 °C). The most promising system of choice for such reductions seems to be the silicone hydride which affords excellent chemoselectivity and yields.

Recently we have studied the reducing characteristics of potassium triphenylborohydrides, $KPh_3BH$[7], and found it is a very mild reducing agent, capable of reducing ketones with an excellent stereo- and chemoselectivity.[8] Moreover $KPh_3BH$ showed a greater tendency of 1,4 reduction for α,β-unsaturated ketones[9] than potassium tri-*s*-butylborohydride K*s*-$Bu_3BH$. This suggests that $KPh_3BH$ could also be an excellent 1,4-reducing agent for α,β-unsaturated acid derivatives. Therefore we have decided to study this possibility for α,β-unsaturated esters, amides and nitriles.

## Results

First we examined the reaction of ethyl methacrylate, an α,β-unsaturated ester, with $KPh_3BH$ alone (Table I, entry 2). The reaction proceeded very slowly at −78 °C, giving only 21% of the saturated reduction product, ethyl isobutyrate, in 10 h. At 0 °C, the reaction accelerated and ethyl methacrylate disappeared rapidly, however, no saturated product was detected. We reasoned this was due to the rapid formation of ester enolate which reacts readily with another substrate molecule, as suggested by Ganem.[2] Therefore we anticipated the addition of a quenching agent which would inhibit the further condensation reaction. We tested several quenching agent such as methanol, phenol, caproic acid and benzenethiol, and found phenol was the best. Thus the addition of a mixture of ethyl methacrylate and phenol (1.5 equiv) to a THF solution of $KPh_3BH$ (2.0 equiv) at 25 °C, followed by the careful oxidative work-up after 15 min reaction afforded pure ethyl isobutyrate in 99.5% yield. We have extended this method to five more representative α,β-unsaturated esters, and the results are summarized in Table 1. Simple esters such as ethyl acrylate, ethyl crotonate and ethyl cinnamate were all reduced smoothly to the corresponding saturated esters, however the more hindered esters, such as ethyl 3,3-dimethyl-acrylate and methyl 1-cyclohexenecarboxylate

**Table 3. Reduction of Representative α,β-Unsaturated Nitriles to the Corresponding Saturated Nitriles with $KPh_3BH$ in the Presence of Phenol[a]**

| entry | substrate | phenol[b] | $KPh_3BH$[b] | temp (°C) | time (h) | yield (%)[c] | |
|---|---|---|---|---|---|---|---|
| | | | | | | product (sat. nitrile) | substrate (unreacted) |
| 1 | acrylonitrile | 0 | 1 | -78 | 3.0 | 0 | 0 |
| | | 0 | 1 | 0 | 0.5 | 0 | 0 |
| | | 3 | 2 | 0 | 0.25 | 78 | 0 |
| | | 3 | 2 | 25 | 0.25 | 62 | 0 |
| | | 6 | 2 | 0 | 0.25 | 84 | 0 |
| 2 | methacrylonitrile | 6 | 2 | 0 | 0.25 | 94 | 0 |
| 3 | crotonitrile | 6 | 2 | 0 | 0.25 | 84 | 0 |
| 4 | cinnamonitrile | 6 | 2 | 0 | 12.0 | 90 | 7 |
| | | 6 | 4 | 0 | 6.0 | 97 | 0 |

[a]A mixture of substrate and phenol was added to $KPh_3BH$ in THF. [b]Mmoles per mmole of substrate. [c]Analyzed by GLC.

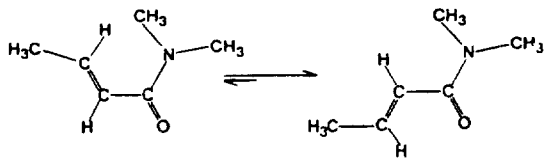
required higher temperature (65 °C) and much excess reagent (4 equiv) for the quantitative reduction. The isolated yield of ethyl hydrocinnamate amounts to 90%. These results show clearly that $KPh_3BH$ is much superior compared to L-Selectride[2] for such 1,4-reduction. For example, the yield of methyl cyclohexanecarboxylate by this system is 95%, whereas only 11% by L-Selectride.

Next, we studied the reaction of N,N-dimethylcrotonamide as a representative of α,β-unsaturated amides. Interestingly, the reaction proceeded smoothly to give the corresponding saturated amide in a yield of 94% in 24 h at room temperature, in the absence of phenol. This suggests that unlike the ester enolate, the possible amide enolate[10] does not react with another amide molecule at such temperature. However, at the elevated reaction temperature of 65 °C the quenching agent, phenol, was necessary. Thus we obtained a quantitative yield of saturated amide in 0.5 h at 65 °C in the presence of 2 equiv of phenol. We have extended this method to four more representative α,β-unsaturated amides and the results are summarized in Table 2.

As shown in Table 2, the reaction of N,N-dimethylacrylamide, N,N-dimethylmethacrylamide, and N,N-dimethylcinnamide also affords excellent yields similarly, however, the more hindered amide such as N,N,3,3-tetramethylacrylamide failed to react in 3 h at 65 °C even with 4 equiv of $KPh_3BH$. The slower reaction of N,N-dimethyl methacrylamide, compared to N,N-dimethylcrotonamide is also interesting to note.

Presumably the steric factor of methyl groups on the double bond seems to bring about such rate difference. In order to proceed via 1,4-reduction, the C-C double bond should be coplanar with the *t*-amide group including two methyl groups on nitrogen, since the C-N bond of amide has a partial double bond character. Thus in the case of the N,N,3,3-tetramethylacrylamide the two β-methyl groups does not allow it to be coplanar. The faster reaction of N,N-dimethylcrotonamide may have been proceed through the coplanar cisoid form, which has much less steric hindrance, whereas N,N-dimethylmethacrylamide may have considerable difficulty to assume the cisoid form due to the α-methyl group.

Finally, we applied this method to the representative α,β-unsaturated nitriles. As shown in the reaction with acrylonitrile, no saturated nitrile could be obtained in the absence of phenol even at -78 °C. Unlike the enolates formed from



transoid form cisoid form

esters and amides, the intermediate produced from α,β-unsaturated nitrile by 1,4 reduction seems to be very reactive for attacking another nitrile molecule. Six equiv of phenol was necessary for the effective quenching. The rather slow reaction with cinnamonitrile may be due to the extended conjugation with benzene ring. The results are summarized in Table 3.

## Experimental

The following are the typical experimental procedures.

**Product analysis.** In a 50 m*l* flask fitted with a rubber syringe cap on an inlet tube, a magnetic stirring bar, and a reflux condenser connected to a gas buret was placed 4 m*l* (2 mmol) of a 0.5 M solution of $KPh_3BH$. With stirring, 1 m*l* of a mixed solution of ethyl methacrylate (1 mmol), phenol (1.5 mmol) and naphthalene (0.5 mmol, an internal standard) was added slowly at 25 °C. After stirring for 15 min, the reaction mixture was oxidized by the addition of 0.4 m*l* of 3N NaOH, followed by 0.5 m*l* of 30% $H_2O_2$ at 30-35 °C for 2 h. The aqueous layer was saturated with anhydrous $K_2CO_3$. The GLC analysis of the THF layer showed a 99.5% yield of ethyl isobutyrate.

**Simplified product isolation.** A mixture of ethyl cinnamate (2 mmol) and phenol (3 mmol) in dry THF (2 m*l*) was added dropwise to a THF solution of $KPh_3BH$ (4 mmol in 8 m*l* THF) in a 100 m*l* round bottom flask under $N_2$ at 25 °C. After 1 h, 3N NaOH (20 m*l*) and hexane (60 m*l*) was added. After the mixture was stirred for 1 h, the aqueous layer was extracted twice with ether (30 m*l*) and the combined organic phase was washed with 3N NaOH until no more phenol was detected by TLC. The solution was washed with water (30 m*l*), and with brine (30 m*l*) and dried over anhydrous $MgSO_4$ and evaporated to afford 0.321 g (90%) of ethyl hydrocinnamate indentical in every respect with an authentic sample.

**Acknowledgement.** We are grateful to the Ministry of Education for the financial support of this work.

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10. We are going to study the reaction of this enolate of amide in near future.


# The Pfeiffer Effect of [Co$^{II}$(acac)$_2$ (diamine)] with Cinchona Alkaloid in Some Organic Solvents

**Chang Eon Oh* and Yang Kim**

*Department of Chemistry, Yeungnam University, Gyongsan 632.* *Received June 1, 1988*

The Pfeiffer effect was examined on the systems of racemic [Co$^{II}$(acac)$_2$(diamine)] with *d*-cinchonine and *l*-cinchonidine as chiral environment substances in methanol, ethanol, chloroform and methanol-chloroform mixture solvents. It was found that the $\Delta$-enantiomer is enriched for the [Co$^{II}$(acac)$_2$(diamine)]—*d*-cinchonine system, but the $\Lambda$-enantiomer is enriched for the-[Co$^{II}$(acac)$_2$(diamine)]—*l*-cinchonidine system. The complexes having no N-H protons such as [Co$^{II}$(acac)$_2$(bpy)] and [Co$^{II}$(acac)$_2$(phen)] were Pfeiffer-inactive in alcoholic solvents, where bpy = 2,2′-bipyridine and phen = 1,10-phenanthroline. This was interpreted to mean that the hydrogen bonding between N-H proton of diamine ligand and C-9 hydroxyl group of alkalid plays an important role in the chiral discrimination. And the rate of antiracemization ($k_{anti}$) by the Pfeiffer effect was also measured for the [Co$^{II}$(acac)$_2$(diamine)]—*d*-cinchonine system in alcoholic solvents. It was found that the rate of appearance of the Pfeiffer effect was enhanced as the concentration of added chloroform is increased.

## Introduction

When a recemic mixture of an optically labile dissymmetric complex is mixed in solution containing a certain optically active compound (called an environment substance), an anomalous change in optical activity is developed. This phenomenon is known as the Pfeiffer effect[1,2], and partial resolution[3-5] of several metal complexes was accomplished by using the Pfeiffer effect. Either the optically active metal complex or chiral organic compound as the environment substance is used in the Pfeiffer effect. A number of the Pfeiffer effect have been reported[6-9] and it has been known that an enantiomerization[10-12] of the complex takes place in favor of either $\Lambda$- or $\Delta$-enantiomer, depending on the spacial demand of the environment substance. This enantiomerization ("equilibrium shift") is known as a prototype of so-called first order asymmetric transformation. Several investigators have studied the Pfeiffer effect of ionic complexes, and notable works have been accomplished by Miyoshi *et al.*[3-5] and Kirschner *et al.*[2,6,7], who investigated a through study of the Co(II), Ni(II) and Zn(II) complexes. Nearly all of their works have been concerned with the charged complexes in aqueous solutions. And in most of the Pfeiffer-active systems which have been reported as yet, racemic metal complexes are all ionic and environment substances are electrolytes or nonelectrolytes. However, little is known yet on the Pfeiffer-active system in which racemic complex and environment substance are all neutral molecules. Furthermore, a paucity[13] of the Pfeiffer effect for neutral complexes was only concerned with the tris-chelate complexes [M(AA)$_3$], where AA is dithiophosphate, dithiocarbamate, dithioxanthate, or acetylacetonate, and M is Co(III) or Cr(III). And the Pfeiffer system for the neutral complexes with mixed ligand has not been reported as yet. In this study, in order to investigate the Pfeiffer effect of the neutral complexes with mixed ligand which is expected neither the electrostatic association nor electrostatic repulsion between complex and environment substance, and to elucidate the solvent effect of their Pfeiffer systems, we report the Pfeiffer effect of [Co$^{II}$(acac)$_2$ (diamine)] complexes with cinchona alkaloid as an environment substance in some organic solvents.

## Experimental

**Preparation of Metal Complexes.** The racemic complexes used in this study are follows: [Co$^{II}$(acac)$_2$(tn)], [Co$^{II}$(acac)$_2$(N-metn), [Co$^{II}$(acac)$_2$(N-meen)], [Co$^{II}$(acac)$_2$(N,N′-dmen)], [Co$^{II}$(acac)$_2$(N,N,N′,N′-tmen)], [Co$^{II}$(acac)$_2$(amp)], [Co$^{II}$(acac)$_2$(bpy)], [Co$^{II}$(acac)$_2$(phen)], where acac = acetylacetonate anion, tn = trimethylenediamine, N-metn = N-methyltrimethylenediamine, N-meen = N-methylethylenediamine, N,N′-dmen = N,N′-dimethylethylenediamine, N,N,N′,N′-tetramethylethylenediamine, and amp = 2-aminomethylpyridine, respectively. These complexes were prepared in a similar way to that for [Co$^{II}$(acac)$_2$(phen)][14]. To a hot benzene solution(50m*l*) of anhydrous bis(acetylacetonato)cobalt(II) (0.01 mole) was added dropwise diamine ligand(0.05 mole) in benzene(10m*l*). The solution was stirred