# Efficient Method for the Preparation of Primary, Inverted Secondary and Tertiary Alkyl Carboxylates from Alcohols and Carboxylic Acids by a New Type of Oxidation–Reduction Condensation Using Simple 1,4-Benzoquinone

Taichi Shintou[†,††] and Teruaki Mukaiyama*[†,††]
[†]*Center for Basic Research, The Kitasato Institute, 6-15-5 Toshima, Kita-ku, Tokyo 114-0003*
[††]*Kitasato Institute for Life Sciences, Kitasato University, 5-9-1 Shirokane, Minato-ku, Tokyo 108-8641*

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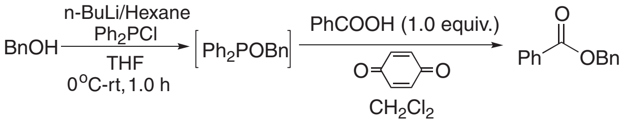
A new type of oxidation–reduction condensation using in situ formed alkoxydiphenylphosphines (i.e., diphenylphosphinite esters), easily available 1,4-benzoquionone and carboxylic acids provides a new and efficient method for the preparation of alkyl carboxylates from the corresponding alcohols under mild and neutral conditions. Further, the yields of the corresponding inverted carboxylates were equally high in the case of chiral secondary or tertiary alcohols.

As shown in our previous reports,[1] oxidation–reduction condensation[2] using in situ-generated alkoxydiphenylphosphine, 2,6-dimethyl-1,4-benzoquinone, and carboxylic acids provided a new and efficient method for the preparation of primary, inverted secondary and tertiary alkyl carboxylates from the corresponding alcohols under mild and neutral conditions.

Now, in order to establish a practical and convenient reactions, a condensation using easily available 1,4-benzoquinone instead of the above mentioned 2,6-dimethyl-1,4-benzoquinone was studied and the desired reaction proceeded smoothly to afford alkyl carboxylates in good to high yields by combined use of alkoxydiphenylphosphines having primary, bulky secondary or tertiary alkoxy groups, 1,4-benzoquinone and carboxylic acids (Scheme 1). In the case of chiral secondary or tertiary alcohols, the corresponding inverted carboxylates were obtained as well in high yields.

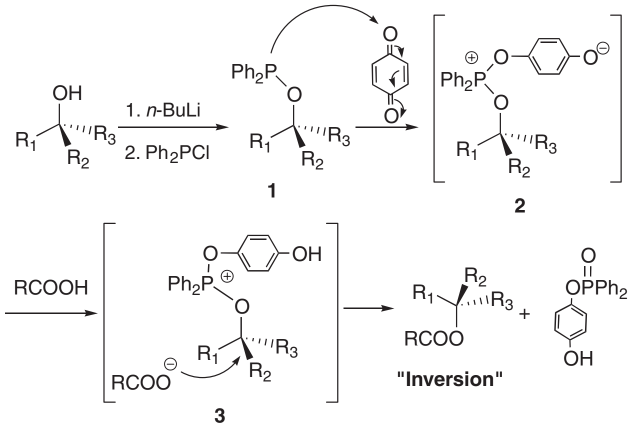
First, by treating benzoic acid with 1.0 equivalent of 1,4-benzoquinone in dichloromethane, benzyl benzoate was obtained in 75% yield within 3 h (Table 1, Entry1). When 1.0 equivalent each of benzoic acid and 1,4-benzoquinone were used, yields of the ester were not influenced by the amount of benzyloxydiphenylphosphine (1.0–1.5 equiv.) (Table 1, Entries 1–4). Next, the effect of the amounts of benzyloxydiphenylphosphine and 1,4-benzoquinone (1:1) was further screened (Table 1, Entries 5–9). Consequently, the ester was obtained in 98% yield when 1.7 equivalents each of in situ-formed benzyloxydiphenylphosphine and 1,4-benzoquinone were treated with benzoic acid at room temperature for 1 h (Table 1, Entry 8, and Figure 1).

**Table 1.** Esterification of benzoic acid using $^{n}$BuLi and benzyl alcohol.



| Entry | $Ph_2POBn$/equiv. | Benzoquinone/equiv. | Time/h | Yield/% |
|---|---|---|---|---|
| 1 | 1.0 | 1.0 | 3.0 | 75 |
| 2 | 1.1 | 1.0 | 3.0 | 75 |
| 3 | 1.3 | 1.0 | 3.0 | 74 |
| 4 | 1.5 | 1.0 | 3.0 | 60 |
| 5 | 1.1 | 1.1 | 1.0 | 76 |
| 6 | 1.3 | 1.3 | 1.0 | 84 |
| 7 | 1.5 | 1.5 | 1.0 | 93 |
| 8 | 1.7 | 1.7 | 1.0 | 98 |
| 9 | 1.9 | 1.9 | 1.0 | 98 |
| 10 | 1.1 | 1.7 | 1.0 | 68 |

Next, esterifications of various in situ-formed alkoxydiphenylphosphines with various carboxylic acids were tried under the conditions shown in Table 2. Benzylation of benzoic acids hav-



**Scheme 1.** Esterifications between alcohols and carboxylic acids by using of 1,4-benzoquinone.

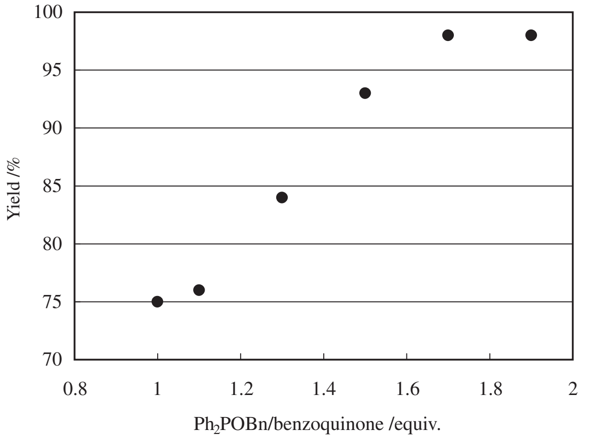
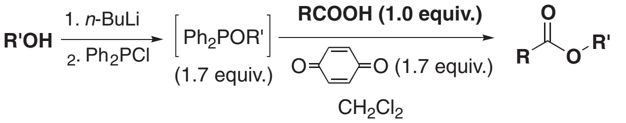
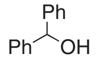
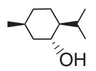
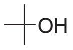
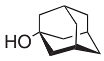
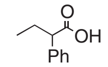
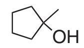
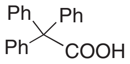
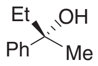


**Figure 1.** Esterification of benzoic acid with *n*-BuLi and benzyl alcohol.

**Table 2.** Esterifications of various carboxylic acids using sveral alcohols



| Entry | R'OH | RCOOH | Time /h | Yield /% | Yield /% [a] |
|---|---|---|---|---|---|
| 1 | BnOH | PhCOOH | 1.0 | 98 | 98 |
| 2 | | $p$-MeO-$C_6H_4COOH$ | 1.0 | 95 | 95 |
| 3 | | $p$-$NO_2$-$C_6H_4COOH$ | 1.0 | 96 | 95 |
| 4 | | $PhCH_2CH_2COOH$ | 1.0 | 92 | 93 |
| 5 | | PhCH=CHCOOH | 1.0 | 98 | 92 |
| 6 | | $CH_3(CH_2)_3COOH$ | 1.0 | 90 | 93 |
| 7 | $p$-MeO-$C_6H_4CH_2OH$ | PhCOOH | 1.0 | 93 | 91 |
| 8 | $CH_3(CH_2)_3OH$ | PhCOOH | 1.0 | 90 | 88 |
| 9 |  | PhCOOH | 3.0 | 90 | 94 |
| 10[b] |  | PhCOOH | 3.0 | 91<br>(>99.9%) | 86<br>(>99.9%) |
| 11[b] | | $p$-$NO_2$-$C_6H_4COOH$ | 3.0 | 96<br>(>99.9%) | 95<br>(>99.9%) |
| 12 |  | PhCOOH | 15.0 | 75 | 69 |
| 13 |  |  | 15.0 | 95 | 96 |
| 14 |  |  | 15.0 | 95 | 96 |
| 15[b] |  | PhCOOH | 15.0 | 95<br>(>99%) | 96<br>(>99%) |

[a] Esterifications of various carboxylic acids with various alcohols using 2,6-dimethyl-1,4-benzoquinone. [Alcohols (1.1–1.2 equiv.), carboxylic acids (1.0 equiv.), 2,6-dimethyl-1,4-benzoquinone (1.0 equiv.)]

[b] Yields in the parenthesis are inversion.

ing electron-donating or electron-withdrawing groups and saturated or unsaturated aliphatic carboxylic acids proceeded smoothly to afford the corresponding carboxylic acid benzyl esters in high to excellent yields under mild conditions (Table 2, Entries 1–6). When primary alcohols such as *n*-buthanol or *p*-methoxybenzyl alcohol having electron-donating or secondary alcohols such as benzhydrol were used, the corresponding esters were obtained in high yields on treatment with benzoic acid for 1–3 h (Table 2, Entries 7–9). Similarly, the reaction of *tert*-butanol and benzoic acid afforded the desired ester in 75% yield under the same conditions (Table 2, Entry 12). The condensations of tertiary alcohol and carboxylic acid such as 1-adamanthanol and 2-phenylbutyric acid or 1-methylcyclopentanol and triphenylacetic acid also proceeded smoothly to afford the corresponding alkyl carboxylates in excellent yields (Table 2, Entries 13 and 14). In addition, it was noted that the corresponding alkyl carboxylates were obtained in excellent yields with perfect inversion of stereochemistry when chiral secondary alcohol such as L-menthol was used (Table 2, Entries 10 and 11). In case of chiral tertiary alcohol such as (*S*)-2-phenyl-2-butanol, the corresponding ester was obtained in 92% yield with 99% inversion (Table 2, Entry 15).

Typical experimental procedure is as follows; to a mixture of carboxylic acid (0.30 mmol) and 1,4-benzoquinone (0.30 mmol) under argon atmosphere was added a dichloromethane (0.3 mL) solution of alkoxydiphenylphosphine[3] (0.51 mmol) at room temperature. After the reaction that was monitored by TLC was completed, the reaction mixture was quenched by adding water and the aqueous layer was extracted with dichloromethane. The organic layers were dried over anhydrous sodium sulfate. After filtration and evaporation, the resulted residue was purified by preparative TLC to afford the corresponding ester. The above reactions were also carried out by one-pot procedure and the same results were obtained even in the presence of lithium chloride.

Thus, a new type of oxidation–reduction condensation using in situ formed alkoxydiphenylphosphines (i.e., diphenylphosphinite esters), carboxylic acids, and 1.7 equivalents of 1,4-benzoquinone provided successfully a new and efficient method for the preparation of alkyl carboxylates from the corresponding alcohols under mild and neutral conditions. Further, the yields of the corresponding inverted carboxylates were equally high in the case of chiral secondary or tertiary alcohols.

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## References and Notes

1 a) T. Mukaiyama, T. Shintou, and W. Kikuchi, *Chem. Lett.*, **2002**, 1126. b) T. Shintou, W. Kikuchi, and T. Mukaiyama, *Chem. Lett.*, **32**, 22 (2003). c) T. Mukaiyama, W. Kikuchi, and T. Shintou, *Chem. Lett.*, **32**, 300 (2003). d) T. Shintou, W. Kikuchi, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **76**, 1645 (2003). e) T. Mukaiyama, T. Shintou, and K. Fukumoto, *J. Am. Chem. Soc.*, **125**, 10538 (2003).

2 Other oxidation-reduction condensation. For examples: a) T. Mukaiyama, I. Kuwajima, and Z. Suzuki, *J. Org. Chem.*, **28**, 2024 (1963). b) I. Kuwajima and T. Mukaiyama, *J. Org. Chem.*, **29**, 1385 (1964). c) T. Mukaiyama, R. Matsueda, and M. Suzuki, *Tetrahedron Lett.*, **22**, 1901 (1970). d) O. Mitsunobu, M. Yamada, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **40**, 935 (1967). e) O. Mitsunobu and M. Yamada, *Bull. Chem. Soc. Jpn.*, **40**, 2380 (1967). f) O. Mitsunobu and M. Eguchi, *Bull. Chem. Soc. Jpn.*, **44**, 3427 (1971). g) O. Mitsunobu, *Synthesis*, **1981**, 1. h) T. Tsunoda, Y. Yamamiya, and S. Ito, *Tetrahedron Lett.*, **34**, 1639 (1993). i) Y.-J. Shi, D. L. Hughes, and J. M. McNamara, *Tetrahedron Lett.*, **44**, 3609 (2003).

3 Preparation of various alkoxydiphenylphosphines. See Ref. 1; into a stirred solution of alcohol (1.5 mmol) in THF (5 mL) was dropped a hexane solution of *n*-BuLi (1.5 mmol) at 0 °C under argon atmosphere. After the solution was stirred at room temperature for 1.0 h, a THF (2 mL) solution of chlorodiphenylphosphine (1.5 mmol) was added at 0 °C. The reaction mixture was stirred for 1.0 h at room temperature and the solvent was concentrated in vacuo.

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