**Communication to the Editor**

**Practical Synthesis of Axially Chiral Dicarboxylates via Pd-Catalyzed External-CO-Free Carbonylation**

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We have developed a safe and practical synthetic method for preparing axially chiral diphenyl dicarboxylates using Pd-catalyzed external-CO-free carbonylation with phenyl formate as a CO surrogate. Optimized conditions consisted of axially chiral [1,1'-binaphthalene]-2,2'-diyl ditriflate and its congeners, each easily prepared from commercially available enantiomerically pure diols, Pd(OAc)₂, 1,3-bis(diphenyolphosphino)propane, ethyldisopropylamine, and no solvent. To demonstrate the potential utility of these products, this method was conducted on gram-scale and the phenyl ester products were converted to other useful compounds, and both processes were carried out without difficulty.

Key words axially chiral dicarboxylate; carbonylation; phenyl formate; carbon monoxide surrogate; palladium; catalysis

Axially chiral compounds have found wide applications as ligands and organocatalysts in asymmetric organic reactions.1–3) Their chiral backbones effectively construct an asymmetric environment around the molecules, enabling catalytic transformations, often with high enantioselectivity. A number of biaryl and spirocyclic chiral ligands are commercially available from multiple suppliers, and many recent papers mentioning the development of novel axially chiral ligands and organocatalysts indicate increasing demand and potential of axially chiral compounds for asymmetric catalysis.

In the search for highly effective chiral ligands and organocatalysts, [1,1'-binaphthalene]-2,2'-dicarboxylic acid and its derivatives such as esters are attractive axially chiral compounds.4–9) However, most previous methods for the synthesis of the enantiomerically pure dicarboxylic acid and dicarboxylates required multiple tedious steps.10–14) In addition, many of the methods include time-consuming optical resolution of racemic dicarboxylic acid. Therefore, it is desirable to develop more practical synthetic methods with fewer steps. Since enantiomerically pure 1,1'-bi-2-naphthol is readily available from many suppliers, it would be an efficient starting point in the synthesis of the targeted dicarboxylates (Chart 1).

Recently, Hamashima and colleagues reported the synthesis of dicarboxylic acid from 1,1'-bi-2-naphthol via lithiation of [1,1'-binaphthalene]-2,2'-diyl diphosphate followed by carbonylation with carbon dioxide.15) While this method affords dicarboxylic acid in high yield in two steps, the involvement of the strongly basic dilithiated intermediate might prove unmanageable with more complex substrates. As another route to [1,1'-binaphthalene]-2,2'-dicarboxylates from 1,1'-bi-2-naphthol, Takaya and colleagues previously reported the Pd-catalyzed alkoxy carbonylation of [1,1'-binaphthalene]-2,2'-diyl ditriflate using carbon monoxide (CO) gas.16) Proving the utility of this pioneering work, many other researchers have used this method to obtain various derivatives.17–19) While this method gives dicarboxylates in good yield under relatively mild, weakly basic conditions, use of the highly toxic CO gas is a major drawback.

To circumvent the use of toxic CO gas, alternative methods using CO surrogates have attracted much attention in recent years.20–23) We recently reported a series of external-CO-free carbonylation of haloarenes utilizing phenyl formate or other formic acid derivatives as CO surrogates.24–28) These CO surrogates can generate CO under mild conditions in a closed reaction vessel, and this CO is consumed during carbonylation in a highly safe and efficient manner. We hypothesized that this external-CO-free carbonylation would be a powerful tool to directly afford not only [1,1'-binaphthalene]-2,2'-dicarboxylates, but also other axially chiral dicarboxylates from the corresponding ditriflates without handling toxic CO gas or strongly basic compounds. We report herein a practical synthetic method for various axially chiral dicarboxylates in an enantiomerically pure form using phenyl formate as a CO surrogate.

We first optimized the reaction conditions for Pd-catalyzed phenoxy carbonylation of (R)-[1,1'-binaphthalene]-2,2'-diyl ditriflate (1), which was easily prepared from enantiomerically pure (R)-1,1'-bi-2-naphthol,29) using phenyl formate as a CO surrogate, as shown in Table 1. Following Takaya's procedure with CO gas,30) we chose Pd(OAc)₂ as a Pd source, 1,3-bis(diphenylphosphino)propane (DPPP) as a ligand, ethyldisopropylamine as a base, and dimethyl sulfoxide (DMSO) as a solvent. However, only a trace amount of the desired phenyl ester 2 was obtained under the external-CO-free conditions (entry 1). Solvent screening (entries 2–5) yielded N,N-dimethylformamide (DMF) as the solvent of choice (entry 5), though a certain amount of monocarbonylated by-product 3 was still present. A review of other phosphate ligands at slightly raised temperatures (entries 6–11) showed that DPPP was the best ligand.31) Notably, subtle differences in the ligand structure significantly influenced the outcome of the reaction. Xantphos and tri(tert-butyl)phosphine, which were effective in the arlyloxy carbonylation of haloarenes,32) were both not suitable for the reaction of 1 with phenyl formate, probably owing to steric repulsion between the substrate and the substituents of these ligands. Decreasing of the amount of DPPP improved the yield (entries 12, 13), probably because

![Chart 1](image)

R = H, Me, Ph, etc.

Chart 1. [1,1'-Binaphthalene]-2,2'-dicarboxylates from 1,1'-Bi-2-naphthol

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Table 1. Optimization of Reaction Conditions for Carbonylation

| Entry | Solvent | Ligand (mol%) | Base (equiv) | X (equiv) | Temp. (°C) | Yield (%) |
|-------|---------|---------------|-------------|-----------|------------|-----------|
| 1     | DMSO    | DPPP (25)     | Pr₂NEt (5)  | 4         | 80         | Trace     |
| 2     | Toluene | DPPP (25)     | Pr₂NEt (5)  | 4         | 80         | 17        |
| 3     | DCE     | DPPP (25)     | Pr₂NEt (5)  | 4         | 80         | 3         |
| 4     | CH₂CN   | DPPP (25)     | Pr₂NEt (5)  | 4         | 80         | 15        |
| 5     | DMF     | DPPP (25)     | Pr₂NEt (5)  | 4         | 100        | 47        |
| 6     | DMF     | DPPP (25)     | Pr₂NEt (5)  | 4         | 100        | Trace     |
| 7     | DMF     | DPPP (25)     | Pr₂NEt (5)  | 4         | 100        | 6         |
| 8     | DMF     | DPPP (25)     | Pr₂NEt (5)  | 4         | 100        | Trace     |
| 9     | DMF     | Xantphos (25) | Pr₂NEt (5)  | 4         | 100        | Trace     |
| 10    | DMF     | PCy₃ (50)     | Pr₂NEt (5)  | 4         | 100        | Trace     |
| 11    | DMF     | Pt(r-Bu)₃·HBF₄ (50) | Pr₂NEt (5) | 4         | 100        | Trace     |
| 12    | DMF     | DPPP (15)     | Pr₂NEt (5)  | 4         | 100        | 65        |
| 13    | DMF     | DPPP (10)     | Pr₂NEt (5)  | 4         | 100        | 56        |
| 14    | DMF     | DPPP (15)     | NMI (5)     | 4         | 100        | 6         |
| 15    | DMF     | DPPP (15)     | NBu₃ (5)    | 4         | 100        | 47        |
| 16    | DMF     | DPPP (15)     | TMP (5)     | 4         | 100        | 62        |
| 17    | DMF     | DPPP (15)     | DABCO (5)   | 4         | 100        | 34        |
| 18    | DMF     | DPPP (15)     | DBU (5)     | 4         | 100        | Trace     |
| 19    | DMF     | DPPP (15)     | NaHCO₃ (5)  | 4         | 100        | 45        |
| 20    | DMF     | DPPP (15)     | Cs₂CO₃ (5)  | 4         | 100        | 8         |
| 21    | —       | DPPP (15)     | Pr₂NEt (5)  | 4         | 100        | 69        |
| 22    | —       | DPPP (15)     | Pr₂NEt (12) | 8         | 120        | 79        |
| 23    | —       | DPPP (15)     | Pr₂NEt (12) | 8         | 120        | 80        |

Table 2. Substrate Scope of Carbonylation

| R       | yield (%) | R       | yield (%) |
|---------|-----------|---------|-----------|
| Me      | 80%       | 9       | 91%       |
| OMe     | 78%       | 10      | not detected |
| Ph      | 66%       | 11      | 77%       |
| CO₂Me   | 41%       | 12      | 90%b      |
| NO₂     | not detected | 13      | 77%       |

* Monophenoxy carbonylated product was obtained in 47% yield. b A racemic substrate was used.
of the suppression of excess ligation to the Pd center. We also
tested other bases (entries 14–20); bulky amines such as ethyl-
diisopropylamine (entry 12) and 2,2,6,6-tetramethylpiperidine
(TMP) (entry 16) were found to be most effective. This ten-
dency is similar to that found in Takaya's studies. Further
studies revealed that the yield could be improved by remov-
ing the solvent (entry 21), increasing the amounts of phenyl
formate and base, raising the temperature to 120°C (entry 22),
and increasing the reaction time (entry 23). It was confirmed
that no racemization occurred during this carbonylation: enan-
tiomerically pure 2 obtained from ditriflate 1 (>99% ee) was
measured to be >99% ee by chiral HPLC.

Under the optimized conditions (Table 1, entry 23), various
enantiomerically pure ditriflates bearing axial chirality were
examined for phenoxycarbonylation (Table 2). Substituents at
the 6 and 6′ positions of the 2,2′-binaphthyl scaffold did not
adversely affect the carbonylation reaction; they instead af-
forded the desired dicarboxylates 4–7 in good yield. Notably,
base-sensitive ester moieties tolerated the reaction conditions
to give 7. The only exception was the derivative bearing nitro
groups (for compound 8). The reaction proceeded smoothly
with a partially saturated substrate to give 9 in high yield. Un-
fortunately, ditriflate with methyl groups on the 3 and 3′ posi-
tions failed to afford product 10. Instead, the monophenoxy-
carbonylated compound was obtained in modest yield. This
carbonylation method was also applicable to the synthesis of
spirocyclic dicarboxylate 11, which was produced in good
yield. Methyl-substituted biphenyl 12, albeit in racemic form,
was also synthesized by this phenoxycarbonylation.

The reaction was tested on gram-scale to evaluate its
practicality (Chart 2). To our delight, more than 1 g of 2 was
obtained in a single reaction which was conducted in a simple
two-necked flask equipped with an empty balloon without any
difficulties.

Owing to their relative electrophilicity when compared
with alkyl esters, the phenyl ester groups could be easily de-
rivatized to other functional groups using nucleophiles (Chart
3). Hydrolysis of 2 afforded dicarboxylic acid 13, and reduc-
tion using lithium aluminum hydride gave diol 14 in high
yield. Bis(2-(trimethylsilyl)ethyl) ester 15, a useful protected
analogue of dicarboxylic acid, was obtained via ester ex-
change. Moreover, 2 was converted into diamide 16 in good
yield.

In summary, a novel and practical synthetic method to
produce axially chiral dicarboxylates was developed using Pd-
catalyzed external-CO-free carbonylation with phenyl formate
as a CO surrogate. Binaphthyl and other ditriflates, which
were readily prepared from the corresponding enantiomeri-
cally pure diols, were directly converted to dicarboxylates, and
they can be used as potential intermediates of chiral ligands
and organocatalysts. Without using a strong base or CO gas
from a cylinder, the reaction can be conducted in a safe and
practical manner. Furthermore, gram-scale synthesis of dicar-
boxylates and subsequent derivatization are readily feasible.
Since various axially chiral diols are commercially available
in the enantiomerically pure form, the present reaction can
offer a general, rapid access to axially chiral dicarboxylates
that would help accelerate the development of more efficient
asymmetric transformations.

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Conflict of Interest The authors declare no conflict of
interest.

Supplementary Materials The online version of this ar-
ticle contains supplementary materials (detailed experimental
procedure, physical data, and NMR spectra of isolated prod-
ucts).

Chart 2. Gram-Scale Synthesis of 2

Chart 3. Derivatization of Diphenyl Ester Product 2
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