

An Efficient Synthesis of 2,6-Di-*tert*-butylphenyl Esters by Palladium-catalysed Carbonylation of 4-Bromobiphenyl

Yoshihiro Kubota, Taka-aki Hanaoka, Kazuhiko Takeuchi and Yoshihiro Sugi*

National Institute of Materials and Chemical Research, AIST, Tsukuba, Ibaraki 305, Japan

2,6-Di-*tert*-butylphenyl biphenyl-4-carboxylates were synthesized in good yields by palladium-catalysed aryloxy carbonylation of 4-bromobiphenyl with the alkali-metal 2,6-di-*tert*-butylphenoxides.

Recently, palladium-catalysed carbonylation has been applied to syntheses of wholly aromatic polyesters and polyamides.¹ The carbonylation-polycondensation of dihalogenobiphenyls with bisphenols is a promising method to synthesize heat-resistant wholly aromatic polyesters.² Substitution of phenoxy moieties by 2,6-di-*tert*-butylphenoxy moieties would make such polyesters not only resistant to hydrolysis but also readily moulded. Therefore, the development of carbonylation of aryl halides with 2,6-di-*tert*-butylphenyl compounds is required. 2,6-Di-*tert*-butylphenyl esters are also important for the substrates of stereo- and regio-selective reactions.³ However, no efficient carbonylation with 2,6-di-*tert*-butylphenols under a moderate pressure of CO at a temperature as low as 100 °C is reported.⁴ We report here an efficient aryloxy carbonylation of 4-bromobiphenyl with alkali-metal 2,6-di-*tert*-butylphenoxides as a model study for the synthesis of biphenylic polyesters containing 2,6-di-*tert*-butylphenyl esters.

We have recently found that phenyl biphenyl-4-carboxylate was obtained in high yield from 4-bromobiphenyl and phenol under less than 5 bar of CO at 100 °C in the presence of PdCl₂, 1,3-bis(diphenylphosphino)propane (dppp) as a ligand, and a cyclic amidine or guanidine as a base.⁵ The use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD)⁶, or 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BEMP)^{6,7} as bases drastically increased the rate of carbonylation relative to NEt₃. A bisphosphine such as dppp was much better than PPh₃ as a ligand. In fact, the phenoxy carbonylation with dppp at 100 °C for 2 h gave a 91% yield of phenyl ester, whereas the yield was 68% with the use of PPh₃. This was consistent with reported results.^{8,9} The base having a pK_a value of more than 11 was found to be essential for the efficient phenoxy carbonylation. Some *o*-substituted aryl esters were also obtained in high yields from 2-methyl-, 2,6-dimethyl-, 2-phenyl- and 2-*tert*-butylphenols under similar conditions.

However, the reaction with 4-methyl-2,6-di-*tert*-butylphenol as nucleophiles did not give any corresponding esters even with the use of DBU as a base because the phenols were too bulky to react with an acyl palladium intermediate. Even with the stronger organic bases such as BEMP and MTBD, the yields of esters were still quite low (Table 1). On the other hand, the carbonylation with 4-methoxy-2,6-di-*tert*-butylphenol by use of potassium *tert*-butoxide in DMF gave the desired ester in 20% yield.[†] This indicates that the potassium salts of 2,6-di-*tert*-butylphenols might be adequately nucleophilic in spite of their bulkiness. Thus, the reaction with various alkali-metal salts of 2,6-di-*tert*-butylphenols was examined.^{‡,§}

The potassium salts of the hindered phenols were found to be particularly effective for this reaction (Scheme 1). The aryloxy carbonylation of 4-bromobiphenyl readily occurred (<3 h) with a potassium 2,6-di-*tert*-butylphenoxide in DMF or benzene under 5 bar of CO in the presence of catalytic amount of PdCl₂ and dppp even at 100–120 °C (Table 2).¶,||,** The esterified products were obtained in 77–84% yields. The yields were greatly dependent on the alkali metal used. With a corresponding sodium salt, an esterified product was obtained in an obviously lower yield than that with a potassium salt. No desired product was obtained with a corresponding lithium salt. The same trend was observed in DMF. Unexpectedly, however, yields were appreciably lower in a polar solvent such as DMF than in an apolar solvent such as benzene. The anticipated side-products of carbonylation of 4-bromobiphenyl included biphenyl as a reduced product and quaterphenyl as a directly coupled product which were easy to detect by GC analysis. The formation of such side-products, however, was not observed.

The difference of reactivity among the counter-cation of phenoxides is ascribed to that of the size among the alkali metal ions. The estimated effective ionic radii of lithium, sodium and potassium ions in crystals of oxides and fluorides are 0.73, 1.13 and 1.51 Å, respectively.¹⁰ The lithium ion is particularly small and is anticipated to be strongly paired with phenoxy anion in the reaction medium. It can therefore be presumed that the lithium salt is more difficult to dissociate, attack the acyl palladium intermediate and regenerate palladium(o) species than the sodium and potassium salts.

The difference of reactivity among the counter-cation of phenoxides is ascribed to that of the size among the alkali metal ions. The estimated effective ionic radii of lithium, sodium and potassium ions in crystals of oxides and fluorides are 0.73, 1.13 and 1.51 Å, respectively.¹⁰ The lithium ion is particularly small and is anticipated to be strongly paired with phenoxy anion in the reaction medium. It can therefore be presumed that the lithium salt is more difficult to dissociate, attack the acyl palladium intermediate and regenerate palladium(o) species than the sodium and potassium salts.

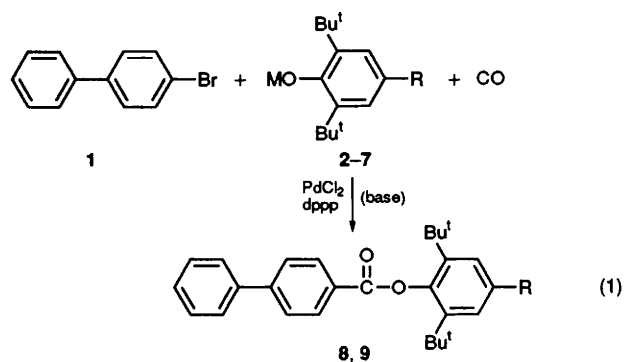


Table 1 Aryloxy carbonylation of 4-bromobiphenyl with bulky phenols^a

Phenol	M	R	Product	Base	Yield(%) ^b
2	H	OMe	8	KOBu ^t	20 ^{c,d}
3	H	Me	9	MTBD	2
3	H	Me	9	BEMP	1
3	H	Me	9	DBU	0

^a Carried out with PdCl₂ (0.05 mmol) and dppp (0.1 mmol) at 120 °C for 3 h. Other conditions were as described in footnote ¶. ^b Yields determined by GC. ^c Carried out in DMF. ^d Formation of *tert*-butyl ester was not observed.

Table 2 Aryloxy carbonylation of 4-bromobiphenyl with bulky phenoxides^a

Phenoxide ^b	M	R	T/°C	Product	Yield(%) ^c
4	K	Me	100	9	84
4	K	Me	120	9	80
5	K	OMe	120	8	77 (63) ^d
6	Na	OMe	120	8	60 (24) ^d
7	Li	OMe	120	8	0 (0) ^d

^a Carried out in benzene as described in footnote ¶. ^b Phenoxides were prepared as described in footnote ‡. ^c Yields determined by GC. ^d Yields for the reaction in DMF, given in parenthesis.

In summary, 2,6-di-*tert*-butyl biphenyl-4-carboxylates **8** and **9** were efficiently synthesized by palladium-catalysed carbonylation of 4-bromobiphenyl with a potassium 2,6-di-*tert*-butylphenoxide under relatively mild conditions for the first time. This mild and effective carbonylation of an aryl bromide to a bulky aryl ester would provide an entry to some advanced materials.

Received, 6th April 1994; Com. 4/02065K

They were separated by column chromatography on silica gel in almost the same yield as that determined by GC analysis. In all cases studied, carbonylation was 100% regioselective.

|| All new compounds provided satisfactory analytical and spectroscopic data.

** The carbonylation with **4** at 100 °C for 3 h showed that dppp (the yield of **9** was 84%) was a better ligand again than PPh₃ (the yield of **9** was 41%) in the present case.

Footnotes

† When potassium *tert*-butoxide was used as a base, a large solvent effect was observed. 4-Bromobiphenyl was carbonylated with PhOH in DMF in the presence of a palladium catalyst and potassium *tert*-butoxide under 5 bar of CO at 100 °C in 74% yield, whereas no reaction occurred in benzene.

‡ The potassium and sodium 2,6-di-*tert*-butyl phenoxides **4–6** were prepared by adding 1.2 mol dm⁻³ THF solution of a 2,6-di-*tert*-butyl phenol to a 1.25 mol dm⁻³ THF suspension of 0.9 equiv. of KH or NaH at -78 °C followed by gradual warming to 20 °C for 40 min. The solvent was evaporated *in vacuo* from the green coloured solution to give the desired salt as slightly green coloured powder which was provided for use. The lithium salt **7** was prepared by adding 0.9 equiv. of 1.6 mol dm⁻³ *n*-hexane solution of *n*-BuLi to 0.6 mol dm⁻³ THF solution of 4-methoxy 2,6-di-*tert*-butylphenol at -78 °C followed by stirring at 20 °C for 30 min. From the resulting white suspension, the solvents were removed *in vacuo* and the resulting white powder was used as such.

§ The treatment of 2,6-di-*tert*-butylphenols with 1 equiv. of KOH, NaOH or LiOH·H₂O in aqueous methanol¹¹ followed by drying did not give corresponding alkali-metal salts.

¶ *Typical procedure:* CO was pressurized into a mixture of 4-bromobiphenyl (2.5 mmol), *n*-docosane (internal standard, 1.25 mmol), dppp (0.2 mmol), PdCl₂ (0.1 mmol), benzene (5 ml), and potassium 4-methyl-2,6-di-*tert*-butylphenoxide (*ca.* 5 mmol) prepared as described above at 5 bar in an autoclave. The reaction vessel and contents were placed in a 100 °C oil-bath. After stirring for 3 h, capillary GC (Shimadzu GC14A; 0.2 mm × 12 m HP Ultra-1 column, 160–280 °C) revealed a 8% recovery of starting bromide and a 84% yield of ester.

References

- 1 M. Yonezma, M. Kakimoto and Y. Imai, *Macromolecules*, 1989, **22**, 2593; 1988, **21**, 1908; R. J. Perry, S. R. Turner and R. W. Blevins, *Macromolecules*, 1993, **26**, 1509.
- 2 Y. Kubota, K. Takeuchi, T. Hanaoka and Y. Sugi, *Bull. Chem. Soc. Jpn.*, 1994, **67**, 563.
- 3 K. Tomioka, M. Shindo and K. Koga, *J. Org. Chem.*, 1990, **55**, 2276; C. H. Heathcock, M. C. Pirrung, S. H. Montgomery and J. Lampe, *Tetrahedron*, 1981, **37**, 4087; M. P. Cook, Jr., *J. Org. Chem.*, 1986, **51**, 1637.
- 4 Formation of 2,6-dimethylphenyl ester has been reported, see: S. Fukuoka, *Jpn. Kokai Tokkyo Koho*, 61, 189, 249 [86, 189, 249], 1986; *Chem. Abstr.* 1987, **106**, 18121g; *Jpn. Kokai Tokkyo Koho* 62, 238, 241 [87, 238, 241], 1987; *Chem. Abstr.*, 1988, **109**, 6225t.
- 5 Y. Kubota, T. Hanaoka, K. Takeuchi and Y. Sugi, *Synlett*, in the press
- 6 R. Schwesinger, *Chimia* 1985, **39**, 269.
- 7 R. Schwesinger and H. Schlemper, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 1167.
- 8 R. E. Dolle, S. J. Schmidt and L. I. Kruse, *J. Chem. Soc., Chem. Commun.*, 1987, 904.
- 9 Y. Sugi, K. Takeuchi, T. Hanaoka, T. Matsuzaki, S. Takagi and Y. Doi, *Sekiyu Gakkaishi*, 1994, **37**, 70.
- 10 Values for a coordination number of four, see: R. D. Shannon and C. T. Prewitt, *Acta Crystallogr., Sect. B*, 1969, **25**, 925; R. D. Shannon, *Acta Crystallogr., Sect. A*, 1976, **32**, 751.
- 11 N. Kornblum and A. P. Lurie, *J. Am. Chem. Soc.*, 1959, **81**, 2705; D. Y. Curtin and D. H. Dybvig, *J. Am. Chem. Soc.*, 1962, **84**, 225; N. Kornblum, R. Seltzer and P. Haberfeld, *J. Am. Chem. Soc.*, 1963, **85**, 1148.