
A Mild and Convenient Preparation of t-Butyl Esters by Carbonylation of Arylhalogenomethyl Derivatives

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An exceptionally mild and efficient, single-pot synthetic procedure is described for the t-butoxy-carbonylation of benzyl chloride derivatives.

The t-butyl ester function as a protecting group has advantages over the corresponding methyl or ethyl esters, owing to its stability under basic conditions. Earlier methods¹ for introducing the group, however, have drawbacks such as the need to use reagents (such as phosgene, isobutene, and BuLi) coupled with multistep procedures, *etc.* Recent reports have, however, indicated improved methods.² Although palladium catalysed carbonylation of benzyl halides is well documented,³ the preparation of t-butyl phenylacetates appears not to have been described. Alper *et al.*,⁴ have, however, reported preparation

of the latter compound by Rh^I catalysed reaction of benzyl chloride with t-butyl borate under CO pressure (10 atm).

Since attempts to synthesize 2,5-dihydroxyphenylacetic acid⁵ (a valuable metabolic intermediate of tyrosine and phenylalanine) by conventional methods of carbonylation were unsuccessful⁶ we have developed a highly convenient method for the preparation of t-butyl phenylacetates by bis(triphenylphosphine)palladium dichloride-triethylbenzylammonium chloride catalysed carbonylation under carbon monoxide at 60–80 °C over 20–30 h. Thus, treatment of PhCH₂Cl with CO,

Table. t-Butoxycarbonylation of halogenomethylarenes

Run	Substrate (ArCH ₂ X)		Temp. (°C)	Time (h)	Product (ArCH ₂ COX)		Yield ^a
	Ar	X			Ar	X	
1	Ph	Cl	70	20	Ph	OBu [†]	60
			80	24			60
			80	24			30 ^b
2	2-EtO ₂ C-5-MeOC ₆ H ₃	Cl	60	30	2-EtO ₂ C-5-MeOC ₆ H ₃	OBu [†]	50
3	<i>o</i> -ClC ₆ H ₄	Cl	80	24	<i>o</i> -ClC ₆ H ₄	OBu [†]	55
4	<i>p</i> -Bu [†] C ₆ H ₄	Cl	80	24	<i>p</i> -Bu [†] C ₆ H ₄	OBu [†]	45
5	<i>p</i> -MeOC ₆ H ₄	Cl	80	24	<i>p</i> -MeOC ₆ H ₄	OBu [†]	45
6	<i>p</i> -O ₂ NC ₆ H ₄	Cl	70	24	<i>p</i> -O ₂ NC ₆ H ₄	OBu [†]	42 ^c
7	<i>p</i> -MeC ₆ H ₄	Cl	70	24	<i>p</i> -MeC ₆ H ₄	OBu [†]	24 ^c
8	PhCOCH ₂ Cl		60	30	PhCOCH ₂ CO ₂ Bu [†]		50
9	2-Naphthyl	Br	80	24	2-Naphthyl	OBu [†]	17 ^c

^a Yields determined by n.m.r. spectrometry, are not optimised; corresponding acetate was a co-product, identified by n.m.r. and/or g.l.c. (3m OV-17 10% on Chromosorb-W). ^b No p.t.c. ^c Poor solubility of substrate.

NaOAc, PPh₃, Bu[†]OH, and Pd(PPh₃)₂Cl₂ (as catalyst) and Et₃NCH₂C₆H₄Cl as a phase transfer catalyst (p.t.c.), at 80 °C and atmospheric pressure gave t-butyl phenylacetate in 60% yield; † without a p.t.c. the yield was 30%.

Applied to a series of arylhalogenomethyl derivatives, this process gave t-butyl esters in fair to good yields (see Table), the various substituents being unaffected by the conditions. Substrates of low solubility gave poor yield (runs 6, 7, and 9). Thus this procedure has the advantage of very mild conditions and simplicity in execution and work-up. t-Butyl esters are converted with a strong base or acid at reflux temperature into the corresponding acid derivatives which are of commercial and synthetic importance.

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† The following general procedure was used: CO was slowly bubbled through t-butyl alcohol (30 ml), whilst [Pd(PPh₃)₂Cl₂] (0.1 mmol) PPh₃ (0.5 mmol), Et₃NCH₂C₆H₅Cl (1 mmol), and NaOAc (11 mmol) were added sequentially. The mixture was then stirred for 1 h at 60–70 °C after which benzyl chloride 10 mmol) was added and the mixture held at reflux for 20 h. Work-up of the reaction mixture gave the t-butyl ester.

References

- B. Abramovitch, J. C. Shivers, B. E. Hudson, and C. R. Hauser, *J. Am. Chem. Soc.*, 1943, **65**, 986; S. Masamune, Y. Hayase, W. Schilling, W. K. Chan, and G. S. Bates, *ibid.*, 1977, **99**, 6756; H. A. Staab and A. Mannschreck, *Chem. Ber.*, 1962, **95**, 1284; G. P. Cowther, E. M. Kaiser, R. A. Woodruff, and C. R. Hauser, *Org. Synth.*, 1971, **51**, 96; J. Inanaya, K. Hirata, H. Saeki, T. Katsuki, and M. Yamaguchi, *Bull. Chem. Soc., Jpn.*, 1979, **52**, 1989.
- T. Mukaiyama, M. Usui, E. Shimada, and K. Saigo, *Chem. Lett.*, 1975, 1045; W. Szeja, *Synthesis*, 1980, 402; B. Ravindranath and P. Srinivas, *Tetrahedron*, 1984, **40**, 1623.
- A. Schoenberg, I. Bartoletti, and R. F. Heck, *J. Org. Chem.*, 1974, **39**, 3318; J. K. Stille, and P. K. Wong, *ibid.*, 1975, **40**, 532; H. Alper, K. Hashem, and J. Haveling, *J. Organomet.*, 1982, **1**, 775.
- H. Alper, N. Hamel, D. J. H. Smith, and J. B. Woell, *Tetrahedron Lett.*, 1985, **26**, 2273.
- S. B. Bostock and A. H. Renfrew, *Synthesis*, 1978, 66.
- L. Casser, M. Foa, and A. Gardano, *J. Organomet. Chem.*, 1976, **121**, C₅₅; T. Takahashi, H. Ikeda, and J. Tsuji, *Tetrahedron Lett.*, 1980, **21**, 3885; B. N. Rao, S. R. Adapa, and M. Pardhasaradhi, *Indian J. Chem., Sect. B*, 1988, **27**, 84.

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