



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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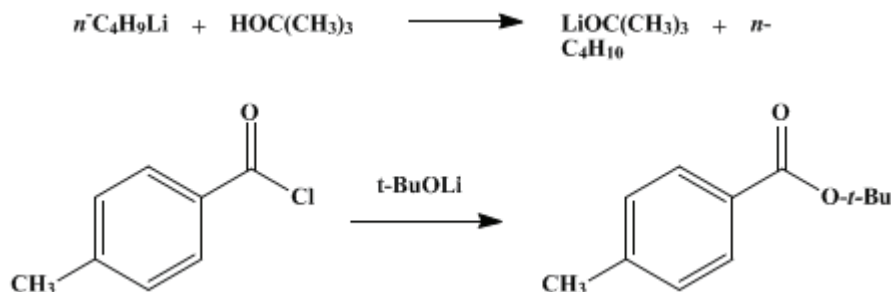
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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ESTERIFICATION OF HINDERED ALCOHOLS: *tert*-BUTYL *p*-TOLUATE

[Benzoic acid, 4-methyl-, 1,1-dimethylethyl ester]



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Checked by A. Brossi, R. A. LeMahieu, and P. LaSalle.

1. Procedure

A 200-ml., one-necked, round-bottomed flask equipped with a Claisen adapter, a condenser, an addition funnel, and a magnetic stirring bar is charged with 50 ml. of *tert*-butyl alcohol (Note 1). Under nitrogen, 22.6 ml. of a 1.55 *M* solution (0.0350 mole) of *n*-butyllithium in hexane (Note 2) is added slowly from a syringe (Note 3), giving a turbid reaction mixture. A water bath is used to keep the mixture near room temperature. After stirring for 15 minutes, a solution of 5.42 g. (0.0351 mole) of *p*-toluoyl chloride (Note 4) in 25 ml. of anhydrous diethyl ether (Note 5) is added dropwise to the stirred mixture. The resulting yellow slurry is stirred at room temperature for 15 hours (Note 6). The yellow suspension (Note 7) is transferred with 100 ml. of ether to a separatory funnel and washed with three 25-ml. portions of saturated sodium chloride, and dried over magnesium sulfate. The ether is removed by distillation, and the residual oil distilled under reduced pressure, yielding a small forerun (0.10 g.) and 5.31–5.51 g. (79–82%) of *tert*-butyl *p*-toluate, b.p. 98–101° (4.2 mm.) (Note 8).

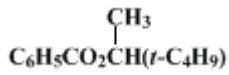
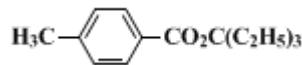
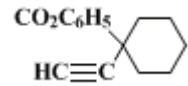
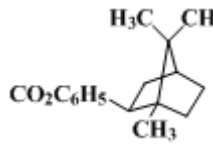

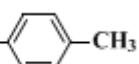
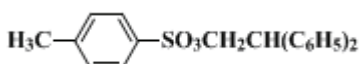
2. Notes

1. *tert*-Butyl alcohol (Eastman Organic Chemicals white label) was dried by distillation from calcium hydride.
2. The solution of 1.55 *M* *n*-butyllithium in hexane was obtained from Foote Mineral Company.
3. Formation of the lithium *tert*-butoxide in this manner is very exothermic and causes the hexane to boil during addition.
4. *p*-Toluoyl chloride was prepared by treating *p*-toluic acid (Eastman Organic Chemicals white label) with thionyl chloride (Eastman Organic Chemicals white label). The *p*-toluoyl chloride used was distilled, b.p. 48–49° (0.1 mm.).
5. Anhydrous ether was distilled from lithium aluminum hydride and stored over sodium ribbon prior to use.
6. In one instance an additional 75 ml. of anhydrous ether was added to make the slurry less viscous. The ester was obtained in the same yield in another run after stirring only 30 minutes.
7. Alternatively, the reaction mixture may be concentrated with a rotary evaporator, removing excess *tert*-butyl alcohol. Ether and water are added, and the mixture transferred to the separatory funnel; the yield of ester is unchanged.
8. With the same procedure *tert*-butyl phenylacetate has been prepared in 47% yield.⁴ When esters of less common alcohols were prepared, anhydrous ether was used as a solvent instead of excess alcohol, with equivalent amounts of alcohol, *n*-butyllithium, and acid chloride employed. Thus, the triethylcarbinol ester of *p*-toluic acid and the 2,2-diphenylethanol ester of benzoic acid have been prepared in 72 and 70% yields, respectively.

3. Discussion

The present procedure⁴ is an especially effective method for the synthesis of esters of aromatic acids and hindered tertiary alcohols or of acid-labile alcohols such as *2,2-diphenylethanol*. The yields are excellent, and the reaction procedure is simple. The method is illustrated by the preparation of *tert-butyl p-toluate*, a compound that could not be prepared by a conventional method⁵ of esterification involving the acid chloride and *tert-butyl alcohol* in the presence of *N,N*-dimethylaniline. Examples of esters prepared by this method are illustrated in Table I.

TABLE I
ESTERS PREPARED BY ALKOXIDE METHODS

Ester	Yield,%	Ester	Yield,%
$C_6H_5CH_2CO_2C(CH_3)_3$	47 ^a	$C_6H_5CO_2CH_2CH(C_6H_5)_2$	70 ^b
		$C_6H_5CO_2C(CH_3)_3$	89 ^c
		$C_6H_5CO_2CCH_3(C_2H_5)_2$	87 ^c
		$C_6H_5CO_2C(C_2H_5)_3$	94 ^c
			76 ^c
		$C_6H_5CO_2CH_2(t-C_4H_9)$	78 ^c
	72 ^b		70 ^c
			69 ^c
$C_6H_5CO_2CH_2$ 	91 ^c		
$CO_2C_6H_5$ 	94 ^c		85 ^d
$(CH_3)_3CCO_2C(CH_3)_3$	64 ^c		
$(CH_3)_3CCO_2C(C_2H_5)_3$	75 ^c		
$C_6H_5CH=CHCO_2C(CH_3)_3$	88 ^c	$(i-C_3H_7)_2CHCO_2C(C_2H_5)_3$	88 ^c
$C_6H_5CH_2CH_2CO_2C(CH_3)_3$	72 ^c	$(t-C_4H_9)CH_2CO_2C(C_2H_5)_3$	86 ^c
		$(t-C_4H_9)_2CHCO_2C(C_2H_5)_3$	30 ^e

a As described in the accompanying procedure.

b As described in the accompanying procedure except ether used as solvent (see (Note 8)).

c Prepared in refluxing tetrahydrofuran with 1.0 equivalent of appropriate alcohol, 1.1 equivalents of *n*-butyllithium, and 1.1 equivalents of acid chloride.⁴

d Prepared by adding an equivalent amount of *p*-toluenesulfonyl chloride to a suspension *2,2*-diphenylethoxide in ether.⁶

e Prepared by adding 0.50 equivalent of acid chloride to an ether suspension of sodium triethylmethoxide, which was obtained from 0.52 equivalent of sodium amide and 0.55 equivalent of triethylcarbinol.⁷

References and Notes

1. Chemistry Department, Duke University, Durham, North Carolina 27706. This work was supported at Duke University by the Army Research Office (Durham).
 2. Chemistry Department, University of Missouri, Columbia, Missouri 65211.
 3. Deceased January 6, 1970.
 4. E. M. Kaiser and R. A. Woodruff, *J. Org. Chem.*, **35**, 1198 (1970).
 5. C. R. Hauser, B. E. Hudson, B. Abramovitch, and J. C. Shivers, *Org. Synth.*, **Coll. Vol. 3**, 142 (1955).
 6. P. J. Hamrick, Jr., and C. R. Hauser, *J. Org. Chem.*, **26**, 4199 (1961).
 7. M. S. Newman and T. Fukunaga, *J. Am. Chem. Soc.*, **85**, 1176 (1963).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

2,2-diphenylethoxide

ether,
diethyl ether (60-29-7)

thionyl chloride (7719-09-7)

sodium chloride (7647-14-5)

nitrogen (7727-37-9)

sodium (13966-32-0)

N,N-dimethylaniline (121-69-7)

magnesium sulfate (7487-88-9)

sodium amide (7782-92-5)

butyllithium,
n-butyllithium (109-72-8)

Tetrahydrofuran (109-99-9)

Triethylcarbinol (597-49-9)

lithium aluminum hydride (16853-85-3)

hexane (110-54-3)

p-Toluic acid (99-94-5)

tert-butyl alcohol (75-65-0)

calcium hydride (7789-78-8)

2,2-diphenylethanol (1883-32-5)

p-Toluenesulfonyl chloride (98-59-9)

Benzoic acid, 4-methyl-, 1,1-dimethylethyl ester,
tert-Butyl p-toluate (13756-42-8)

sodium triethylmethoxide

tert-butyl phenylacetate

lithium tert-butoxide (1907-33-1)

p-toluoyl chloride (874-60-2)

triethylcarbinol ester of p-toluic acid

2,2-diphenylethanol ester of benzoic acid