

A NEW SYNTHESIS OF ARYL *t*-BUTYL ETHERS

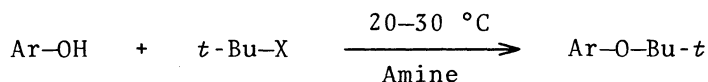
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Aryl *t*-butyl ethers were prepared in high yields by *O*-alkylations of phenols with *t*-butyl halides in the presence of pyridine or aliphatic amines for a few hours at 20–30 °C.

Well-known syntheses of aryl *t*-butyl ethers are the acid-catalyzed addition of cresol to 2-methylpropene,¹⁾ the reaction of phenylmagnesium bromide with *t*-butyl peroxybenzoate,²⁾ the substitution of bromobenzene with potassium *t*-butoxide,³⁾ and the reaction of iodobenzene with copper(I) *t*-butoxide.⁴⁾

In this paper, the reactions of phenols with *t*-butyl halides in the presence of amines were investigated to find a more available synthesis of the ethers:



For example, *t*-butyl bromide (2.740 g, 20 mmol) was added to a chilled mixture of phenol (18.82 g, 200 mmol) and pyridine (1.582 g, 20 mmol) in a 50 cm³ Erlenmeyer flask, with which a syringe was connected through a rubber stopper in order to trap the gas evolved. The homogeneous mixture was stirred magnetically for 2 h at 30 °C, poured into water–ethylene glycol (8/1 vol/vol), and extracted with pentane (40 cm³×3). The upper organic layer was washed with 5% aqueous sodium hydroxide (40 cm³×1) and water (40 cm³×2), dried over sodium sulfate, and distilled under reduced pressure, giving 2.250 g (75%) of pure *t*-butyl phenyl ether: bp 72.5–73.0 °C/16 Torr; n_D^{20} 1.4875 (lit.⁵⁾ 1.4880); IR (neat) 1240 (C–O–C), 1396, 1370 (*t*-Bu), 785, and 698 cm⁻¹ (aromatic); NMR (CDCl₃) δ =1.28 (9H, s, *t*-Bu) and 7.05 (5H, m, aromatic). The lower aqueous layer was extracted with diethyl ether (40 cm³×3). The ethereal extract was washed with water, dried, and distilled under reduced pressure, giving phenol (13.8 g, >80% recovered).

The reaction of *p*-cresol (21.63 g, 200 mmol) with *t*-butyl bromide (20 mmol) by use of pyridine (20 mmol) was carried out and worked up in a similar manner as above, giving 2.458 g (75%) of pure *t*-butyl *p*-tolyl ether: bp 89.5–90.0 °C/16 Torr; n_D^{20} 1.4876 (lit.⁶⁾ 1.4879); IR (neat) 1240 (C–O–C), 1396, 1371 (*t*-Bu), and 848 cm⁻¹ (*p*-tolyl).

On the other hand, small scale reactions of phenols with *t*-butyl halides by use of various amines were studied in detail. The amines used were pyridine, butylamine, hexylamine, diisopropylamine, triethylamine, and *N*-ethyldiisopropylamine. The products in the solution were determined by GLPC comparison with

Table 1. Reactions of Phenols with *t*-Butyl Halides in the Presence of Amines

Substrates ^{a)}			Temp. (°C)	Time (h)	Yield ^{b)} of Aryl <i>t</i> -butyl ether (%)
ArOH	<i>t</i> -BuX	Amine			
PhOH	X = Br	none	30	8	0
PhOH	Br	pyridine	30	2	90, 75 ^{c)}
PhOH	Br	pyridine	20	4	91
PhOH	Br	<i>n</i> -C ₆ H ₁₃ NH ₂	30	2	88
PhOH	Br	(<i>i</i> -Pr) ₂ NH	30	2	85
PhOH	Br	Et ₃ N	30	2	74
PhOH	Br	(<i>i</i> -Pr) ₂ N·Et	30	2	67
PhOH	Cl	pyridine	30	5	66
<i>p</i> -cresol	Br	pyridine	30	2	88, 75 ^{c)}
<i>p</i> -cresol	Br	<i>n</i> -BuNH ₂	30	2	83

a) The molar ratio of substrates: ArOH/*t*-BuX/Amine=10/1/1.

b) GLPC yield based on *t*-butyl halide. c) Isolated yield.

authentic samples using internal standards. The results are summarized in Table 1. The gas chromatogram showed that the reaction of phenol with *t*-butyl bromide in the presence of pyridine at 30 °C gave 90% of *t*-butyl phenyl ether, 8% of 2-methylpropene, and 2% of *p*-*t*-butylphenol. In the absence of amines, the elimination and *C*-alkylation products were exclusively given under comparable conditions. The primary and secondary aliphatic amines used were effective for the preparation of the ethers, while tertiary amines such as triethylamine and *N*-ethyldiisopropylamine were not so favorable. *t*-Butyl chloride also reacted slowly with phenol to give the ether in reasonable yield. Similar results were obtained with the corresponding reactions of *p*-cresol with *t*-butyl bromide.

Some of these reactions provide one of the best convenient procedures for the syntheses of aryl *t*-butyl ethers since they are one-step reactions using readily available chemicals, and give the ethers in high yields under very mild conditions.

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