CHEMISTRY LETTERS, pp. 57-58, 1978. Published by the Chemical Society of Japan

A NEW SYNTHESIS OF ARYL *t*-BUTYL ETHERS

Hiromitsu MASADA and Yutaka OISHI

Department of Industrial Chemistry, Faculty of Engineering, Kanazawa University, Kodatsuno, Kanazawa 920

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:

$$\text{Ar–OH} + t\text{-Bu–X} \xrightarrow[\text{Amine}]{\text{20–30 °C}} \text{Ar–O–Bu-}t$$

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 cm^3 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 $cm^3 \times 3$). The upper organic layer was washed with 5% aqueous sodium hydroxide (40 $cm^3 \times 1$) and water (40 $cm^3 \times 2$), 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 ($CDCl_3$) δ=1.28 (9H, s, *t*-Bu) and 7.05 (5H, m, aromatic). The lower aqueous layer was extracted with diethyl ether (40 $cm^3 \times 3$). 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.	Time	Yield[b] of Aryl
ArOH	*t*-BuX	Amine	(°C)	(h)	*t*-butyl ether (%)
PhOH	X = Br	none	30	8	0
PhOH	Br	pyridine	30	2	90, 75[c]
PhOH	Br	pyridine	20	4	91
PhOH	Br	n-$C_6H_{13}NH_2$	30	2	88
PhOH	Br	$(i\text{-Pr})_2NH$	30	2	85
PhOH	Br	Et_3N	30	2	74
PhOH	Br	$(i\text{-Pr})_2N\cdot Et$	30	2	67
PhOH	Cl	pyridine	30	5	66
p-cresol	Br	pyridine	30	2	88, 75[c]
p-cresol	Br	n-$BuNH_2$	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.

References

1) D. R. Stevens, *J. Org. Chem.*, 20, 1232 (1955).
2) C. Frisell and S. Lawesson, *Org. Synth.*, 41, 91 (1961).
3) M. R. V. Sahyun and D. J. Cram, *Org. Synth.*, 45, 89 (1965).
4) G. M. Whitesides, J. S. Sadowski, and J. Lilburn, *J. Am. Chem. Soc.*, 96, 2829 (1974).
5) S. Lawesson and C. Frisell, *Arkiv Kemi*, 17, 393 (1961); *Chem. Abstr.*, 57, 2058b (1962).
6) J. B. Mckinley, *J. Am. Chem. Soc.*, 69, 1624 (1947).

(Received November 1, 1977)