ELSEVIER

Journal of Fluorine Chemistry 76 (1996) 201–202

JOURNAL OF FLUORINE CHEMISTRY

2,5-Di-t-butyl-4-fluorophenol

Suzanne T. Purrington *, Gary M. Green

Chemistry Department, North Carolina State University, P.O. Box 8204, Raleigh, NC 27695-8204, USA

Received 26 July 1995; accepted 16 September 1995

Abstract

Treatment of 4-fluorophenol with excess t-butyl chloride and aluminum chloride results in the formation of 2,5-di-t-fluorobutylphenol.

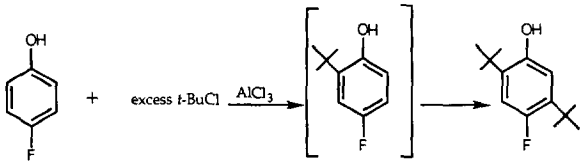
Keywords: Synthesis; Di-t-butylfluorophenol; IR spectroscopy; NMR spectroscopy; Mass spectrometry

1. Introduction

2,6-Di-t-butyl-4-substituted phenols are usually prepared by the Lewis acid-catalyzed butylation of the parent phenol [1]. These hindered phenols have been widely used as antioxidants [1]. We sought a synthesis of 2,6-di-t-butyl-4-fluorophenol that did not employ the use of the expensive reagent, xenon difluoride [2].

2. Results and discussion

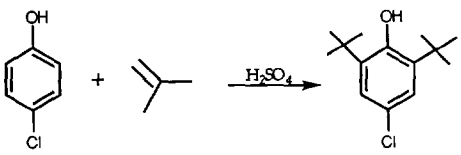
Thus, we treated 4-fluorophenol with excess t-butyl chloride in the presence of aluminum chloride. The compound that resulted was 2,5-di-t-butyl-4-fluorophenol, as shown in Eq. (1). No mono-t-butylated compound was observed.



(1)

1 2

The formation of 2,6-di-t-butyl-4-chlorophenol occurs when *p*-chlorophenol is t-butylated [3], as shown in Eq. (2). The steric bulk of the 4-chlorine substituent does not allow substitution in the 5-position.



(2)

* Corresponding author.

SSDI 0022-1139(95)03366-1

The reaction of 4-methoxyphenol with t-butylating reagents is sensitive to the reaction conditions [4]. Both the 2,6-di-t-butyl and the 2,5-di-t-butyl compounds are formed. Although the methoxy group is not as strong a donor as the hydroxy group, the influence of the t-butyl in 2-t-butyl-4-methoxyphenol, the reaction intermediate, is sufficient to direct the second t-butyl to the 5-position.

In nitration reactions, the fluorine substituent is deactivating compared with hydrogen, but activating compared with chlorine [5]. In the chlorophenol, the alkylation is directed by the –OH group, but in the fluorophenol, the fluorine in the intermediate 2-t-butyl-4-fluorophenol directs the entering group exclusively to the 5-position. The fluorine 2p orbital can overlap with the aromatic carbon better than the 3p orbital in the chloro compound. The π-donor effect of fluorine, the small size of fluorine and the 2-t-butyl directing effect all combine to give rise solely to 2,5-di-t-butyl-4-fluorophenol.

3. Experimental details

^{1}H NMR spectra were obtained at 300.075 MHz on a Varian Gemini 300 NMR spectrometer; chemical shifts are reported in ppm downfield from tetramethylsilane, using the peak for $CDCl_3$ (δ 7.26 ppm) as a reference. ^{19}F NMR spectra were obtained at 282.33 MHz on a Varian Gemini 300 NMR spectrometer; chemical shifts are reported in ppm downfield from internal $CFCl_3$ (δ 0 ppm) as a reference. High-resolution mass spectra were obtained on a JEOL HX110HF mass spectrometer using electron impact ionization. ^{13}C NMR spectra were obtained at 75.43 MHz on a GE-300 NMR spectrometer. IR spectra were obtained on a Perkin-Elmer 1430 Ratio Recording Infrared Spectrometer.

3.1. Preparation of 2,5-di-t-butyl-4-fluorophenol

To a mixture of 4-fluorophenol (8.852 g, 79.0 mmol) and aluminum chloride (4.502 g, 33.76 mmol) was added t-butyl chloride (23.45 g, 253.3 mmol). This reaction mixture was stirred for 24 h, after which it was placed into ice water (200 ml) and extracted with benzene (150 ml, 3×50 ml). The benzene solution was washed with 10% NaOH (150 ml), dried with magnesium sulfate and evaporated in vacuo to leave a blue residue (1.80 g, 10.2% crude yield). Sublimation of the blue residue resulted in colorless crystals, m.p. 92–93 °C. IR: 3590 cm^{-1}. ^1H NMR (300 MHz) δ: 6.90 (d, J=15.6 Hz, 1H); 6.57 (d, J=8.1 Hz, 1H); 4.92 (s, 1H); 1.39 (s, 9H); 1.34 (s, 9H) ppm. ^{19}F NMR (282 MHz) δ: 120.92 (dd, ^3J=15 Hz, ^4J=8 Hz) ppm. ^{13}C NMR (75 MHz) δ: 29.4, 29.8, 33.7, 34.2, 114.8, 115.2, 134.8, 135.0, 149.4, 155.8 ppm. HRMS: calc. for $C_{14}H_{21}FO$, 224.1576. Found, 224.1572.

Acknowledgments

Mass spectra were obtained at the Mass Spectrometry Laboratory for Biotechnology Research. Partial funding for the facility is from the National Science Foundation and the North Carolina Biotechnology Center.

References

[1] K.U. Ingold, *J. Phys. Chem., 64* (1960) 1636.
[2] I. Takemoto and K. Yamasaki, *Biosci. Biotech. Biochem., 58* (1994) 594.
[3] H. Hart and F.A. Cassio, Jr., *J. Am. Chem. Soc., 73* (1951) 3179.
[4] (a) C.D. Cook, R.G. Inskeep, A.S. Rosenberg and E.C. Curtis, Jr., *J. Am. Chem. Soc., 77* (1955) 1672; (b) K.U. Ingold, *Can. J. Chem., 38* (1960) 1092.
[5] (a) R.G. Coombes, D.H.G. Crout, J.G. Hoggett, R.B. Moodie and K. Schofield, *J. Chem. Soc. B,* (1970) 347; (b) N.C. Deno and R. Stein, *J. Am. Chem. Soc., 78* (1956) 578.