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Short Note

Synthesis of 2-Fluoromethyl-7-methylnaphthalene

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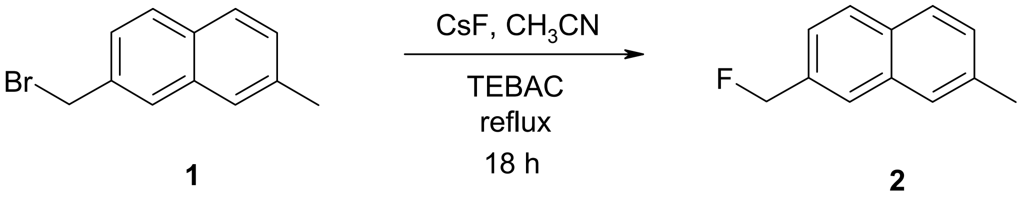
1. Introduction

In connection with our investigation of competitive mesolytic cleavages [1] of radical anions we needed 2-fluoromethyl-7-methylnaphthalene, **2**, as a gas chromatography standard. Our initial attempt was to prepare **2** via the corresponding known alcohol 2-hydroxymethyl-7-methylnaphthalene [2]. Treatment of the alcohol with the Olah's reagent (HF/pyridine) [3], according to the procedure of Olah and co-workers for fluorination of alcohols [4] did not result in the desired fluoride. The alternative strategy was to employ halogen exchange using the bromo derivative **1** with a proper source of nucleophilic fluoride. The choice of fluoride source was cesium fluoride, which has appreciable solubility in polar aprotic organic solvents [5], especially when used together with a quaternary ammonium salt [5]. We would like to report a convenient procedure for preparation of 2-fluoromethyl-7-methylnaphthalene.



2. Experimental Section

2.1. General

Melting points were determined using Mel-Temp apparatus and were uncorrected. NMR spectra were recorded on Bruker 400 MHz instrument using deuterated chloroform as solvent and tetramethylsilane as internal standard. The number of hydrogens on each carbon was determined from ^{13}C NMR and ^{135}DEPT spectra. The mass spectra were recorded on Kratos MS-25 RFA double focusing mass spectrometer in chemical ionization (CI) mode. Gas chromatography was performed on a Varian 3700 instrument with packed column. The column was 1/8'' in diameter and 50 cm in length packed with 5% OV-101 on supelcoport and was purchased from Supelco. The carrier gas was helium (30mL/min flow), the detection was accomplished with flame ionization and monitored with HP-3390A reporting integrator. Preparative flash chromatography [6] was performed using Merck silica gel 60 (230-400 mesh) and TLC was carried out using Merck pre-coated plates (60 F_{254}, 250 µm).

2.2. 2-Bromomethyl-7-methylnaphthalene (1)

A mixture of 2,7-dimethylnaphthalene [7], (0.981 g, 6.28 mmol), *N*-bromosuccinimide (1.141 g, 6.42 mmol), benzoyl peroxide (0.038g, 0.16 mmol) in 30 mL of degassed carbon tetrachloride was refluxed under argon for six hours. The mixture was allowed to cool to room temperature then it was cooled on ice and succinimide was removed via filtration. The filtrate was washed with saturated sodium bicarbonate (30 mL), water (2 x 30 mL) and dried over sodium sulfate. The yellow solid that was left behind upon removal of solvent contained **1**, unreacted 2,7-dimethylnaphthalene, and 2,7-bis(bromomethyl)naphthalene. The desired product, 2-bromomethyl-7-methylnaphthalene, **1**, was isolated by flash chromatography, eluting with 10% methylene chloride in hexanes, as a white solid weighing 0.819 g (55%).

Mp 99-100 °C (lit.[8] 100 °C).

R_f (10% dichloromethane in hexanes) = 0.42.

GC: Rt = 7.93 min (100 °C, 3 min, 8 °C/min to 280 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, J = 8.4 Hz, 1H), 7.73-7.69 (m, 2H), 7.57 (s, 1H), 7.42 (s, 1H), 7.42 (dd, J = 8.4 Hz, J = 1.7 Hz, 1H), 7.31 (dd, J = 8.4 Hz, J = 1.7 Hz, 1H), 4.65 (s, 2H, Ar-CH_2-Br), 2.50 (s, 3 H, Ar-CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.6, 135.5, 133.8, 131.7, 129.3, 128.9, 127.9, 127.6, 127.4, 126.3 (*Ar*), 34.7 (Ar-CH_2-Br), 22.1 (Ar-CH_3).

2.3. 2-Fluoromethyl-7-methylnaphthalene (2)

A mixture of 2-bromomethyl-7-methylnaphthalene, **1**, (0.150 g, 0.605 mmol), dry cesium fluoride (0.396 g, 2.61 mmol), triethylbenzylammonium chloride (TEBAC) (0.003 g, 0.02 mmol) in dry acetonitrile (6 mL) was refluxed under nitrogen for 18 hours. The mixture was cooled to room temperature, filtered and the solid residue was washed with dichloromethane. The crude 2-fluoromethyl-7-methylnaphthalene was dissolved in dichloromethane, 0.3 g of silica gel was added and the solvent was removed. This resulting solid was applied onto an equilibrated silica gel column and eluted with 10% dichloromethane in hexane to yield 0.044 g (42%) of **2** as a white crystalline solid.

Mp 85-87 °C (dec.).

R_f (10 % dichloromethane in hexanes) = 0.34.

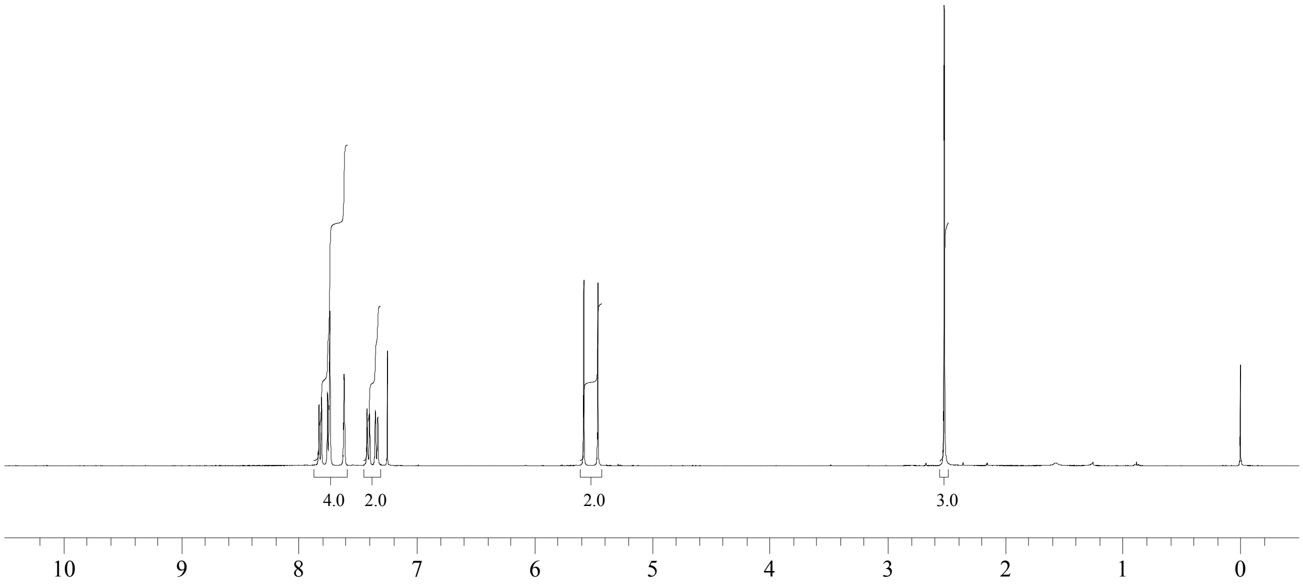
GC Rt = 1.46 min (100 °C, 3 min, 8 °C/min to 280 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, 8.4 Hz, 1H), 7.75 (m, 2H), 7.61 (s, 1H), 7.41 (d, 8.4 Hz, 1H), 7.34 (d, 8.4 Hz, 1H), 5.52 (d, $^2J_{H\text{-}F}$ = 47.8 Hz, 2H), 2.52 (s, 3H).

^{13}C NMR (100 MHz): δ = 136.32 (C), 133.83 (d, $^2J_{C\text{-}F}$ = 17 Hz, C), 133.60 (C), 131.84 (d, $J_{C\text{-}F}$ = 2 Hz, C), 128.99 (d, $J_{C\text{-}F}$ = 1 Hz, CH), 128.40 (CH), 127.77 (d, $J_{C\text{-}F}$ = 1 Hz, CH), 127.28 (d, $J_{C\text{-}F}$ = 1 Hz, CH), 126.36 (d, $^3J_{C\text{-}F}$ = 7 Hz, CH), 124.35 (d, $J_{C\text{-}F}$ = 5 Hz, CH), (*Ar*), 85.11 (d, $^1J_{C\text{-}F}$ = 165 Hz, Ar-CH_2-F), 21.93 (Ar-CH_3).

CI-MS (m/z, rel. intensity): 176 (10%), 175 (MH^+, 82%), 174 (MH^+ - H, 97%), 173 (16%), 159 (16%), 156 (15%), 155, (MH^+ - HF, 100%), 141 (11%).

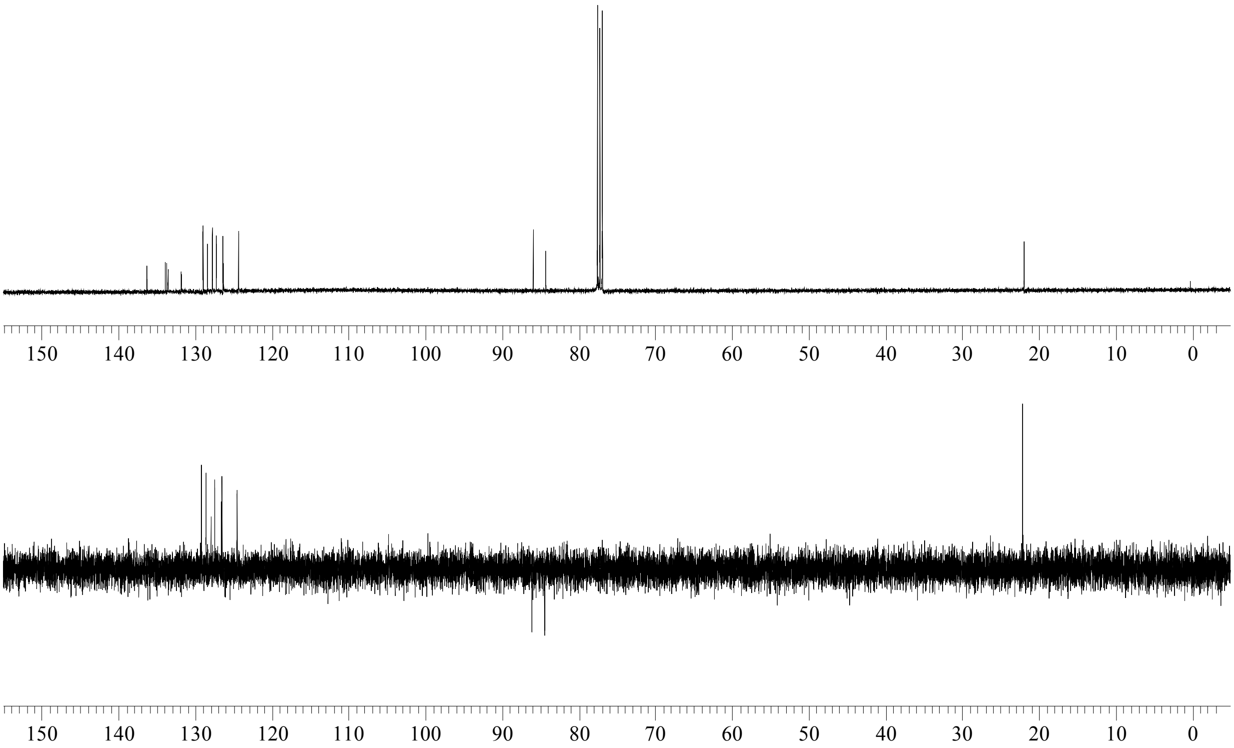
Figure 1. ^{1}H NMR spectrum of 2-fluoromethyl-7-methylnaphthalene (2) in $CDCl_3$ (400 MHz). The singlet at 0 ppm is TMS and the singlet at 7.25 ppm is the residual $CHCl_3$ from the $CDCl_3$.



3. Conclusion

The reaction of 2-bromomethyl-7-methylnaphthalene with cesium fluoride in refluxing acetonitrile, in the presence of triethylbenzylammonium chloride gave the desired product **2** as a white crystalline solid. The structure of **2** was unambiguously determined by spectroscopic means (^{1}H NMR, ^{13}C NMR, ^{135}DEPT NMR and MS). The presence of the benzylic fluorine could be seen from the ^{1}H NMR spectrum (doublet centered at 5.52 ppm, arising from two bond hydrogen-fluorine coupling, with coupling constant of 47.8 Hz) and from the ^{13}C NMR spectrum (doublet centered at 85.11 ppm arising from one bond carbon-fluorine coupling with coupling constant of 165 Hz. Both values are in excellent agreement with the literature values for benzylic fluorides [9,10].

Figure 2. ^{13}C NMR spectrum (top), and ^{135}DEPT NMR spectrum (bottom) of **2** in $CDCl_3$ (100 MHz).



Note: The compound is volatile so do not dry it for prolonged times *in vacuo*. It decomposes when kept in halogenated solvents for several days (especially $CHCl_3$).

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