

Short Note

Synthesis of 2,7-Bis(fluoromethyl)naphthalene

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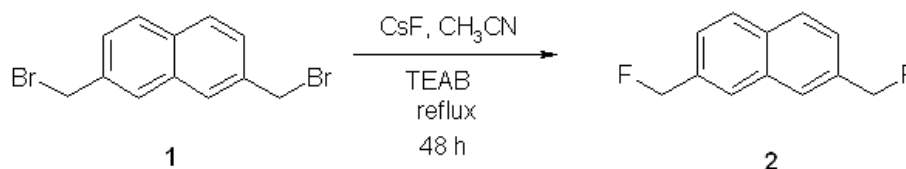
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1. Introduction

In connection with our investigation of the competitive mesolytic cleavages [1] of radical anions we have prepared several symmetrically substituted 2,7-bis(halomethyl)naphthalene derivatives. The starting material for these derivatives was 2,7-bis(bromomethyl)naphthalene **1**, which could be conveniently obtained by benzylic bromination of the commercially available 2,7-dimethylnaphthalene using the procedure described by Reid and co-workers [2]. Our initial attempts of preparing 2,7-bis(fluoromethyl)naphthalene by treatment of the known 2,7-bis(hydroxymethyl)naphthalene [3] with Olah's HF/pyridine reagent [4,5] met with failure. 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 [6], especially when used together with a quaternary ammonium salt [6]. We would like to report a convenient procedure for preparation of 2,7-bis(fluoromethyl)naphthalene.



2. Experimental

2.1. General

All chemicals were obtained from commercial sources and were used without further purification. Melting points were determined using Mel-Temp apparatus and were uncorrected. NMR spectra were recorded on Bruker 400 MHz instrument using CDCl₃ as solvent and tetramethylsilane as internal standard. The IR spectra were recorded on Perkin Elmer Model 1600 instrument between sodium chloride plates in carbon tetrachloride. The mass spectra were recorded on Kratos MS-25 RFA double focusing mass spectrometer in electron impact (EI) 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 [7] was performed using Merck silica gel 60 (230-400 mesh) and TLC was carried out using Merck pre-coated plates (60 F₂₅₄, 250 μm).

2.2. 2,7-Bis(bromomethyl)naphthalene (1)

2,7-Bis(bromomethyl)naphthalene (**1**) was prepared by the procedure described by Reid et.al.

Mp 144-146 °C (lit. [2] 145-147 °C).

R_f = 0.32 (10% dichloromethane in hexane).

GC Rt = 11.87 min (100 °C, 3 min, 8 °C/min 280 °C).

¹H NMR (400 MHz, CDCl₃): δ = 7.83-7.79 (m, 4H), 7.51 (d, J = 8.8 Hz, 2H), 4.65 (s, 4H).

¹³C NMR (100 MHz, CDCl₃): δ = 136.1, 133.2, 132.9, 128.8, 128.1, 127.7 (*Ar*), 33.9 (*Ar-CH₂-Br*).

2.3 2,7-Bis(fluoromethyl)naphthalene (2)

A mixture of 2,7-bis(bromomethyl)naphthalene, **1**, (1.258 g, 4.01 mmol), dry cesium fluoride (1.341 g, 8.82 mmol), tetraethylammonium bromide (0.050 g, 0.238 mmol) in dry acetonitrile (20 mL) was refluxed for 24 hours with vigorous stirring under argon. Additional cesium fluoride was added (1.341 g, 2.61 mmol) and the mixture was refluxed for an additional 24 hours. The reaction mixture was cooled to room temperature, diluted with methylene chloride (75 mL) and transferred to a separatory funnel. The organic layer was washed with water (5 × 50 mL), saturated sodium chloride (1 × 50 mL) and dried over sodium sulfate. The solvents were removed *in vacuo* and the resulting white powder was subjected to column chromatography (SiO₂) eluting with 10% dichloromethane in hexane to yield 0.477 g (62%) of **2** as a white crystalline solid.

Mp 127-129 °C; R_f = 0.21 (10% methylene chloride in hexanes).

GC Rt = 4.41 min (100 °C, 3 min, 8 °C/min 280 °C).

¹H NMR (400 MHz, CDCl₃): δ = 7.86 (d, J = 8.4 Hz, 2H), 7.82 (broad s, 2H), 7.49 (d, J = 8.4 Hz, 2H), 5.53 (d, ²J_{H-F} = 47.8 Hz, 4H).

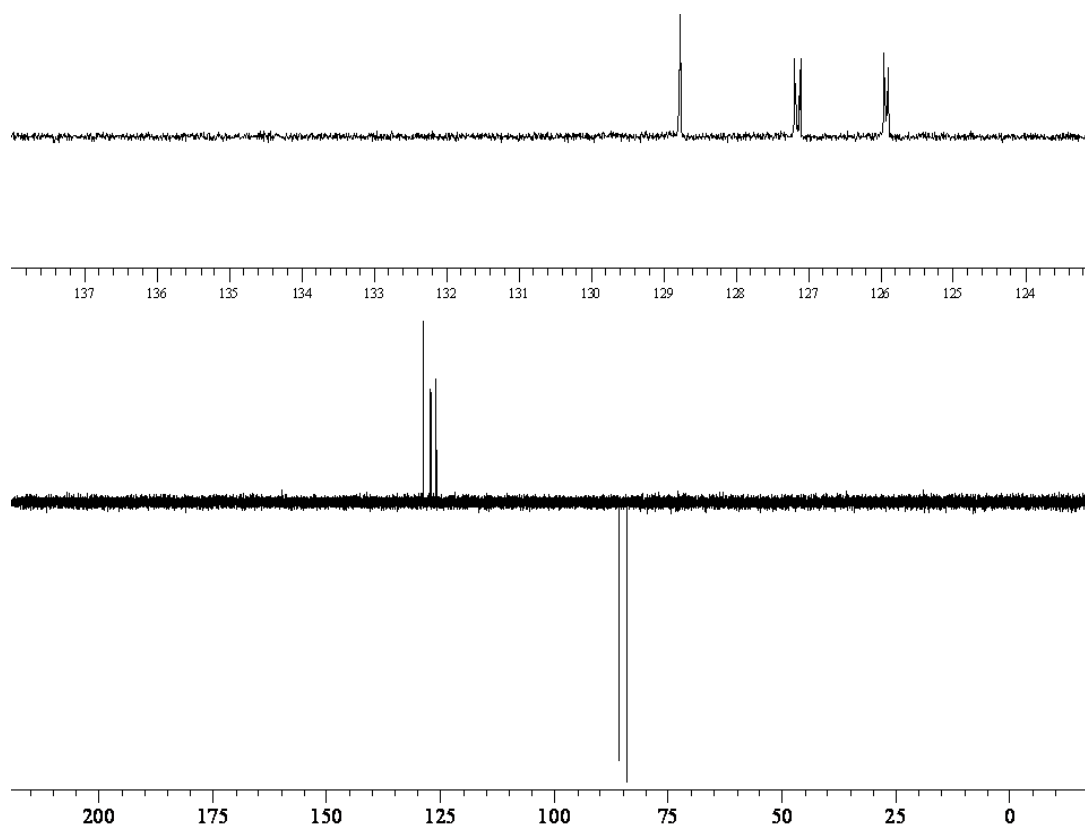
^{13}C NMR (100 MHz, CDCl_3): δ = 134.68 (d, $^2J_{\text{C-F}} = 17$ Hz), 133.68, 133.26, 128.76, 127.14 (d, $^3J_{\text{C-F}} = 8$ Hz, CH), 125.92 (d, $^3J_{\text{C-F}} = 6$ Hz) (*Ar*), 84.99 (d, $^1J_{\text{C-F}} = 166$ Hz, Ar- $\text{CH}_2\text{-F}$).

$^{135}\text{DEPT}$ NMR: 128.76 (\uparrow , CH), 127.14 (\uparrow , d, $^3J_{\text{C-F}} = 8$ Hz, CH), 125.92 (\uparrow , d, $^3J_{\text{C-F}} = 6$ Hz, CH), 84.99 (\downarrow , d, $^3J_{\text{C-F}} = 6$ Hz, Ar- $\text{CH}_2\text{-F}$).

IR (CCl_4 , cm^{-1}): 3060, 3033, 2955, 2894, 1614, 1518, 1465, 1439, 1381, 1362, 1340, 1272, 1205, 1172, 1032, 1014, 990, 956, 904.

EI-MS (m/z , rel. intensity): 193 ($\text{M}^+ + 1$, 10%), 192 (M^+ , 78%), 191 ($\text{M}^+ - 1$, 30%), 190 (7%), 173 ($\text{M}^+ - \text{F}$, 6%), 172 ($\text{M}^+ - \text{HF}$, 16%), 170 (17%), 159 (100%), 133 (13%).

Figure 1. ^{13}C NMR spectrum of 2,7-bis(fluoromethyl)naphthalene (**2**) in CDCl_3 (100 MHz).

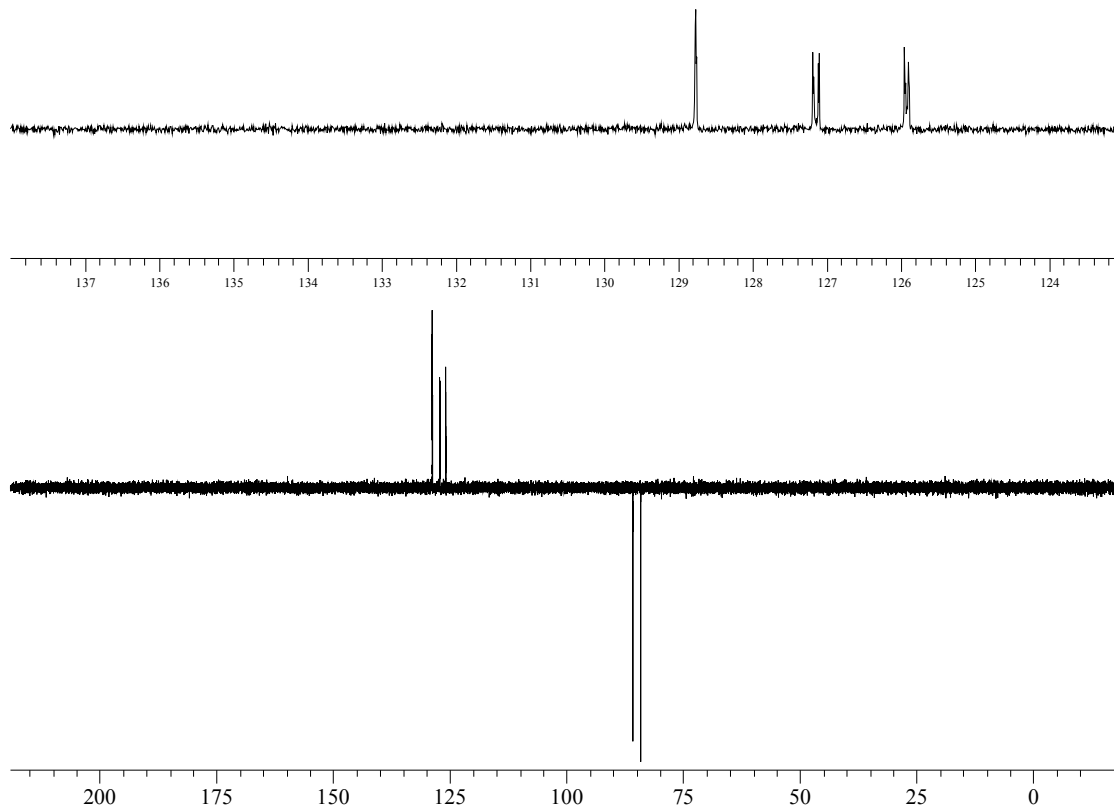


3. Conclusion

The reaction of 2,7-bis(bromomethyl)naphthalene with cesium fluoride in refluxing acetonitrile, in the presence of tetraethylammonium bromide gave the desired product **2** as a white crystalline solid. The reaction can be conveniently monitored by thin-layer chromatography or gas chromatography. It is important to push the halogen exchange to completion, because the intermediate 2-bromomethyl-7-fluoromethylnaphthalene has similar polarity with **2**. The structure of **2** was unambiguously determined by spectroscopic means (^1H NMR, ^{13}C NMR, $^{135}\text{DEPT}$ NMR, IR and MS). The presence of the benzylic fluorine could be seen from the ^1H NMR spectrum (doublet centered at 5.53 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 85.0 ppm arising from one bond carbon-fluorine coupling

with coupling constant 166 Hz). Both values are in excellent agreement with the literature values for benzylic fluorides [8,9].

Figure 2. 135 DEPT NMR spectrum of 2,7-bis(fluoromethyl)naphthalene (**2**) in CDCl_3 (400 MHz).



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