Fluoronaphthalene Building Blocks via Arynes: A Solution to the Problem of Positional Selectivity

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When 3-fluoro- and 3-chloro-1,2-didehydrobenzenes are generated in the presence of 2-(trimethylsilyl)furan, two regioisomeric cycloadducts are formed in a 1:2 ratio. However, regioselectivity can be installed by fitting one bulky trimethylsilyl group into sterically critical positions of each of the two reaction components. Thus 3-fluoro-6-trimethylsilyl-1,2-didehydrobenzene and 2-(trimethylsilyl)furan give one cycloadduct exclusively. In this way, the Diels–Alder reaction between suitably adorned arynes and similarly designed furans can open an entry to naphthalene derivatives that have unprecedented substituent patterns that qualify them as building blocks for pharmaceutical or agricultural research. The acid-catalyzed isomerization of model 1,4-epoxy-1,4-dihydronaphthalenes, the aryne/furan cycloadducts, exhibits unexpected effects on rates and regioselectivity.

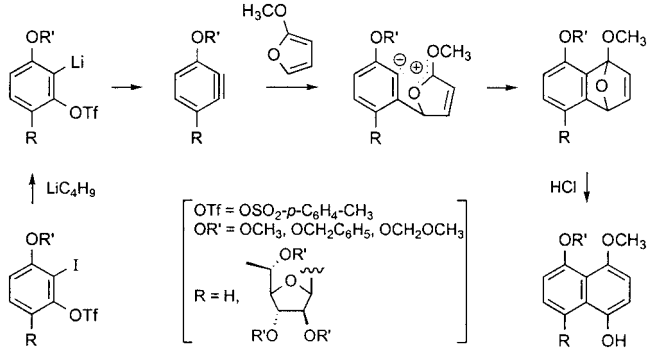
Introduction

The "holy grail" of the regiochemically exhaustive functionalization[1] of benzene-like arenes can be easily attained by applying a set ("toolbox"[1]) of tailor-made organometallic methods. It is more difficult to achieve the same goal in the naphthalene series. First of all, there are seven vacant positions in a monosubstituted naphthalene (as opposed to three in the benzene series) and, moreover, it is not obvious how to tackle those located in the unsubstituted ring as orientational effects level off rapidly with distance.

Although known for half a century,[2] the synthetic potential of the aryne route to naphthalene derivatives is still underevaluated. Based on this potential, we have recently been able to elaborate a facile access to trifluoromethyl-[3,4] and trifluoromethoxy-substituted[5] naphthalenecarboxylic acids. As in previous work from this laboratory, the carboxy entity represents just the most typical functional group, and the methods employed are designed to tolerate any kind of electrophile.

While featuring fluorinated and trimethylsilylated 1,2-didehydrobenzenes ("arynes") as reactive intermediates, the present article focuses on a widely ignored selectivity problem. The issue is whether one of the two possible regioisomers is preferentially formed when an unsymmetrically substituted aryne is allowed to combine with a monosubstituted furan or other diene. This issue has been addressed just once in relation with fluorinated products. 3-Fluoro-1,2-didehydrobenzene and 2-methylfuran have been found to afford the head-to-head and head-to-tail cycloadducts in a 2:3 ratio.[6] Other unsymmetrical arynes such as 4-fluoro-1,2-didehydrobenzene,[7] 3,4,5-trifluoro-1,2-didehydrobenzene,[8] 3,4,6-trifluoro-1,2-didehydrobenzene,[8,9] 3,4,6-trifluoro-5-methoxy-1,2-didehydrobenzene[9] and 3-bromo-4,5,6-trifluoro-1,2-didehydrobenzene[10] have so far only been intercepted with symmetrical reagents such as furan and thiophene. 3,4- and 3,5-Difluoro-1,2-didehydrobenzene have not yet been investigated as reactive species at all.[11,12]

The sole case of effective regiocontrol was reported with 3-alkoxy-substituted arynes (alkoxy = methoxy, benzyloxy, methoxymethoxy) which fuse with 2-methoxyfuran in high yields (74–82%) and exclusive head-to-head orientation.[13] The same selectivity was realized with 6-alkyl-substituted 3-alkoxy-1,2-didehydrobenzenes[14,15] (Scheme 1).



Scheme 1. The exceptionally encountered regioselectivity of cycloaddition reactions between 3-alkoxy1,2-didehydroarenes and 2-methoxyfuran.

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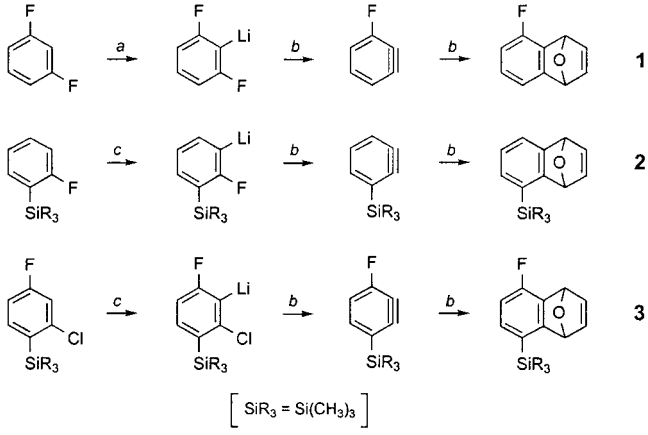
Although these authors refrained from any mechanistic speculation, one can hardly rationalize the regiochemical outcome without invoking zwitterionic intermediates (Scheme 1).

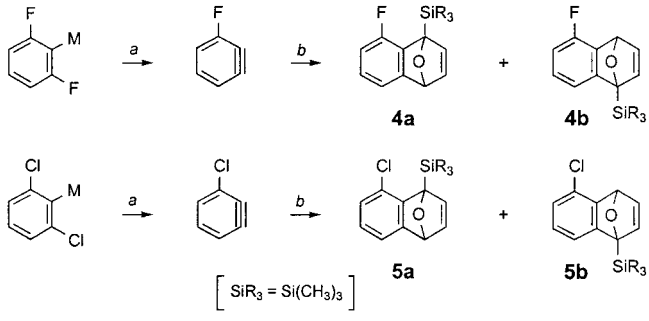
Results

Our objective was to dock a monofluorodehydrobenzene at a monosubstituted furan in a regiochemically controlled fashion. To proceed systematically, we first allowed 3-fluoro-1,2-didehydrobenzene, 3-trimethylsilyl-1,2-didehydrobenzene, and 3-fluoro-6-trimethylsilyl-1,2-didehydrobenzene, generated from 1,3-difluorobenzene, (2-fluorophenyl)trimethylsilane, and (2-chloro-4-fluorophenyl)trimethylsilane, respectively, by treatment with butyllithium or *sec*-butyllithium, to react with unsubstituted furan. The fluoro- or trimethylsilyl-bearing 1,4-epoxy-1,4-dihydronaphthalenes **1** (45%), **2** (42%), and **3** (73%) were obtained in acceptable yields (Scheme 2).



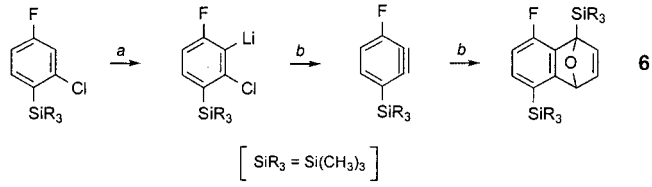
Scheme 2. Trapping of 3-fluoro-1,2-didehydrobenzene, 3-trimethylsilyl-1,2-didehydrobenzene, and 3-fluoro-6-trimethylsilyl-1,2-didehydrobenzene with furan. *a*: *sec*-Butyllithium in tetrahydrofuran (THF) at –75 °C. *b*: Transfer through Teflon tubing into furan kept at +25 °C *c*: Butyllithium in THF at –75 °C.

Next, 3-fluoro-1,2-didehydrobenzene and the 3-chloro congener were generated in the presence of a substituted diene, namely 2-(trimethylsilyl)furan. The bulky substituent was found to discriminate little between the possible reactant arrangements. The products **4** and **5** were formed in poor yields (25% and 23%, respectively) as regioisomeric mixtures **a** and **b** in a 1:2 ratio in both cases (Scheme 3).



Scheme 3. Trapping of 3-fluoro- and 3-chloro-1,2-didehydrobenzene with 2-(trimethylsilyl)furan. *a*: M = H; *sec*-butyllithium in THF at –75 °C (→ M = Li). *b*: Transfer through Teflon tubing into a solution of 2-(trimethylsilyl)furan in THF.

Finally, 3-fluoro-6-trimethylsilyl-1,2-didehydrobenzene, produced as described above, was fused with 2-(trimethylsilyl)furan. The cycloadduct **6** was isolated in unexpectedly good yield (62%) and, more importantly, as a sole regioisomer (Scheme 4). This means that the desired regioselectivity can indeed be achieved if both the aryne and diene components are subjected to steric crowding.



Scheme 4. Perfect regioselective cycloaddition between 3-fluoro-6-trimethylsilyl-1,2-didehydrobenzene and 2-(trimethylsilyl)furan. *a*: *sec*-Butyllithium in THF at –75 °C. *b*: Addition of 2 equiv. of 2-(trimethylsilyl)furan and rapid heating to +60 °C.

These findings constitute proof of concept and the starting point for further work in this field. The next step should be an attempt to promote cycloadditions between 3-fluoro-6-trimethylsilyl-1,2-didehydrobenzene and 2-(trimethylsilyl) furans that carry a second substituent, for example, bromine, methoxymethoxy, or methyl, at the 5-position. The resulting 1,4-epoxy-1,4-dihydronaphthalenes could then be deoxygenated to the corresponding naphthalenes with zinc powder[5] or low-valent titanium,[3] and the two trimethylsilyl groups located in different environments could possibly be induced to undergo a consecutive displacement by protodesilylation,[16,17] bromodesilylation,[16,18] or iododesilylation.[16,19] Alternatively, the 1,4-epoxy-1,4-dihydronaphthalenes could be converted into phenols by acid catalysis, again regioselectively.

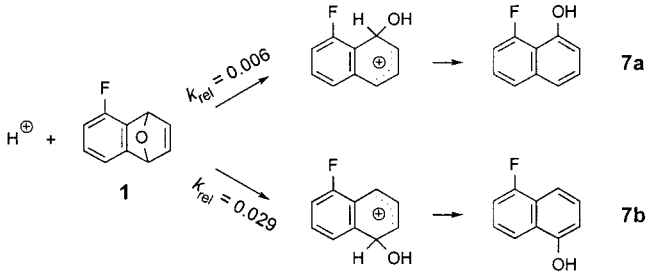
In anticipation of such future endeavors we have examined the acid-catalyzed ring-opening of the 1,4-epoxy-1,4-dihydronaphthalenes **1** and **2** (Table 1). The fluorine-substi-

Table 1. Reaction rates k_{rel}, relative to the unsubstituted 1,4-epoxy-1,4-dihydronaphthalene, calculated from the amounts of substituted 1,4-epoxy-1,4-dihydronaphthalenes and 1,4-epoxy-1,4-dihydronaphthalene before ($[A]_0$ and $[B]_0$) and after ($[A]_t$ and $[B]_t$) their simultaneous reaction with hydrochloric acid in ethanol at reflux.

Substituent	$[A]_0$	$[B]_0$	$[A]_t$	$[B]_t$	k_{rel}
5-F[a]	1.00	1.00	0.88	0.03	0.0035
5-SiR_3[b]	1.05	1.22	0.71	0.05	0.12[c]
5-F-8-SiR_3[d]	1.02	1.07	1.02	0.02	–[e]
5-SiR_3[f]	1.04	1.05	0.99	0.69	0.15[c]

[a] 1,4-Epoxy-1,4-dihydro-5-fluoronaphthalene. [b] 1,4-Epoxy-1,4-dihydro-5-(trimethylsilyl)naphthalene. [c] Trimethylsilyl-substituted naphthols were never observed and they evidently undergo fast desilylation to 1-naphthol (see below). [d] 1,4-Epoxy-1,4-dihydro-5-fluoro-8-(trimethylsilyl)naphthalene. [e] 1,4-Epoxy-1,4-dihydro-5-fluoro-8-(trimethylsilyl)naphthalene gave no ring opening. [f] 1,4-Epoxy-1,4-dihydro-5-(trimethylsilyl)naphthalene competing with 1-(trimethylsilyl)naphthalene (undecane as an inert reference compound for quantification).

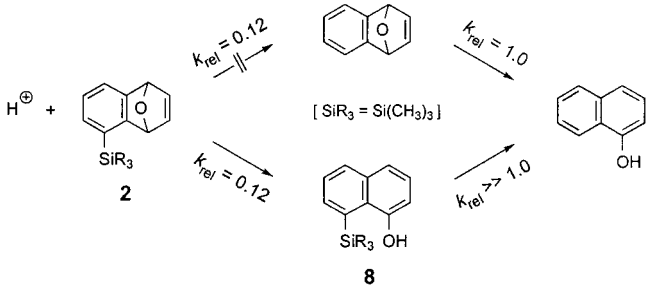
tuted cycloadduct gave a 17:83 mixture of 8-fluoro-1-naphthol (**7a**) and 5-fluoro-1-naphthol (**7b**). However, the reaction occurred only 0.035 times as fast as the corresponding conversion of the unsubstituted 1,4-epoxy-1,4-dihydronaphthalene into 1-naphthol (Scheme 5). Apparently the electron-retaining inductive effect of the halogen destabilizes the allyl cation[5] formation, in particular, if not partially compensated by an electron-donating mesomeric effect. For comparison, the solvolysis rate of *p*-, *m*- and *o*-fluoro-substituted cumyl chloride is 2.1, 0.025, and 0.050, respectively, relative to that of the parent compound.[20,21]



Scheme 5. The rate-retarding effect of a remote fluorine substituent on the acid-catalyzed isomerization of 1,4-epoxy-5-fluoro-1,4-dihydronaphthalene (**1**) to 5- and 8-fluoronaphthol.

The reluctance of fluorinated aryne cycloadducts to undergo acid-catalyzed opening of the heterocyclic ring can be overcome by increasing the acid concentration. Under such conditions, 1,4-epoxy-1,4-dihydro-5,6,7,8-tetrafluoronaphthalene was smoothly isomerized to afford 5,6,7,8-tetrafluoro-1-naphthol in 70%[22] and 93% yield.[23]

The silyl-substituted cycloadduct **2** was found to undergo 1,4-epoxide opening 0.12 times as fast as the unsubstituted parent compound. However, the only detected product was the silyl-free 1-naphthol. An initial protodesilylation via an *ipso*-cyclohexadienyl cation[24] is improbable for several reasons. Thus, we tentatively assume a relatively slow acid-mediated isomerization to give the 1-(8-hydroxynaphthyl)-trimethylsilane (**8**), which rapidly loses the trimethylsilyl group after hydroxy-assisted *ipso*-protonation (Scheme 6). To support this hypothesis, one would have to prepare the silane **8** and study its protolysis behavior separately.



Scheme 6. Neighboring group-assisted protodesilylation of 1-(8-hydroxynaphthyl)trimethylsilane (**8**).

Conclusions

Up to now, a single systematic investigation has been devoted to the preparation of functionalized fluoronaphthalenes. Four mono- and four difluoronaphthoic acids were made accessible by reaction sequences relying, in most cases, on an intramolecular Friedel–Crafts acylation as the key step.[25]

The concepts outlined above now open a wide avenue leading to naphthalene derivatives that qualify as promising building blocks for life-sciences oriented research. The cornerstone of the synthesis plan is the early introduction of an electronegative substituent such as OH, Cl, F, CF_3, or OCF_3. This can be achieved by fusing a correspondingly substituted aryne to a furan. The latter may carry substituents at the 2- and 5-positions to increase the structural variety of the cycloadducts. If bulky trialkylsilyl groups are present in both components (the dienophile and diene), the cycloaddition reaction proceeds regioselectively, whereas without this bias, product mixtures will be obtained. Ultimately, the trialkylsilyl groups can (and should sooner or later) be replaced either by hydrogen or by heavy halogen atoms (bromine or iodine). Substituents and, in particular, functional groups can be introduced at will in the neighborhood of the electron-withdrawing, generally halogen-containing entity by *ortho* metalation and subsequent trapping with an appropriate electrophilic reagent. To modify the other ring, one may again rely on metalation as the key step, this time occurring at a position adjacent to an *O*-acetal-protected hydroxy group or rather on a halogen/metal permutation that replaces a foresightedly positioned bromine atom by lithium. Thus, the organometallic approach to structure elaboration offers a unique choice of possibilities also in the naphthalene field.

Experimental Section

General: Starting materials were purchased from Acros Organics (B-2440 Geel), Aldrich-Fluka (CH-9479 Buchs), and Apollo Scientific (UK-SK62QR Stockport) unless literature sources or details of the preparation are given. Solutions of butyllithium in hexane (1.5 M) were supplied by Chemetall (60271 Frankfurt, Germany), and potassium *tert*-butoxide was a gift from Callery (Pittsburgh, PA 15230, USA). All commercial reagents were used without further purification. Air and moisture sensitive compounds were stored in Schlenk tubes or Schlenk burettes. They were protected by and handled under 99.995% pure nitrogen, using appropriate glassware (Glasgerätebau Pfeifer, 98711 Frauenfeld, Germany). Tetrahydrofuran was dried by distillation with sodium wire after the characteristic blue color of in situ generated sodium biphenyl ketyl (benzophenone sodium radical anion) had been found to persist.[26,27] The temperature of dry ice/toluene baths is consistently indicated as –75 °C, of ice baths as 0 °C and "room temperature" (22–26 °C) as 25 °C. Boiling ranges (b.p.) refer to ordinary atmospheric conditions (725 ± 5 Torr) if no reduced pressure is specified. If melting points are missing it means that all attempts to crystallize the liquid at temperatures down to –75 °C failed. The purity of distilled compounds was checked using at least two capillary columns (30 m long) loaded with stationary phases of different polarities. The stationary phases employed are encoded as DB-1 (of the silicone type) and DB-WAX (belonging to the polyethylene glycol family). ^1H and $^{13}C\{^1H\}$ NMR spectra of samples dissolved in deuterochloroform were recorded at 400 and 101 MHz, respectively. Chemical shifts δ refer to the signal of tetramethylsilane (δ

= 0.00 ppm) and coupling constants *J* are given in Hz. Coupling patterns are abbreviated as s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet), symm. m (symmetrical multiplet), dd (doublet of doublets), dt (doublet of triplets), etc. Elementary analyses were performed by the laboratory of I. Beetz (96301 Kronach, Germany). The expected percentages were calculated with the atomic weight numbers listed in the 1993 IUPAC recommendations.

Starting Materials

(2-Fluorophenyl)trimethylsilane: *sec*-Butyllithium (0.25 mol) in cyclohexane (0.20 L) was added to a solution of fluorobenzene (24 mL, 24 g, 0.25 mol) in tetrahydrofuran (0.25 L) at –75 °C in the course of 15 min. After 15 min, the white suspension was treated with chlorotrimethylsilane (32 mL, 27 g, 0.25 mol) and, when the temperature had reached +25 °C, the mixture was poured into water (20 mL). After evaporation of the solvents from the filtered solution, distillation afforded a colorless oil. Yield: 35.3 g (84%). B.p. 60–62 °C/20 Torr (ref.[28]: b.p. 60 °C/15 Torr). n_D^{20} = 1.4760 (ref.[28]: n_D^{20} = 1.4780). ^{1}H NMR: δ = 7.4 (m, 1 H), 7.3 (m, 1 H), 7.12 (tt, *J* = 7.3, 1.0 Hz, 1 H), 6.98 (td, *J* = 8.5, 1.0 Hz, 1 H), 0.31 (d, *J* = 1.0 Hz, 9 H) ppm.

(2-Chloro-4-fluorophenyl)trimethylsilane: A solution of 1-bromo-2-chloro-4-fluorobenzene (5.2 g, 25 mmol) in tetrahydrofuran (50 mL) was added dropwise in the course of 45 min to a solution of butyllithium (25 mmol) in hexanes (50 mL) at –100 °C. The mixture was treated with chlorotrimethylsilane (3.2 mL, 2.7 g, 25 mmol), allowed to reach +25 °C, and washed with water (50 mL). Upon distillation a colorless oil was collected. Yield: 3.90 g (77%). B.p. 35–36 °C/1 Torr. n_D^{20} = 1.4931. ^{1}H NMR: δ = 7.42 (dd, *J* = 8.2, 6.8 Hz, 1 H), 7.10 (dd, *J* = 9.0, 2.4 Hz, 1 H), 6.98 (td, *J* = 8.4, 2.4 Hz, 1 H), 0.37 (s, 9 H) ppm. ^{13}C NMR: δ = 164.8 (s), 162.3 (s), 136.8 (d, *J* = 8 Hz), 134.2 (s), 116.8 (d, *J* = 23 Hz), 113.2 (d, *J* = 19 Hz), –0.8 (s, 3 C) ppm. $C_9H_{12}ClFSi$ (202.73): calcd. C 53.32, H 5.97; found C 53.18, H 5.96.

2-(Trimethylsilyl)furan: Butyllithium (0.25 mol) in hexanes (0.15 L) was transferred into a solution of furan (18 mL, 17 g, 0.25 mol) and *N*,*N*′,*N*′,*N*′′,*N*′′-pentamethyldiethylenetriamine (52 mL, 43 g, 0.25 mol) in the course of 15 min at 25 °C. At 0 °C, excess chlorotrimethylsilane (50 mL) was added all at once to the white suspension. Direct distillation afforded a colorless oil. Yield: 20.5 g (58%). B.p. 50–52 °C/50 Torr. n_D^{20} = 1.4430 (ref.[29]: n_D^{20} = 1.447). ^{1}H NMR: δ = 7.66 (d, *J* = 1.5 Hz, 1 H), 6.64 (d, *J* = 3.2 Hz, 1 H), 6.40 (dd, *J* = 3.2, 1.5 Hz, 1 H), 0.29 (s, 9 H) ppm.

1,4-Epoxy-1,4-dihydronaphthalenes

1,4-Epoxy-1,4-dihydro-5-fluoronaphthalene (1): Butyllithium (0.10 mol) in hexanes (70 mL) was added to a solution of 1,3-difluorobenzene (9.9 mL, 11 g, 0.10 mol) in tetrahydrofuran (0.10 L) at –75 °C. After 15 min, the white suspension was transferred through Teflon tubing into furan (73 mL, 68 g, 1.0 mol) kept at +25 °C. The reaction mixture was diluted with hexanes (0.25 L) and filtered through a pad of alumina. After evaporation of the solvents, the residue was distilled. A slightly yellow oil was obtained. Yield: 7.30 g (45%). B.p. 57–58 °C/1 Torr. ^{1}H NMR: δ = 7.0 (m, 3 H), 6.96 (symm. m, 1 H), 6.68 (td, *J* = 8.3, 0.6 Hz, 1 H), 5.97 (br. s, 1 H), 5.74 (br. s, 1 H) ppm. ^{13}C NMR: δ = 157.1 (s), 154.6 (s), 152.7 (d, *J* = 5 Hz), 142.8 (d, *J* = 55 Hz), 133.6 (d, *J* = 21 Hz), 127.6 (d, *J* = 6 Hz), 116.3 (d, *J* = 3 Hz), 113.8 (d, *J* = 22 Hz), 82.5 (d, *J* = 1 Hz), 79.4 (d, *J* = 1 Hz) ppm. $C_{10}H_7FO$ (162.05): calcd. C 74.07, H 4.35; found C 74.01, H 4.21.

1,4-Epoxy-1,4-dihydro-5-(trimethylsilyl)naphthalene (2): (2-Fluorophenyl)trimethylsilane (8.4 g, 50 mmol) was added dropwise to a solution of *sec*-butyllithium (50 mmol) in cyclohexane (40 mL) and tetrahydrofuran (40 mL) cooled in a dry ice/toluene bath for 45 min. At –75 °C, the yellow suspension was transferred through Teflon tubing into furan (73 mL, 68 g, 1.0 mol) whilst stirring. The mixture was diluted with hexanes (0.25 L) and filtered through a pad of alumina. After evaporation of the solvents, the residue was distilled to give a viscous yellow oil. Yield: 4.50 g (42%). B.p. 83–86 °C/1 Torr. ^{1}H NMR: δ = 7.25 (symm. m, 1 H), 7.09 (dd, *J* = 7.7, 1.0 Hz, 1 H), 7.03 (dd, *J* = 5.5, 1.8 Hz, 1 H), 7.01 (dd, *J* = 5.5, 1.8 Hz, 1 H), 6.95 (t, *J* = 7.3 Hz, 1 H), 5.84 (symm. m, 1 H), 5.70 (symm. m, 1 H), 0.33 (s, 9 H) ppm. ^{13}C NMR: δ = 155.0, 147.5, 143.2, 142.8, 132.0, 129.6, 124.0, 120.9, 82.6, 82.0, –0.4 (3 C) ppm. $C_{13}H_{16}OSi$ (216.35): calcd. C 72.17, H 7.45; found C 72.23, H 7.40.

1,4-Epoxy-1,4-dihydro-5-fluoro-8-(trimethylsilyl)naphthalene (3): A solution of (2-chloro-4-fluorophenyl)trimethylsilane (2.0 g, 10 mmol) in tetrahydrofuran (10 mL) was treated with a solution of butyllithium (10 mmol) in tetrahydrofuran (10 mL) at –75 °C. After 2 h, the solution was transferred through Teflon tubing into furan (15 mL, 14 g, 0.20 mol). The reaction mixture was diluted with hexanes (50 mL) and filtered through a pad of alumina. Chromatography using alumina as the support (50 mL) and hexanes as the eluent afforded a yellow oil. Yield: 0.87 g (73%). ^{1}H NMR: δ = 7.1 (m, 3 H), 6.67 (t, *J* = 8.4 Hz, 1 H), 5.97 (symm. m, 1 H), 5.84 (symm. m, 1 H), 0.31 (s, 9 H) ppm. ^{13}C NMR: δ = 158.9 (d, *J* = 4 Hz), 158.1 (s), 155.6 (s), 142.8 (d, *J* = 8 Hz), 132.5 (d, *J* = 5 Hz), 132.3 (s), 128.6 (d, *J* = 4 Hz), 112.9 (d, *J* = 21 Hz), 82.2 (d, *J* = 2 Hz), 79.0 (s), –0.3 (s, 3 C) ppm. $C_{13}H_{15}FOSi$ (234.34): calcd. C 66.63, H 6.45; found C 66.40, H 6.54.

1,4-Epoxy-1,4-dihydro-1-trimethylsilyl-5-fluoronaphthalene (4a): At dry ice temperature, butyllithium (10 mmol) in hexanes (7.0 mL) was added to a solution of 1,3-difluorobenzene (0.98 mL, 1.1 g, 10 mmol) and undecane (1.0 g) in tetrahydrofuran (20 mL). After 15 min at –75 °C, the white suspension was transferred through Teflon tubing into excess 2-(trimethylsilyl)furan (4.0 mL, 3.5 g, 25 mmol) kept at +50 °C. The mixture was washed with water (50 mL) and separated. According to gas chromatography (30 m, DB-1, 100 °C; 30 m, DB-WAX, 100 °C; undecane as the "internal standard" for quantification), the organic layer contained 1,4-epoxy-1,4-dihydro-1-trimethylsilyl-5-fluoronaphthalene (**4a**) and 1,4-epoxy-1,4-dihydro-1-trimethylsilyl-8-fluoronaphthalene (**4b**) in 17% and 8% yield, respectively. As these compounds decomposed upon attempted separation and purification by column or preparative gas chromatography, the structures are only tentatively assigned. ^{1}H NMR (of the mixture of isomers **4a** and **4b**): δ = 7.0 (m, 1 H), 6.7 (m, 2 H), 6.41 (dd, *J* = 3.0, 1.5 Hz, 0.33 H), 5.98 (dd, *J* = 2.5, 1.8 Hz, 0.67 H), 0.33 (s, 0.33×9 H), 0.32 (d, *J* = 1.3 Hz, 0.67×9 H) ppm.

1,4-Epoxy-1,4-dihydro-1-trimethylsilyl-5-chloronaphthalene (5a): In an analogous manner to that described for compounds **4a** and **4b**, starting from 1,3-dichlorobenzene (1.1 mL, 1.5 g, 10 mmol) instead of 1,3-difluorobenzene, 1,4-epoxy-1,4-dihydro-1-trimethylsilyl-5-chloronaphthalene (**5a**) and 1,4-epoxy-1,4-dihydro-1-trimethylsilyl-8-chloronaphthalene (**5b**) were formed in 15% and 8% yield, respectively. ^{1}H NMR (of the mixture of isomers **5a** and **5b**): δ = 7.0 (m, 1 H), 6.9 (m, 2 H), 5.87 (dd, *J* = 1.8, 1.0 Hz, 0.33 H), 5.71 (d, *J* = 1.8 Hz, 0.67 H), 0.35 (s, 0.67×9 H), 0.30 (s, 0.33×9 H) ppm.

1,4-Epoxy-1,4-dihydro-1-trimethylsilyl-5-fluoro-8-(trimethylsilyl)-naphthalene (6): A solution of 2-chloro-4-(fluorophenyl)trimethylsilane (5.1 g, 25 mmol) and butyllithium (25 mmol) in tetrahydrofuran (50 mL) was kept at –75 °C for 2 h, before excess 2-(trimethylsilyl)furan (8.0 mL, 7.0 g, 50 mmol) was added all at

once, and the vessel was immediately plunged into hot water (60 °C). After 15 min, the reaction mixture was diluted with pentanes (25 mL) and filtered through a pad of alumina. Crystallization from pentanes afforded colorless prisms. Yield: 4.75 g (62%). M.p. 60–62 °C. ^{1}H NMR: δ = 7.1 (m, 2 H), 6.99 (d, J = 5.5 Hz, 1 H), 6.65 (dd, J = 9.3, 8.3 Hz, 1 H), 5.86 (dd, J = 2.8, 1.8 Hz, 1 H), 0.31 (s, 9 H), 0.30 (d, J = 1.0 Hz, 9 H) ppm. ^{13}C NMR: δ = 160.8 (d, J = 5 Hz), 158.0 (s), 155.5 (s), 145.7 (s), 142.8 (s), 135.1 (d, J = 20 Hz), 132.0 (d, J = 6 Hz), 127.7 (d, J = 3 Hz), 112.8 (d, J = 22 Hz), 83.8 (s), 0.0 (s, 3 C), –3.5 (d, J = 3 Hz, 3 C) ppm. $C_{16}H_{23}FOSi_2$ (306.52): calcd. C 62.69, H 7.56; found C 62.32, H 7.50.

Acid-Catalyzed Isomerization

5-Fluoronaphthol (7b): A solution of 1,4-epoxy-1,4-dihydro-5-fluoronaphthalene (**1**, 1.6 g, 10 mmol) in ethanol (10 mL) and concentrated hydrochloric acid (2.0 mL) were heated to reflux for 20 h. A 87:13 mixture of 5-fluoronaphthol (**7b**) and 8-fluoronaphthol (**7a**) was isolated after the evaporation of the solvents. The crude material was crystallized from toluene and hexanes (1:1 v/v) to afford pure 5-fluoronaphthol (**7b**) as colorless needles. M.p. 132–133 °C (ref.[30]: m.p. 135–136 °C). ^{1}H NMR: δ = 7.96 (d, J = 8.3 Hz, 1 H), 7.69 (d, J = 8.3 Hz, 1 H), 7.4 (m, 2 H), 7.16 (ddd, J = 10, 7.3, 1.3 Hz, 1 H), 6.87 (d, J = 7.4 Hz, 1 H), 5.25 (s, 1 H) ppm.

Competition Kinetics: Pairs of substrates (approx. 1.0 mmol each) and naphthalene (0.10 g, as an inert reference compound for quantification) were dissolved in ethanol (5.0 mL). Samples were analyzed by gas chromatography (30 m, DB-1, 100 °C; 30 m, DB-WAX, 100 °C) to determine the substrate/standard peak areas before the reaction. Concentrated hydrochloric acid (1.0 mL) was added to the reaction mixture, which was heated to reflux for 2 h. The reaction mixture was analyzed again by gas chromatography to assess the amounts of unconsumed material. The standard logarithmic formula[31,32] was used to calculate the relative rate constants.

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