*flavus* do not contain significant amounts of this metabolite.

## Experimental Section

**General.** Strains of *A. flavus* (e.g., NRRL 13462) were obtained from the Agricultural Research Service (ARS) collection at the USDA Northern Regional Research Center in Peoria, IL. The sclerotia were prepared by solid substrate fermentation on autoclaved corn kernels using general procedures that have been previously described[2] and were stored at 4 °C until extracted. Proton and carbon NMR data were obtained in $CD_3OD$ or $CDCl_3$ on a Bruker WM-360 spectrometer, and chemical shifts were recorded by using the signal for the residual protiated solvent (3.30 ppm for $CD_3OD$) as a reference. Carbon multiplicities were established by a delayed decoupling experiment. All long-range C–H correlations were obtained through selective INEPT experiments. Proton signals studied with the selective INEPT technique were individually subjected to four separate experiments, optimizing for 4, 7, 10, or 15 Hz. Details of other experimental procedures and insect bioassays have been described elsewhere.[2-4]

**Isolation and Properties of Aflavazole (6).** Ground *A. flavus* sclerotia (NRRL 13462, 24.7 g) were exhaustively extracted with hexane, followed by chloroform, and the chloroform extract (513 mg) was subjected to flash chromatography on a reversed phase column (1 × 10 cm; $C_{18}$; 40–63 μm particles) using a step gradient from 50 to 70% $MeOH-H_2O$ in 5% increments. Compound 6 was contained in fractions eluting at 60% MeOH. Separation of the resulting fractions by reversed phase HPLC (5-μm $C_{18}$ column; 250 × 10 mm; 70:30 $MeOH-H_2O$ at 2.0 mL/min) afforded compound 6 (8.6 mg) as a light yellow crystalline solid with the following properties: mp 156–160 °C dec; $[\alpha]_D$ +2.8° (*c* 0.35, MeOH); HPLC retention time under the above conditions, 25.3 min; UV (MeOH) 341 (ε 1600), 327 (1300), 297 (7600), 263 (7500), 243 (17300), 219 (15300); $^1H$ NMR, $^{13}C$ NMR, selective INEPT, and NOESY data, Table I; EIMS (70 eV) 417 (($M^+$; rel intensity 100), 399 (37), 381 (13), 316 (40), 284 (8), 272 (13), 258 (32), 254 (16), 244 (36), 231 (42), 217 (62), 204 (29), 194 (47), 182 (20), 168 (21), 130 (60); HREIMS, obsd 417.2694, calcd for $C_{28}H_{35}NO$, 417.2669.

**Acknowledgment.** This work was conducted under Cooperative Research Agreement No. 58-5114-M-010 between the USDA Agricultural Research Service and the University of Iowa. The University of Iowa NMR and Mass Spectrometry Central Resource Facilities are gratefully acknowledged. We also thank the National Science Foundation (CHE-8905894) for financial support.

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# Silicon-Modified Metal–Ammonia Reduction of Fluorene

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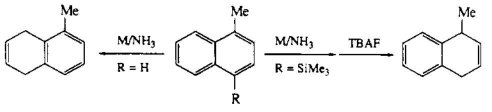
*Received April 10, 1990*

The metal–ammonia reduction of aromatic and polynuclear aromatic compounds, known as the Birch reduction when alcohols are employed as proton sources, represents an important method for the synthesis of hydroaromatic compounds.[1] The regiochemistry of this reduction is dictated primarily by the electron density distribution in the anionic intermediates. We have been exploring methods for regiochemical control in this reaction and have shown that a trimethylsilyl group can be used to alter regiochemistry, and, after its subsequent removal, afford a "misoriented" Birch reduction product.[2] For example, 1-methylnaphthalene (1, R = H) reduces exclusively in the unsubstituted ring providing 2, whereas reduction of 1-methyl-4-(trimethylsilyl)naphthalene followed by desilylation with tetrabutylammonium fluoride (TBAF) affords only 3. Presumably, the driving force for this change in regiochemistry comes from the stabilization of negative charge by an α-silicon (4).[3] This study shows that remote silyl substituents, which are not α to a site bearing a negative charge in the reaction intermediate, can also be used to alter the course of metal–ammonia reduction.



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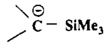

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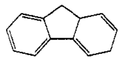
The metal–ammonia reduction of fluorene was reinvestigated[4] after an earlier report[5] suggested the 3,9a-dihydro isomer 5 to be the primary product, in conflict with HMO calculations that predicted 6. In fact, the reduction of fluorene produces a mixture of dihydro isomers 6 and 7 in 39% and 37% yields, respectively, together with 8% of an unidentified tetrahydro product and 11% recovered starting material. The dihydro products were not easily isolable, and analytical samples were obtained by trapping off the gas chromatograph. Reduction of 9,9-dimethylfluorene also produced a mixture of dihydro isomers, analogous to 6 and 7, in 38% and 24% yields, respectively.



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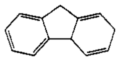

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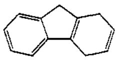

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In contrast, reduction of 9,9-bis(trimethylsilyl)fluorene produced the single dihydro isomer 8 together with a minor amount of recovered starting material. Subsequent treatment with TBAF in THF for 30 min provided 1,4-dihydrofluorene (7) as a crystalline solid. Similar reduction, but with excess metal and in the presence of *tert*-butyl alcohol, afforded the tetrahydro isomer 9, which also underwent smooth desilylation with TBAF to produce a crystalline solid (10).

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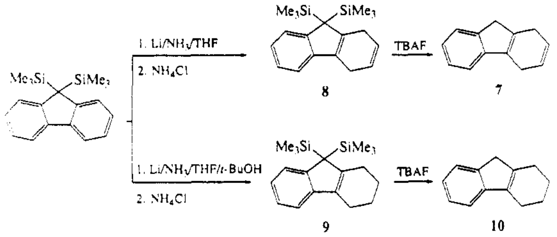
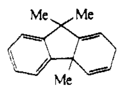


Insight into the role of the trimethylsilyl groups in this process may be gained by consideration of the reductive methylation of 9,9-dimethylfluorene, which leads to two



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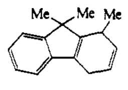

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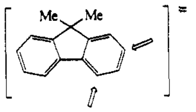

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trimethyl dihydro isomers, **11** and **12**.[4] These products arise by protonation of the intermediate dianion (eq 1) by

$$\mathrm{ArH} \xrightarrow{e^-} [\mathrm{ArH}]^{\bullet-} \xrightarrow{e^-} [\mathrm{ArH}]^{2-} \xrightarrow{\mathrm{NH_3}} \mathrm{ArH_2}^- \qquad (1)$$

ammonia, affording a monoanion that persists in solution and is subsequently alkylated in a second step. From the positions of methylation, it is clear that protonation of the dianion **13** takes place at the 2- and 4-positions, respectively, prior to alkylation with a preference for the 2-position (4:1).

The simplest explanation for the observed behavior is a steric effect leading to exclusive protonation at the 4-position when the larger trimethylsilyl substituents are present instead of methyl. In the presence of alcohol and excess metal, slow isomerization of the initial product to the 1,2-dihydro (or 3,4-dihydro) isomer is followed by rapid reduction to the tetrahydro product **19**.

## Experimental Section

**9-(Trimethylsilyl)fluorene** was prepared by a slightly modified literature procedure.[6] Fluorene (10.0 g, 60 mmol) was stirred with 1.1 equiv of *n*-butyllithium (1.6 M) in THF under nitrogen for 3 hours. An excess of chlorotrimethylsilane was added, and the mixture was stirred for an additional 18 h. Addition of water followed by typical ether extraction produced a residue that was recrystallized from ethanol to give 13.2 g (92%) of 9-(trimethylsilyl)fluorene, mp 96–97 °C (lit. mp 95–97 °C).[6]

**9,9-Bis(trimethylsilyl)fluorene** was prepared from 9-(trimethylsilyl)fluorene (13.2 g, 55 mmol) according to the above procedure to afford 15.3 g (89%), mp 109–110 °C (lit. mp 109–110 °C).[6]

**1,4-Dihydrofluorene (7).** 9,9-Bis(trimethylsilyl)fluorene (0.5 g, 1.6 mmol) was added to 100 mL of anhydrous ammonia/THF (3:1) in a previously flame-dried flask fitted with a Dewar condensor and an argon inlet. The mixture was cooled to ca. −78 °C with a dry ice/acetone bath, and lithium metal (0.055 g, 8.0 mmol) was added. After stirring for 1 h, saturated ammonium chloride solution was added, and the crude product was isolated by ether partition. Chromatography on neutral alumina (hexane) followed by recrystallization from ethanol gave 1,4-dihydro-9,9-bis(trimethylsilyl)fluorene (**8**) (0.32 g, 63%), mp 96–97 °C. To this material in dry THF was then added 1.0 M tetrabutylamonium fluoride solution (5.0 equiv), and the mixture was stirred for 30 min. Saturated ammonium chloride was added, and the product was isolated by ether partition. Chromatography on alumina (hexane) followed by recrystallization from ethanol gave 1,4-dihydrofluorene (0.14 g, 83% from **8**), mp 116–117 °C (lit.[4] mp 110–111 °C). The $^1$H NMR spectrum was in agreement with authentic literature data.[4] $^{13}$C NMR (CDCl$_3$): $\delta$ 24.4, 27.7, 40.7, 118.2, 123.8, 124.4, 124.6, 124.9, 126.5, 133.8, 138.4, 143.0, 145.8.

**1,2,3,4-Tetrahdydrofluorene (10).** 9,9-Bis(trimethylsilyl)fluorene (0.5 g, 1.6 mmol) was added to 100 mL of anhydrous ammonia/THF (3:1) in a previously flame-dried flask fitted with a Dewar condensor and an argon inlet. The mixture was cooled to ca. −78 °C with a dry ice/acetone bath, and 5.0 mL of *tert*-butyl alcohol was added followed by lithium metal (0.095 g, 13.8 mmol). After stirring for 30 min, saturated ammonium chloride solution was added, and the product was isolated as described above to give 1,2,3,4-tetrahydro-9,9-bis(trimethylsilyl)fluorene (**9**) (0.47 g, 94%), mp 82–84 °C. This material in dry THF was then reacted with 1.0 M tetrabutylammonium fluoride solution as described above for **8** to give 1,2,3,4-tetrahydrofluorene (0.23 g, 90% from **9**), mp 55–57 °C (lit.[7] mp 57 °C). $^1$H NMR (CDCl$_3$): $\delta$ 7.3 (m, 4 H), 3.3 (s, 2 H), 2.5 (m, 4 H), 1.9 (m, 4 H).

**Acknowledgment.** We would like to acknowledge support of this work from the Division of Chemical Sciences, Office of Basic Energy Sciences of the U.S. Department of Energy. We also thank the National Science Foundation for an equipment grant that allowed purchase of the QE-300 NMR instrument.

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