N, 4.74. Found: C, 44.58; H, 7.55; N, 4.73.

Acknowledgment. We gratefully acknowledge helpful discussions with J. C. Vederas, P. L. Ornstein, J. W. Fisher, D. A. Evans, and D. D. Schoepp. We are also indebted to T. K. Elzey for assistance of with the ^{13}C NMR experiments and the physical chemistry department for providing analytical and spectral data.

Supplementary Material Available: The portion of the ^1H NMR spectra of **2a** and **2b** treated with (*S*)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol (TAE) used to establish enantiomeric purity, and the ^1H NMR spectra of the methoxy region of **4a** as compared to a diastereomeric mixture of **4a** and **4b** (2 pages). Ordering information is given on any current masthead page.

Diazotative Deaminosilylation of β-Amino Silanes

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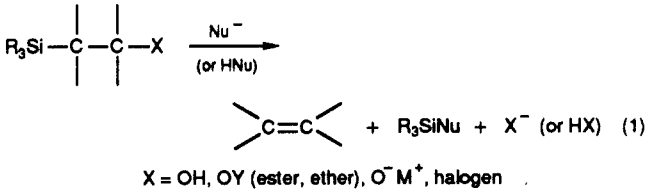
Received August 7, 1989

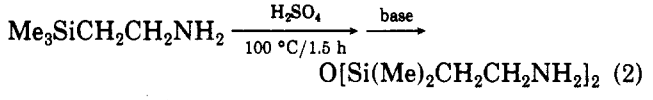
Introduction

The utilization of β-functional organosilanes as precursors to alkenes via elimination under thermolytic, acidic, or basic conditions is a useful synthetic technique.[1] Although a variety of functionalities have commonly been employed for this purpose (eq 1), the use of amino groups



(1)

is rare. Indeed, early work along these lines was discouraging, as Sommer and co-workers found that, in total contrast to the behavior of (β-hydroxyethyl)silanes, heating (β-aminoethyl)trimethylsilane with concentrated sulfuric acid caused silicon–methyl cleavage instead of β-elimination (eq 2).[2] We are aware of no other report concerning



(2)

the attempted elimination of a primary β-amino silane, although several authors have detailed the successful elimination of β-silyl quaternary,[3,4] and secondary[3] amines and of tertiary amine oxides.[4] The current approach to deaminosilylation of primary amines was predicated on the expectation that diazotization would produce a diazonium ion[5] which would suffer elimination directly or via a β-silyl carbocation[6] (Scheme I). Of the many methods available for diazotization,[7] the one initially reported by Friedman[8] employing isoamyl nitrite (iAmONO) was used, as this seemed to offer the best prospects for convenience, completeness of reaction, and maximization of the alkene/substitution-product ratio. Although this approach has proven successful, the outcome is not without complications when viewed as a synthetic method, and these results are detailed herein.

Scheme I

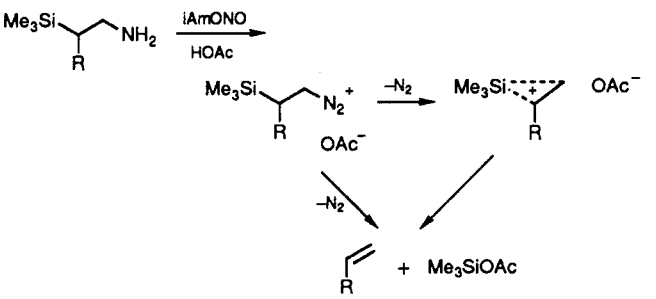
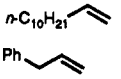
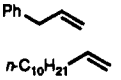
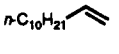
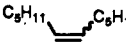
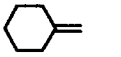


Table I. Deaminosilylation of β-Amino Silanes[a]

silane	product	% yield[b]
2		62[c]
5		68
6		52[c]
9		50
12		26

[a] In glacial HOAc with iAmONO (70 °C) followed by $BF_3{\cdot}Et_2O$; see Experimental Section for details. [b] VPC yields except where noted. [c] Isolated yield. [d] Stereochemistry undetermined.

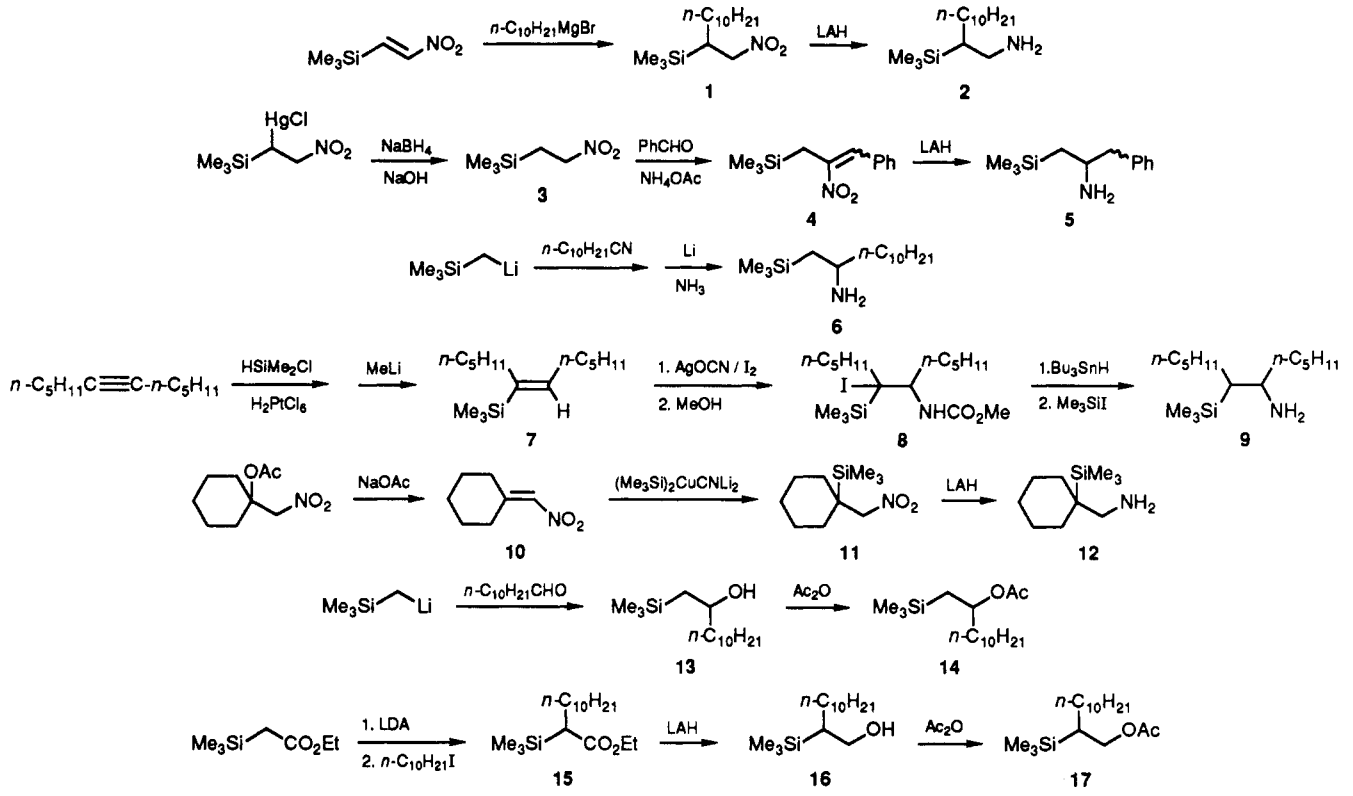
Preparation of Materials

Scheme II outlines the preparation of the β-amino silanes and reference compounds employed in this work. Few entries to the primary β-amino silane moiety are extant,[9] and we purposefully explored a diversity of approaches to this sytem in order to expand the available synthetic methodology. Yields of all products were sufficient to our needs, and optimization of conditions was thus not generally carried out. Two aspects of these syntheses are worthy of note: (a) the preparation of **3**, the parent member of its class ((β-nitroalkyl)silanes) and (b) stereospecific (presumably anti) addition of iodine isocyanate to alkenylsilane **7** with regiochemistry opposite that expected for all-carbon analogues.[10] This would here lead to only the *S,S/R,R* enantiomeric pair of adducts, a prediction consistent with the ^1H NMR homogeneity of the product obtained. It is of interest to note that the silylated dodecanamines employed in this study are not extracted into 3 N hydrochloric acid from the usual organic

(1) Colvin, E. *Silicon in Organic Synthesis*; Butterworths: London, 1981.
(2) Sommer, L. H.; Marans, N. S.; Goldberg, G. M.; Rockett, J.; Pioch, R. P. *J. Am. Chem. Soc.* **1951**, *73*, 882.
(3) Nametkin, N. S.; Perchenko, N.; Grushevenko, I. A.; Kamneva, G. L.; Derenkovskaya, T. I.; Kuzovkina, M. E. *Izv. Akad. Nauk SSSR* **1973**, 865.
(4) Bac, N. V.; Langlois, Y. *J. Am. Chem. Soc.* **1982**, *104*, 7666.
(5) Review: Patai, S., Ed. *The Chemistry of Diazonium and Diazo Groups*; Wiley: New York, 1978.
(6) The heightened stability of β-silyl carbocations is well documented. See ref 1.
(7) See: Baumgarten, R. J.; Curtis, V. A. In *The Chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives*; Patai, S., Ed.; Wiley: New York, 1982; Chapter 22.
(8) (a) Bayless, J. H.; Mendicino, F. D.; Friedman, L. *J. Am. Chem. Soc.* **1965**, *87*, 5790. (b) Friedman, L.; Bayless, J. H. *J. Am. Chem. Soc.* **1969**, *91*, 1790.
(9) For some other approaches, see: (a) Sommer, L. H.; Rockett, J. *J. Am. Chem. Soc.* **1951**, *73*, 5130. (b) Limburg, W. W.; Post, H. W. *Recl. Trav. Chim. Pays-Bas* **1962**, *81*, 430. (c) Duboudin, F.; LaPorte, O. *J. Organomet. Chem.* **1979**, *174*, C18.
(10) Hassner, A.; Lorber, M. E.; Heathcock, C. *J. Org. Chem.* **1967**, *32*, 540. Our results confirm identical regiochemistry postulated for the addition of INCO to $Et_3SiCH{=}CH_2$ by Vakhrushov, L. P.; Filipov, E. F.; Chernov, N. F.; Ageev, V. P. *J. Gen. Chem. USSR* **1975**, *45*, 1878. Parallel stereo- and regiochemistry is exhibited by the addition of INCS to alkenylsilanes: Thomas, E. J.; Whitham, G. H. *J. Chem. Soc., Chem. Commun.* **1979**, 212.

0022-3263/90/1955-4474$02.50/0

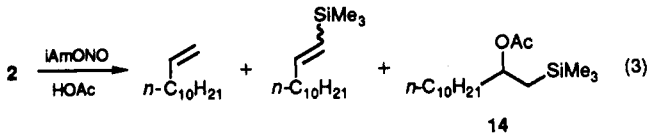
Scheme II



solvents, nor does the hydrochloride of **2** precipitate from pentane upon introduction of anhydrous HCl. A methanol–12 N hydrochloric acid mixture, however, was immiscible with pentane and retained the amine hydrochloride upon extraction.

Results and Discussion

Diazotization of **2** with iAmONO in acetic acid as solvent led to a complex mixture of primary products whose principal components (eq 3) were 1-dodecene, *cis*- and *trans*-1-(trimethylsilyl)-1-dodecene, and **14**. These were



(3)

obtained in a respective ratio of 5:1:3, with the yield of 1-dodecene being 30–40% based on starting **2**. The presence of lesser amounts of compounds **13**, **16**, and **17** was also indicated by VPC retention time comparisons using authentic samples. While the complexity of products (some structurally rearranged) was disconcerting, it was recognized that all byproducts were in principle convertable to 1-dodecene under conditions of higher acidity.[1] Thus, subsequent addition of boron trifluoride etherate to the reaction mixture in situ quickly resulted in the formation of 1-dodecene at the expense of all other products. Table I summarizes our results with **2** and other β-amino silanes. It is interesting to note that no detectable (NMR analysis) isomerization of initially formed alkenes occurs under the conditions employed; this is particularly striking in the instances of allylbenzene and methylenecyclohexane. Overall yields of olefins, however, are generally only fair to good, and results are especially poor for **12**. At least in part, this was found to result from the reactivity of initially formed olefin with the iAmONO–HOAc reagent, since 45% of the methylenecyclohexane employed in a control experiment was destroyed over the usual reaction time (before BF_3 addition). Attempts to reduce the usual quantities of iAmONO used for diazotization (1.5 equiv) were counterproductive, as amine conversion was then incomplete.

The formation of skeletally rearranged products upon diazotization of **2** is of interest and, together with other products, can be discussed within the context of Scheme III (*Si* = $SiMe_3$). The key determinant is seen to be the site of nucleophilic attack on an intermediate diazonium ion (A) or silicon-stabilized β-carbocation (B). Thus, attack at C-1 of A leads to unrearranged substitution products **16**, **17**. Nitrogen expulsion from A prior to nucleophilic attack may instead form B. Since silyl groups are known to equilibrate within such ions,[11] the majority of charge would be expected to reside at the secondary (C-2) position. By targeting this site, nucleophilic attack on B would then give rise to products **13**, **14**, while proton abstraction from C-1 would now lead directly to alkenylsilane product.[12] Either intermediate (A or B) would generate 1-dodecene upon nucleophilic attack at silicon.

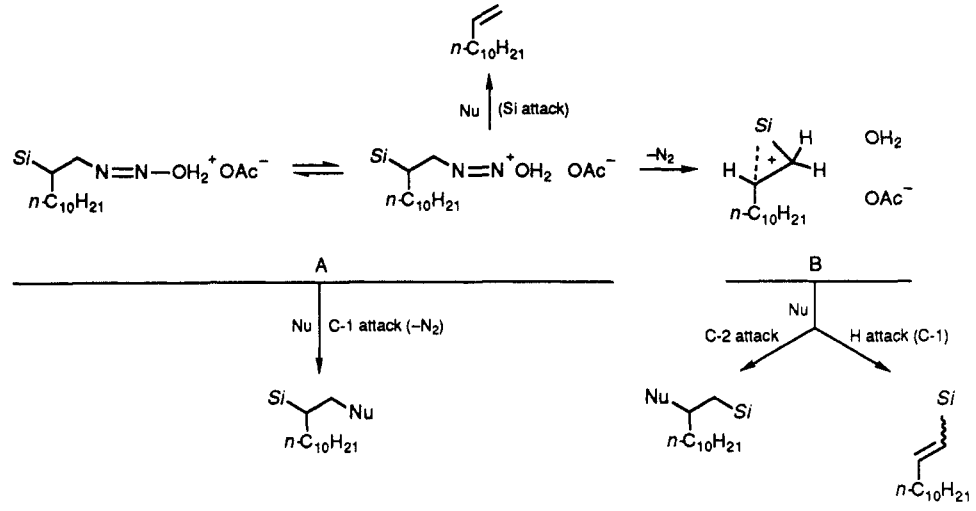
Experimental Section

NMR spectra were recorded using $CDCl_3$ solutions ($CHCl_3$ taken as δ 7.24) on an IBM WP200SY spectrometer. IR spectra were determined from neat films using a Sargent-Welch 3-200 spectrophotometer. VPC analyses employed a 2 ft × 0.25 in. 20% SE-30 column; samples for analytical and spectral data were generally isolated by preparative VPC. Elemental analyses were performed by P. Rider of these laboratories or by Spang Microanalytical Laboratory, Eagle Harbor, MI. Unless stated otherwise, all reactions were carried out under N_2 and anhydrous $MgSO_4$

(11) (a) Jarvie, A. W. P.; Holt, A.; Thompson, J. *J. Chem. Soc. B* **1969**, 852. (b) Cooke, M. A.; Eaborn, C.; Walton, D. R. M. *J. Organomet. Chem.* **1970**, *24*, 301.

(12) Alkenylsilane could also be envisioned as arising via proton abstraction from C-1 of A to give a (β-diazoalkyl)silane which could undergo a 1,2-silyl group migration concerted with loss of nitrogen. To our knowledge, however, such species are yet unknown.

Scheme III[a]



[a] *Si* = $SiMe_3$.

used to dry organic phases during workup. Ethereal solvents were distilled from sodium benzophenone ketyl immediately before use. All distillations employed short-path apparatus unless indicated otherwise. Column chromatography used "flash" silica gel; a "Chromatotron" (Harrison Research, Palo Alto, CA) was used for centrifical thick-layer chromatography.

General Method for Elimination of β-Amino Silanes by Diazotization. Samples of amine (50 mg, 0.20 mmol) were dissolved in 0.5 mL of glacial acetic acid in a snap-cap vial whose cap was punctured by a 26 gauge needle open to the atmosphere. After equilibrating 10 min in a 70 °C bath, an equivalent of iAmONO was added, followed 15 min later by an additional 0.5 equiv (0.25 equiv for **12**). After 20 min more, 2 drops of BF_3 etherate was added, and the reaction continued at 70 °C for 6–8 min (2 min for **12**). The mixture was poured into water–pentane, the organic phase was extracted with $NaHCO_3$ solution, and the organic phase was made up to 10 mL in a volumetric flask. VPC peak areas of olefinic products were then compared to those obtained from standard solutions of authentic olefins. Results are shown in Table I. Preparative runs were carried out for **2** and **6**. Amine (360 mg, 1.4 mmol) in 3.6 mL of HOAc was treated at 70 °C with 0.19 mL (1.4 mmol) of iAmONO, followed 15 min later by an additional 0.095 mL (0.70 mmol) of iAmONO. After 20 min more, 14 drops of $BF_3{\cdot}Et_2O$ was added, and the reaction mixture was held at 70 °C for 10 min more. Isolation was followed by chromatography on 5 in. × 1 in. silica gel using hexane elution. 1-Dodecene, homogeneous by both VPC and ^1H NMR analysis, was obtained from **2** (145 mg, 62% yield) and from **6** (121 mg, 52% yield). Analyses of reaction mixtures obtained without BF_3 addition were carried out by adding hexadecane as internal standard during workup followed by VPC analysis (180 °C) using predetermined relative response ratios. All reaction products were found to be stable to the VPC conditions used except **16**, which showed variable decomposition (up to $^1/_3$ of total peak area) on injection. Isomers of 1-(trimethylsilyl)-1-dodecene were identified from their NMR spectra.[13]

A run which included 1 equiv of KF in a mixture of **2**, iAmONO, and HOAc as solvent did not lead to conversion of the substitution and rearrangement byproducts to 1-dodecene, even after 2.5 h at 70 °C.

1-Nitro-2-(trimethylsilyl)dodecane (1). The Grignard reagent prepared from 11.2 g (50.7 mmol) of 1-bromododecane, 2.0 g (82 mmol) of magnesium powder (325 mesh), and 45 mL ether was transferred by syringe, the solids were washed with 20 mL of THF, and an additional 30 mL of THF added. After cooling to −78 °C, (2-nitroethenyl)trimethylsilane[14] (2.9 g, 20 mmol) in 20 mL of THF was added dropwise.[15] After 5 min, aqueous NH_4Cl was added at −78 °C, and the mixture was then poured into 1 N HCl and ether. After workup, chromatography using 3% ether–hexane afforded 4.05 g (71%) of **1**: ^1H NMR δ 0.05 (s, 9 H), 0.86 (m, 3 H), 1.2–1.7 (m, 19 H), 4.35 (*ABX* pattern, 2 H); IR 1550, 1375, 1250, 830 cm^{-1}. Anal. Calcd for $C_{15}H_{33}NO_2Si$: C, 62.67; H, 11.57; N, 4.87. Found: C, 62.67; H, 11.77; N, 4.55.

2-(Trimethylsilyl)-1-dodecanamine (2). A solution of 3.0 g (10 mmol) of **1** in 5 mL of ether was slowly added to 4.0 g (100 mmol) of $LiAlH_4$ in 65 mL of ether. After the exothermic reaction had subsided, the mixture was refluxed 1.5 h and then allowed to stand to 25 °C for 16 h. After cooling to 0 °C, 30% KOH, water, and ether were added, and the slurry was filtered through Celite. The organic phase was washed with saturated NaCl and dried over KOH pellets (2×). After evaporation, the residue was chromatographed on a 3.5 × 1.5 in. column packed in acetonitrile. Elution with 5% triethylamine–acetonitrile gave 1.74 g (63%) of **2**: ^1H NMR δ 0.00 (s, 9 H), 0.64 (m, 1 H), 0.86 (m, 3 H), 1.23 (br s, 18 H), 2.6–2.9 (*ABX* pattern, 2 H); IR 1250, 835 cm^{-1}. Anal. Calcd for $C_{15}H_{35}NSi$: C, 69.96; H, 13.70. Found: C, 70.18; H, 13.86.

(2-Nitroethyl)trimethylsilane (3). A solution of (1-(chloromercuri)-2-nitroethyl)trimethylsilane[14] (5.0 g, 13 mmol) in 10 mL of THF was added dropwise to 0.25 g (6.6 mmol) of $NaBH_4$ in 20 mL of 3 N NaOH and 10 mL of THF at 0 °C.[16] Addition over 5 min was accompanied by effervescence and Hg precipitation. After 10 min, the mixture was added to dilute HCl, extracted with pentane, washed with water, dried, and evaporated. Distillation afforded 1.12 g (59%) of **3**: bp 47–49 °C (3 mmHg); ^1H NMR δ 0.06 (s, 9 H), 1.35 (m, 2 H), 4.33 (m, 2 H); IR 1550, 1377, 1251, 840 cm^{-1}. Anal. Calcd for $C_5H_{13}NO_2Si$: C, 40.79; H, 8.90. Found: C, 40.64; H, 9.01.

2-Nitro-1-phenyl-3-(trimethylsilyl)propene (4). A mixture of benzaldehyde (0.86 g, 8.1 mmol), 1.0 g (6.8 mmol) of **3**, 0.28 g (3.6 mmol) of ammonium acetate, and 2.8 mL of degassed glacial acetic acid was heated at 120 °C for 2.25 h.[17] After addition to water–pentane, the organic phase was extracted with $NaHSO_3$ and $NaHCO_3$ solutions, dried, and evaporated. Kugelrohr distillation at 40 °C (1 mmHg) removed unreacted starting materials. The residue (0.97 g) was chromatographed with 3% ether–hexane to afford 0.85 g (53%) of **4**: ^1H NMR δ 0.05 (s, 9 H), 2.43 (s, 2 H), 7.40 (s, 5 H), 7.90 (s, 1 H); IR 1640, 1518, 1320, 1251, 850 cm^{-1}.

(13) Dumont, W.; Van Ende, D.; Krief, A. *Tetrahedron Lett.* **1979**, 485. *cis*-1-(Trimethylsilyl)-1-dodecene: ^1H NMR δ 0.08 (s, 9 H), 0.84 (m, 3 H), 1.26 (br s, 16 H), 2.05 (m, 2 H), 5.43 (dt, *J* = 14, 1.1 Hz, 1 H), 6.28 (dt, *J* = 14, 7 Hz, 1 H). *trans*-1-(Trimethylsilyl)-1-dodecene: ^1H NMR δ 0.01 (s, 9 H), 0.84 (m, 3 H), 1.26 (br s, 16 H), 2.05 (m, 2 H), 5.58 (dt, *J* = 19, 1.5 Hz, 1 H), 6.00 (dt, *J* = 19, 6 Hz, 1 H).

(14) Cunico, R. F. *Synth. Commun.* **1988**, *18*, 917.

(15) See: Hayama, T.; Tomoda, S.; Takeuchi, Y.; Nomura, Y. *Tetrahedron Lett.* **1983**, *24*, 2795.

(16) Method of Brown, H. C.; Geoghegan, P., Jr. *J. Am. Chem. Soc.* **1967**, *89*, 1522.

(17) See: Gairand, C. B.; Lappin, G. R. *J. Org. Chem.* **1953**, *18*, 1.

Anal. Calcd for $C_{12}H_{17}NO_2Si$: C, 61.24; H, 7.28. Found: C, 61.39; H, 7.30.

1-Phenyl-3-(trimethylsilyl)-2-propanamine (5). A solution of 0.70 g (18 mmol) of $LiAlH_4$ in 30 mL of THF was treated dropwise with 0.85 g (3.6 mmol) of **4**. After a 2.5-h reflux, 0.7 mL of water, 0.7 mL of 15% NaOH, and 2.1 mL of water were added sequentially, and the solids were filtered off and washed with ether. The filtrate was washed with water, dried, and evaporated. The residue was chromatographed on a 4 × 0.75 in. column packed in acetonitrile using 5% triethylamine–acetonitrile as eluent to give 0.20 g (27%) of **5**: ^1H NMR δ 0.05 (s, 9 H), 1.77 (*ABX* pattern, 2 H), 2.07 (br s, 2 H), 2.41 and 2.80 (*ABX* pattern, 2 H), 3.13 (br s, 1 H), 7.2 (m, 5 H); IR 1250, 830 cm^{-1}. Anal. Calcd for $C_{12}H_{21}NSi$: C, 69.49; H, 10.21; N, 6.76. Found: C, 68.89; H, 9.92; N, 6.50.

1-(Trimethylsilyl)-2-dodecanamine (6).[18] A solution of (trimethylsilyl)methyllithium was prepared from 1.7 g (240 mmol) of ether-washed Li sand (1% Na) and 3.4 g (28 mmol) of (chloromethyl)trimethylsilane in 60 mL of ether using a few drops of 1,2-dibromoethane as initiator. Undecanenitrile (3.3 g, 20 mmol) was then added dropwise, and stirring was continued for 1 h. Ammonia (100 mL) was then condensed into the reaction mixture over a 2-h period with intermittent dry ice bath cooling, followed 30 min later by addition of 4 g of sodium benzoate. After the mixture was stirred overnight, hydrolysis with NH_4Cl solution was followed by filtration through Celite, and the organic phase was extracted with water and dried (KOH pellets). Distillation gave 2.9 g (56%) of **6**, bp 85–105 °C (0.3 mmHg), which VPC (160 °C) indicated contained 5–10% of a lower eluting impurity: ^1H NMR δ 0.01 (s, 9 H), 0.70 (*ABX* pattern, 2 H), 0.86 (m, 3 H), 1.10 (s, 2 H), 1.24 (s, 18 H), 2.85 (m, 1 H); IR 1245, 840 cm^{-1}. Anal. Calcd for $C_{15}H_{35}NSi$: C, 69.96; H, 13.70; N, 5.44. Found: C, 70.01; H, 13.56; N, 5.41.

(*E*)-6-(Trimethylsilyl)-6-dodecene (7). A mixture of 16.6 g (100 mmol) of 6-dodecyne, 10 g (100 mmol) of chlorodimethylsilane, and several drops of a chloroplatinic acid–isopropyl alcohol solution was held at reflux (Hg trap) overnight. The reaction mixture was then added in ether to 76 mL (130 mmol) of 1.6 N methyllithium in ether and hydrolyzed 2 h later with NH_4Cl solution. Workup and distillation gave 16 g (62%) of **7**: bp 76 °C (0.3 mmHg); ^1H NMR δ 0.02 (s, 9 H), 0.87 (m, 6 H), 1.3 (m, 12 H), 2.05 (m, 4 H), 5.68 (t, J = 7 Hz, 1 H); IR 1610, 1247, 835 cm^{-1}. Anal. Calcd for $C_{15}H_{32}Si$: C, 74.91; H, 13.41. Found: C, 75.14; H, 13.37.

6-Iodo-7-(methoxycarboxamido)-6-(trimethylsilyl)dodecane (8). A solution of silver cyanate (15.8 g, 105 mmol) in 100 mL of THF was cooled to −20 °C and treated at once with 8.9 g (35 mmol) of iodine. After 3 h at −20 °C, the mixture was filtered through a sintered glass tube into a jacketed addition funnel cooled to −78 °C. The INCO solution was then added to a solution of 7.2 g (30 mmol) of **7** in 50 mL of THF held at −78 °C. The reaction was allowed to warm to 25 °C and stirred overnight. Solvent was removed by rotary evaporator (45 °C), and pentane was added to the residue. Solids were filtered off, the solvent was removed, and the residue was refluxed in a mixture of 50 mL of ether and 50 mL of methanol for 28 h. The solvent was removed to give 11.0 g of material which was shown by IR and NMR analysis to contain small amounts of starting olefin and intermediate isocyanate (the latter indicated by absorptions at δ 3.25 (dd, OCNC*H*) and 0.26 (s, $SiMe_3$) in the ^1H NMR and at 2260 cm^{-1} in the IR spectrum). Chromatography of a 0.35-g sample of this crude material (chromatotron, 2% ether–hexane) gave 0.30 g of pure **8**, indicating an overall yield of 9.4 g (71%); ^1H NMR δ 0.25 (s, 9 H), 0.85 (m, 6 H), 1.1–1.7 (m, 14 H), 2.07–2.45 (m, 2 H), 3.04 (m, 1 H), 3.65 (s, 3 H), 4.75 (d, J = 10 Hz, 1 H, NH); IR 3410, 3330, 1725, 1250, 1218, 837 cm^{-1}. Anal. Calcd for $C_{17}H_{36}INO_2Si$: C, 46.25; H, 8.22; N, 3.17. Found: C, 46.04; H, 8.44; N, 3.12.

7-(Trimethylsilyl)-6-dodecanamine (9). A solution of 1.0 g (2.7 mmol) of crude **8**, 0.87 g (3 mmol) of tri-*n*-butyltin hydride, and 0.01 g of azobisisobutyronitrile in 10 mL of benzene was refluxed 18 h. NMR analysis showed complete disappearance of **8**, as adjudged by the replacement of $SiMe_3$ absorption at δ 0.25 by one at δ 0.02. The residue from solvent removal was added to a solution of iodotrimethylsilane prepared by mixing 0.46 g (1.8 mmol) of iodine and 0.26 g (1.8 mmol) of hexamethyldisilane in 10 mL of chloroform.[19] After a 2.5-h reflux period, 0.32 mL of chlorotrimethylsilane in 0.5 mL of methanol was added, and volatiles were removed 20 min later. The residue was added to a solution of 10 mL of methanol and 0.5 mL of concentrated HCl, and extraction with pentane was carried out. Aqueous $NaHCO_3$ was added to the methanol layer, the mixture was extracted with pentane, and the pentane phase was dried. Kugelrohr distillation gave 0.35 g (50% overall) of **9**: bp 70–75 °C (0.3 mmHg); ^1H NMR δ 0.02 (s, 9 H), 0.7–1.7 (m, 25 H), 3.92 (br s, 1 H, CHN); IR 3360, 1250, 835 cm^{-1}. Anal. Calcd for $C_{15}H_{35}NSi$: C, 69.95; H, 13.70; N, 5.44. Found: C, 69.79; H, 13.76; N, 5.24.

(Nitromethylidene)cyclohexane (10).[20] 1-Acetoxy-1-(nitromethyl)cyclohexane[21] was prepared from 1-(nitromethyl)-cyclohexanol.[22] A mixture of 13.5 g (62 mmol) of acetoxy compound, 5.9 g (72 mmol) of anhydrous sodium acetate, and 70 mL of THF was stirred and refluxed for 6.5 h. The cooled suspension was filtered through sintered glass, and the filtrate was evaporated and distilled to give 6.9 g (70%) of light yellow-green liquid, bp 50–52 °C (0.2 mmHg). NMR analysis indicated that the distillate contained less than 10% of the unconjugated nitro isomer, as determined from its vinylic (δ 5.92) and nitromethyl (δ 4.79) absorptions. The desired **10** showed ^1H NMR δ 1.65 (m, 6 H), 2.19 (t, J = 6 Hz, 2 H), 2.83 (t, J = 6 Hz, 2 H), 6.89 (s, 1 H).

1-(Nitromethyl)-1-(trimethylsilyl)cyclohexane (11). Methyllithium (1.6 N, 10.7 mL, 17 mmol) in ether was slowly added to a mixture of 15 mL of HMPT and 3.1 g (4.4 mL, 21 mmol) of hexamethyldisilane at −5 °C.[23] The initially deep red solution lightened to a greenish-orange during addition. After 10 min at 0 °C, 20 mL of THF was added at −15 °C followed by 0.76 g (8.5 mmol) of CuCN. After stirring at −5 °C for 25 min, the turbid solution was cooled to −78 °C, and 0.83 g (5 mmol) of **10** in 3 mL of THF was added dropwise. The now yellow-green solution was stirred 1 h at −78 °C, allowed to warm to −30 °C, and hydrolyzed by dropwise addition of acetic acid–water. Workup involved cross-extraction with water–pentane followed by Kugelrohr distillation to give 0.44 g (41%) of **11**: bp 75 °C (0.15 mmHg); ^1H NMR δ 0.02 (s, 9 H), 1.15–1.75 (m, 10 H), 4.54 (s, 2 H); ^{13}C NMR −3.7, 20.4, 26.0, 26.8, 28.8, 79.3; IR 1548, 1250, 835 cm^{-1}. Anal. Calcd for $C_{10}H_{21}NO_2Si$: C, 55.76; H, 9.83; N, 6.51. Found: C, 55.92; H, 9.75; N, 6.40.

1-(Aminomethyl)-1-(trimethylsilyl)cyclohexane (12). A solution of 2.9 g (13 mmol) of **11** in 5 mL of ether was slowly added to a solution of 2.3 g (61 mmol) of $LiAlH_4$ in 35 mL of ether at 0 °C. After 3 h at 25 °C, 2.3 mL of water, 2.3 mL of 15% NaOH, and 7 mL of water were added sequentially. The resulting suspension was filtered, solids were washed with ether, and the organic phases were dried and evaporated. Distillation gave 0.80 g (33%) of **12**: bp 85–95 °C (5 mmHg); ^1H NMR δ −0.03 (s, 9 H), 1.1–1.7 (m, 12 H), 2.81 (s, 2 H); ^{13}C NMR δ −3.0, 20.6, 26.2, 26.3, 28.3, 45.0; IR 3300, 1250, 835 cm^{-1}. Anal. Calcd for $C_{10}H_{23}NSi$: C, 64.79; H, 12.50; N, 7.56. Found: C, 64.84; H, 12.71; N, 7.42.

1-(Trimethylsilyl)-2-dodecanol (13). To the Grignard reagent prepared from 1.5 g (12 mmol) of (chloromethyl)trimethylsilane and 0.39 g (16 mmol) of Mg turnings in 10 mL of ether was added a solution of 1.3 g (7.6 mmol) of undecanal in 5 mL of ether. After workup, evaporation gave 1.65 g (84%) of **13** which was greater than 95% pure by VPC (170 °C): ^1H NMR δ 0.02 (s, 9 H), 0.8–0.9 (m, 5 H, CH_3 + CH_2Si), 1.24 (s, 16 H), 1.40 (br s, 3 H, CH_2OH), 3.77 (m, 1 H); IR 3350, 1250, 840 cm^{-1}. Anal. Calcd for $C_{15}H_{34}OSi$: C, 69.70; H, 13.26. Found: C, 69.64; H, 13.31.

2-Acetoxy-1-(trimethylsilyl)dodecane (14). A mixture of 0.65 g (2.5 mmol) of **13**, 0.20 g (2.5 mmol) of pyridine, 0.004 g of *p*-(*N*,*N*-dimethylamino)pyridine, and 0.30 g (3 mmol) of acetic anhydride in 2 mL of ether was stored at 25 °C for 25 h. Addition

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of pentane was followed by sequential extraction with water, 1 N HCl, and $NaHCO_3$ solution, and the organic phase was dried and evaporated to give 0.56 g (74%) of **14**, which VPC (180 °C) showed to be greater than 95% one component: ^1H NMR δ 0.00 (s, 9 H), 0.86 (m, 3 H), 0.91 (*ABX* pattern, 2 H), 1.23 (s, 16 H), 1.5 (m, 2 H, CH_2CO), 1.99 (s, 3 H), 4.96 (AB*X* pattern, 1 H); IR 1735, 1250, 840 cm^{-1}. Anal. Calcd for $C_{17}H_{36}O_2Si$: C, 67.94; H, 12.08. Found: C, 68.00; H, 12.11.

Ethyl 2-(Trimethylsilyl)dodecanoate (15). A solution of 1.1 g (1.5 mL, 11 mmol) of diisopropylamine in 10 mL of THF was treated at -78 °C with 3.5 mL (11 mmol) of 3.15 N *n*-BuLi in hexane. After 10 min, 1.6 g (10 mmol) of ethyl (trimethylsilyl)acetate in 2 mL of THF was added dropwise. HMPT (0.9 g, 5 mmol) was added 30 min later, followed by 2.7 g (10 mmol) of 1-iododecane. The reaction mixture was stirred at -78 °C for an additional 4 h and at 25 °C overnight, whereupon it was poured into 1 N HCl-pentane, and the organic phase was washed with K_2CO_3 solution. After drying and evaporation, Kugelrohr distillation gave 2.4 g of material, bp 90-100 °C (0.4 mmHg) which VPC (180 °C) showed contained 70% of **15**, 20% starting ester, and 10% 1-iododecane. Pure **15** was isolated by preparative VPC: ^1H NMR δ 0.03 (s, 9 H), 0.85 (m, 3 H), 1.22 (br s over t, 21 H), 1.65-1.95 (m, 2 H), 4.08 (q, J = 7 Hz, 3 H); IR 1719, 1251, 845 cm^{-1}. Anal. Calcd for $C_{17}H_{36}O_2Si$: C, 67.94; H, 12.08. Found: C, 68.13; H, 11.99.

2-(Trimethylsilyl)-1-dodecanol (16). A solution of 1.5 g (3.5 mmol) of **15**, 70% pure by VPC, in 2 mL of ether was slowly added to 0.87 g (15 mmol) of $LiAlH_4$ in 25 mL of ether. After an 18-h reflux, 3.0 mL of 1.5 N NaOH was added at 0 °C, and the resulting slurry filtered through Celite. After workup, Kugelrohr disillation gave 0.91 g of material, bp 80-90 °C (0.4 mmHg) which VPC (180 °C) showed contained **16** contaminated with 15% of a lower eluting impurity: ^1H NMR δ 0.00 (s, 9 H), 0.86 (m, 4 H, CH_3 + CHSi), 1.24 (br s, 18 H), 1.35 (s, 1 H, OH), 3.60-3.85 (*ABX* pattern, 2 H); IR 3350, 1250, 840 cm^{-1}. Anal. Calcd for $C_{15}H_{34}OSi$: C, 69.70; H, 13.26. Found: C, 69.76; H, 13.37.

1-Acetoxy-2-(trimethylsilyl)dodecane (17). A mixture of 0.39 g (1.5 mmol) of **16**, 0.20 g (2.5 mmol) of pyridine, 0.004 g of *p*-(*N*,*N*-dimethylamino)pyridine, and 0.25 g (2.5 mmol) of acetic anhydride in 2 mL of ether was allowed to stand at 25 °C for 18 h. After workup, evaporation gave 0.23 g of water-white **17**, which VPC (180 °C) indicated contained 15% of a lower eluting impurity: ^1H NMR δ 0.00 (s, 9 H), 0.86 (m, 3 H), 0.9 (m, 1 H), 1.24 (br s, 18 H), 2.01 (s, 3 H), 4.0-4.3 (*ABX* pattern, 2 H); IR 1740, 1237, 1250, 838 cm^{-1}. Anal. Calcd for $C_{17}H_{36}O_2Si$: C, 67.94; H, 12.08. Found: C, 67.92; H, 12.19.

An Improved Synthesis of *anti*-Benzo[*c*]phenanthrene-3,4-diol 1,2-Epoxide via 4-Methoxybenzo[*c*]phenanthrene

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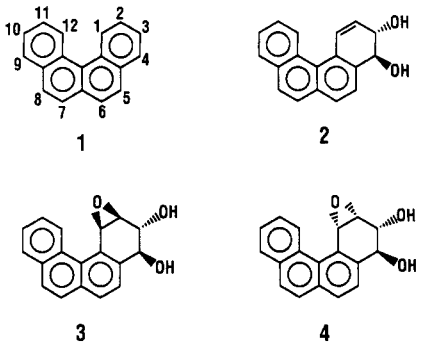
Received January 26, 1990

Benzo[*c*]phenanthrene (**1**) is a relatively weak carcinogen[1] widely distributed in the environment.[2] Metabolism of **1** on the benzo ring occurs almost exclusively at the 3,4-position to give *trans*-benzo[*c*]phenanthrene-3,4-diol[3] (**2**), the precursor to the bay region benzo[*c*]-phenanthrene-3,4-diol 1,2-epoxides (BcPhDE). BcPhDE exists as a pair of diastereoisomers: *syn*-BcPhDE (**3**) and *anti*-BcPhDE (**4**). Each diastereoisomer consists of a pair of enantiomers. Both diastereoisomers are highly mutagenic to bacteria and Chinese hamster V79 cells and have shown exceptionally high tumor-initiating activity on mouse skin.[4,5a] However in the newborn mouse tumor



1 **2** **3** **4**

model, **4** is more potent than **3**.[5b] The diol epoxides **3** and **4** covalently bind to calf thymus DNA at exocyclic nitrogens of guanine and adenine almost in equal proportions.[6] Similarly the enantiomeric diol epoxides (**3**, **4**) also bind to DNA in embryo cell cultures of mouse, hamster, and rat.[7] However, the major adducts obtained via metabolic activation of **1** in cell cultures were only due to **4**. During our preparation of 1-(N^2-deoxyguanosyl/N^6-deoxyadenosyl-3′-phosphate)-2,3,4-trihydroxy-1,2,3,4-tetrahydrobenzo[*c*]phenanthrene, as markers for the ^{32}P postlabeling assay,[8] we required substantial amounts of the *anti*-BcPhDE (**4**). The methods[9] available for the preparation of **4** either required multiple steps or resulted in low yields and were not suitable for our purpose. In the present study, we report the synthesis of 4-methoxybenzo[*c*]phenanthrene (**5**), the key intermediate for the preparation of **4**.

Initially, we prepared 4-hydroxybenzo[*c*]phenanthrene (**6**) using Harvey's procedure.[10] The critical step in the synthesis was the generation of the anion **7**. The formation of **7** occurs within a small range of temperatures (-42 °C to -38 °C); which is close to the boiling point of the reaction medium, liquid ammonia (-33 °C), hence care must be taken to control the reaction temperature. The cyclization of **8** to **9** was temperature dependent. At 130 °C, **8** afforded a 1:1 mixture of **9** and **10**, in contrast to exclusively **9** at 115 °C. Oxidation of **6** was carried out with Fremy's salt to afford benzo[*c*]phenanthrene-3,4-dione (**11**).[11] Subsequent steps involved $NaBH_4$ reduction of

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