Notes

Masked 2-Arylacroleins: Versatile Three-Carbon Units for Organic Synthesis

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Introduction

2-Arylpropenals $H_2C{=}C(Ar)CHO$ are of considerable synthetic value for the preparation of tryptophans,[1] vinylic peroxyketals,[2] 2,2′-bipyridines,[3] and functionalized cycloheptenes.[4] Accordingly, a variety of methods have been developed for the preparation of 2-arylpropenals based on transformations of various styrenes as follows: (i) reaction of Grignards derived from α-bromo styrenes with ethyl orthoformate;[5] (ii) oxidation with selenium dioxide,[6] or bromination followed by hydrolysis,[7] of α-methylstyrenes; and (iii) three-step cyclopropanation, ring opening, and hydrolysis of styrenes.[8] Further routes use 2-arylethanols[9] and α-chloroacetals as starting materials.[10]

However, the application of 2-arylpropenals in synthesis is accompanied by several problems. The compounds are highly toxic.[11] The double bond in $H_2C{=}C(Ar)CHO$, activated by both the aryl and the carbonyl group, is highly reactive; consequently, these molecules are claimed to be unstable above −6 °C,[8] although 2-(4-methoxycarbonylphenyl)propenal was isolated apparently at room temperature[12] and although 2-phenylpropenal can be distilled at 79−82 °C at reduced pressure.[6] At room temperature, atropaldehyde (2-phenylpropenal) undergoes a spontaneous hetero Diels−Alder dimerization to give the corresponding dihydropyran.[6] Furthermore, while conjugate additions occur readily, to our best knowledge, the only 1,2-additions of carbon nucleophiles to 2-arylpropenals are allylmagnesium chloride, propynyl bromide in the presence of aluminum amalgam to 2-phenylpropenal,[13] and 1-bromo-2-phenylpropene in the presence of zinc and ammonium chloride to 2-(4-methoxycarbonylphenyl)propenal.[14] Hence, the development of a route to masked 2-arylpropenals is considerably attractive. We now describe such substrates in which the double bond is masked, allowing for clean 1,2-addition to the aldehyde moiety. Deprotection of the double bond regenerates the unsaturation and renders a formal 1,2-addition to 2-arylpropenals.

Results and Discussion

Our previous work[15] described the easy preparation of compounds **1a**−**f** from 1-arylmethylbenzotriazoles (Scheme 1) and demonstrated that, when treated with *n*-BuLi, **1a**−**f** provide useful masked α-arylalkenyllithium reagents. New heteroaryl **1h** and methylthio **1g** analogues have now been prepared, and we report that deprotonation of **1a**−**h** and subsequent formylation with *N*,*N*-dimethylformamide affords compounds **2a**−**h** in good yields (Scheme 1). Compounds **2a**−**h** show low solubility in hexanes, making them readily available in the pure state by recrystallization from this solvent. The main reason for the interest in structures **2a**−**h** is their resemblance to atropaldehydes in which the double bond is protected in the form of a *β*-benzotriazolyl silane. *β*-Benzotriazolylalkylsilanes substrates were previously shown to generate the corresponding styrene by vicinal elimination of silicon.[15]

To test the reactivity of the aldehyde group in substrates **2** and to open a new entry to 1-alkyl-2-arylallyl alcohols, a series of nucleophilic additions followed by vicinal elimination of silicon was undertaken. Addition of *n*-BuLi at −78 °C to **2d** afforded the *O*-trimethylsilylallyl alcohol **4a** in 98% yield, and similar condensation with secondary alkyllithium gave the expected alcohol **4b** in 51% yield (Scheme 1). Such 1,4 shifts of silicon from carbon to oxygen are well precedented.[16,17] The addition of Grignard reagents to **2b** and **2e** went smoothly to give the corresponding compounds **6a**−**c** in 87% average yield. In this case, no elimination with [1,4]-C→O silicon rearrangement occurred, even upon reflux in THF for 3 h. Therefore, eliminations to give **7a**,**b** were accomplished at room temperature in THF in the presence of TBAF. To test whether the presence of the 2-chloro substituent in the aryl ring hampered the rearrangement, compound **2b** was reacted with trimethylsilylmethylmag-

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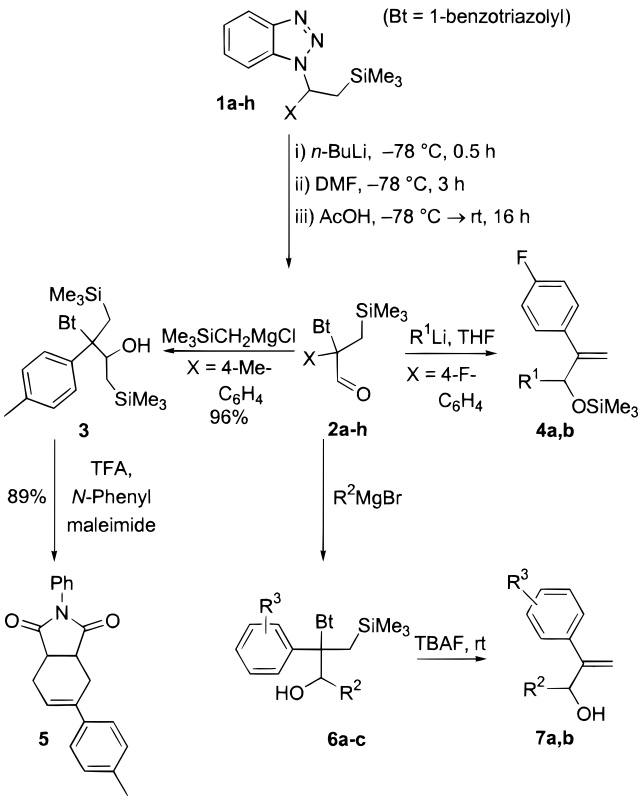
Scheme 1



1,2	a	b	c	d	e	f	g	h
X	2-Me-C_6H_4	4-Me-C_6H_4	2-F-C_6H_4	4-F-C_6H_4	2-Cl-C_6H_4	4-MeO-C_6H_4	SMe	5-Me-thien-2-yl
Yield of **2** (%)	71	70	68	73	65	82	84	86

4	a	b
R^1	*n*-Bu	*s*-Bu
Yield (%)	98	51

6	a	b	c
R^2	Me	Ph	Ph
R^3	4-Me	4-Me	2-Cl
Yield (%)	81	94	86

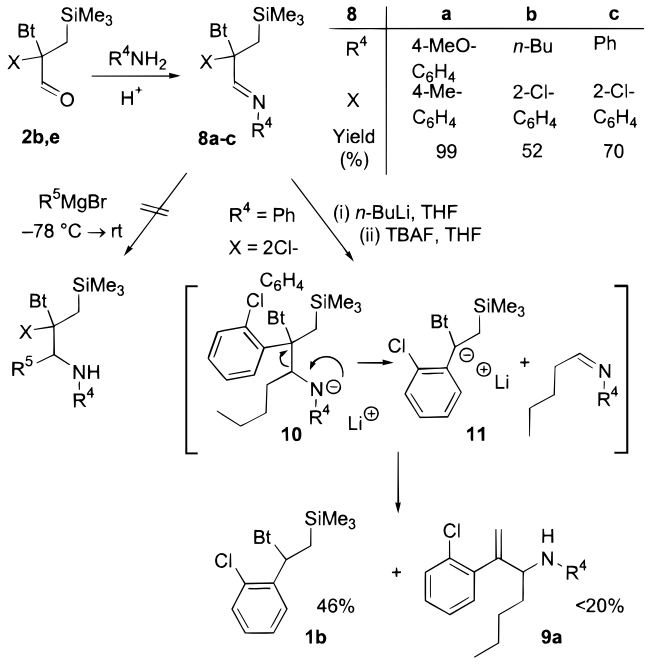
7	a	b
R^2	Me	Ph
R^3	4-Me	4-Me
Yield (%)	94	85

nesium chloride. The addition product **3** was isolated quantitatively and again did not rearrange upon reflux for 3 h in THF. Elimination of the benzotriazole, hydroxyl, and both trimethylsilyl groups in **3** by trifluoroacetic acid in the presence of *N*-phenylmaleimide rapidly afforded the cycloadduct **5** in 89% yield (Scheme 1).

The reactivities of aldehydes **2a**−**h** are less than those of normal aliphatic aldehydes, presumably for steric reasons, and are more like those of aromatic aldehydes. This is in accord with the upfield peak for the formyl groups in the ^{13}C NMR of **2a**−**h** (190−191 ppm), which are characteristic of aromatic rather than aliphatic aldehydes. Perhaps the bond between the C_α and the carbonyl is longer than for regular aliphatic aldehydes due to steric crowding. This is further supported by the reaction of **2b** with 4-anisidine, which proceeded under mild conditions, and in quantitative yield, to give imine **8a**. Similar condensations of *n*-butylamine and aniline with compound **2e** gave the corresponding imines **8b**,**c** in good yields (Scheme 2).

Surprisingly, imines **8a**,**c** did not show normal reactivity for aromatic imines. Thus, attempted condensations using alkyllithium or Grignard reagents, even upon heating, gave only unchanged starting materials. Con-

Scheme 2



8	a	b	c
R^4	4-MeO-C_6H_4	*n*-Bu	Ph
X	4-Me-C_6H_4	2-Cl-C_6H_4	2-Cl-C_6H_4
Yield (%)	99	52	70

densation of *n*-BuLi with imine **8c** and subsequent elimination of the silicon group in the presence of tetrabutylammonium fluoride (TBAF) (1 M in THF) gave, as the only isolated compound, **1b** in 46% yield. The expected amine **9a** composed ca. 15% of the crude reaction mixture as estimated by ^1H NMR (Scheme 2). Possibly, hindered intermediate **10** cleaves to anion **11**, which leads to **1b**.

1-(Trimethylsilyl)benzotriazole is an alternative to Lewis acids to increase the electrophilicity of azomethine carbon of imines toward the addition of Grignard reagents,[18,19] and initial reversible addition of 1-(trimethylsilyl)benzotriazole to the imine is followed by nucleophilic displacement of the benzotriazolyl group by a Grignard reagent to afford the corresponding secondary amine. This device succeeded in the present case: Grignard reagents added to equimolar solutions of imines **8** and 1-(trimethylsilyl)benzotriazole in dry toluene evidently formed the expected condensation products **12**, which rearranged into the desired allylamines **9b**−**d** after the mixture was heated overnight at 80 °C (Scheme 3). This one-pot two-step procedure constitutes a general and versatile access to 1,2-disubstituted allylic amines since ortho or para substitution of the aryl ring did not affect the course of the rearrangement and amines **9** are obtained with a characteristic 50% overall yield.

Conclusions

Novel masked 2-arylacrolein three-carbon units **2** have been developed. They allow, for the first time, the preparation of the products **7** of formal 1,2-additions onto the aldehyde moieties of 2-arylacroleins to provide access to the corresponding 2-substituted allyl alcohols. The analogous imines **8** give 1,2-disubstituted allylamines **9**. Easy deprotection of the double bond is achieved smoothly in the presence of tetrabutylammonium fluoride to generate the allyl alcohols or by simple heating for the allylamines.

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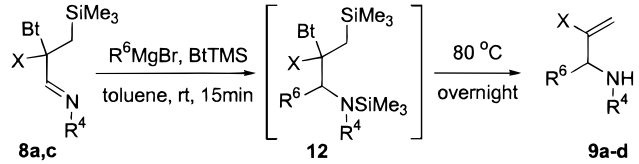
Scheme 3



9	b	c	d
R^4	4-MeO-C_6H_4	Ph	4-MeO-C_6H_4
R^6	Me	Me	nBu
X	4-Me-C_6H_4	2-Cl-C_6H_4	4-Me-C_6H_4
Yield (%)	62	47	44

Experimental Section

General Methods. Melting points were determined with a capillary melting point apparatus equipped with a digital thermometer. NMR spectra were taken in $CDCl_3$ with tetramethylsilane as internal standard for ^1H (300 MHz) or solvent as internal standard for ^{13}C (75 MHz). Tetrahydrofuran (THF) was distilled under nitrogen immediately before use from sodium/benzophenone. Chloromethyltrimethylsilane was purchased from Gelest, Inc. Column chromatography was conducted with silica gel grade 230−400 mesh. All organometallic reactions were carried out under argon in oven-dried glassware. All remaining reagents were reagent grade and were used without purification.

General Procedure for the Synthesis of Compounds 1a−h. Compounds **1a−h** were synthesized according to a previously described procedure.[15] The corresponding 1-substituted 1*H*-benzotriazole (0.004 mol) was dissolved in THF (100 mL) and cooled to −78 °C. *n*-BuLi in hexanes (1.46 M, 3.01 mL, 0.0044 mol) was added and stirred at −78 °C for 30 min. After the addition of chloromethyltrimethylsilane (0.491 g, 0.0044 mol), the reaction mixture was stirred at −78 °C for 3 h, and the mixture was allowed to reach rt in 16 h. Aqueous sodium bicarbonate solution (saturated, 40 mL) was added, and the resulting mixture was stirred at room temperature for 1 h. The aqueous layer was extracted with ethyl ether (2 × 30 mL), the combined organic layers were washed with brine (2 × 30 mL) and dried ($MgSO_4$), and the solvent was removed to give a residue. The residue was dissolved in hot hexanes (5 mL) and allowed to slowly cool to room temperature. The pure product was collected on a fritted funnel.

1-[(4-Methoxyphenyl)-2-(trimethylsilyl)ethyl]-1*H*-benzotriazole (1f): white prisms (91% yield); mp 90.4−91.0 °C (hexanes); ^1H NMR δ −0.15 (s, 9H), 1.94 (dd, J = 14.6, 8.3 Hz, 1H), 2.09 (dd, J = 14.6, 8.2 Hz, 1H), 3.75 (s, 3H), 5.95 (t, J = 8.1 Hz, 1H), 6.83 (d, J = 8.7 Hz, 2H), 7.26−7.42 (m, 5H), 8.02 (d, J = 8.2 Hz, 1H); ^{13}C NMR δ −1.7, 23.5, 55.1, 60.8, 110.0, 114.0, 119.8, 123.6, 126.7, 128.0, 132.0, 132.8, 146.3, 159.3. Anal. Calcd for $C_{18}H_{23}N_3OSi$: C, 66.42; H, 7.12; N, 12.91. Found: C, 66.21; H, 7.12; N, 12.99.

1-[1-(Methylthio)-2-(trimethylsilyl)ethyl]-1*H*-benzotriazole (1g): colorless prisms (77% yield); mp 58.3−60.3 °C (hexanes); ^1H NMR −0.12 (s, 9H), 1.63 (dd, J = 14.9, 6.7 Hz, 1H), 1.79−1.87 (dd, overlapped, 1H), 1.83 (s, 3H), 6.11 (dd, J = 9.5, 6.9 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 8.2 Hz, 1H), 7.87 (d, J = 8.3 Hz, 1H), 8.07 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ −1.9, 14.2, 23.5, 63.7, 111.6, 120.0, 124.1, 126.9, 130.7, 146.9. Anal. Calcd for $C_{12}H_{19}N_3OSiS$: C, 54.30; H, 7.21; N, 15.83. Found: C, 54.45; H, 7.58; N, 15.69.

1-[1-(5-Methylthiophen-2-yl)-2-(trimethylsilyl)ethyl]-1*H*-benzotriazole (1h):[16] light yellow prisms (90% yield); mp 78.4−80.3 °C (hexanes); ^1H NMR δ −0.15 (s, 9H), 1.93 (dd, J = 14.6, 7.4 Hz, 1H), 2.05 (dd, J = 14.6, 8.8 Hz, 1H), 2.39 (s, 3H), 6.28 (t, J = 8.0 Hz, 1H), 6.56 (d, J = 2.3 Hz, 1H), 6.88 (d, J = 3.3 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 7.0 Hz, 1H), 7.42 (d, J = 8.2 Hz, 1H), 8.03 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ −1.8, 15.2, 24.1, 57.1, 110.4, 120.1, 123.8, 124.6, 125.5, 127.0, 131.7, 140.4, 141.9, 146.6. Anal. Calcd for $C_{16}H_{21}N_3SSi$: C, 60.90; H, 6.72; N, 13.32. Found: C, 61.10; H, 6.96; N, 13.59.

General Procedure for the Synthesis of Compounds 2a−h. The corresponding **1** (0.005 mol) was dissolved in THF (50 mL) and cooled to −78 °C. *n*-BuLi in hexanes (1.41 M, 4.00 mL, 0.0055 mol) was added and the resulting mixture stirred at −78 °C for 30 min. *N*,*N*-Dimethylformamide was added (0.39 mL, 0.0055 mol), and the reaction mixture was stirred at −78 °C for 3 h. Glacial acetic acid (2 mL) was added, and the mixture was allowed to reach rt in 16 h. Aqueous sodium bicarbonate solution (saturated, 40 mL) was added, and the mixture was stirred at room temperature for 1 h. The aqueous layer was extracted with ethyl ether (2 × 30 mL), the combined organic layers were washed with brine (2 × 30 mL) and dried ($MgSO_4$), and the solvent was removed. The resulting residue was dissolved in hot hexanes (5 mL) and allowed to slowly cool to room temperature. The product was collected on a fritted funnel.

2-(1*H*-Benzotriazol-1-yl)-2-(2-methylphenyl)-3-(trimethylsilyl)propanal (2a): white prisms (71% yield); mp 134.9−135.8 °C (hexanes); ^1H NMR δ −0.28 (s, 9H), 1.53 (s, 3H), 2.09 (d, J = 14.3 Hz, 1H), 2.37 (d, J = 14.4 Hz, 1H), 6.54 (d, J = 9.2 Hz, 1H), 7.06 (d, J = 7.2 Hz, 1H), 7.17 (t, J = 7.2 Hz, 1H), 7.28−7.41 (m, 3H), 7.73 (d, J = 7.7 Hz, 1H), 8.08 (d, J = 8.3 Hz, 1H), 10.85 (s, 1H); ^{13}C NMR δ −0.8, 20.2, 25.5, 75.8, 110.8, 120.1, 124.2, 126.7, 127.2, 127.3, 129.4, 132.6, 133.1, 135.8, 137.0, 146.4, 195.1. Anal. Calcd for $C_{19}H_{23}N_3OSi$: C, 67.62; H, 6.87; N, 12.45. Found: C, 67.79; H, 7.02; N, 12.56.

2-(1*H*-Benzotriazol-1-yl)-2-(4-methylphenyl)-3-(trimethylsilyl)propanal (2b): white prisms (70% yield); mp 134.3−136.3 °C (hexanes); ^1H NMR δ −0.37 (s, 9H), 1.87 (d, J = 14.5 Hz, 1H), 2.34 (s, 3H), 2.44 (d, J = 14.4 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 7.09 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.25 (t, J = 8.2 Hz, 1H), 7.33 (t, J = 7.8 Hz, 1H), 8.09 (d, J = 8.2 Hz, 1H), 10.20 (s, 1H); ^{13}C NMR δ −1.0, 21.0, 22.7, 74.9, 111.5, 120.2, 124.2, 126.8, 127.2, 130.0, 132.1, 133.3, 139.1, 146.4, 191.4. Anal. Calcd for $C_{19}H_{23}N_3OSi$: C, 67.62; H, 6.87; N, 12.45. Found: C, 67.62; H, 7.20; N, 12.51.

2-(1*H*-Benzotriazol-1-yl)-2-(2-fluorophenyl)-3-(trimethylsilyl)propanal (2c): colorless prisms (68% yield); mp 141.9−143.1 °C (hexanes); ^1H NMR δ −0.26 (s, 9H), 2.04 (d, J = 14.3 Hz, 1H), 2.35 (d, J = 14.3 Hz, 1H), 6.70 (d, J = 8.1 Hz, 1H), 7.02 (t, J = 8.8 Hz, 1H), 7.22−7.36 (m, 3H), 7.41−7.46 (m, 2H), 8.10 (d, J = 8.2 Hz, 1H), 10.44 (d, J = 4.1 Hz, 1H); ^{13}C NMR δ −1.1, 23.1, 74.5, 111.2, 116.3 (d, J = 21.6 Hz), 120.3, 124.3, 127.5, 128.9 (d, J = 8.4 Hz), 132.1 (d, J = 22.5 Hz), 132.3, 146.4, 162.8 (d, J = 248.6 Hz), 191.3. Anal. Calcd for $C_{18}H_{20}FN_3OSi$: C, 63.32; H, 5.90; N, 12.31. Found: C, 63.68; H, 5.95; N, 12.39.

2-(1*H*-Benzotriazol-1-yl)-2-(4-fluorophenyl)-3-(trimethylsilyl)propanal (2d): white needles (73% yield); mp 102.0−103.5 °C (hexanes); ^1H NMR δ-0.26 (s, 9H), 2.04 (d, J = 14.3 Hz, 1H), 2.36 (d, J = 14.3 Hz, 1H), 6.71 (d, J = 8.2 Hz, 1H), 7.01 (t, J = 8.5 Hz, 1H), 7.21−7.35 (m, 3H), 7.39−7.46 (m, 2H), 8.09 (d, J = 8.1 Hz, 1H), 10.45 (d, J = 4.4 Hz, 1H); ^{13}C NMR δ −0.7, 23.8, 73.6 (d, J = 3.1 Hz), 110.7, 116.9 (d, J = 22.7 Hz), 120.3, 124.1, 124.9 (d, J = 3.2 Hz), 127.2, 128.4 (d, J = 3.2 Hz), 131.6 (d, J = 8.9 Hz), 133.4, 146.4, 160.2 (d, J = 250.3 Hz), 192.6 (d, J = 3.5 Hz). Anal. Calcd for $C_{18}H_{20}FN_3OSi$: C, 63.32; H, 5.90; N, 12.31. Found: C, 63.58; H, 6.00; N, 12.31.

2-(1*H*-Benzotriazol-1-yl)-2-(2-chlorophenyl)-3-(trimethylsilyl)propanal (2e): colorless prisms (65% yield); mp 130.2−130.9 °C (hexanes); ^1H NMR δ −0.27 (s, 9H), 2.05 (d, J = 14.0 Hz, 1H), 2.33 (d, J = 14.1 Hz, 1H), 6.51 (d, J = 8.5 Hz, 1H), 7.18 (t, J = 7.1 Hz, 1H), 7.27−7.40 (m, 3H), 7.46 (t, J = 7.9 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 8.2 Hz, 1H), 11.0 (s, 1H); ^{13}C NMR δ −0.8, 25.6, 74.7, 110.4, 124.0, 127.3, 129.3, 130.8, 131.7, 132.3, 133.6, 135.9, 146.3, 195.8. Anal. Calcd for $C_{18}H_{20}N_3OSiCl$: C, 60.40; H, 5.63; N, 11.74. Found: C, 60.56; H, 5.72; N, 11.81.

2-(1*H*-Benzotriazol-1-yl)-2-(4-methoxyphenyl)-3-(trimethylsilyl)propanal (2f): white needles (82% yield); mp 97.4−97.9 °C (hexanes); ^1H NMR δ -0.23 (s, 9H), 1.99 (d, J = 14.4 Hz, 1H), 2.57 (d, J = 14.3 Hz, 1H), 3.95 (s, 3H), 6.89 (d, J = 8.1 Hz, 1H), 7.04 (d, J = 8.5 Hz, 2H), 7.27 (d, J = 8.5 Hz, 2H), 7.38−7.51 (m, 2H), 8.25 (d, J = 8.2 Hz, 1H), 10.37 (s, 1H); ^{13}C NMR δ −1.0, 22.7, 55.3, 74.6, 111.6, 114.7, 120.2, 124.2, 127.3, 128.1, 128.4, 132.1, 146.4, 160.1, 191.2. Anal. Calcd for $C_{19}H_{23}N_3O_2Si$: C, 64.56; H, 6.56; N, 11.89. Found: C, 64.93; H, 6.95; N, 12.05.

2-(1*H*-Benzotriazol-1-yl)-2-(methylthio)-3-(trimethylsilyl)-propanal (2g): white prisms (84% yield); mp 80.4−81.4 °C (hexanes); ^{1}H NMR δ -0.38 (s, 9H), 1.75 (d, J = 14.6 Hz, 1H), 1.90 (s, 3H), 1.96 (d, J = 14.6 Hz, 1H), 7.41 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 6.2 Hz, 1H), 7.94 (d, J = 7.5 Hz, 1H), 8.08 (d, J = 8.2 Hz, 1H), 9.85 (s, 1H); ^{13}C NMR δ −1.1, 12.5, 22.8, 74.8, 112.0, 120.3, 124.5, 127.7, 132.2, 146.4, 184.0. Anal. Calcd for $C_{13}H_{19}N_3OSSi$: C, 53.21; H, 6.53; N, 14.32. Found: C, 53.38; H, 6.82; N, 14.34.

2-(1*H*-Benzotriazol-1-yl)-2-(5-methylthiophen-2-yl)-3-(trimethylsilyl)propanal (2h): light yellow prisms (86% yield); mp 131.7−132.7 °C (hexanes); ^{1}H NMR δ -0.36 (s, 9H), 1.94 (d, J = 14.6 Hz, 1H), 2.35 (d, J = 14.5 Hz, 1H), 2.47 (s, 3H), 6.65−6.68 (m, 2H), 6.98 (d, J = 8.6 Hz, 1H), 7.31−7.37 (m, 2H), 8.09 (d, J = 6.9 Hz, 1H), 10.12 (s, 1H); ^{13}C NMR δ −1.1, 15.3, 24.3, 72.8, 111.4, 120.2, 124.2, 126.0, 127.4, 132.2, 137.3, 142.9, 146.3, 188.8. Anal. Calcd for $C_{17}H_{21}N_3OSSi$: C, 59.44; H, 6.16; N, 12.23. Found: C, 59.76; H, 6.30; N, 12.30.

3-(1*H*-Benzotriazol-1-yl)-3-(4-methylphenyl)-1,4-bis(trimethylsilyl)butan-2-ol (3). 2-(1*H*-Benzotriazol-1-yl)-2-(4-methylphenyl)-3-(trimethylsilyl)propanal **2b** (0.337 g, 0.001 mol) was dissolved in THF (100 mL) and cooled to −78 °C. Me_3SiCH_2-MgCl in THF (1.0M, 4.0 mL, 0.004 mol) was added and the mixture stirred at −78 °C for 2 h. The mixture was allowed to reach rt in 16 h. Brine was added (30 mL), and the aqueous layer was extracted with ethyl ether (2 × 30 mL). The combined organic layers were dried (Na_2SO_4), and the solvent was removed to give the pure product (yield 96%): white solid; mp 191.0−191.4 °C (hexanes); ^{1}H NMR δ −0.28 (s, 9H), 0.17 (s, 9H), 0.55 (d, J = 14.0 Hz, 1H), 0.90 (d, J = 14.0 Hz, 1H), 2.09 (dd, J = 24.0, 15.0 Hz, 2H), 2.45 (s, 3H), 4.03 (brs, 1H), 5.42−5.46 (m, 1H), 6.74 (d, J = 8.3 Hz, 1H), 7.12 (d, J = 7.9 Hz, 2H), 7.20 (d, J = 7.9 Hz, 2H), 7.27 (t, J = 8.0 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 8.16 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ −0.6, −0.4, 18.4, 21.0, 26.2, 72.2, 75.4, 112.8, 119.9, 123.8, 126.8, 128.3, 133.0, 137.0, 137.3, 146.4. Anal. Calcd for $C_{23}H_{35}N_3OSi_2$: C, 64.88; H, 8.30; N, 9.87. Found: C, 64.98; H, 8.35; N, 9.94.

General Procedure for the Synthesis of Compounds 4a,b. 2-(1*H*-Benzotriazol-1-yl)-2-(4-fluorophenyl)-3-(trimethylsilyl)propanal **2d** (0.341 g, 0.001 mol) was dissolved in THF (100 mL) and cooled to −78 °C. The appropriate lithiating reagent (0.0011 mol) was added, and the mixture was stirred at −78 °C for 2 h. The mixture was allowed to reach rt in 16 h. Brine was added (30 mL), the aqueous layers were extracted with ethyl ether (2 × 30 mL), the combined organic layer was dried (Na_2SO_4), and the solvent was removed to give a residue. The residue was distilled under vacuum (4 mmHg) to afford the pure product as the first fraction.

[1-Butyl-2-(4-fluorophenyl)prop-2-enyl]oxy(trimethyl)-silane (4a): colorless oil (98% yield); bp 105 °C (4 mmHg); ^{1}H NMR δ −0.14 (s, 9H), 0.54 (t, J = 6.9 Hz, 3H), 0.93−1.13 (m, 6H), 4.19 (t, J = 5.9 Hz, 1H), 4.89 (s, 1H), 4.99 (s, 1H), 6.70 (t, J = 8.6 Hz, 2H), 7.07 (t, J = 8.6 Hz, 2H); ^{13}C NMR δ −0.4, 14.0, 22.5, 28.0, 36.7, 75.2, 113.1, 114.9 (d, J = 12.0 Hz), 128.7 (d, J = 7.5 Hz), 136.3, 151.0, 162.3 (d, J = 244.5 Hz). Anal. Calcd for $C_{16}H_{25}FOSi$: C, 68.52; H, 9.00. Found: C, 68.31; H, 9.28.

[2-(4-Fluorophenyl)-1-(1-methylpropyl)prop-2-enyl]oxy-(trimethyl)silane (4b): colorless oil (51% yield), mixture of diastereomers A/B = 1:2; bp 125 °C (4 mmHg); ^{1}H NMR δ −0.16 (s, 9H), 0.73−0.84 (m, 6H), 0.97−1.20 (m, 1H), 1.20−1.42 (m, 2H), 4.43 (m, 1H), 5.24−5.26 (m, 2H), 6.99 (t, J = 9.0 Hz, 2H), 7.32−7.37 (m, 1H), 7.40−7.45 (m, 1H); ^{13}C NMR δ 0.2 (A + B, 2C), 11.5 (A), 11.8 (B), 12.9 (B), 15.8 (A), 23.7 (A), 26.6 (B), 38.1 (B), 38.4 (A), 77.9 (B), 80.6 (A), 114.1 (A + B), 114.8 (d, J = 9.0 Hz, A), 115.1 (d, J = 9.0 Hz, B), 128.6 (d, J = 7.5 Hz, A), 129.0 (d, J = 8.3 Hz, B), 136.8 (A + B), 149.8 (d, J = 15.0 Hz, A + B), 162.3 (d, J = 247.5 Hz, A + B). Anal. Calcd for $C_{16}H_{25}FOSi$: C, 68.52; H, 9.00. Found: C, 68.42; H, 9.34.

5-(4-Methylphenyl)-2-phenyl-3a,4,7,7a-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione (5). 3-(1*H*-Benzotriazol-1-yl)-3-(4-methylphenyl)-1,4-bis(trimethylsilyl)butan-2-ol **3** (50 mg, 0.114 mmol) and *N*-phenylmaleimide (78 mg, 0.455 mmol) were dissolved in dry CH_2Cl_2 (1 mL). Trifluoroacetic acid (26 μL, 0.341 mmol) was added slowly under vigorous stirring. After 10 min, aqueous 5% NaOH solution (1 mL) was introduced, and the mixture was extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layers were dried ($MgSO_4$), and solvent was removed to give an oil. Purification by flash chromatography on silica gel (hexanes/Et_2O gradient) afforded **5** as a colorless solid (32 mg, 89%): mp 113.5−113.6 °C; ^{1}H NMR δ 2.33 (s, 3H), 2.40 (m, 1H), 2.60 (dd, J = 6.6, 15.3 Hz, 1H), 2.91 (ddd, J = 2.0, 6.9, 18.4 Hz, 1H), 3.23 (dd, J = 1.8 , 15.2 Hz, 1H), 3.32 (brt d, J = 2.1, 7.1 Hz, 1H), 3.40 (brt d, J = 2.2, 6.8 Hz, 1H), 6.16 (brt, J = 3.2 Hz, 1H), 7.11−7.15 (m, 4H), 7.26 (d, J = 8.0 Hz, 2H), 7.32−7.41 (m, 3H); ^{13}C NMR δ −21.1, 25.2, 27.6, 39.5, 40.1, 122.2, 125.4, 126.4, 128.5, 129.1, 129.2, 132.0, 137.3, 137.5, 139.9, 178.9, 179.1; HRMS (EI) calcd for $C_{21}H_{20}NO_2$ (M + 1) 318.1494, found 318.1540. Anal. Calcd for $C_{21}H_{19}NO_2$: N, 4.41. Found: N, 4.75.

General Procedure for the Synthesis of Compounds 6a−c. Compounds **2** (0.001 mol) were dissolved in THF (100 mL) and cooled to −78 °C. The appropriate Grignard reagent in THF (0.004 mol) was added, and the mixture was stirred at −78 °C for 2 h. The mixture was allowed to reach rt over 16 h. Brine was added (30 mL), and the aqueous layer was extracted with ethyl ether (2 × 30 mL). The combined organic layers were dried (Na_2SO_4), and the solvent was removed. The obtained residue was purified by flash chromatography to afford the desired compound.

3-(1*H*-Benzotriazol-1-yl)-3-(4-methylphenyl)-4-(trimethylsilyl)butan-2-ol (6a): white solid (81% yield); mixture of diastereomers A/B = 3:1; mp 121.3−122.3 °C; ^{1}H NMR δ −0.52 (s, 9H, A), −0.47 (s, 9H, B), 0.90 (d, J = 6.3 Hz, 3H, B), 0.97 (d, J = 6.4 Hz, 3H, A), 1.82 (s, 2H, A + B), 2.17 (s, 3H, A+B), 4.91 (q, J = 6.3 Hz, 1H, B), 5.19 (q, J = 6.1 Hz, 1H, A), 6.53 (d, J = 8.2 Hz, 1H, A), 6.65 (d, J = 8.2 Hz, 1H, B), 6.84 (m, 2H, A + B), 6.96 (m, 2H, A + B), 7.03 (brt, J = 7.8 Hz, 1H, A + B), 7.13 (m, 1H, A + B), 7.90 (d, J = 8.1 Hz, 1H, A + B); ^{13}C NMR δ −0.7 [0.1], 17.0, 21.0, 25.8, 70.0, 73.5 [74.4], 112.7, 119.9 [120.0], 123.9 [124.0], 126.5, 126.9 [127.0], 128.0, 128.5, 129.3, 132.7, 136.4, 137.6. Anal. Calcd for $C_{20}H_{27}N_3OSi$: C, 67.94; H, 7.71; N, 11.89. Found: C, 67.61; H, 8.08; N, 12.15.

2-(1*H*-Benzotriazol-1-yl)-2-(4-methylphenyl)-1-phenyl-3-(trimethylsilyl)propan-1-ol (6b): colorless oil (94% yield); mixture of diastereomers A/B = 1:2; ^{1}H NMR δ −0.34 (s, 9H, A), −0.31 (s, 9H, B), 1.80 (d, J = 14.8 Hz, 1H, A + B), 2.08 (d, 1H, J = 14.8 Hz, A + B), 2.30 (s, 3H, B), 2.34 (s, 3H, A), 4.50 (brs, OH, A + B), 6.01 (s, 1H, B), 6.31 (s, 1H, A), 6.58 (d, J = 8.3 Hz, 1H, A), 6.73−6.97 (m, 4H, A+B), 6.98 (d, J = 7.8 Hz, 2H, A + B), 7.07−7.31 (m, 5H, A + B), 8.06 (d, J = 8.3 Hz, 1H, A + B); ^{13}C NMR δ −0.3 [0.1], 21.0, 26.4, 74.0 [75.7], 76.5 [80.2], 113.0 [113.5], 115.5, 119.7 [119.8], 124.0 [124.2], 126.8, 127.0, 127.2, 127.6, 127.9, 128.3, 128.9 [129.1], 129.5, 136.1, 137.7 [137.8], 138.9, 146.2; HRMS (EI) calcd for $C_{25}H_{30}N_3OSi$ (M + 1) 416.2158, found 416.2113.

2-(1*H*-Benzotriazol-1-yl)-2-(2-chlorophenyl)-1-phenyl-3-(trimethylsilyl)propan-1-ol (6c): white prisms (86% yield); mp 208.7−210.1 °C; ^{1}H NMR δ -0.14 (s, 9H), 1.89 (d, J = 15.0 Hz, 1H), 2.53 (d, J = 15.0 Hz, 1H), 5.80 (s, 1H), 6.13 (s, 1H), 6.44 (d, J = 6.0 Hz, 2H), 6.84 (d, J = 8.1 Hz, 1H), 7.10−7.26 (m, 6H), 7.42 (t, J = 7.2 Hz, 1H), 7.63 (t, J = 7.2 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 8.27 (d, J = 7.2 Hz, 1H); ^{13}C NMR δ −0.3, 24.5, 72.3, 76.2, 114.7, 118.4, 122.8, 125.2, 127.0, 127.3, 127.8, 128.5, 129.7, 130.5, 131.9, 133.8, 134.9, 136.6, 140.0, 145.8. Anal. Calcd for $C_{24}H_{26}ClN_3OSi$: C, 66.11; H, 6.02; N, 9.64. Found: C, 66.06; H, 6.23; N, 9.69.

General Procedure for the Synthesis of Compounds 7a,b. The corresponding **6** (0.30 mmol) were dissolved in dry THF (3 mL), and a 1 M solution of tetrabutylammonium fluoride in THF (450 μL, 0.45 mmol) was added. The resulting mixtures were allowed to react until complete conversion of the starting material as verified by TLC, and the solvent was removed. The residue obtained was purified by flash chromatography on silica gel (hexanes/Et_2O gradient) to afford **7** as pure product.

3-(4-Methylphenyl)but-3-en-2-ol (7a): colorless oil (94% yield); ^{1}H NMR δ 1.31 (d, J = 6.5 Hz, 3H), 1.90 (d, J = 4.1 Hz, 1H), 2.34 (s, 3H), 4.81 (qd, J = 6.5, 4.1 Hz, 1H), 5.25 (s, 1H), 5.32 (s, 1H), 7.14 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H); ^{13}C NMR δ 21.1, 22.6, 69.5, 110.8, 126.7, 129.1, 136.9, 137.4, 152.9; HRMS (EI) calcd for $C_{11}H_{14}O$ 162.1045, found 162.1033.

2-(4-Methylphenyl)-1-phenylprop-2-en-1-ol (7b): colorless oil (85% yield); ^{1}H NMR δ 2.28 (s, 3H), 5.42 (s, 1H), 5.47 (s, 1H), 5.67 (s, 1H), 7.04 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.3 Hz, 2H), 7.23−7.25 (m, 1H), 7.29 (t, J = 6.9 Hz, 2H), 7.38 (d, J = 7.1 Hz, 2H); ^{13}C NMR δ 21.1, 75.9, 113.2, 126.8, 127.0, 127.7, 128.4,

129.0, 136.3, 137.4, 141.9, 150.1; HRMS (EI) calcd for $C_{16}H_{16}O$ 224.1201, found 224.1202.

General Procedure for the Synthesis of Compounds 8a−c. The corresponding **2** (0.002 mol) and the amine (0.002 mol) were dissolved in methanol (5 mL) and heated to reflux for 10 h in the presence of one drop of acetic acid. The solvent was removed to give a residue that was purified by either flash chromatography for compound **8b** or by recrystallization in hot hexanes (2 mL) for compounds **8a**,**c**.

***N*-[(*E*)-2-(1*H*-Benzotriazol-1-yl)-2-(4-methylphenyl)-3-(trimethylsilyl) propylidene]-4-(methoxy)aniline (8a):** colorless prisms (99% yield); mp 129.8−130.5 °C (hexanes); ^{1}H NMR δ −0.33 (s, 9H), 2.12 (d, J = 14.3 Hz, 1H), 2.31 (s, 3H), 2.71 (d, J = 14.3 Hz, 1H), 3.78 (s, 3H), 6.85 (d, J = 8.7 Hz, 3H), 7.08−7.09 (m, 6H), 7.20 (t, J = 7.1 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 8.06 (d, J = 8.3 Hz, 1H), 8.72 (s, 1H); ^{13}C NMR δ −0.25, 20.9, 26.0, 55.4, 72.4, 112.3, 114.2, 120.0, 122.2, 123.8, 126.2, 126.7, 129.6, 132.5, 138.0, 138.4, 143.5, 146.7, 158.4, 160.5. Anal. Calcd for $C_{26}H_{30}N_4OSi$: C, 70.55; H, 6.83; N, 12.66. Found: C, 70.79; H, 7.19; N, 12.80.

***N*-[(*E*)-2-(1*H*-Benzotriazol-1-yl)-2-(2-chlorophenyl)-3-(trimethylsilyl) propylidene]butan-1-amine (8b):** yellow oil (52% yield); ^{1}H NMR δ −0.17 (s, 9H), 0.96 (t, J = 7.4 Hz, 3H), 1.35 (sextet, J = 7.4 Hz, 2H), 1.66 (quintet, J = 7.4 Hz, 2H), 2.36 (d, J = 13.8 Hz, 1H), 2.64 (d, J = 13.8 Hz, 1H), 3.57−3.63 (m, 1H), 3.69−3.75 (m, 1H), 6.73 (d, J = 8.3 Hz, 1H), 6.98 (d, J = 8.5 Hz, 1H), 7.23−7.44 (m, 3H), 7.53 (t, J = 7.2 Hz, 1H), 7.98 (d, J = 7.8 Hz, 1H), 8.17 (d, J = 8.2 Hz, 1H), 9.31 (s, 1H); ^{13}C NMR δ 0.5, 13.8, 20.3, 27.5, 32.3, 60.4, 71.6, 111.0, 153.5, 120.0, 123.7, 126.8, 127.0, 128.6, 129.4, 129.9, 131.8, 132.4, 133.7, 139.2, 146.6, 163.2; HRMS (EI) calcd for $C_{22}H_{30}ClN_4Si$ (M + 1) 413.1928, found 413.1923.

***N*-[(*E*)-2-(1*H*-Benzotriazol-1-yl)-2-(2-chlorophenyl)-3-(trimethylsilyl)propylidene]aniline (8c):** colorless solid (70% yield); mp 108.1−108.7 °C (hexanes); ^{1}H NMR δ −0.15 (s, 9H), 2.40 (d, J = 14.0 Hz, 1H) 2.84 (d, J = 14.0 Hz, 1H), 6.77 (d, J = 8.3 Hz, 1H), 7.22−7.50 (m, 9H), 7.59 (t, J = 7.6 Hz, 1H), 8.09 (d, J = 8.0 Hz, 1H), 8.20 (d, J = 8.3 Hz, 1H), 9.59 (s, 1H); ^{13}C NMR δ −0.5, 27.5, 71.9, 111.1, 120.2, 120.7, 123.9, 126.2, 126.9, 127.1, 127.3, 128.7, 129.0, 130.0, 131.8, 133.6, 138.9, 146.7, 150.7, 163.7. Anal. Calcd for $C_{24}H_{25}ClN_4OSi$: C, 66.56; H, 5.83; N, 12.94. Found: C, 66.54; H, 6.14; N, 13.05.

General Procedure for the Synthesis of Compounds 9b−d. Compounds **8** (0.34 mmol) and 1-(trimethylsilyl)benzotriazole (0.37 mmol) were dissolved in dry toluene (4 mL), and the desired Grignard reagent (3 M in Et_2O, 1.4 mmol) was added. The resulting deep red solution was allowed to react for 15 min at room temperature before reacting overnight at 80 °C. The mixture was cooled to room temperature and quenched with water (3 mL). The aqueous phase was neutralized (aqueous saturated NH_4Cl) and extracted with Et_2O and EtOAc. The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed. The obtained residue was submitted to flash chromatography on silica gel (hexanes/Et_2O gradient) to afford compounds **9b−d** as pure light yellow oils.

***N*-[1-Methyl-2-(4-methylphenyl)prop-2-enyl]-4-(methoxy)-aniline (9b):** light yellow oil (62% yield); ^{1}H NMR δ 1.57 (d, J = 6.6 Hz, 3H), 2.60 (s, 3H), 3.98 (s, 3H), 4.58 (q, J = 6.6 Hz, 1H), 5.49 (s, 1H), 5.51 (s, 1H), 6.82 (d, J = 8.9 Hz, 2H), 7.01 (d, J = 8.9 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.0 Hz, 2H); ^{13}C NMR δ 21.1, 22.0, 53.2, 55.7, 111.7, 114.4, 114.8, 126.5, 129.0, 137.2, 137.7, 141.4, 150.5, 151.8. Anal. Calcd for $C_{18}H_{21}NO$: N, 5.24. Found: N, 5.27.

***N*-[2-(2-Chlorophenyl)-1-methylprop-2-enyl]aniline (9c):** light yellow oil (47% yield); ^{1}H NMR δ 1.37 (d, J = 6.7 Hz, 3H), 4.52 (q, J = 6.7 Hz, 1H), 5.19 (s, 1H), 5.60 (s, 1H), 6.81 (d, J = 7.8 Hz, 3H), 7.28−7.35 (m, 5H), 7.48−7.51 (m, 1H); ^{13}C NMR δ 21.0, 53.4, 113.3, 115.7, 117.3, 126.4, 127.4, 128.4, 129.2, 129.4, 130.8, 131.9, 140.0, 148.8; HRMS (EI) calcd for $C_{16}H_{17}ClN$ (M + 1) 258.1049, found 258.1045.

***N*-[1-Butyl-2-(4-methylphenyl)prop-2-enyl]-*N*-[4-methoxyphenyl]amine (9d):** light yellow oil (44% yield); ^{1}H NMR δ 1.14 (t, J = 7.1 Hz, 3H), 1.50−2.01 (m, 6H), 2.63 (s, 3H), 4.01 (s, 3H), 4.46 (t, J = 4.9 Hz, 1H), 5.51 (s, 2H), 6.80 (d, J = 8.6 Hz, 2H), 7.04 (d, J = 8.6 Hz, 2H), 7.42 (d, J = 7.8 Hz, 2H), 7.56 (d, J = 7.8 Hz, 2H); ^{13}C NMR δ 14.0, 21.1, 22.6, 28.5, 35.2, 55.7, 58.1, 112.7, 114.2, 114.8, 126.4, 129.0, 137.1, 137.9, 141.8, 149.4, 151.8. Anal. Calcd for $C_{21}H_{27}NO$: N, 4.53. Found: N, 4.49.

Supporting Information Available: NMR spectra for obtained compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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