A Four-Carbon Unit Reagent for the Regiospecific Synthesis of 2-Alkyl-Substituted 1,3-Butadienes

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2-Alkyl-substituted butadienes are synthesized starting from a masked butadiene reagent, which allows the regiospecific synthesis of 2-alkylbutadienes by lithiation and subsequent reaction with alkyl halides or aliphatic aldehydes. The regioselectivity of the reaction with allylic halides and aliphatic and aromatic aldehydes is studied.

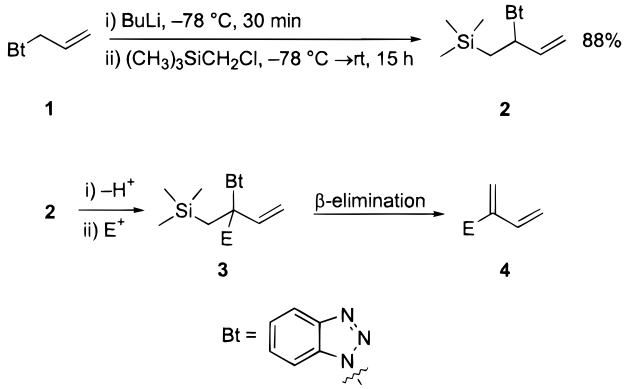
Introduction

Numerous studies have been performed on the regiospecific synthesis of 2-substituted 1,3-butadienes due to their use in the Diels−Alder reaction for the construction of complex molecules.[1] The recent syntheses of Bacatin III−steroid hybrid by Danishefsky[2] and (±)-Ipsenol by Najera[3] demonstrate the utility of such strategies.

Previous syntheses of 2-alkyl-substituted 1,3-dienes can be divided into two categories. The first uses preformed 1,3-butadien-2-yl reagents which are prepared (i) by nickel(II)-catalyzed coupling of diethyl 1-methylene-2-propenyl phosphates with Grignard reagents[4] or (ii) from 2-lithio-1,3-butadiene synthesized via a Shapiro reaction[5] or by lithium−halogen exchange upon 2-chloro-1,3-butadiene.[1a,6] These are excellent approaches, but sometimes require starting materials which are not readily available and occasionally afford the rearranged allene as a byproduct.[1a,6b]

The second category of syntheses of 2-alkyl-substituted 1,3-butadienes build the backbone of the diene by a variety of multistep approaches: (i) elaboration of 1-substituted 2,3-butadienes using boronate reagents developed by Brown,[7] trimethylsilyl reagents developed by Takano[8] or diethyl phosphate esters;[9] (ii) elaboration of propargylic ethers;[10] (iii) addition of bromomethanesulfonyl bromide to 2-substituted propenes followed by a Ramberg−Bäcklund elimination of sulfur dioxide and hydrogen bromide;[11] (iv) transition metal-catalyzed methods including β-vinylation of α-olefins catalyzed by Ni and Zr,[12] and palladium-catalyzed 1,2-elimination of methylvinylcarbinol acetates;[13] (v) silicon-[2,3,14] and tin[15]-directed synthesis of dienes.

Scheme 1



We have recently shown that easily accessible 2-benzotriazolylethylsilanes undergo vicinal elimination of silicon and the benzotriazole residue under various conditions to afford ethylenes.[16] We now describe the use of 1-{1-[(trimethylsilyl)methyl]prop-2-enyl}-1*H*-benzotriazole (**2**) (Scheme 1) as a four-carbon unit for regiospecific synthesis of 2-alkyl-substituted 1,3-butadienes.

Results and Discussion

1-Allyl-1*H*-benzotriazole (**1**) (Scheme 1) was prepared from allyl bromide and benzotriazole by the previously reported procedure.[17] Lithiation of **1** was accomplished with BuLi in THF at −78 °C for 30 min. 1-{1-[(Trimeth-

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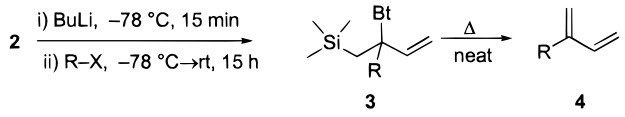
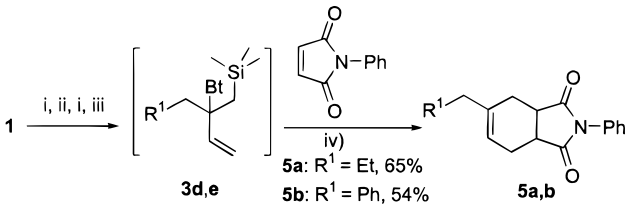
Scheme 2



		Elimination conditions		Yield (%)	
3, 4	R–X	temp (°C)	time (h)	**3**	**4**
a	$C_6H_{13}Br$	120-130	7	82	70
b	$C_{10}H_{21}Cl$	120-125	6	90	64
c	$C_{12}H_{25}Br$	130-135	8	86	90
d	C_3H_7I	25	2	87	[a]
e	$PhCH_2Br$	75-80	6	85	[a]

[a] See Scheme 3.

Scheme 3

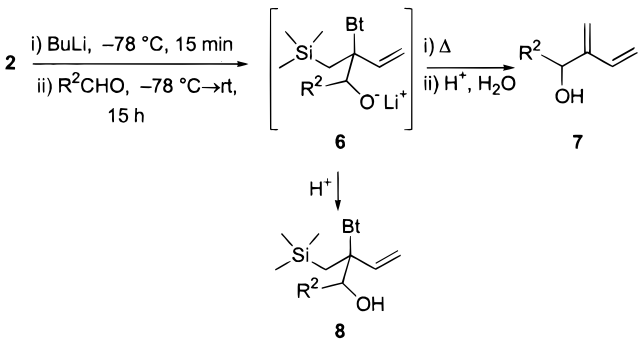


Reaction conditions: i) BuLi, –78 °C, 30 min; ii) $(CH_3)_3SiCH_2Cl$, –78 °C→rt; iii) R^1CH_2Br, –78 °C→rt; iv) (**5a**) TFA, 25 °C, 2 h; (**5b**) neat, 75–80 °C, 6 h.

ylsilyl)methyl]prop-2-enyl}-1*H*-benzotriazole (**2**) was obtained in 88% yield as a colorless stable oil by nucleophilic substitution of chlorine in chloromethyltrimethylsilane by the anion derived from **1**. Reagent **2** can be lithiated with BuLi, and the resulting carbanion behaves as a masked 1,3-butadien-2-yl reagent. Reagent **2** is similar to some others previously used[1a,5,6] for the synthesis of 2-alkyl-substituted dienes, but importantly rearrangement to allenes is suppressed with reagent **2** because the second double bond is formed by vicinal elimination of silicon after the reaction with electrophiles. A regiospecific synthesis of 2-alkyl-substituted 1,3-butadienes is thus possible as illustrated in Scheme 1 without the drawback of side-product formation. Elimination of silicon is in most cases accomplished thermally by heating the intermediate adducts **3** neat at 75−135 °C for 6−8 h. Dienes **4** were obtained pure after the byproduct benzotriazole was removed by washing with dilute aqueous sodium hydroxide solution.

Thus, lithiation of **2** followed by reaction with alkyl halides afforded the corresponding adducts **3a**−**e** in excellent yields. The vicinal elimination of silicon worked well with medium and long chain alkyl groups in the 2-position to yield 2-alkyl-1,3-butadienes **4a**−**c** in excellent yields after simple heating at 120−135 °C for 6−8 h (Scheme 2). When short chain alkyl adducts **3d** and **3e** were heated under similar conditions, polymers were the only observed products. However, these difficulties were overcome by trapping the corresponding **3d** and **3e** in the presence of a dienophile. This approach is depicted in Scheme 3 where reagent **1** is transformed into Diels−Alder adduct **5b** by heating the corresponding adduct **3e** with *N*-phenylmaleimide at 75−80 °C for 6 h. *N*-Phenylmaleimide does not react with **3d** on heating at 95 °C for 6 h, and starting material was recovered; at 135 °C for 6 h, 60% of the starting material **3d** and unidentified products were obtained. However, **5a** is formed by mixing *N*-phenylmaleimide with **3d** under acidic condition (Scheme 3). Here, the role of TFA is to protonate benzotriazole which then leaves and forms a carbocation that is quaternary, allylic, and β to a silicon (highly stabilized). The trifluoroacetate anion acts as a nucleophile to react with the trimethylsilyl group, and the elimination is then accomplished. Thus the isolation of intermediates **3** is superfluous if the preparation of dienes **4** has been carried out for the sole purpose of reacting them with a dienophile in a Diels−Alder protocol.

Scheme 4



		Elimination conditions		Yield (%)	
7, 8	R^2CHO	temp (°C)	time (h)	**7**	**8**
a	$PhCH_2CH_2CHO$	56	3	74[a]	80
b	$PhCH(CH_3)CHO$	56	5	60[a]	75[b]
c	$CH_3CH(CH_3)CHO$	56	5	72	81[b]

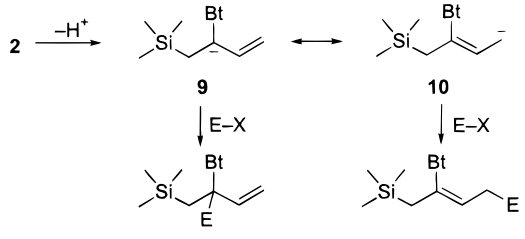
[a] Yield based on one pot reaction from **1**. [b] Not separated, yield based on GC-MS of crude product

The reaction of lithiated **2** with aliphatic aldehydes afforded alcohols **8a**−**c** as a mixture of diastereomers in good yields (Scheme 4). However, when the reaction (without isolation of the intermediate alkoxide derived from **6a**−**c**) was performed in THF solution and refluxed for 3−5 h, dienes **7a**−**c** were isolated in good yields. This outcome is the result of a [1,4]-C → O silicon migration followed by hydrolysis of the intermediate silyl ether.

The regiochemistry of the reaction **2** → **3** (Scheme 1) is dependent upon the nature of the electrophile, as shown by a study of the reactions of the anion derived from **2** with electrophiles under the reaction conditions used for alkyl halides. The adducts **3** or **8** and **11a**−**e** were obtained as mixtures in high yields and analyzed by GC-MS and ^1H NMR. The results are summarized in Scheme 5.

The carbanion derived from **2** has an ambident character: it can react either α to the benzotriazolyl group (carbanion **9** in Scheme 5) or γ to the benzotriazolyl group (carbanion **10** in Scheme 5). In contrast to the simple halides of Scheme 2, cinnamyl bromide **12** reacted predominantly in the γ position. Moderately hindered aldehydes **13** and **14** reacted predominantly at the α-position, similar to their simple analogue of Scheme 4. However, highly hindered **15** prefers the γ-orientation in a ratio of 1:9.5. Under the same reaction conditions 4-chlorobenzaldehyde shows an intermediate position with a 1:0.66 = α:γ ratio (Scheme 5).

Scheme 5



E–X	Products	3 (8) + 11 Yield (%)	Ratio α : γ
12 Ph, Br	**3f, 11a**	90	1:11.5
13 Ph, CHO	**8b, 11b**	80	1:0.15[b]
14 CHO	**8c, 11c**	90	1:0.1[b]
15 CHO	**8d, 11d**	84	1:9.5
16 Cl, CHO	**8e, 11e**	82	1:0.66[a]

[a]The corresponding **8e** and **11e** were separated. [b]The mixture was subjected to elimination

Conclusions

A four-carbon unit reagent for the regiospecific syntheses of 2-alkyl and 2-(hydroxyalkyl)butadienes has been developed. This new approach shows advantages over the previously described methods in its high regioselectivity, easily available precursors and stable masked butadienes which can be deprotected thermally during the Diels–Alder process. The regiochemistry of the reaction of the allyl carbanion with electrophiles is influenced by steric and electronic factors.

Experimental Section

General Methods. NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard for ^1H (300 MHz) or solvent as the internal standard for ^{13}C (75 MHz). THF was distilled from sodium/benzophenone under nitrogen immediately prior to use. All reactions with air-sensitive compounds were carried out under an argon atmosphere. 1-Allyl-1*H*-benzotriazole (**1**) was prepared according to the previously reported procedure.[17] All reagents were used as purchased from commercial suppliers without further purification.

Preparation of 1-{1-[(Trimethylsilyl)methyl]prop-2-enyl}-1*H*-1,2,3-benzotriazole (2). To a solution of **1** (5 mmol) in THF (50 mL) at −78 °C under argon was added *n*-BuLi (1.52 M, 3.7 mL, 5.2 mmol). After stirring for 30 min, a solution of chloromethyltrimethylsilane (0.73 mL, 5.2 mmol) in THF (5 mL) was added. The reaction mixture was allowed to warm to room temperature overnight before being washed with water (2 × 20 mL), extracted with ethyl ether (2 × 20 mL), and dried (Na_2SO_4). The oil remaining after the solvent was removed under reduced pressure was subjected to column chromatography with hexanes:ethyl acetate = 20:1 to give the pure product as a colorless oil (1.08 g, 88%): ^1H NMR δ −0.13 (s, 9H), 1.52 (dd, J = 14.6 and 7.1 Hz, 1H), 1.70 (dd, J = 14.8 and 8.8 Hz, 1H), 5.15 (d, J = 9.0 Hz, 1H), 5.20 (s, 1H), 5.51 (q, J = 7.5 Hz, 1H), 6.09−6.20 (m, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.42 (t, J = 7.5 Hz, 1H), 7.53 (d, J = 8.3 Hz, 1H), 8.03 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ −1.5 (3C), 22.2, 59.9, 110.2, 116.7, 120.0, 123.7, 126.8, 131.9, 138.0, 146.4. Anal. Calcd for $C_{13}H_{19}N_3Si$: C, 63.63; H, 7.80; N, 17.12. Found: C, 63.37; H, 8.15; N, 17.42.

General Procedure for the Synthesis of Compounds 3a−e and 11a. To a solution of **2** (0.98 g, 4 mmol) in THF (50 mL) at −78 °C under argon was added *n*-BuLi (1.52 M, 2.9 mL, 4.1 mmol). After the mixture was stirred for 15 min, a solution of the appropriate alkyl halide (4.1 mmol) in THF (5 mL) was added. The reaction mixture was allowed to warm to room temperature overnight, before being washed with water (2 × 20 mL), extracted with ethyl ether (2 × 20 mL), and dried (Na_2SO_4). The crude oil left after the solvent was removed under reduced pressure was subjected to column chromatography with hexanes:ethyl acetate = 8:1 to give the pure product.

1-{1-Hexyl-1-[(trimethylsilyl)methyl]prop-2-enyl}-1*H*-1,2,3-benzotriazole (3a): colorless oil (1.00 g, 82%): ^1H NMR δ −0.26 (s, 9H), 0.72 (t, J = 6.8 Hz, 3H), 1.09−1.20 (m, 8H), 1.70 (d, J = 14.8 Hz, 1H), 1.79 (d, J = 14.9 Hz, 1H), 2.18−2.38 (m, 2H), 5.16 (d, J = 17.6 Hz, 1H), 5.27 (d, J = 11.0 Hz, 1H), 6.12 (dd, J = 17.6 and 10.8 Hz, 1H), 7.18−7.29 (m, 2H), 7.52 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H); ^{13}C NMR δ −0.1 (3C), 13.9, 22.4, 23.5, 26.9, 29.2, 31.5, 39.2, 69.1, 112.7, 115.1, 119.9, 123.3, 126.1, 132.3, 142.2, 147.0. Anal. Calcd for $C_{19}H_{31}N_3Si$: C, 69.24; H, 9.50; N, 12.75. Found: C, 68.92; H, 9.75; N, 12.71.

1-{1-Decyl-1-[(trimethylsilyl)methyl]prop-2-enyl}-1*H*-1,2,3-benzotriazole (3b): colorless oil (1.39 g, 90%): ^1H NMR δ −0.18 (s, 9H), 0.84 (t, J = 5.7 Hz, 3H), 1.12−1.28 (m, 16H), 1.78 (d, J = 14.9 Hz, 1H), 1.87 (d, J = 14.9 Hz, 1H), 2.25−2.42 (m, 2H), 5.24 (d, J = 17.4 Hz, 1H), 5.35 (d, J = 10.7 Hz, 1H), 6.20 (dd, J = 17.4 and 10.7 Hz, 1H), 7.26−7.36 (m, 2H), 7.60 (d, J = 7.9 Hz, 1H), 8.03 (d, J = 7.9 Hz, 1H); ^{13}C NMR δ −0.1 (3C), 14.0, 22.6, 23.5, 26.9, 29.2, 29.3, 29.4, 29.6, 29.7, 31.8, 39.2, 69.1, 112.7, 115.0, 120.0, 123.3, 126.1, 132.3, 142.3, 147.0. Anal. Calcd for $C_{23}H_{39}N_3Si$: C, 71.63; H, 10.19; N, 10.90. Found: C, 71.95; H, 10.47; N, 10.66.

1-{1-Dodecyl-1-[(trimethylsilyl)methyl]prop-2-enyl}-1*H*-1,2,3-benzotriazole (3c): colorless oil (1.33 g, 86%): ^1H NMR δ −0.16 (s, 9H), 0.87 (t, J = 6.1 Hz, 3H), 1.18−1.27 (m, 20H), 1.80 (d, J = 14.9 Hz, 1H), 1.89 (d, J = 14.9 Hz, 1H), 2.26−2.44 (m, 2H), 5.26 (d, J = 17.5 Hz, 1H), 5.38 (d, J = 10.8 Hz, 1H), 6.22 (dd, J = 17.5 and 10.8 Hz, 1H), 7.30 (t, J = 6.6 Hz, 1H), 7.36 (t, J = 6.6 Hz, 1H), 7.62 (d, J = 8.1 Hz, 1H), 8.05 (d, J = 8.1 Hz, 1H); ^{13}C NMR δ −0.1 (3C), 14.1, 22.6, 23.5, 26.9, 29.2, 29.3, 29.4, 29.5, 29.6, 31.8, 39.2, 69.1, 112.7, 115.0, 120.0, 123.3, 126.1, 132.3, 142.2, 147.0. Anal. Calcd for $C_{25}H_{43}N_3Si$: N, 10.16. Found: N, 10.32.

1-{1-Propyl-1-[(trimethylsilyl)methyl]prop-2-enyl}-1*H*-1,2,3-benzotriazole (3d): colorless oil (1.50 g, 87%): ^1H NMR δ −0.10 (s, 9H), 0.91 (t, J = 6.9 Hz, 3H), 0.97−1.05 (m, 1H), 1.33−1.43 (m, 1H), 1.87 (d, J = 14.8 Hz, 1H), 1.96 (d, J = 14.5 Hz, 1H), 2.31−2.52 (m, 2H), 5.33 (d, J = 17.6 Hz, 1H), 5.44 (d, J = 10.7 Hz, 1H), 6.28 (dd, J = 17.6 and 10.7 Hz, 1H), 7.35−7.45 (m, 2H), 7.68 (d, J = 8.2 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H); ^{13}C NMR δ −0.2 (3C), 13.9, 16.8, 26.8, 41.3, 69.0, 112.7, 115.0, 119.9, 123.3, 126.1, 132.3, 142.1, 146.9. Anal. Calcd for $C_{16}H_{25}N_3Si$: C, 66.84; H, 8.78. Found: C, 66.62; H, 8.59.

1-{1-Benzyl-1-[(trimethylsilyl)methyl]prop-2-enyl}-1*H*-1,2,3-benzotriazole (3e): colorless oil (2.90 g, 85%): ^1H NMR δ −0.11 (s, 9H), 1.62 (d, J = 14.6 Hz, 1H), 2.06 (d, J = 14.6 Hz, 1H), 3.59 (s, 2H), 5.36 (d, J = 17.6 Hz, 1H), 5.47 (d, J = 10.9 Hz, 1H), 6.35 (dd, J = 10.9 and 17.5 Hz, 1H), 6.61(d, J = 7.3 Hz, 1H), 7.00−7.20 (m, 3H), 7.32−7.40 (m, 2H), 7.58 (d, J = 8.5 Hz, 1H), 8.06 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 0.3 (3C), 27.6, 46.0, 69.1, 112.7, 115.7, 120.0, 123.4, 126.3, 126.8, 127.8, 130.4, 132.7, 135.3, 141.5, 146.9. HRMS (M + 1, FAB) calcd for $C_{20}H_{26}N_3Si$: 336.1896 (M + 1). Found: 336.1898.

1-(1*Z*,5*E*)-6-Phenyl-1-[(trimethylsilyl)methyl]hexa-1,5-dienyl-1*H*-1,2,3-benzotriazole (11a): yellow oil (1.21 g, 84%): ^1H NMR δ −0.15 (s, 9H), 2.47−2.55 (m, 6H), 5.78 (t, J = 6.7 Hz, 1H), 6.28−6.39 (m, 1H), 6.54 (d, J = 15.7 Hz, 1H), 7.24−7.46 (m, 7H), 7.64 (d, J = 8.0 Hz, 1H), 8.09 (d, J = 8.0

Hz, 1H); ^{13}C NMR δ −1.6 (3C), 21.2, 27.5, 32.8, 110.9, 119.9, 120.7, 123.8, 125.9, 127.1, 127.4, 128.4, 129.2, 131.0, 132.1, 135.2, 137.2, 145.9. Anal. Calcd for $C_{22}H_{27}N_3Si$: N, 11.62. Found: N, 11.62.

General Procedure for the Synthesis of Compounds 4a−c. The corresponding **3a−c** (2 mmol) was heated under argon and stirred at 130−135 °C for 8−12 h. The cold reaction mixture was dissolved in diethyl ether (40 mL), washed with NaOH solution (10%, 2 × 20 mL) and water (2 × 20 mL), and then dried (Na_2SO_4). After the solvent was removed under reduced pressure, the remaining crude oil was subjected to column chromatography with hexanes:ethyl acetate = 40:1 to afford the pure product.

2-Hexylbuta-1,3-diene (4a): colorless oil (lit.[12] oil) (0.20 g, 70%): ^{1}H NMR δ 0.93 (t, J = 6.9 Hz, 3H), 1.20−1.45 (m, 6H), 1.45−1.60 (m, 2H), 2.24 (t, J = 8.0 Hz, 2H), 5.02−5.03 (m, 2H), 5.07 (d, J = 10.9 Hz, 1H), 5.26 (d, J = 17.6 Hz, 1H), 6.40 (dd, J = 17.6 and 10.7 Hz, 1H); ^{13}C NMR δ 14.1, 22.7, 28.2, 29.3, 31.4, 31.8, 113.0, 115.4, 139.1, 146.7.

2-Decylbuta-1,3-diene (4b): colorless oil (0.32 g, 64%): ^{1}H NMR δ 0.91 (t, J = 6.8 Hz, 3H), 1.20−1.40 (m, 14H), 1.49−1.54 (m, 2H), 2.22 (t, J = 8.0 Hz, 2H), 5.01−5.02 (m, 2H), 5.07 (d, J = 10.8 Hz, 1H), 5.25 (d, J = 17.6 Hz, 1H), 6.40 (dd, J = 17.6 and 10.7 Hz, 1H); ^{13}C NMR δ 14.1, 22.7, 28.2, 29.4, 29.6, 29.7, 31.4, 32.0, 113.0, 115.4, 139.1, 146.7; HRMS (EI) calcd for $C_{14}H_{26}$: 194.2035. Found: 194.2013.

2-Dodecylbuta-1,3-diene (4c): colorless oil (0.40 g, 90%): ^{1}H NMR δ 0.91 (t, J = 6.5 Hz, 3H), 1.20−1.35 (m, 18H), 1.46−1.53 (m, 2H), 2.22 (t, J = 7.6 Hz, 2H), 5.00−5.02 (m, 2H), 5.07 (d, J = 10.8 Hz, 1H), 5.25 (d, J = 17.6 Hz, 1H), 6.40 (dd, J = 17.6 and 10.8 Hz, 1H); ^{13}C NMR δ 14.1, 22.7, 28.2, 29.4, 29.6, 29.7, 31.4, 32.0, 113.0, 115.4, 139.1, 146.7; HRMS (EI) calcd for $C_{16}H_{30}$: 222.2348. Found: 222.2351.

General Procedure for the Synthesis of Compounds 5a,b. BuLi in hexanes (1.4 M, 3.7 mL, 5.1 mmol) was added to a solution of **1** (0.80 g, 5 mmol) in THF (50 mL) at −78 °C. After stirring for 30 min at −78 °C, a solution of chloromethyltrimethylsilane (0.63 g, 5.1 mmol) in THF (5 mL) was added, and the reaction mixture was allowed to warm to room temperature overnight. The reaction mixture was cooled to −78 °C and BuLi in hexanes (1.4 M, 3.6 mL, 5.0 mmol) was added. After 15 min a solution of 1-iodopropane (0.48 mL, 5.0 mmol), in the case of **5a**, or benzyl bromide (0.86 g, 5.0 mmol) in THF (5 mL), in the case of **5b**, was added. After the reaction reached rt overnight, the mixture was washed with water (2 × 20 mL), extracted with diethyl ether (2 × 20 mL), and dried (Na_2SO_4). After the filtration of the drying agent, the solvent was removed from the filtrate, and the remaining oil was purified as previously described to afford **3d,** in the case of **5a**, or the solution was used without purification, in the case of **5b**. In the case of **5a**, *N*-phenylmaleinimide was added (0.45 g, 2.6 mmol) to a solution of **3d** (0.50 g, 1.7 mmol) in methylene chloride (30 mL) followed by slow addition of trifluoroacetic acid (0.8 mL, 10 mmol). After being stirred for 2 h at room temperature, the mixture was washed with sodium hydroxide aqueous solution (0.5 M, 20 mL) and dried (Na_2SO_4) and had the solvent removed. In the case of **5b**, *N*-phenylmaleinimide was added (1.04 g, 6.0 mmol) to the ether solution, and the mixture was heated under reflux for 1 h. The solvent was removed by distillation under a stream of nitrogen, and the remaining oil was heated at 75−80 °C for 6 h. The cold reaction mixture was dissolved in diethyl ether (40 mL), washed with sodium carbonate (10%, 40 mL) and water (40 mL), and then dried (Na_2SO_4). In both cases the remaining crude oil was subjected to column chromatography with hexanes:ethyl acetate = 2:1 to give the pure product.

2-Phenyl-5-propyl-3a,4,7,7a-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione (5a): colorless oil (0.40 g, 65% yield): ^{1}H NMR δ 0.86 (t, J = 7.1 Hz, 3H), 1.25−1.48(m, 2H), 2.02 (t, J = 7.4 Hz, 2H), 2.25−2.32 (m, 2H), 2.61−2.74 (m, 2H), 3.20−3.30 (m, 2H), 5.62 (m, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.36−7.49 (m, 3H); ^{13}C NMR δ 13.7, 20.4, 24.3, 27.6, 39.2, 39.4, 39.7, 119.9, 126.3, 128.4, 129.0, 132.0, 140.6, 179.1, 179.3. Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.80; H, 7.12; N, 5.20. Found: C, 75.46; H, 7.24; N, 5.42.

2-Phenyl-5-(phenylmethyl)-3a,4,7,7a-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione (5b): yellow oil (0.86 g, 54%): ^{1}H NMR δ 2.22−2.34 (m, 2H), 2.58 (d, J = 15.5 Hz, 1H), 2.69 (dd, J = 15.5 and 6.6 Hz, 1H), 3.15−3.20 (m, 2H), 3.34 (s, 2H), 5.62−5.66 (m, 1H), 7.09−7.26 (m, 6H), 7.34−7.46 (m, 4H); ^{13}C NMR δ 24.4, 27.6, 39.3, 39.6, 43.7, 121.6, 126.3, 128.4, 128.9, 129.0, 132.0, 138.5, 139.9, 178.7, 179.1. HRMS (M + 1, FAB) calcd for $C_{21}H_{19}NO_2$: 318.1494 (M + 1). Found: 318.1497.

General Procedure for the Synthesis of Compounds 8a,e and 11b−e. To a solution of **2** (0.98 g, 4 mmol) in THF (50 mL) at −78 °C under argon was added BuLi (1.52 M, 2.9 mL, 4.1 mmol). After the mixture was stirred for 15 min, a solution of the appropriate aldehyde (4.1 mmol) in THF (5 mL) was added. The reaction mixture was allowed to warm to room temperature overnight before being washed with water (2 × 20 mL), extracted with diethyl ether (2 × 20 mL), and dried (Na_2SO_4). The crude oil left after the solvent was removed under reduced pressure was subjected to column chromatography to give the pure product.

4-(1*H*-1,2,3-Benzotriazol-1-yl)-1-phenyl-4-[(trimethylsilyl)methyl]hex-5-en-3-ol (8a): yellow oil (1.52 g, 80%), 1.3:1 mixture of diastereomers (minor diastereomer in square brackets): ^{1}H NMR δ −0.10 (s, 9H) [−0.24 (s, 9H)], 1.71−2.21 (m, 4 + [4]H), 2.85−2.95 (m, 2H) [3.15−3.30 (m, 2H)], 4.08 (s, 1H) [4.09 (s, 1H)], 4.74−4.79 (m, 1H) [5.10−5.13 (m, 1H)], 5.36 (d, J = 18.0 Hz, 1H) [5.53 (d, J = 18.0 Hz, 1H)], 5.58 (d, J = 11.4 Hz, 1H) [5.70 (d, J = 11.4 Hz, 1H)], 6.32 (dd, J = 17.5 and 10.8 Hz, 1H) [6.55 (dd, J = 17.5 and 10.8 Hz, 1H)], 7.34−7.58 (m, 7 + [7]H), 7.77 (d, J = 7.8 Hz, 1H) [7.78 (d, J = 7.8 Hz, 1H)], 8.22 (d, J = 7.8 Hz, 1 + [1]H); ^{13}C NMR δ −0.1 [−0.8] (3C), 22.5 [23.0], 32.5 [32.4], 33.0 [32.9], 73.4 [73.2], 75.6 [73.7], 113.1 [112.8], 117.3 [117.6], 119.9, 123.7 [123.8], 125.7 [125.8], 126.7 [126.9], 128.2 [128.3], 128.4 [128.5], 132.6 [132.7], 139.5 [138.2], 141.7 [141.9], 146.2 [146.4]. HRMS calcd for $C_{25}H_{43}N_3Si$: 380.2158 (M + 1). Found: 380.2144 (M + 1, FAB).

2-(1*H*-1,2,3-Benzotriazol-1-yl)-1-(4-chlorophenyl)-2-[(trimethylsilyl)methyl]but-3-en-1-ol (8e): hexanes:diethyl ether = 1:1 (eluent); yellow oil (0.79 g, 52%), 2.7:1 mixture of diastereomers (minor diastereomer in square brackets): ^{1}H NMR δ −0.01 (s, 9H) [−0.13 (s, 9H)], 1.75 (d, J = 15.0 Hz, 2H) [2.14 (d, J = 15.0 Hz, 2H)], 5.37 (d, J = 17.7 Hz, 2H) [5.68 (d, J = 10.8 Hz, 2H)], 5.78 (s, 1H) [6.11 (s, 1H)], 6.41 (dd, J = 18.0 and 12.0 Hz, 1H) [6.70 (dd, J = 18.0 and 12.0 Hz, 1H)], 7.17 (d, J = 8.7 Hz, 2 + [2]H), 7.38−7.64 (m, 4 + [4]H), 7.84 (d, J = 8.0 Hz, 1 + [1]H), 8.27 (d, J = 8.0 Hz, 1 + [1]H); ^{13}C NMR δ 0.3 [-0.1] (3C), 24.1 [23.6], 73.4 [73.3], 79.4, 113.8 [113.1], 117.4 [119.2], 120.0 [120.1], 123.8 [124.0], 126.7 [127.0], 127.9 [127.7], 129.7 [130.1], 133.4, 134.0, 136.8, 138.7, 146.4. Anal. Calcd for $C_{20}H_{24}N_3ClOSi$: C, 62.24; H, 6.27; N, 10.89. Found: C, 61.86; H, 6.56; N, 11.03.

6-(1*H*-1,2,3-Benzotriazol-1-yl)-6-[(trimethylsilyl)methyl]-2-methylhex-5-en-3-ol (11c): hexanes:EtOAc = 8:1; yellow oil (0.34 g, 22%): ^{1}H NMR δ −0.20 (s, 9H), 1.01 (d, J = 6.7 Hz, 6H), 1.75−1.85 (m, 1H), 2.39−2.51 (m, 2H), 2.46 (s, 2H), 3.55−3.60 (m, 1H), 5.87 (t, J = 7.2 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ −1.5 (3C), 17.4, 18.8, 21.3, 32.7, 33.5, 76.3, 111.0, 118.5, 120.0, 124.0, 127.6, 132.2, 136.4, 146.0. Anal. Calcd for $C_{17}H_{27}N_3OSi$: N, 13.24. Found: N, 13.35.

6-(1*H*-1,2,3-Benzotriazol-1-yl)-6-[(trimethylsilyl)methyl]-2,2-dimethylhex-5-en-3-ol (11d): hexanes:EtOAc = 8:1; yellow oil (1.37 g, 83%): ^{1}H NMR δ −0.20 (s, 9H), 1.00 (s, 9H), 2.24−2.54 (m, 5H), 3.42 (m, 1H), 5.91 (t, J = 7.2 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.6 Hz, 1H), 7.68 (d, J = 8.3 Hz, 1H), 8.02 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ −1.5 (3C), 21.1, 25.7 (3C), 30.0, 35.0, 79.3, 111.1, 119.6, 119.8, 123.9, 127.5, 132.1, 135.9, 145.9. Anal. Calcd for $C_{17}H_{27}N_3OSi$: N, 12.67. Found: N, 12.61.

4-(1*H*-1,2,3-Benzotriazol-1-yl)-1-(4-chlorophenyl)-5-(trimethylsilyl)-3-penten-1-ol (11e): hexanes:EtOAc = 3:1; yellow oil (0.45 g, 30%): ^{1}H NMR δ −0.22 (s, 9H), 2.39(s, 2H), 2.66−2.81 (m, 2H), 3.00 (br s, 1H), 4.89 (t, J = 6.6 Hz, 1H), 5.74 (t, J = 7.2 Hz, 1H), 7.08−7.50 (m, 7H), 8.00 (d, J = 8.2 Hz, 1H); ^{13}C NMR δ −1.6 (3C), 21.3, 37.5, 73.0, 110.9, 116.9, 119.9, 124.1, 127.2, 127.7, 128.7, 132.1, 133.5, 137.0, 142.4,

145.8. Anal. Calcd for $C_{20}H_{24}N_3OSiCl$: C, 62.23; H, 6.28; N, 10.89. Found: C, 61.87; H, 6.61; N, 11.01.

General Procedure for the Synthesis of Compounds 7a−c. To a solution of **2** (0.98 g, 4 mmol) in THF (50 mL) at −78 °C under argon was added *n*-BuLi (1.52 M, 2.9 mL, 4.1 mmol). After the mixture was stirred for 15 min, a solution of the appropriate aldehyde (4.1 mmol) in THF (5 mL) was added. The reaction mixture was allowed to warm to room temperature overnight and then refluxed in THF under argon for 3 h. Upon being cooled, the reaction mixture was washed with saturated aqueous ammonium chloride solution (40 mL), HCl (10%, 2 × 20 mL), and water (2 × 20 mL) before being extracted with diethyl ether (2 × 20 mL) and dried (Na_2SO_4). The crude oil left after the solvent was removed under reduced pressure was subjected to column chromatography to give the pure product.

4-Methylidene-1-phenylhex-5-en-3-ol (7a): yellow oil (lit.[8a] oil), 0.69 g, 74%: ^{1}H NMR δ 1.80−2.02 (m, 3H), 2.67−2.83 (m, 2H), 4.41 (dd, J = 7.3 and 3.8 Hz, 1H), 5.05 (d, J = 11.3 Hz, 1H), 5.15 (s, 1H), 5.20 (d, J = 18.0 Hz, 1H), 5.26 (s, 1H), 6.32 (dd, J = 18.0 and 11.3 Hz, 1H), 7.15−7.30 (m, 5H); ^{13}C NMR δ 32.0, 37.9, 70.6, 114.1, 114.3, 125.8, 128.3, 128.5, 136.1, 141.9, 149.1.

3-Methylidene-1,1-methylphenylpent-4-en-2-ol (7b): yellow oil, 0.45 g, 60%: ^{1}H NMR δ 1.23 (d, J = 7.1 Hz, 3H), 1.79 (s, 1H), 3.02−3.11 (m, 1H), 4.51 (d, J = 4.4 Hz, 1H), 5.09 (d, J = 11.0 Hz, 1H), 5.16 (s, 1H), 5.20 (s, 1H), 5.33 (d, J = 17.6 Hz, 1H), 6.31 (dd, J = 17.9 and 11.3 Hz, 1H), 7.17−7.32 (m, 5H); ^{13}C NMR δ 13.6, 42.9, 75.3, 114.1, 115.3, 126.3, 127.7, 128.3, 136.4, 144.5, 147.0. Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.58. Found: C, 82.61; H, 8.48.

2-Methyl-4-methylidenehex-5-en-3-ol (7c): yellow oil (lit.[1a] oil), 0.56 g, 72%: ^{1}H NMR δ 0.93 (d, J = 6.6 Hz, 6H), 1.72 (br s, 1H), 1.80−2.00 (m, 1H), 4.12 (d, J = 5.8 Hz, 1H), 5.10 (d, J = 11.1 Hz, 1H), 5.17 (s, 1H), 5.20 (s, 1H), 5.36 (d, J = 17.9 Hz, 1H), 6.33 (dd, J = 11.0 and 17.6 Hz, 1H); ^{13}C NMR δ 16.9, 19.6, 32.0, 77.2, 114.4, 114.6, 136.2, 148.3.

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