Silicon-Substituted Dienes in the Intramolecular Diels-Alder Reaction: Nagilactone Model Studies

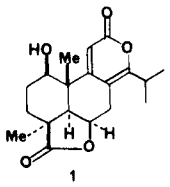
Steven D. Burke,* Sharon M. Smith Strickland, and Tory H. Powner

Department of Chemistry, University of South Carolina, Columbia, South Carolina 29208

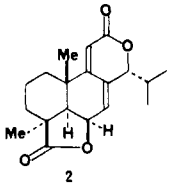
Received January 27, 1982

The syntheses of 1-(2-propenoxy)-3-[*trans*-β-(trimethylsilyl)vinyl]cyclohex-2-ene (**6a**), 1-(2-methyl-2-propenoxy)-3-[*trans*-β-(trimethylsilyl)vinyl]cyclohex-2-ene (**7a**), 1-(3-methyl-2-butenoxy)-3-[*trans*-β-(trimethylsilyl)vinyl]cyclohex-2-ene (**8a**), and the 5,5-dimethyl analogues **6b**, **7b**, and **8b** are described. The thermolyses of these substrates to give the tricyclic adducts **9a,b**, **10a,b**, and **11a** are described, demonstrating the viability of the trimethylsilyl-terminated butadiene unit as a useful moiety for the intramolecular Diels-Alder cycloaddition with unactivated olefin sites in cases with minimal steric demand. The desilylated substrate **14** corresponding to the triene **6b** was prepared and thermolyzed to give the tricyclic adduct **15**. Qualitatively, the substrates **6b** and **14** were found to be comparable in reactivity, thus the trimethylsilyl substituent in **6b** exerts no major influence on the course of the cycloaddition. Finally, the tricyclic lactones **20a,b** were prepared by the thermolysis of the mixed fumarates **19a,b**.

We have initiated a program targeting for total synthesis the nagilactones, isolated from the seeds and root bark of *Podocarpus nagi*.[1] Members of this class of natural products show biological activity as antitumor agents,[2] plant growth promoters,[3] and insect larvae toxins.[4] Nagilactones A (**1**)[1a] and F (**2**)[1a] are representative structures.



1

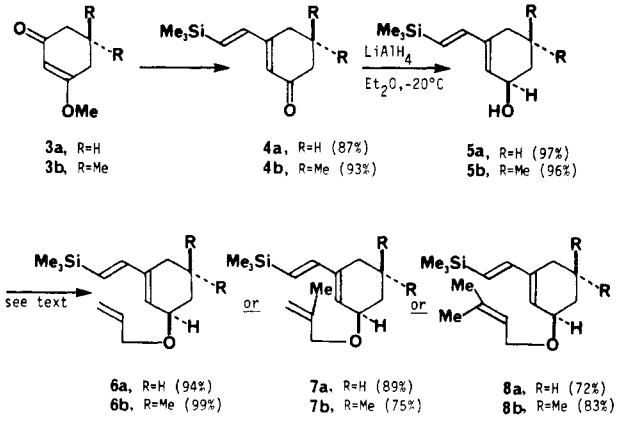


2

We report herein preliminary studies that demonstrate the viability of the trimethylsilyl-substituted butadiene unit[5] as an intramolecular Diels-Alder partner with *unactivated* dienophilic components for the rapid construction of a tricyclic model system.

It was felt that advantage could be derived from utilizing a heteroatom-carbon bond as a tether to force the key carbon-carbon bond-forming process to occur in an intramolecular fashion, fusing two rings simultaneously to a preestablished six-membered carbocycle (eq 1).[6] Within certain limitations (vide infra), this general strategy proved feasible, affording a short and efficient entry to the desired tricyclics.

Scheme I[15]



3a, R=H; **3b**, R=Me

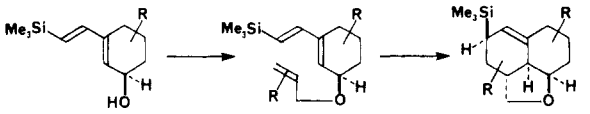
4a, R=H (87%); **4b**, R=Me (93%)

5a, R=H (97%); **5b**, R=Me (96%)

6a, R=H (94%); **6b**, R=Me (99%)

7a, R=H (89%); **7b**, R=Me (75%)

8a, R=H (72%); **8b**, R=Me (83%)



(1)

The preparation of ethers **6a,b**, **7a,b**, and **8a,b** as substrates for the intramolecular Diels-Alder reaction is outlined in Scheme I. For example, addition of *trans*-β-(trimethylsilyl)vinyllithium[7] to a solution of the vinylogous ester **3a** in tetrahydrofuran (THF; −78 → 25 °C) followed by an aqueous acid quench provided 3-[*trans*-β-(trimethylsilyl)vinyl]cyclohex-2-en-1-one (**4a**) in 87% yield. Reaction at −20 °C with an ethereal suspension of lithium aluminum hydride gave in 97% yield the corresponding alcohol **5a**.[8] Conversion to the allyl ether **6a** was

(1) For a comprehensive bibliography of the structural elucidation of the nagilactones, see: (a) Hayashi, Y.; Matsumoto, T.; Sakan, T. *Heterocycles* **1978**, *10*, 123. For a completed synthesis of nagilactone F, see: (b) Hayashi, Y.; Matsumoto, T.; Hyono, T.; Nishikawa, N.; Uemura, M.; Nishizawa, M.; Togami, M.; Sakan, T. *Tetrahedron Lett.* **1979**, 3311. For synthetic efforts in closely related systems, see: (c) Adinolfi, M.; Mangoni, L.; Barone, G.; Laonigro, G. *Ibid.* **1972**, 695. (d) Adinolfi, M.; Mangoni, L.; Barone, G.; Laonigro, G. *Gazz. Chim. Ital.* **1973**, *103*, 1271. (e) Mangoni, L.; Adinolfi, M.; Laonigro, G.; Caputo, R. *Tetrahedron* **1972**, *28*, 611. (f) Welch, S. C.; Hagan, C. P.; White, D. H.; Fleming, W. P.; Trotter, J. W. *J. Am. Chem. Soc.* **1977**, *99*, 549.

(2) (a) Hayashi, Y.; Sakan, T.; Sakurai, Y.; Tashiro, T. *Gann* **1975**, *66*, 587. (b) Kupchan, S. M.; Baxter, R. L.; Ziegler, M. F.; Smith, P. M.; Bryan, R. F. *Experentia* **1975**, *31*, 137. (c) Hayashi, Y.; Matsumoto, T.; Tashiro, T. *Gann* **1979**, *70*, 365 and references cited therein.

(3) (a) Hayashi, T.; Yokoi, J.; Watanabe, Y.; Sakan, T.; Masuda, Y.; Yamamoto, R. *Chem. Lett.* **1972**, 759. (b) Hayashi, Y.; Sakan, T. "Plant Growth Substances 1973"; Hirokawa Publishing Co.: Tokyo, 1974. (c) Galbraith, M. N.; Horn, D. H. S.; Ito, S.; Kodama, M.; Sasse, J. M. *Agric. Biol. Chem.* **1972**, *36*, 2393.

(4) Russell, G. B.; Fenemore, P. G.; Singh, P. *J. Chem. Soc., Chem. Commun.* **1973**, 166.

(5) For other examples of 1-trimethylsilyl-substituted dienes as intermolecular Diels-Alder substrates, see: (a) Jung, M. E.; Gaede, B. *Tetrahedron* **1979**, *35*, 621. (b) Fleming, I.; Percival, A. *J. Chem. Soc., Chem. Commun.* **1978**, 178. (c) Fleming, I.; Percival, A. *Ibid.* **1976**, 681. (d) Sleta, T. M.; Standnichuk, M. D.; Petrov, A. A. *Zh. Obshch. Khim.* **1968**, *38*, 374. (e) Standnichuk, M. D.; Petrov, A. A. *Ibid.* **1963**, *33*, 3563. (f) Sadykh-Zade, S. I.; Petrov, A. D. *Ibid.* **1958**, *28*, 1542. (g) Carter, M. J.; Fleming, I.; Percival, A. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2415. For an account of an intramolecular Diels-Alder reaction involving a 1-trimethylsilyl-substituted diene, see: (h) Oppolzer, W.; Burford, S. C.; Marazza, F. *Helv. Chim. Acta* **1980**, *63*, 555.

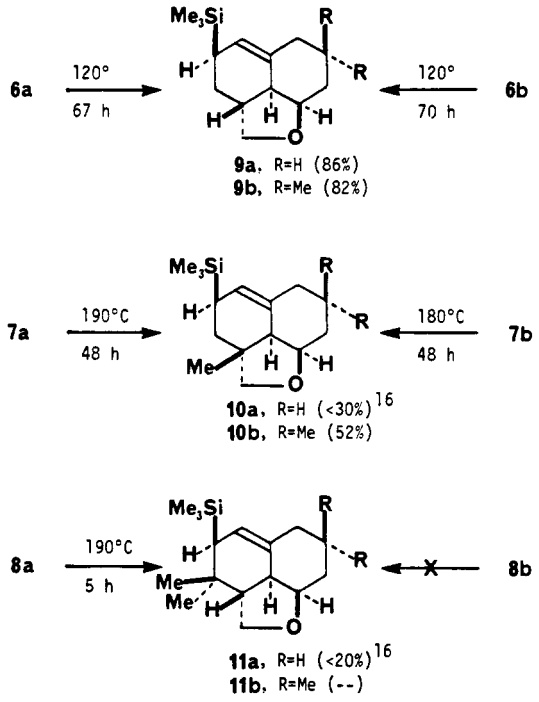
(6) The following articles review the intramolecular Diels-Alder cycloadditions: (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. (b) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63. (c) Mehta, G. *J. Chem. Educ.* **1976**, *53*, 551.

(7) Cunico, R. R.; Clayton, F. J. *J. Org. Chem.* **1976**, *41*, 1480.

(8) For a report describing with experimental detail the synthesis of alcohol **5b** for a separate study, see: Burke, S. D.; Murtiashaw, C. W.; Dike, M. S.; Strickland, S. M. S.; Saunders, J. O. *J. Org. Chem.* **1981**, *46*, 2400.

0022-3263/83/1948-0454$01.50/0

Scheme II



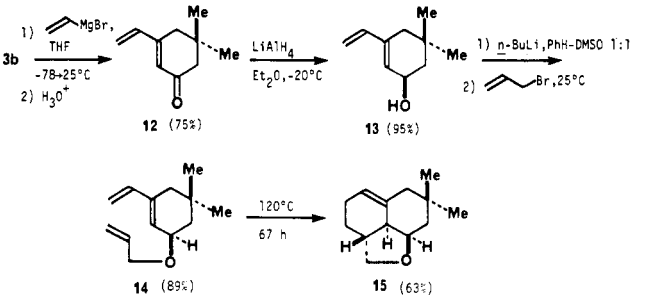
effected in 94% yield by treatment of **5a** in 1:1 benzene–dimethyl sulfoxide with *n*-butyllithium (1.5 equiv, 0 → 25 °C) followed by the addition of 3 equiv of allyl bromide. The sequential conversion of **3b** to **6b** was accomplished by similar means.

The prenyl ethers **8a** and **8b** were prepared from the alcohols **5a** and **5b** in 72% and 83% yields, respectively, in a manner strictly analogous to the preparation of the allyl ethers **6a,b**. However, the methallyl ethers **7a** and **7b** were formed in satisfactory yields (89% and 75%, respectively) only when the appropriate lithium alkoxide, derived from **5a** or **5b**, was converted to the corresponding quaternary ammonium alkoxide[9] and the O-methallylation was done at elevated temperature. For example, treatment of **5a** in 1:1 *o*-xylene–dimethyl sulfoxide with *n*-BuLi (1.5 equiv, 0 → 25 °C) was followed by the addition of tetra-*n*-butylammonium iodide (10 mol %) and methallyl chloride (3 equiv). After having stirred at reflux for 30 min, the reaction mixture afforded the methallyl ether **7a** in 89% yield after chromatography.

With the allyl (**6a,b**), methallyl (**7a,b**), and prenyl (**8a,b**) ethers thus secured, it remained to find optimal conditions for the intramolecular Diels–Alder cycloaddition reaction of each. This range of substrates was chosen to provide a probe of the effect of increasing steric demand in the transition state upon the efficacy of the cycloaddition. When the allyl ether **6a** was sealed in a Pyrex tube as a neat, degassed liquid and heated at 120 °C for 67 h, there was obtained in 86% yield after chromatography the corresponding tricyclic **9a** as a low-melting (32 °C) solid (Scheme II). Similarly, thermolysis of **6b** as a neat liquid in a sealed Pyrex tube at 120 °C for 70 h provided the tricyclic adduct **9b** in 82% yield. As the steric demand in the dienophilic partner increased, the cycloaddition became less favorable, with elimination processes competing effectively. This is reflected (Scheme II) in the diminished yields of tricyclic adducts observed in the thermolyses of the methallyl ethers (**7a,b**) and the prenyl ethers (**8a,b**).

(9) Czernecki, S.; Georgoulis, C.; Provelenghiou, G. *Tetrahedron Lett.* **1976**, 3535.

Scheme III



As a part of a study of the *intermolecular* Diels–Alder cycloaddition of 1-(trimethylsilyl)butadiene with standard dienophiles, Fleming noted surprisingly low regioselectivities along with reactivities 10- and 1000-fold less than butadienes lacking the silyl substituent.[5g] Although regiochemical control was not an issue in our Diels–Alder reactions, we were curious to see how the trimethylsilyl group influenced the diene reactivity in these *intramolecular* cycloadditions.[10] To this end (Scheme III), we prepared the analogous "desilylated" Diels–Alder substrate **14** for comparison with **6b**. As shown in the scheme, the conversion of **3b** to **14** followed closely the methodology for **6b** (vide supra; see Experimental Section for details).

Thermolysis of **14** as a neat liquid in a sealed Pyrex tube was then examined at various temperatures. We found that the reactivities of **6b** and **14** toward intramolecular cycloaddition were roughly equal. Indeed, the optimal conditions for the production of the cycloadduct **15** were 120 °C for 67 h—nearly identical with those employed for the **6b** → **9b** conversion. Lower temperatures (80 °C, 102 h, 7.5% of **15**; 100 °C, 165 h, 35% of **15**) resulted in incomplete conversion of **14** and thus decreased yields of the tricyclic **15**. Higher temperatures (e.g., 200 °C, 46 h, 23% of **15**, 20% elimination) again gave diminished amounts of the cycloadduct **15**, with elimination of the allyloxy substituent competing effectively, along with polymerization. Thus, we found the trimethylsilyl group to exert little influence on the rate of this *intramolecular* cycloaddition, as one might expect.

Of course, the nagilactone natural products (e.g., **1** and **2**) have γ-lactones, *not* tetrahydrofurans, as structural subunits. Although methods exist[11] for the oxidation of cyclic ethers to lactones, their general brutality encouraged us to examine a more direct lactone generation. Thus, we prepared the acrylates **16a,b**. These proved to be rather sensitive compounds, difficult to purify, which gave only products of elimination and polymerization upon thermolysis or subjection to Lewis acid catalysis (Et_2AlCl). In order to avoid manipulating the unstable acrylates **16a,b**, we then prepared the dimethylfulvene acrylate generator **18**.[12] This, too, failed to yield **17**, the expected product of intramolecular Diels–Alder cycloaddition.

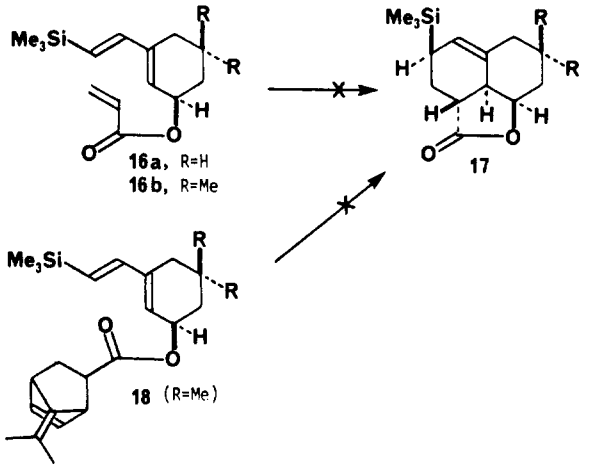
The failure of the acrylates **16a,b** to demonstrate the desired reactivity led us to examine the mixed fumarates **19a,b**, prepared in high yield by the acylation of the corresponding allylic alcohols **5a,b** with *trans*-β-carbethoxyacryloyl chloride.[13] The fumaryl residues in **19a** and **19b** proved to be acceptable cycloaddends, providing the tri-

(10) We acknowledge a referee, similarly curious, who suggested that we include the data on the "desilylated" material.

(11) For recent advances, see: (a) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936–3938. (b) Smith, A. B.; Scarborough, R. M. *Synth. Commun.* **1980**, *10*, 205–211.

(12) Ichihara, A.; Kimura, R.; Yamada, S.; Sakamura, S. *J. Am. Chem. Soc.* **1980**, *102*, 6353–6355 and references cited therein.

(13) Eisner, U.; Elvidge, J. A.; Linstead, R. P. *J. Chem. Soc.* **1951**, 1501–1512.



cyclic lactones **20a** and **20b** in 82% and 80% yield (Scheme IV) upon thermolysis in benzene solution at 120 °C for 90 h.

The stereochemical course of the cycloadditions described was inferred qualitatively by considering the possible transition-state orientations and, more rigorously, by homonuclear decoupling ^1H NMR experiments at 400 MHz. Examination of molecular models for the allyl ether and mixed fumarate intramolecular Diels–Alder substrates revealed that the transition-state orientation in which the tether between the diene and dienophilic units is exo is readily accessible. However, the alternative orientation in which the tether is endo with respect to the diene is quite strained. We therefore expected the stereochemistry shown for the tricyclic adducts, and these expectations were confirmed by high-field ^1H NMR. For example, the coupling constant data derived from extensive homonuclear decoupling experiments on the tricyclic adducts **9b** and **20b** are summarized in Chart I.

It should be noted that in this synthetic access to the tricyclic adducts there is demonstrated an introduction of four (or five) asymmetric centers with complete relative stereocontrol, including an allylsilane moiety[14] for further elaboration. The tricyclic adducts **9a,b** and **20a,b** are thus available in yields of 60–72% from the corresponding vinylogous esters **3a,b**. This signals that the trimethylsilyl-terminated butadiene fragment is a willing partner in the intramolecular Diels–Alder reaction, even with unactivated olefinic sites. Further studies on this and related entries to the nagilactones are in progress.

Experimental Section

General Procedures. Melting points were recorded on a Büchi capillary melting point apparatus. Melting and boiling points are uncorrected. Infrared (IR) spectra were recorded on a Beckman IR 4210 spectrometer. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded at 60 (Varian EM 360), 90 (Varian EM 390), 200 (Bruker WP-200) or 400 MHz (Bruker WH-400) as indicated. Carbon magnetic resonance (^{13}C NMR) spectra were recorded on a Varian CFT-20 or an IBM NR-80 spectrometer. Multiplicities cited for the ^{13}C spectra were derived from off-resonance ^1H decoupling experiments or the application of the INEPT pulse sequence[17] technique. Chemical shifts for proton and carbon resonances are reported in parts per million (δ) relative to Me_4Si (δ 0.0).

Scheme IV

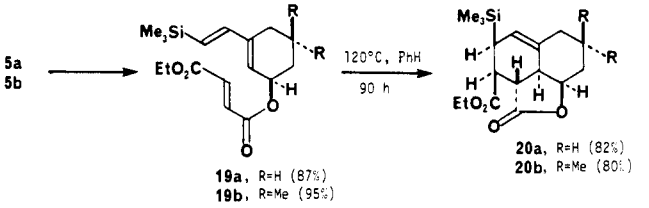
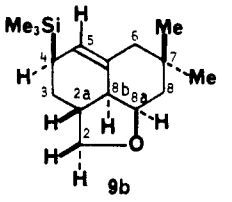
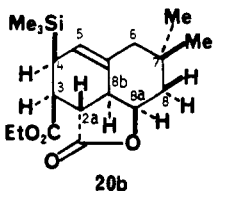


Chart I



Coupling	J (Hz)
$H_{2\alpha}$-$H_{2\beta}$(gem)	7.0
$H_{2\alpha}$-H_{2a}	11.4
$H_{2\beta}$-H_{2a}	5.7
H_{2a}-H_{8b}	13.7
H_5-H_{8b}	2.2
$H_{8\alpha}$-$H_{8\beta}$(gem)	14.9
$H_{8\alpha}$-H_{8a}	4.6
$H_{8\beta}$-H_{8a}	12.6
H_{8a}-H_{8b}	9.0



Coupling	J (Hz)
H_{2a}-H_3	11.2
H_{2a}-H_{8b}	14.6
H_3-H_4	8.3
$H_{8\alpha}$-$H_{8\beta}$(gem)	14.2
$H_{8\alpha}$-H_{8a}	4.9
$H_{8\beta}$-H_{8a}	13.2
H_{8a}-H_{8b}	8.0

Analytical thin-layer chromatography (TLC) was done on Analtech precoated TLC plates with silica gel GHLF, 250-μm layer thickness. Preparative TLC was done on Analtech plates precoated with silica gel GF, 1000-μm layer thickness. Column chromatography was done with Merck silica gel 60, 70–230 mesh ASTM, or Baker silica gel, 40–100 mesh.

"Dry" solvents were prepared as follows. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl immediately before use. Dimethyl sulfoxide (Me_2SO) was distilled in vacuo from CaH_2 and stored over 4-Å molecular sieves. Benzene and *o*-xylene were dried by azeotropic distillation and were stored over sodium ribbon.

All reactions were run under an atmosphere of dry nitrogen. Liquid reagents were introduced via syringe through a rubber septum. Solid reagents were added under a stream of nitrogen.

Elemental analyses were performed by Robertson Laboratory, Florham Park, NJ.

3-[*trans*-β-(Trimethylsilyl)vinyl]cyclohex-2-en-1-one (4a). To a solution of *trans*-β-(trimethylsilyl)vinyllithium[7] (0.026 mol) in 45 mL of dry THF at −78 °C was added dropwise a solution of 3.24 g (0.026 mol) of 3-methoxycyclohex-2-en-1-one (**3a**) in 6 mL of THF. The reaction mixture was allowed to warm to room temperature over 4.5 h and was then quenched at 0 °C with 6 mL of 5% aqueous HCl. The reaction mixture was then partitioned between brine and ether, and the combined ether extracts were dried ($MgSO_4$) and concentrated. Purification by chromatography on 100 g of silica gel (elution with hexanes followed by 1:10 ether–hexanes) afforded 4.35 g (87%) of the dienone **4a** as an oil, homogeneous by TLC and spectroscopic analysis, which crystallized at subambient temperature; R_f 0.41 (1:2 ether–hexanes); IR ($CDCl_3$) 3034, 2999, 2961, 2899, 2879, 2839, 1695, 1672,

(14) For key reports of allylsilane transpositional functionalization, see: (a) Au-Yeung, B.-W.; Fleming, I. *J. Chem. Soc., Chem. Commun.* **1977**, 81. (b) Au-Yeung, B.-W.; Fleming, I. *Ibid.* **1977**, 79. (c) Carter, M. J.; Fleming, I. *Ibid.* **1976**, 679. (d) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, 1295. (e) Deleris, G.; Dunogues, J.; Calas, R. *J. Organomet. Chem.* **1975**, *93*, 43. (f) Calas, R.; Dunogues, J.; Pillot, J.-P.; Biran, C.; Pisciotti, F.; Arreguy, B. *Ibid.* **1975**, *85*, 149. (g) reference 5g. (h) For a review of allylsilane chemistry, see: (h) Chan, T. H.; Fleming, I. *Synthesis* **1979**, 761.

(15) In each scheme, all yields reported are for spectroscopically and chromatographically homogeneous material. All structural assignments are supported by IR, ^1H NMR, ^{13}C NMR, and mass spectral analysis. All potentially chiral products were produced as racemates; a single enantiomer is shown for simplicity.

(16) In each trial, this product was contaminated by an inseparable isomeric byproduct.

(17) Morris, G. A.; Freeman, R. *J. Am. Chem. Soc.* **1979**, *101*, 760–762.

1608, 1571, 1562, 1510, 1457, 1432, 1419, 1383, 1350, 1328, 1303, 1252, 1242, 1209, 1190, 1159, 1147, 1122, 1074, 1053, 990, 970, 911, 892, 874, 861, 838, 739, 696, 665, 621 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 6.26 (AB q, 2 H, J_{AB} = 18.1 Hz, $\Delta\nu_{AB}$ = 16.1 Hz), 5.62 (br s, 1 H), 2.36–1.31 (br m, 6 H), 0.03 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 200.26 (s), 156.98 (s), 143.98 (d), 138.50 (d), 127.80 (d), 37.53 (t), 24.18 (t), 21.97 (t), –1.82 (q). Distillation [bath temperature 80 °C (0.2 mmHg)] provided an analytical sample of **4a**.

Anal. Calcd for $C_{11}H_{18}OSi$: C, 67.98; H, 9.34. Found: C, 67.64; H, 9.34.

3-[*trans*-β-(Trimethylsilyl)vinyl]cyclohex-2-en-1-ol (5a). To a suspension of 1.65 g (43.4 mol) of lithium aluminum hydride in 343 mL of dry diethyl ether at –20 °C was added dropwise a solution of the ketone **4a** (8.0 g, 41.2 mmol) in 82 mL of Et_2O. After the reaction had stirred for 1.75 h at –20 °C, it was warmed to 0 °C and quenched by the sequential addition of 2.3 mL of H_2O, 2.3 mL of 15% aqueous NaOH, and 7.5 mL of H_2O.[18] The resulting white granular precipitate of aluminum salts was removed by filtration, and the filtrate was dried ($MgSO_4$) and concentrated. Elution through a column of silica gel with 2:3 ether–hexanes gave 7.8 g (97%) of the allylic alcohol **5a** as an oil, homogeneous by TLC and spectroscopic criteria, which crystallized at subambient temperature; R_f 0.57 (2:1 ether–hexanes); IR (CCl_4) 3614, 3352, 3022, 2954, 2900, 2865, 2844, 1634, 1582, 1452, 1435, 1402, 1386, 1371, 1346, 1319, 1296, 1250, 1207, 1176, 1158, 1119, 1102, 1068, 1031, 989, 960, 925, 872, 850, 726, 692, 642, 622, 608 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 6.03 (AB q, 2 H, J_{AB} = 18.8 Hz, $\Delta\nu_{AB}$ = 38.4 Hz), 5.62 (br d, 1 H), 4.30–3.94 (br m, 1 H), 2.13 (br s, 1 H), 2.07–1.28 (br m, 6 H), –0.02 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 146.18 (d), 138.80 (s), 131.78 (d), 127.44 (d), 65.79 (d), 31.69 (t), 23.62 (t), 18.87 (t), –1.50 (q). Distillation [bath temperature 65 °C (0.02 mmHg)] afforded an analytical sample of **5a**.

Anal. Calcd for $C_{11}H_{20}OSi$: C, 67.28; H, 10.27. Found: C, 67.12; H, 10.59.

1-(2-Propenoxy)-3-[*trans*-β-(trimethylsilyl)vinyl]cyclohex-2-ene (6a). To a solution of 1.33 g (6.78 mmol) of alcohol **5a** in 15 mL of dry benzene and 15 mL of dry dimethyl sulfoxide at 0 °C was added dropwise 5.9 mL (10.2 mmol) of *n*-butyllithium in hexane solution. After the reaction mixture had stirred at 0 °C for 10 min, it was warmed to ambient temperature, and 1.8 mL (20.3 mmol) of allyl bromide was added dropwise. The reaction mixture was allowed to stir 90 min at room temperature and then was quenched at 0 °C with saturated aqueous ammonium chloride. The organic products were partitioned between brine and ether. The combined ether extracts were dried ($MgSO_4$) and concentrated. Chromatography on 100 g of silica gel (elution with 1:20 ether–hexanes) provided 1.51 g (94%) of the allyl ether **6a** as an oil, homogeneous by TLC and spectroscopic methods; R_f 0.84 (1:4 ether–hexanes); IR (CCl_4) 3098, 3000, 2966, 2950, 2910, 2875, 1653, 1588, 1463, 1457, 1444, 1441, 1433, 1416, 1392, 1350, 1338, 1325, 1313, 1298, 1267, 1256, 1214, 1196, 1185, 1166, 1157, 1143, 1130, 1124, 1110, 1086, 1070, 1036, 993, 954, 932, 902, 876, 847, 732, 718, 697, 672, 653, 626 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 6.04 (AB q, 2 H, J_{AB} = 18.9 Hz, $\Delta\nu_{AB}$ = 64.2 Hz), 6.04–4.91 (m, 4 H), 4.00–3.75 (m, 3 H), 2.17–1.23 (br m, 6 H), 0.02 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 146.25 (d), 139.59 (s), 135.13 (d), 129.39 (d), 127.38 (d), 116.03 (t), 72.69 (d), 68.83 (t), 28.32 (t), 23.08 (t), 18.92 (t), –1.40 (q). Distillation [bath temperature 60–65 °C (0.02 mmHg)] gave an analytical sample of **6a**.

Anal. Calcd for $C_{14}H_{24}OSi$: C, 71.12; H, 10.23. Found: C, 71.20; H, 10.51.

1-(2-Methyl-2-propenoxy)-3-[*trans*-β-(trimethylsilyl)vinyl]cyclohex-2-ene (7a). To a solution of 0.91 g (4.65 mmol) of the alcohol **5a** in 22 mL of dry *o*-xylene and 22 mL of dry dimethyl sulfoxide at 0 °C was added dropwise 4.2 mL (7.2 mmol) of *n*-butyllithium in hexane. After the reaction mixture had stirred at 0 °C for 15 min, it was warmed to room temperature, and 0.17 g (0.46 mmol) of tetrabutylammonium iodide was added. Methallyl chloride (1.4 mL, 14.4 mmol) was then added dropwise, and the reaction mixture was stirred 65 min at room temperature and then for 30 min at 135 °C. The solution was allowed to cool to ambient temperature and was quenched with 3 mL of saturated aqueous ammonium chloride. The organic products were partitioned between brine and ether. The combined ether extracts were dried ($MgSO_4$) and concentrated. Purification was effected by chromatography on 200 g of silica gel (elution with 1:100 ether–hexanes) to yield 1.03 g (89%) of the methallyl ether **7a** as an oil, homogeneous by TLC and spectroscopic methods; R_f 0.66 (1:10 ether–hexanes); IR (CCl_4) 3100, 3079, 3031, 2954, 2948, 2898, 2864, 2842, 1655, 1581, 1450, 1437, 1401, 1373, 1342, 1318, 1307, 1291, 1260, 1248, 1208, 1188, 1177, 1160, 1150, 1103, 1082, 1053, 1031, 1004, 986, 949, 901, 868, 847, 724, 691, 649, 622 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 6.15 (AB q, 2 H, J_{AB} = 19.2 Hz, $\Delta\nu_{AB}$ = 63.5 Hz), 5.78 (br s, 1 H), 4.93 (br s, 1 H), 4.81 (br s, 1 H), 4.10–3.70 (br m, 1 H), 3.90 (s, 2 H), 2.26–1.36 (br m, 6 H), 1.72 (br s, 3 H), 0.06 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 146.24 (d), 142.20 (s), 139.26 (s), 129.50 (d), 126.98 (d), 111.30 (t), 72.32 (d), 71.67 (t), 28.19 (t), 23.73 (t), 19.10 (q), 18.85 (t), –1.63 (q). Distillation [bath temperature 61 °C (0.02 mmHg)] provided an analytical sample of **7a**.

Anal. Calcd for $C_{15}H_{26}OSi$: C, 71.94; H, 10.46. Found: C, 72.21; H, 10.70.

1-(3-Methyl-2-butenoxy)-3-[*trans*-β-(trimethylsilyl)vinyl]cyclohex-2-ene (8a). A solution of 5.4 mL (9.30 mmol) of *n*-butyllithium in hexane was added dropwise to a solution of 1.22 g (6.20 mmol) of the alcohol **5a** in 20 mL of dry benzene and 20 mL of dry Me_2SO at 0 °C. After the reaction mixture had stirred 10 min, it was warmed to room temperature, and 1.45 mL (12.42 mmol) of prenyl bromide was added dropwise. The mixture was stirred at ambient temperature for 30 min and was then cooled to 0 °C and quenched with 6 mL of saturated aqueous ammonium chloride. The reaction mixture was then partitioned between ether and brine, and the combined ether extracts were dried ($MgSO_4$) and concentrated. Chromatography on 150 g of silica gel (elution with 1:20 ether–hexanes) gave 1.18 g (72%) of the prenyl ether **8a**, homogeneous by TLC and spectroscopic criteria; R_f 0.56 (1:10 ether–hexanes); IR (CCl_4) 3026, 2961, 2942, 2866, 1729, 1677, 1644, 1635, 1584, 1453, 1442, 1380, 1355, 1346, 1334, 1319, 1294, 1265, 1252, 1211, 1183, 1163, 1153, 1118, 1105, 1077, 1061, 1039, 989, 952, 922, 915, 899, 884, 842, 727, 694, 652, 623 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 6.03 (AB q, 2 H, J_{AB} = 19.4 Hz, $\Delta\nu_{AB}$ = 65.3 Hz), 5.69 (br s, 1 H), 5.21 (br t, 1 H, J = 6.9 Hz), 3.88 (d, 2 H, J = 6.9 Hz), 3.96–3.71 (br m, 1 H), 2.15–1.31 (br m, 6 H), 1.66 (s, 3 H), 1.58 (s, 3 H), 0.00 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 146.35 (d), 139.41 (s), 135.93 (s), 129.64 (d), 127.20 (d), 121.46 (d), 72.50 (d), 64.27 (t), 28.33 (t), 25.45 (q), 23.81 (t), 18.98 (t), 17.64 (q), –1.51 (q). Distillation [bath temperature 60 °C (0.075 mmHg)] provided an analytical sample of **8a**.

Anal. Calcd for $C_{16}H_{28}OSi$: C, 72.66; H, 10.67. Found: C, 72.95; H, 10.94.

2aβ,3,4β,6,7,8,8aα,8bα-Octahydro-4-(trimethylsilyl)-2*H*-naphtho[1,8-*bc*]furan (9a). A neat sample (1.3 g, 5.51 mmol) of the allyl ether **6a** was degassed and sealed under nitrogen in a Pyrex tube. After this heated for 67 h at 120 °C, TLC analysis of the reaction indicated that the starting material had been consumed. The product was purified by direct chromatography on 250 g of silica gel. Elution with 1:20 ether–hexanes provided 1.12 g (86%) of the tricyclic Diels–Alder adduct **9a** as a low-melting solid (mp 32 °C) which was homogeneous by TLC and spectroscopic criteria; R_f 0.19 (1:10 ether–hexanes); IR ($CDCl_3$) 2942, 2914, 2892, 2860, 1472, 1456, 1446, 1430, 1415, 1406, 1399, 1369, 1357, 1343, 1321, 1314, 1282, 1271, 1258, 1246, 1200, 1187, 1153, 1131, 1124, 1108, 1086, 1055, 1033, 1018, 1000, 980, 926, 847, 832, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.24 (d, 1 H, J = 2.0 Hz), 4.06 (ddd, 1 H, J = 11.4, 8.9, 4.4 Hz), 3.91 (dd, 1 H, J = 7.4, 5.6 Hz), 3.32 (dd, 1 H, J = 10.6, 7.4 Hz), 2.35 (br dd, 1 H, J = 10.0, 8.9 Hz) 2.25–2.07 (m, 3 H), 1.94–1.66 (m, 5 H), 1.57–1.44 (m, 1 H), 1.15–1.01 (m, 1 H), 0.01 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 135.49 (s), 120.04 (d), 75.98 (d), 70.78 (t), 46.19 (d), 41.19 (d), 27.94 (t), 26.12 (d, t, 2 C), 23.11 (t), 19.53 (t), –3.20 (q).

Anal. Calcd for $C_{14}H_{24}OSi$: C, 71.12; H, 10.23. Found: C, 70.83; H, 10.50.

2aβ,3,4β,6,7,8aα,8bα-Octahydro-7,7-dimethyl-4-(trimethylsilyl)-2*H*-naphtho[1,8-*bc*]furan (9b). A neat sample (1.09 g, 4.12 mmol) of the allyl ether **6b** was degassed and sealed under nitrogen in a Pyrex tube. The crude product derived from heating the sealed tube at 120 °C for 70 h was directly chromatographed on 125 g of silica gel. Elution with 1:20 ether–hexanes gave 0.89 g (82%) of the tricyclic Diels–Alder adduct **9b** as an

(18) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. I, p 584.

oil: R_f 0.27 (1:10 ether–hexanes); IR ($CDCl_3$) 3011, 2949, 2930, 2862, 1475, 1458, 1451, 1438, 1362, 1346, 1322, 1308, 1274, 1246, 1214, 1203, 1168, 1125, 1094, 1082, 1054, 1022, 1013, 964, 932, 834, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.20 (br d, 1 H, J = 2.2 Hz), 4.18 (ddd, 1 H, J = 12.6, 9.0, 4.6 Hz), 3.90 (dd, 1 H, J = 7.0, 5.7 Hz), 3.30 (dd, 1 H, J = 11.4, 7.0 Hz), 2.30 (br m, 1 H, J = 13.7, 9.0, 2.2 Hz), 1.95–1.85 (m 2 H), 1.85–1.67 (m, 4 H), 1.50 (dd, 1 H, J = 14.9, 4.6 Hz), 0.98 (s, 3 H), 0.93 (dd, 1 H, J = 14.9, 12.6 Hz), 0.87 (s, 3 H), 0.00 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 134.59 (s), 119.60 (d), 74.03 (d), 71.13 (t), 46.70 (d), 43.64 (q), 43.04 (q), 39.95 (d), 31.39 (s), 31.17 (t), 30.03 (t), 26.57 (d), 23.17 (t), −3.19 (q).

Anal. Calcd for $C_{16}H_{28}OSi$: C, 72.66; H, 10.67. Found: C, 72.85; H, 10.81.

2aβ,3,4β,6,7,8,8aα,8bα-Octahydro-2a,7,7-trimethyl-4-(trimethylsilyl)-2*H*-naphtho[1,8-*bc*]furan (10b). A neat sample (0.266 g, 0.96 mmol) of the methallyl ether **7b** was degassed and sealed under nitrogen in a Pyrex tube. The reaction product derived from heating this tube for 48 h at 180 °C was purified by chromatography on silica gel. Elution with 1:20 ether–hexanes yielded 0.139 g (52%) of the tricyclic Diels–Alder adduct **10b** as an oil (crystalline at subambient temperatures): R_f 0.59 (1:4 ether–hexanes): IR ($CDCl_3$) 2952, 2930, 2902, 2854, 2820, 2808, 1464, 1450, 1422, 1399, 1385, 1364, 1344, 1312, 1307, 1286, 1259, 1247, 1221, 1206, 1180, 1149, 1137, 1115, 1080, 1051, 1029, 1017, 1006, 990, 981, 962, 951, 922, 864, 848, 832, 800, 776, 681, 624, 612 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.38 (d, 1 H, J = 2.4 Hz), 4.21 (ddd, 1 H, J = 10.7, 10.3, 6.9 Hz), 3.80 (d, 1 H, J = 7.3 Hz), 3.36 (d, 1 H, J = 7.3 Hz), 2.36 (br d, 1 H, J = 10.3 Hz), 2.21 (d, 1 H, J = 18.1 Hz), 1.95 (br d, 1 H, J = 18.1 Hz), 1.82 (ddd, 1 H, J = 8.6, 6.9, 2.4 Hz), 1.74–1.60 (m, 2 H), 1.15 (dd, 1 H, J = 10.7, 8.6 Hz), 0.96 (dd, 1 H, J = 11.7, 11.7 Hz), 0.96 (s, 3 H), 0.86 (s, 3 H), 0.74 (s, 3 H), 0.05 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 138.67 (s), 121.09 (d), 78.47 (t), 73.67 (d), 47.99 (d), 46.51 (s), 43.44 (t), 42.85 (t), 32.59 (q), 31.63 (s), 25.63 (d), 23.99 (m, 2 C), 22.45 (q), −3.22 (q).

5,5-Dimethyl-3-vinylcyclohex-2-en-1-one (12). To a solution of 25 mL of 1.3 M vinylmagnesium bromide in THF (32.5 mmol) at −78 °C was added dropwise a solution of 5.0 g (32.4 mmol) of 3-methoxy-5,5-dimethylcyclohex-2-en-1-one (**3b**) in 7.5 mL of THF over 15 min. The reaction mixture was allowed to stir at −78 °C for 2 h and was allowed to warm to 25 °C over 1.5 h. After addition of 25 mL of 5% aqueous HCl, the reaction mixture was stirred for 12.5 h and then partitioned between ether and saturated aqueous $NaHCO_3$. The combined ether extracts were dried ($MgSO_4$) and concentrated. Purification by chromatography on 200 g of silica gel (elution with 1:9 ether–hexanes) gave 3.63 g (75%) of the dienone **12** as a colorless oil, homogeneous by TLC and spectroscopic analysis; R_f 0.51 (1:2 ether–hexanes); IR ($CHCl_3$) 3091, 3012, 3000, 2959, 2923, 2882, 2869, 1651, 1618, 1582, 1462, 1407, 1375, 1302, 1278, 1244, 1207, 1139, 1117, 1022, 986, 962, 923, 899, 873, 848 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 6.67–5.35 (vinylic ABX, 3 H), 5.90 (br s, 1 H), 2.35 (br s, 2 H), 2.26 (br s, 2 H), 1.07 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 198.79 (s), 153.48 (s), 137.23 (d), 126.21 (d), 119.63 (t), 50.57 (t), 37.39 (t), 32.27 (s), 27.52 (q).

5,5-Dimethyl-3-vinylcyclohex-2-en-1-ol (13). To a suspension of 1.19 g (31.4 mmol) of lithium aluminum hydride in 249 mL of dry Et_2O at −20 °C was added dropwise a solution of the ketone **12** (4.5 g, 30 mmol) in 40 mL of Et_2O. After the reaction had stirred for 1.75 h at −20 °C, it was warmed to 0 °C and quenched by the sequential addition of 2.0 mL of H_2O, 2.0 mL of 15% aqueous NaOH, and 7.0 mL of H_2O.[18] The resulting white granular precipitate of aluminum salts was removed by filtration, and the filtrate was dried ($MgSO_4$) and concentrated to give 4.33 g (95%) of the allylic alcohol **13** as colorless plates (mp 41–42 °C), homogeneous by TLC and spectroscopic criteria; R_f 0.44 (1:2 ether–hexanes); IR ($CHCl_3$) 3594, 3087, 3000, 2949, 2926, 2904, 2867, 2847, 2828, 1638, 1604, 1459, 1384, 1364, 1346, 1278, 1220, 1168, 1147, 1132, 1096, 1040, 1019, 1017, 992, 968, 943, 908, 890, 869, 846 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 6.58–4.90 (vinylic ABX, 3 H), 5.70 (br s, 1 H), 4.33 (br s, 1 H), 2.83 (br s, 1 H), 1.92 (br s, 2 H), 1.88–1.15 (m, 2 H), 1.07 (s, 3 H), 0.90 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 139.19 (d), 135.88 (s), 130.39 (d), 112.06 (t), 66.00 (d), 44.82 (t), 37.29 (t), 31.33 (q), 30.35 (s), 25.71 (q).

5,5-Dimethyl-1-(2-propenoxy)-3-vinylcyclohex-2-ene (14). To a solution of 1.0 g (6.56 mmol) of the alcohol **13** in 29 mL of dry benzene and 29 mL of dry Me_2SO at 0 °C was added dropwise 6.36 mL (9.85 mmol) of *n*-butyllithium in hexane. The reaction mixture was allowed to warm to room temperature, and 1.7 mL (19.7 mmol) of allyl bromide was added dropwise. The reaction mixture was stirred for 16 h at 25 °C, cooled to 0 °C, and quenched with 8.5 mL of saturated aqueous NH_4Cl. After extraction of the aqueous layer with 3 × 75 mL of Et_2O, the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography on 35 g of silica gel (elution with 1:20 ether–hexanes) provided 1.15 g (89%) of the allyl ether **14** as an oil, homogeneous by TLC and spectroscopic analysis; R_f 0.90 (1:2 ether–hexanes); IR ($CHCl_3$) 3079, 3000, 2948, 2918, 2859, 2829, 1636, 1602, 1455, 1419, 1374, 1363, 1346, 1310, 1289, 1269, 1224, 1172, 1139, 1118, 1101, 1068, 1035, 1019, 990, 929, 902, 863, 843 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 6.58–4.88 (m, 7 H), 4.22–3.89 (m, 3 H), 1.92 (br s, 2 H), 1.58 (ABX, 2 H, J_{AB} = 12.3 Hz, J_{AX} = 5.7 Hz, J_{BX} = 9.0 Hz, $\Delta\nu_{AB}$ = 39.5 Hz), 1.07 (s, 3 H), 0.92 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 139.15 (d), 136.53 (s), 135.06 (d), 127.67 (d), 116.02 (t), 111.96 (t), 73.05 (d), 68.78 (t), 41.38 (t), 37.41 (t), 31.13 (q), 30.15 (s), 26.08 (q). Distillation [bath temperature 44 °C (0.035 mmHg)] provided an analytical sample of **14**.

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.42; H, 10.47.

2aβ,3,4,6,7,8,8aα,8bα-Octahydro-7,7-dimethyl-2*H*-naphtho[1,8-*bc*]furan (15). A neat sample (90 mg, 0.47 mmol) of the allyl ether **14** was degassed and sealed under nitrogen in a Pyrex tube. The tube was heated at 120 °C for 67.5 h, and the crude product was purified by preparative thin-layer chromatography (elution with 20:1 hexanes–ether) to give 57 mg (63%) of the tricyclic Diels–Alder adduct **15** as an oil: R_f 0.61 (1:1 ether–hexanes); IR ($CHCl_3$) 2996, 2948, 2928, 2895, 2860, 2837, 1454, 1432, 1381, 1372, 1361, 1342, 1323, 1310, 1239, 1188, 1163, 1126, 1105, 1064, 1034, 1011, 992, 969, 941, 920, 902, 885, 859, 844, 826 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.22 (br s, 1 H), 4.20 (ddd, 1 H, J = 12.8, 8.6, 4.4 Hz), 3.95 (dd, 1 H, J = 7.3, 6.1 Hz), 3.38 (dd, 1 H, J = 11.30, 7.3 Hz), 2.38–0.90 (br, 9 H), 1.51 (dd, 1 H, J = 12.7, 4 Hz), 1.00 (s, 3 H), 0.90 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 136.89 (s), 119.25 (d), 74.45 (d), 71.54 (t), 46.86 (d), 43.63 (t), 43.14 (t), 41.37 (d), 31.73 (s), 31.55 (q), 30.38 (q), 26.02 (t), 22.80 (t). Distillation [bath temperature 68–71 °C (0.07 mmHg)] provided an analytical sample of **15**.

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.24; H, 10.57.

1-[(*trans*-β-carbethoxyacryloyl)oxy]-5,5-dimethyl-3-[*trans*-β-(trimethylsilyl)vinyl]cyclohex-2-ene (19b). To a solution of 1.11 g (5.0 mmol) of the alcohol **5b** in 40 mL of THF and 0.6 mL of pyridine and 25 °C was added slowly dropwise 2.44 g (15 mmol) of *trans*-β-carbethoxyacryloyl chloride. After the reaction mixture had stirred for 14.5 h at 25 °C, there was added 30 mL of H_2O. The THF was removed by rotary evaporator, and the product was partitioned between Et_2O and H_2O. The combined ether layers were washed with 5% aqueous HCl, followed by saturated aqueous $NaHCO_3$. The ether extracts were dried (Na_2SO_4) and concentrated. Chromatography on 30 g of silica gel (elution with 1:10 ether–hexanes) gave 1.67 g (95%) of the mixed fumarate **19b** as a colorless oil, homogeneous by TLC and spectroscopic criteria; R_f 0.76 (1:4 ether–hexanes); IR ($CHCl_3$) 2955, 1723, 1711, 1635, 1576, 1464, 1447, 1429, 1365, 1296, 1255, 1205, 1156, 1094, 1024, 1007, 980, 933, 860, 838 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 6.85 (s, 2 H), 6.55 (d, 1 H, J = 19.5 Hz), 5.86 (d, 1 H, J = 19.5 Hz), 5.69 (br s, 1 H), 5.57 (br m, 1 H), 4.25 (q, 2 H, J = 6.6 Hz), 2.02 (br s, 2 H), 1.99–1.38 (m, 2 H), 1.31, (t, 3 H, J = 6.6 Hz), 1.09 (s, 3 H), 0.99 (s, 3 H), 0.09 (s, 9 H); ^{13}C NMR ($CDCl_3$) 164.70 (s), 164.46 (s), 145.53 (d), 139.85 (s), 133.69 (d), 133.36 (d), 129.06 (d), 125.12 (d), 70.76 (d), 61.00 (t), 40.67 (t), 37.57 (t), 30.24 (q), 30.12 (s), 26.88 (q), 13.89 (q), −1.47 (q). Preparative TLC (elution with 1:4 ether–hexanes) provided an analytical sample of **19b**.

Anal. Calcd for $C_{19}H_{30}O_4Si$: C, 65.10; H, 8.63. Found: C, 65.34; H, 8.56.

3β-Carbethoxy-2aβ,3β,4β,6,7,8,8aα,8bα-octahydro-7,7-dimethyl-4-(trimethylsilyl)-2*H*-naphtho[1,8-*bc*]furan-2-one (20b). The mixed fumarate **19b** (1.0 g, 2.93 mmol) in 10 mL of benzene was sealed under nitrogen in a Pyrex tube and heated for 90 h at 120 °C. The solution was then concentrated, and the crude product was purified by chromatography on silica gel. Elution with 1:4 ether–hexanes gave 820 mg (82%) of the tricylic lactone **20b** as white crystals (mp 83–84 °C), homogeneous by TLC

and spectroscopic analysis; R_f 0.23 (1:4 ether–hexanes); IR ($CHCl_3$) 3011, 2947, 2887, 2858, 2829, 1776, 1728, 1457, 1368, 1363, 1335, 1305, 1246, 1186, 1161, 1138, 1112, 1090, 1058, 1035, 1004, 966, 935, 905, 857, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.39 (br s, 1 H), 4.68 (ddd, 1 H, J = 13.2, 8.0, 4.9 Hz), 4.21 (m, 2 H), 3.13 (dd, 1 H, J = 11.2, 8.3 Hz), 2.84 (br m, 1 H), 2.67 (dd, 1 H, J = 14.6, 11.2 Hz), 2.14 (br m, 1 H), 2.03 (m, 2 H), 1.79 (dd, 1 H, J = 14.2, 4.9 Hz), 1.37 (dd, 1 H, J = 14.2, 13.2 Hz), 1.31 (t, 3 H, J = 7.1 Hz), 1.08 (s, 3 H), 1.02 (s, 3 H), 0.09 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 173.76 (s), 172.79 (s), 136.34 (s), 121.87 (d), 75.98 (d), 60.78 (t), 42.77 (t), 42.10 (d), 41.60 (d), 41.50 (d), 38.75 (t), 32.09 (s), 31.52 (d), 31.52 (q), 29.96 (q), 13.79 (q), -1.54 (q).

Anal. Calcd for $C_{19}H_{30}O_4Si$: C, 65.10; H, 8.63. Found: C, 65.17; H, 8.60.

Acknowledgment. Grateful acknowledgement is extended to the donors of the Petroleum Research Fund, administered by the American Chemical Society, to Research Corp., and to the National Institutes of Health for their generous support of this research. High-field NMR spectra were obtained through the National Science Foundation Regional NMR Center at the University of South Carolina (Grant CHE 78-18723).

Registry No. **3a**, 16807-60-6; **3b**, 4683-45-8; **4a**, 84132-55-8; **4b**, 76999-36-5; **5a**, 84132-56-9; **5b**, 76999-38-7; **6a**, 84132-57-0; **6b**, 84132-61-6; **7a**, 84132-58-1; **7b**, 84142-96-1; **8a**, 84132-59-2; **8b**, 84132-62-7; **9a**, 84132-60-5; **9b**, 84132-63-8; **10a**, 84192-49-4; **10b**, 84132-64-9; **11a**, 84132-69-4; **12**, 21634-43-5; **13**, 84132-65-0; **14**, 84132-66-1; **15**, 84132-67-2; **19a**, 84132-70-7; **19b**, 84132-68-3; **20a**, 84132-71-8; **20b**, 84143-12-4; *trans*-β-(trimethylsilyl)vinyllithium, 55339-31-6; methallyl chloride, 563-47-3; prenyl bromide, 870-63-3; vinylmagnesium bromide, 593-60-2; *trans*-β-carbethoxyacryloyl chloride, 26367-48-6.

On the Relation between Elution Order and Absolute Stereochemistry of Alkylarylcarbinols from a Pirkle Column

Masaji Kasai,[1a] Cleanthis Froussios,[1b] and Herman Ziffer*[†]

Laboratory of Chemical Physics, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20205

Received May 11, 1982

A study of the relation between the absolute stereochemistry of a series of alkylarylcarbinols and two groups of benzocycloalkenols with their elution order from an HPLC column containing a chiral stationary phase has shown that the enantiomer more strongly retained by the column in each group of compounds has the same absolute stereochemistry except for benzoin and its *p*-methyl derivative. The enantiomer more strongly retained in the acyclic series does *not* have the same absolute stereochemistry as that retained in the two cyclic series examined. Better separations were observed in the acyclic series for the acetate esters than the free alcohols, while the reverse situation occurred for the benzocycloalkenols. In each series of compounds the enantiomer of the alcohols and corresponding acetates more strongly retained on the column differs in absolute stereochemistry. These results are *not* in accord with the current model for "chiral recognition" on the chiral phase employed. The reliability of using elution order to assign the absolute stereochemistry of previously unassigned compounds is compared with other methods currently in use.

While many theoretical and empirical relations between chiroptical data and absolute stereochemistry are known, it is impossible to assign the absolute stereochemistry of many compounds from circular dichroism or optical rotatory dispersion measurements. The traditional solution of this dilemma is to transform the compound in question chemically into one that can be analyzed. However, alternative approaches have explored the uses of other physical properties that can be related to the absolute stereochemistry of an enantiomer. One measurement that has been used with some success is the elution order of diastereomers from a chromatographic column. The approach has been used with satisfactory results for amino acids[2a] and terpenoid acids.[2b] However, a significant number of exceptions to such correlations exist in the literature;[3] for example, Schooley and his associates[3a,b] have shown that the elution order differs for the amides from 1-(1-naphthyl)ethylamine and 3-methyl- and 3-ethyl-3-hydroxyglutaric acid, of the same absolute stereochemistry. Thus, an assignment made for the ethyl derivative based on the elution order of the methyl analogue would be in error. Despite these reports the approach is very attractive as the measurement is nondestructive and can be used to characterize nanogram quantities of material. Recently some theoretical rationalizations for the interactions between the substrate and the chiral phase have been proposed[4] that may improve the reliability of the method.

Pirkle and co-workers[5] have prepared a series of chiral phases bonded ionically to a silanized silica column that can separate a racemate without the necessity of converting the latter into a mixture of diastereomers. Their reports suggest that this approach may avoid the limitations observed with the elution order of diastereomers. These investigators also proposed a theoretical model that was employed in designing these columns. So that the "chiral recognition" needed for separation could be achieved, the

[†] This paper is dedicated to Dr. Ulrich Weiss on the occasion of his 75th birthday.

(1) (a) On leave from Kyowa Hakko Kogyo Co. Ltd., Tokyo Research Laboratory, 3-6-6, Asahi-machi, Machida-shi, Tokyo, 194, Japan. (b) Present address: Laboratory of Organic Chemistry, University of Athens, Athens 144, Greece.

(2) (a) H. Furukawa, Y. Mori, Y. Takeuchi, and K. Ito, *J. Chromatogr.*, **136**, 428–431 (1977). (b) C. G. Scott, M. J. Petrin, and T. McCorkle, *ibid.*, **125**, 157–161 (1976).

(3) (a) B. J. Bergot, R. J. Anderson, D. A. Schooley, and C. A. Henrick, *J. Chromatogr.*, **155**, 97–105 (1978). (b) B. J. Bergot, F. C. Baker, E. Lee, and D. A. Schooley, *J. Am. Chem. Soc.*, **101**, 7432–7434 (1979). (c) G. Solladié and F. Matloubi-Moghadam, *J. Org. Chem.*, **47**, 91–94 (1982).

(4) G. Helmchen, H. Völter, and W. Schühle, *Tetrahedron* Lett., 1417–1420 (1977).

(5) (a) W. H. Pirkle, J. M. Finn, J. L. Schreiner, and B. C. Hamper, *J. Am. Chem. Soc.*, **103**, 3964–3966 (1981). (b) W. H. Pirkle and J. L. Schreiner, *J. Org. Chem.*, **46**, 4988–4991 (1981). (c) W. H. Pirkle, D. W. House, and J. M. Finn, *J. Chromatogr.*, **192**, 143–158 (1980). (d) W. H. Pirkle and J. M. Finn, *J. Org. Chem.*, **46**, 2935–2938 (1981).