ethanol–water: yield 3.42 g (first crop) (48.7%).

5,5′-Bis(2-cyano-2-(ethoxycarbonyl)vinyl)-3,3′,4,4′-tetramethyl-2,2′-bipyrrole (56). 2-(2-Carbethoxy-2-cyanovinyl)-5-iodo-3,4-dimethylpyrrole[27] (**55**) (3.44 g, 0.010 mol) was dissolved in *N,N*-dimethylformamide (20 mL) in a loosely stoppered Erlenmeyer flask. Copper bronze (5 g, BDH) was added at room temperature, and the stirred suspension was heated slowly. The original green color became orange–brown after the addition of the copper. As the solution was warmed, yellow solids (presumably the copper chelate of the iodopyrrole) crystallized out, making the copper bronze appear to clot. Iodine crystals (ca. 0.2 g) were added to activate the copper bronze. The mixture was then heated to, and just maintained at, the boiling point, with continued stirring, for 1 h.

The yellow solids redissolved, and a permanent deep burgundy-red color set in as the reaction progressed. The mixture was allowed to cool somewhat, before being diluted with tetrahydrofuran (100 mL) and filtered to remove the excess copper. The solids were rinsed with tetrahydrofuran (300–400 mL) until the washings were nearly colorless and then with a solution of concentrated hydrochloric acid (20 mL) in THF (80 mL) and finally with water (400 mL), all of the washings and filtrates being collected together. The solids deposited from the aqueous solution were collected and rinsed with water. The bipyrrole is a striking purple color; in an especially finely divided form, the color is a pure Harvard crimson. If any bipyrrole appeared to remain in solution (a red color), it was recovered by further aqueous dilution. Addition of yet more water allowed the recovery of a modest quantity of the deiodinated monomer, 2-(2-cyano-2-(ethoxycarbonyl)vinyl)-3,4-dimethylpyrrole.[24]

The combined solids were boiled with dichloromethane (300–400 mL) in several portions and filtered hot, to remove gray cuprous iodide, which was rinsed until the filtrates were only pale orange. The solvent was displaced with ethanol at the boiling point and concentrated to approximately 50 mL, before being allowed to cool. The solids, most of which had crystallized during the concentration, were collected and rinsed with ethanol and then hexane. The yield of dark purple fluffy needles was 0.76 g (35%).

An analytical sample was recrystallized from dichloromethane–95% ethanol: mp infusible below 300 °C. Anal. Calcd for $C_{24}H_{26}N_4O_4$: C, 66.34; H, 6.03; N, 12.90. Found: C, 65.90; H, 5.95; N, 12.75. IR (KBr) 3400, 2200, 1710, 1570 cm^{-1}; MS, *m/e* 434; NMR (CF_3CO_2H) δ 1.47 (t, J = 7 Hz, 6 H), 2.33 (s, 12 H), 4.50 (q, J = 7 Hz, 4 H), 8.26 (s, 2 H), 9.72 (s, 2 H).

Preparation of a Zn(II) Derivative of Decamethylsapphyrin (57). Decamethylsapphyrin (**12**) (55 mg, 0.10 mmol) in chloroform (80 mL) was heated to reflux for 1 h and then allowed to cool to room temperature. A solution containing zinc acetate dihydrate (100 mg), anhydrous sodium acetate (120 mg), and methanol (3 mL) was added. The resulting solution was stirred at room temperature for 4 h and then allowed to stand at room temperature for 1 day. Chloroform (80 mL) was added and the solution was washed twice with water (20 mL) and dried over a small amount of anhydrous magnesium sulfate. The solution was evaporated to give a sparkling solid that was in turn dissolved in chloroform and put in a desiccator containing petroleum ether. Several days later, the crystals were collected: yield 37 mg; IR (KBr) 1590 cm^{-1}; vis ($CHCl_3$) λ_{max} 696, 681, 630, 584, 462 nm; MS (see above).

Preparation of Cobalt(II) Decamethylsapphyrin (58). To methanol (10 mL) were added $CoCl_2 \cdot 6H_2O$ (100 mg, 0.42 mmol) and anhydrous sodium acetate (360 mg, 4.4 mmol). The mixture was stirred thoroughly, and NaCl was removed by filtration. Decamethylsapphyrin (**12**) (50 mg, 0.097 mmol) was added to chloroform (80 mL), heated at reflux for 1 h, and allowed to cool to room temperature. The two solutions were combined, stirred for 1 h, and then allowed to stand at room temperature for 2 days. Chloroform (40 mL) was added and the resulting solution was extracted with water (15 mL). The organic layer was dried over $MgSO_4$ and concentrated to 10 mL. This solution was placed in a desiccator containing petroleum ether. After 5 days (when the volume of solution had increased to 18 mL), 33 mg of sparkling, dark blue crystals were collected: vis ($CHCl_3$) λ_{max} 692, 638, 595, 468 nm.

Acknowledgment. We thank the National Institutes of Health (GM04229 (R.B.W.) and GM29198 (D.D.)) and the Canadian Natural Sciences and Engineering Research Council for financial support. M.M.K. thanks the N.I.H. for a predoctoral fellowship (1966–1970). The work reported here is taken in part from the Harvard Ph.D. Theses of M.M.K., 1970, and J.B.P. III, 1973.

Registry No. 2, 86568-79-8; **4**, 86568-80-1; **6**, 86584-08-9; **12**, 86568-81-2; **13**, 51952-99-9; **14**, 86568-82-3; **15**, 86568-83-4; **16**, 4424-76-4; **17**, 86568-84-5; **18**, 86568-85-6; **19**, 86568-86-7; **20**, 86568-87-8; **21**, 50634-34-9; **22**, 65038-94-0; **23**, 86568-88-9; **24**, 86568-89-0; **25**, 59435-08-4; **26**, 86568-90-3; **30**, 86584-09-0; **31**, 86568-91-4; **32**, 86568-92-5; **39**, 2199-46-4; **46**, 59435-00-6; **47**, 59700-08-2; **50**, 59434-99-0; **55**, 59435-16-4; **56**, 86568-93-6; **57**, 86568-98-1; **58**, 86568-99-2; sapphyrin dihydrochloride, 86568-94-7; decamethylsapphyrin dihydrochloride, 86568-95-8; 2-((benzyloxy)carbonyl)-3,4-dimethyl-2-chloroformylpyrrole, 86568-96-9; 2,2′-dipyrrole, 10087-64-6; 2-(2-cyano-2-(methoxycarbonyl)vinyl]-5-dichloromethyl-3,4-dimethylpyrrole, 86568-97-0; 2-(2-cyano-2-(methoxycarbonyl)vinyl)-3,4-dimethylpyrrole, 59434-99-0.

Electron Spin Resonance and Chemical Studies on the 6-(Trimethylsilyl)cyclohexadienyl and Related Radicals[1]

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Received March 28, 1983

Abstract: Various 3,6-disubstituted cyclohexadienyl radicals were generated and investigated by ESR at low temperature. Analysis of the ESR parameters indicated that the significant out-of-plane deformation of the carbon framework of 6-Me_3Si- and 6-Me_3Ge-substituted cyclohexadienyl radicals (**1**, **6**, and **7**) occurred to gain stabilization due to the effective hyperconjugation between the substituted methylene pseudo-π orbital and the π SOMO, while the 6-unsubstituted (**2**, **3**, and **4**) and 6-*t*-Bu (**5**) cyclohexadienyl radicals were essentially planar. Investigation of the fate of the 3,6-bis(trimethylsilyl)cyclohexadienyl radical (**6**) showed strong evidence for the temperature-dependent reversibility of the silyl radical addition to aromatics. The spontaneous elimination of the trimethylsilyl radical from **6** was proved by spin-trapping experiments.

Cyclohexadienyl and a wide variety of substituted cyclohexadienyl radicals have been studied by ESR spectroscopy.[2-12] One of the interesting features of cyclohexadienyl radicals is the large hyperfine splitting constants (hfsc's) of the methylene protons

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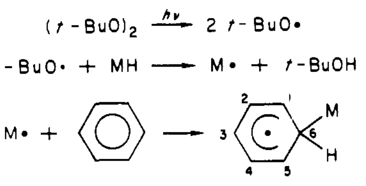
(1) Part 178: Chemistry of Organosilicon Compounds.

(2) (a) Fischer, H. *Kolloid Z. Z. Polym.* **1962**, *180*, 64. (b) *Z. Naturforsch. A*, **1962**, *17*, 693. (c) *J. Chem. Phys.* **1962**, *37*, 1094.

(3) (a) Fessenden, R. W.; Schuler, R. H. *J. Chem. Phys.* **1963**, *38*, 773. (b) *Ibid.* **1963**, *39*, 2147. (c) Ohnishi, S.-I.; Tanei, T.; Nitta, I. *Ibid.* **1962**, *37*, 2402.

0002-7863/83/1505-6436$01.50/0

Scheme I



1a, $M = Si(CH_3)_3$
b, $M = Si(C_2H_5)_3$
c, $M = Si(CH_3)_2Si(CH_3)_3$

and the large drop in hfsc caused by the replacement of one of the methylene protons by an electron-withdrawing group such as OH[4] and F.[5] The methylene proton hfsc of the parent cyclohexadienyl radical is 47.9 G, while the corresponding hfsc of the 6-hydroxycyclohexadienyl[13] radical is 36.0 G.[4] Whiffen[14] has interpreted these unusually large methylene proton hfsc's in terms of the effective hyperconjugation between the methylene pseudo-π orbital and the singly occupied molecular orbital of the pentadienyl moiety.

Recently, Yim and Wood have ascribed the reduction of the magnitude of the β-proton hfsc values with the introduction of an electron-withdrawing group at the saturated position to less effective hyperconjugation lowering the energy level of the methylene pseudo-π orbital.[5]

On the other hand, 6-silylcyclohexadienyl radicals, which have an electron-donating substituent at the 6-position, also show significantly small proton hfsc's for the residual β proton (ca. 35–40 G).[6,7] We have proposed in previous communications[7c–e] that the substituent effects of a 6-silyl group on the β-proton hfsc's should be related to the enhanced hyperconjugation between the C–Si σ bond and the π fragment, which results in significant deformation of the planar carbon framework. These proposals are based on the temperature dependence of the hfsc and on both CNDO/2[7c] and ab initio MO[7e] calculations. We report here ESR spectra of 6-*tert*-butyl-, 6-(trimethylsilyl)-, 6-(trimethylgermyl)-, and 6-deuterio-substituted cyclohexadienyl radicals and discuss the relationship between ESR parameters and the structures of these radicals.

Cyclohexadienyl radicals are known to be key intermediates in free-radical aromatic substitutions.[15] Typically, the intermediate cyclohexadienyl radicals have been detected by ESR combined with rapid flow techniques for hydroxy radical substitution and with a technique of introducing sterically bulky groups into aromatics for free-radical aromatic silylations.[6,7a,b] More recently, several 6-silylcyclohexadienyl radicals have been observed by ESR[6c,7d] as intermediates of free-radical silylation on benzene.

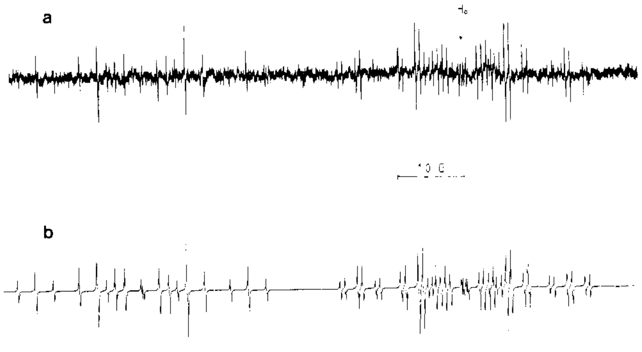


Figure 1. ESR spectrum of **2** generated from 1,4-cyclohexadiene at −100 °C in solution: (a) observed and (b) simulated.

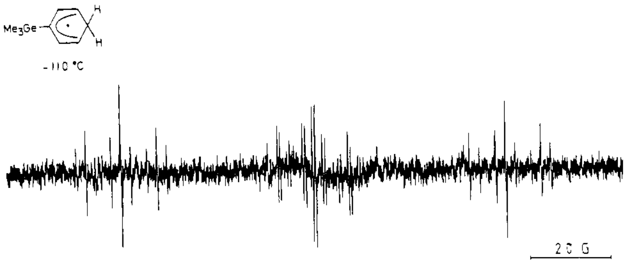
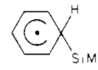
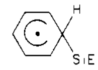
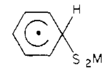


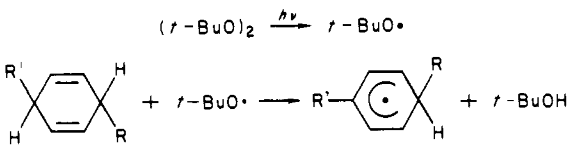
Figure 2. ESR spectrum of **3** generated from 3-(trimethylgermyl)-cyclohexadiene at −110 °C in solution.

Table I. Experimental ESR Parameters for 6-Silylcyclohexadienyl Radicals Generated by the Route in Scheme I

radical	temp/ °C	$a_{1,5}$/G	$a_{2,4}$/G	a_3/G	a_6/G	$\lvert Q\rvert^a$
 SiMe3 1a	−60	8.34	2.43	12.45	37.8	24.3
 SiEt3 1b	−60	8.34	2.43	12.43	40.2	24.3
 Si2Me5 1c	−60	8.30	2.40	12.28	38.1	24.1

[a] Q is defined as $\Sigma_{i=1}^{5} a_i$.

Scheme II



2, R = R' = H
3, R = H; R' = $Ge(CH_3)_3$
4, R = D; R' = $Ge(CH_3)_3$
5, R = $C(CH_3)_3$; R' = $Si(CH_3)_3$
6, R = $Si(CH_3)_3$; R' = $Si(CH_3)_3$
7, R = $Ge(CH_3)_3$, R' = $Ge(CH_3)_3$

One of the most interesting aspects of the free-radical silylation may be concerned with the reversibility of the addition step. The fate of the 3,6-bis(trimethylsilyl)cyclohexadienyl radical, generated by hydrogen abstraction of the corresponding cyclohexa-1,4-diene, has been investigated in this context, affording strong evidence for the temperature-dependent reversibility.

Results and Discussion

Generation and ESR Spectra of 6-Substituted Cyclohexadienyl Radicals. Recently, two groups[6,7a,b] have reported independently

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(4) (a) Dixon, W. T.; Norman, R. O. C. *Proc. Chem. Soc., London* **1963**, 97. (b) *J. Chem. Soc.* **1964**, 4857. (c) Jefcoate, C. R. E.; Norman, R. O. C. *J. Chem. Soc. B* **1968**, 48.

(5) (a) DiGregorio, S.; Yim, M. B.; Wood, D. E. *J. Am. Chem. Soc.* **1973**, *95*, 8455. (b) Yim, M. B.; Wood, D. E. *Ibid.* **1975**, *97*, 1004.

(6) (a) Griller, D.; Dimroth, K.; Fyles, T. M.; Ingold, K. U. *J. Am. Chem. Soc.* **1975**, *97*, 5526. (b) Effio, A.; Griller, D.; Ingold, K. U.; Scaiano, J. C.; Sheng, S. J. *Ibid.* **1980**, *102*, 6063. (c) Griller, D.; Marriott, P. R.; Nonhebel, D. C.; Perkins, M. J.; Wong, P. C. *Ibid.* **1981** *103*, 7761.

(7) (a) Sakurai, H.; Nozue, I.; Hosomi, A. *Chem. Lett.* **1976**, 129. (b) *J. Am. Chem. Soc.* **1976**, *98*, 8279. (c) Kira, M.; Sakurai, H. *Ibid.* **1977**, *99*, 8455. (d) *Chem. Lett.* **1981**, 927. (e) *Ibid.* **1982**, 221.

(8) (a) Mishra, S. P.; Symons, M. C. R. *Tetrahedron Lett.* **1973**, 4061. (b) Edwards, J.; Hills, D. J.; Mishra, S. P.; Symons, M. C. R. *J. Chem. Soc., Chem. Commun.* **1974**, 556.

(9) Cookson, P. G.; Davies, A. G.; Roberts, B. P. *J. Chem. Soc., Chem. Commun.* **1976**, 289.

(10) (a) Leone, J. A.; Koski, W. S. *J. Am. Chem. Soc.* **1966**, *88*, 656. (b) Shiga, T.; Kishimoto, T.; Tomita, E. *J. Phys. Chem.* **1973**, *77*, 330.

(11) (a) Filby, W. G.; Gunther, K. *J. Phys. Chem.* **1974**, *78*, 1521. (b) *Ibid.* **1974**, *60*, 3355.

(12) (a) Helcké, G. A.; Fantechi, R. *Mol. Phys.* **1969**, *17*, 65. (b) Fantechi, R.; Helcké, G. A. *Ibid.* **1971**, *22*, 737.

(13) The ring of the cyclohexadienyl radicals is numbered as indicated in Scheme I following *Chem. Abstr.*, while several authors favor an alternative method,[5b,6] where the saturated carbon is designated as the 1-position.

(14) Wiffen, W. T. *Mol. Phys.* **1963**, *6*, 223.

(15) Perkins, M. J. In "Free Radicals", Kochi, J. K., Ed.; John Wiley & Sons: New York, 1973; Vol. II, Chapter 16.

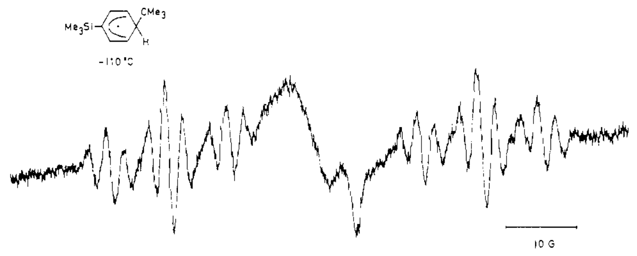


Figure 3. ESR spectrum of **5** generated from 3-*tert*-butyl-6-(trimethylsilyl)cyclohexadiene at −110 °C in solution.

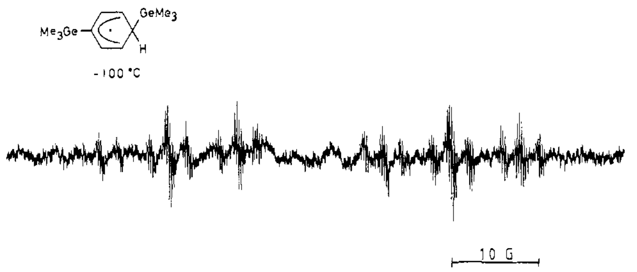
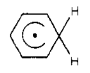
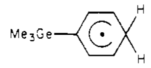
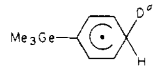
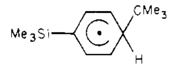
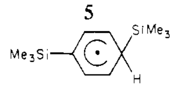
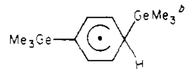


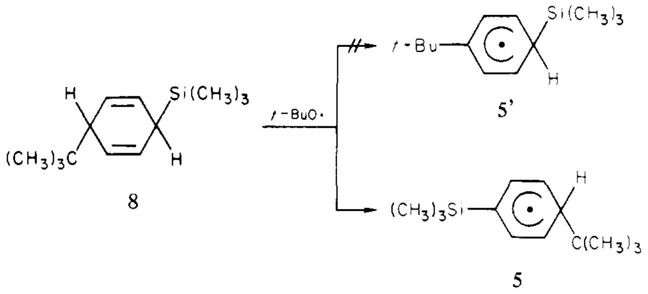
Figure 4. ESR spectrum of **7** generated from 3,6-bis(trimethylgermyl)cyclohexadiene at −100 °C in solution.

Table II. Experimental ESR Parameters for Substituted Cyclohexadienyl Radicals Generated by the Route in Scheme II

radical	temp/ °C	$a_{1,5}$/G	$a_{2,4}$/G	a_3/G	a_6/G
 **2**	−100	9.13	2.65	13.56	48.1
 **3**	−110	8.73	2.39		47.5
 **4**	−110	8.72	2.38		47.71
 **5**	−110	8.40	2.43		43.55
 **6**	−100	8.00	2.15		35.9
 **7**	−100	7.83	2.09		32.22

[a] The deuterium hfsc was 7.01 G. [b] The additional splitting of 0.24 G was assigned as due to 9 protons on the 6-trimethylgermyl group.

Scheme III



that 2,4-di-*tert*-butyl-6-(trimethylsilyl)cyclohexadienyl and related radicals are produced by addition of a silyl radical to an appropriate benzene. These radicals are found to be rather persistent in allowing extensive ESR studies since the bulky *tert*-butyl groups protect the radicals sterically from any secondary reactions.

The reaction was partly successful as a general route to a 6-silylcyclohexadienyl radical from parent benzene (Scheme I).[7d] Although the steady-state concentrations were fairly low, detection and analysis of the ESR spectra were crucial not only for proving the actual intermediacy of 6-silylcyclohexadienyl radicals in free-radical silylations on benzene itself but also for elucidating the radical structures by analyzing the proton hfsc's which fortunately can be obtained for all the ring positions. The proton hfsc's of **1a–c** are listed in Table I.

Hydrogen abstraction from an appropriate 1,4-cyclohexadiene[7c] by the photochemically generated *tert*-butoxy radical is also a good route to 6-silyl- and 6-germyl-substituted cyclohexadienyl radicals (Scheme II). Photolysis of a mixture of cyclohexa-1,4-diene, di-*tert*-butyl peroxide, and cyclopropane (ca. 1:1:1) in a cavity of an ESR spectrometer gave a well-resolved spectrum of the cyclohexadienyl radical (**2**) as shown in Figure 1. The peak-to-peak line width was less than 50 mG. The hfsc's are well in accord with those in the literature.[3a] Similarly, 3,6-disubstituted cyclohexadienyl radicals (**3–7**) have been investigated. The ESR spectra of **3**, **5**, and **7** are shown in Figures 2, 3, and 4, respectively. According to the previous analysis for **2**[3] and 6-hydroxycyclohexadienyl radicals,[4a,b] where $a_{1,5}$ should be about 9 G, $a_{2,4} \sim 2.5$ G, $a_3 \sim 13$ G, and a_6 more than 30 G, the proton hfsc's of **3–7** are easily assigned to the positions as shown in Table II.

The radical derived from 3-*tert*-butyl-6-(trimethylsilyl)cyclohexa-1,4-diene (**8**) cannot be assigned unequivocally to **5**;[16] a possible alternative should be **5'** (Scheme III). However, the magnitude of a_6 being larger than 43 G suggests strongly that the radical is not **5'** but **5**, since the former radical should have an a_6 value smaller than 41 G, as was found for **1a–c** and **6**, as well as for 2,4-di-*tert*-butyl-6-silylcyclohexadienyl radicals.[6,7] The selective hydrogen abstraction from **8** by the *tert*-butoxy radical to produce **5** may be attributed partly to the higher thermal stability of **5** than **5'** due to the electron-accepting effect of a silyl group at the 3-position, although the 6-silyl group in **5'** also can be expected to stabilize the radical by σ–π conjugation.[7c,17]

The results suggest that the stabilization by the σ–π conjugation of 6-silyl groups in cyclohexadienyl radicals is not important enough to be determine the direction of hydrogen abstraction from the cyclohexadiene. Similar selective hydrogen abstractions are found in the production of **3** and **4** from 3-(trimethylgermyl)-cyclohexa-1,4-diene and the 6-deuterio derivative, respectively.

Out-of-Plane Distortion of the Cyclohexadienyl Ring due to Group 4B Metal Substituents at the 6-Position. The a_6 values of cyclohexadienyl radicals decrease remarkably with the introduction of a silyl or a germyl substituent at the 6-position, as shown in Table I. Comparing the a_6 values between **2** and **1a** and between **3** and **7**, the decrease due to the introduction of 6-trimethylsilyl and 6-trimethylgermyl groups amounts to 10.2 and 15.3 G, respectively, while the reduction caused by a 6-*tert*-butyl group is not evident. It already has been reported that replacement of one

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[16] So far as we know, only one example of 6-alkyl-substituted cyclohexadienyl radicals has been reported up to date.[12] The radical generated by irradiation of mesitylene in the cavities of a zeolite was assigned to the 2,4,6-trimethylcyclohexadienyl radical whose ^{1}H hfsc at the 6-position was determined as 86.5 G. An unusually large a_6 suggests that the radical may be the isomer, 1,3,5-trimethylcyclohexadienyl radical, whose a_6 should be estimated as 43.3 G from the spread of 86.5 G of the triplet due to two equivalent protons at the 6-position. The absence of a central group of lines may be caused partly by the relatively large second-order splittings and partly by overlaying of the different radical(s).

[17] A somewhat similar effect was observed in the predominant formation of α group 4B metallic radicals from $(CH_3CH_2)_4M$ (M = Si, Ge, and Sn) by Krusic and Kochi (Krusic, P. J.; Kochi, J. K. *J. Am. Chem. Soc.* **1969**, *91*, 6161). However, relative rates of hydrogen abstraction with the *tert*-butoxy radical for structurally similar carbon and silicon compounds indicate rather little difference in the reactivity (Sakurai, H.; Hosomi, A.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1970**, *44*, 568), so that the predominant formation of **5** may not be a simple result of reactivities.

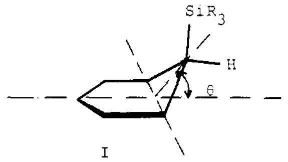
Table III. Calculated $\rho_{1,5}$ Values and a_6 Values for the Supposed Planar Cyclohexadienyl Radicals

radical	$\rho_{1,5}$ [a]	a_6/G obsd	a_6/G calcd [b]	θ/deg [c]
2	0.344	48.1	48.1	0
1a	0.315	37.9	44.0	6.5
1b	0.315	40.2	44.0	4.2
1c	0.313	38.1	43.8	6.1
3	0.329	47.5	46.0	−1.7
5	0.317	43.6	44.3	0.9
6	0.302	35.9	42.2	7.0
7	0.295	32.2	41.3	10.0

[a] Estimated by using eq 3. [b] Estimated by using eq 2. [c] The distortion angle θ's are defined as shown in eq 4.

of the methylene protons with an electronegative group such as OH or F results in the reduction of the remaining methylene proton hfsc's.[4,5b] Yim and Wood[5b] have pointed out that the methylene group orbital of π symmetry is lowered in energy because of replacement of hydrogen by fluorine resulting in less effective hyperconjugation. Since the 6-substituents are all electropositive in our case, these considerations cannot be applied to explain the decrease of a_6 values with 6-silyl and germyl substituents. Electropositive substituents should make the hyperconjugation between the substituted methylene pseudo-π orbital and the cyclohexadienyl SOMO more effective so that the a_6 values should increase in silyl- and germyl-substituted cyclohexadienyl radicals.

Deformation of the equilibrium structure of the cyclohexadienyl radical can be another factor that could account for the effects. Yim and Wood have predicted the potential curve for out-of-plane deformation of the methylene carbon of the cyclohexadienyl radical is rather shallow on the basis of the unrestricted INDO calculations.[5b] We have observed the negative temperature dependence of the a_6 value of **2** (the $da_6/dT = -6.6$ mG/°C) and verified the ease of the out-of-plane vibration from the planar carbon framework.[7c] On the other hand, the 3,6-bis(trimethylsilyl)cyclohexadienyl radical (**6**) has shown a small but positive temperature dependence of the a_6 value ($da_6/dT = 2.6$ mG/°C). Such a positive da_6/dT can be expected when the 6-trimethylsilyl group occupies the axial position at the bent structure at low temperatures, as shown in I. The small a_6 value also can be explained for such an equilibrium geometry, since the remaining 6-proton must occupy the equatorial position. The preferred conformation is stabilized to some extent by σ–π conjugation between the C–Si σ and π systems.[18]



I

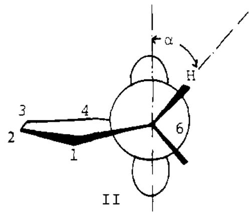
Unrestricted ab initio MO calculations for the equilibrium geometry of **2** and the 6-silylcyclohexadienyl radical (**1d**) also support the conclusion on the equilibrium structure of such cyclohexadienyl radicals. Namely, the parent cyclohexadienyl radical was calculated to be essentially planar, while **1d** showed the energy minimum at $\theta = +4°$, where θ is defined as the angle of out-of-plane distortion from the planar carbon framework as shown in I.[7e]

In the present study, the 6-trimethylgermyl group has been found to reduce the a_6 value more effectively than the 6-trimethylsilyl group, indicative of the larger out-of-plane distortion of the cyclohexadienyl with the former substituent than with the latter. It is suggested that the more effective σ–π conjugation results in a larger out-of-plane distortion from the planar carbon framework in the equilibrium geometry.

The distortion angle θ in I may be estimated experimentally by using the well-known Heller–McConnell equation[19] in connection with Wiffen's consideration.[14] The following equation for the a_6 value is derived:

$$a_6 = (\rho_1^{1/2} + \rho_5^{1/2})^2(A + B\cos^2\alpha) \qquad (1)$$

where ρ_1 and ρ_5 are the π spin densities on carbons 1 and 5, and α is the dihedral angle between pπ orbitals of carbon 1 (and 5) and the C$_6$–H bond as depicted in II. Since the relatively small constant A can usually be ignored, the equation is simplified as follows:



II

$$a_6 = 4\rho_1 B\cos^2\alpha \qquad (2)$$

Prior to determining the $\rho_{1,5}$ values, we should mention that the ring proton hfsc's are slightly modified by the introduction of silyl and germyl groups at the third position. Comparing the proton hfsc's between **1a** and **6**, and between **2** and **3**, the respective absolute values of $a_{1,5}$, $a_{2,4}$, and a_6 are found to be reduced in amounts of 0.34, 0.28, and 1.9 G, by introducing a 3-trimethylsilyl, and 0.40, 0.26, and 0.60 G, by introducing a 3-trimethylgermyl group. Well-known electron-accepting effects of Me$_3$Si and Me$_3$Ge groups due to d–π and/or σ^*–π interaction on π radicals[20] may be responsible for such a small reduction of the proton hfsc's. Thus, the magnitude of $\rho_{1,5}$'s depends on the 3-substituents. The $\rho_{1,5}$ values also varied with the 6-substituent. As we have already mentioned, introduction of an electropositive substituent at the 6th position results in the effective σ–π conjugation between the pseudo-π orbital of the substituted methylene group and the pentadienyl π system. The π spin density of the cyclohexadienyl radical should be reduced by this spin-delocalization mechanism. Actually the apparent $|Q|$ values ($=|\sum_{i=1}^{5}\alpha_i|$, where a_2 and a_4 were reasonably taken as to be positive) for **1a–c** were found to be ca. 2 G smaller than those of the parent cyclohexadienyl ($Q = -26.52$ G) as shown in the last column of Table I.

We can estimate the appropriate $\rho_{1,5}$ values for variously substituted cyclohexadienyl radicals from the McConnell relationship:[21]

$$\rho_{1,5} = Q/a_{1,5} \qquad (3)$$

where Q is taken to be −26.52 G as observed for the cyclohexadienyl radical itself. The $\rho_{1,5}$ values are thus determined for **1a–c** and **2–7** as shown in Table III.

The constant B of eq 2 is calculated to be 46.6 G in order to reproduce the observed a_6 for the cyclohexadienyl radical, **2**, where the dihedral angle is assumed to be 30° for the planar carbon framework. If we suppose the planar ring structures for all the substituted cyclohexadienyl radicals, the a_6 values are easily derived from eq 2 and are shown in the 4th column of Table III. The calculated values are fairly in accord with the experimental ones for **3–5**, while significant deviations in the values are found for **1a–c**, **6**, and **7**. Thus, silyl groups as well as a trimethylgermyl group at the 6-position of the cyclohexadienyl radical are suggested to cause the strong out-of-plane deformation of the methylene

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(18) Inter alia: (a) Kawamura, T.; Kochi, J. K. *J. Am. Chem. Soc.* **1972**, *94*, 649. (b) Symons, M. C. R. *Ibid.* **1972**, *94*, 8589. (c) *Tetrahedron Lett.* **1975** 793. (d) Griller, D.; Ingold, K. U. *J. Am. Chem. Soc.* **1973**, *95*, 6459. (e) *Ibid.* **1974**, *96*, 6715. (f) Sakurai, H.; Uchida, T.; Kira, M. *J. Organomet. Chem.* **1976**, *107*, 15. (g) Kira, M.; Watanabe, M.; Sakurai, H. *J. Am. Chem. Soc.* **1980**, *102*, 5202.

(19) Heller, C.; McConnell, H. M. *J. Chem. Phys.* **1960**, *32*, 1535.

(20) (a) Bedford, J. A.; Bolton, J. R.; Carrington, A.; Prince, R. H. *Trans. Faraday Soc.* **1963**, *59*, 53. (b) Kira, M.; Watanabe, M.; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 7780 and references cited therein.

(21) McConnell, H. M. *J. Chem. Phys.* **1956**, *24*, 632.

Table IV. Temperature Dependence of a_6 Values for 6-Substituted Cyclohexadienyl Radicals

radical	(da_6^H/dT)/ (mG/°C)	radical	(da_6^H/dT)/ (mG/°C)
2	−6.4	6	2.6
3	−7.9	7	5.0
5	−7.2		

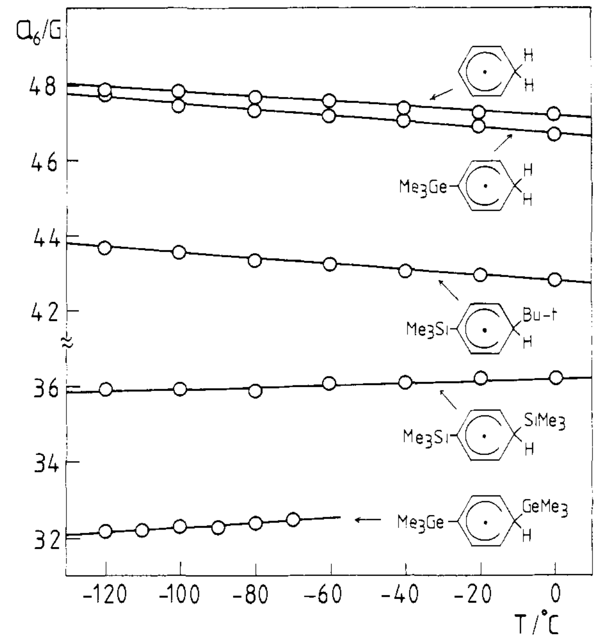


Figure 5. Plots of a_6 values against temperatures for substituted cyclohexadienyl radicals.

carbon. If we assume that the deviation of calculated a_6 values from the experimental is caused only by the out-of-plane deformation of methylene carbon, which varies the dihedral angle α, the distortion angle θ can be calculated as follows, where θ (deg) = $\alpha - 30$ is also assumed.

$$\theta(\text{deg}) = [\cos^{-1}(a_6/4\rho_1 B)^{1/2}] - 30 \qquad (4)$$

As shown in the last column of Table III, 6-trimethylsilyl- and 6-trimethylgermyl-substituted cyclohexadienyl radicals have the distortion angles of 6–7° and 10°, respectively. In spite of the rough estimation where the deformation of the $C_{1,5}$ pπ orbital is not reflected upon, these values are acceptable in comparison with the value calculated by the ab initio MO method for **1d** (θ = 4.3°).[7e]

Distortion of the Ring Structure and the Temperature Dependence of a_6 Values. In a previous study,[7c] we found a negative temperature dependence of a_6 for the planar cyclohexadienyl radical and a positive temperature dependence for a distorted cyclohexadienyl radical, in accordance with the INDO calculated dependence of a_6's on the distortion angle.[5b]

This was confirmed for a wide variety of cyclohexadienyl radicals. Thus, as shown in Table IV and Figure 5, 6-unsubstituted cyclohexadienyl radicals, **2** and **3**, and 6-*tert*-butylcyclohexadienyl radical, **5**, have revealed a rather large negative temperature dependence of the a_6 values, da_6/dT = −6.4 to −7.9 mG/°C, in contrast to the 6-trimethylsilyl and 6-trimethylgermyl derivatives, **6** and **7**, for which the da_6/dT values are +2.6 and +5.0 mG/°C, respectively. The larger temperature coefficient of a 6-trimethylgermyl-substituted cyclohexadienyl radical (**7**) than that of a trimethylsilyl-substituted one (**6**) may be taken as another indication of a larger distortion angle of **7**.

It thus can be concluded that the cyclohexadienyl ring is distorted by replacement of one of the methylene protons with an electropositive group to gain more effective hyperconjugation between the substituted methylene pseudo-π orbital and the ring π system.

Deuterium isotope effects observed in radical **4** are rather difficult to interpret. If we consider that the introduction of deuterium results in the freezing of the appropriate vibrations,[22] the observed negative temperature dependence for **3** as well as that for **2** suggests that ΔD defined in eq 5 should be negative.

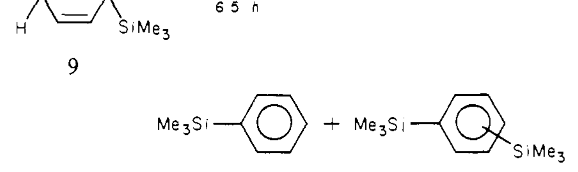
$$\Delta D = a^H(\mathbf{4}) - 6.5144a^D(\mathbf{4}) \qquad (5)$$

On the contrary, the actual ΔD was positive, ca. 2.0 G. Although the origin of the positive deuterium effect remains uncertain, other vibration modes such as methylene H–C–H wagging as well as C–H stretching may be responsible for such isotope effects. On the other hand, the small secondary isotope effect $\Delta D'$, which is defined as in eq 6, can be reasonably explained by the freezing of the out-of-plane deformation of the carbon framework by a deuterium substitution.

$$\Delta D' = a_6^H(\mathbf{3}) - a_6^H(\mathbf{4}) \qquad (6)$$

Fate of the 3,6-Bis(trimethylsilyl)cyclohexadienyl Radical. As determined by ESR, the 3,6-bis(trimethylsilyl)cyclohexadienyl radical (**6**) exists as a paramagnetic species of the highest steady-state concentration during the reaction of 3,6-bis(trimethylsilyl)cyclohexa-1,4-diene (**9**) and photochemically generated *tert*-butoxy radicals at low temperatures. In order to shed light on the fate of this interesting radical, we have investigated the products of the reaction of **9** with *tert*-butoxy radicals generated thermally as well as photochemically.

When a 1:1 mixture of **9** and di-*tert*-butyl peroxide (DTBP) was heated in a sealed tube under nitrogen at 130 °C for a period of 6.5 h, the main products were analyzed to be phenyltrimethylsilane (**10**) and *p*- (**11**) and *m*-bis(trimethylsilyl)benzene (**12**) in 62, 17, and 5% yields, respectively. The material balance on the basis of the six-membered rings was over 80%. In contrast, the photochemical reaction of **9** with DTBP in hexane at 0 °C for a period of 3.5 h afforded a remarkably different product distribution:



9

(7)

10, 62%

11, p-isomer, 17%
12, m-isomer, 5%
13, o-isomer, 0%

$$\mathbf{9} \xrightarrow[3.5\ \text{h}]{\text{DTBP, HP-lamp}} \underset{1\%}{\mathbf{10}} + \underset{35\%}{\mathbf{11}} + \underset{0\%}{\mathbf{12}} + \underset{0\%}{\mathbf{13}} \qquad (8)$$

Poor material balance of the latter reaction may originate in the competitive photochemical isomerization of **9**, which was revealed by an independent experiment[23] in the absence of DTBP. It should be noted that **10**, which is proposed by the elimination of a trimethylsilyl radical from the intermediate radical **6**, mainly is

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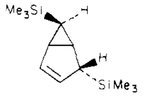
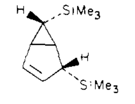
[22] Kochi, J. K.; Bakuzis, P.; Krusic, P. J. *J. Am. Chem. Soc.* **1973**, *95*, 1516 and references cited therein.

[23] When a hexane solution of **9** in a quartz tube was irradiated by a high-pressure mercury lamp under argon at 0 °C for a period of 3.5 h, isomerization products were obtained as a mixture of **15** and **16** in the total yield of 63%. After separating by TLC and GLC, satisfactory elemental analysis and mass spectra were obtained for **15** and **16**, respectively. The structure of these products was determined by NMR analysis. The details of this novel photoisomerization will be reported later.

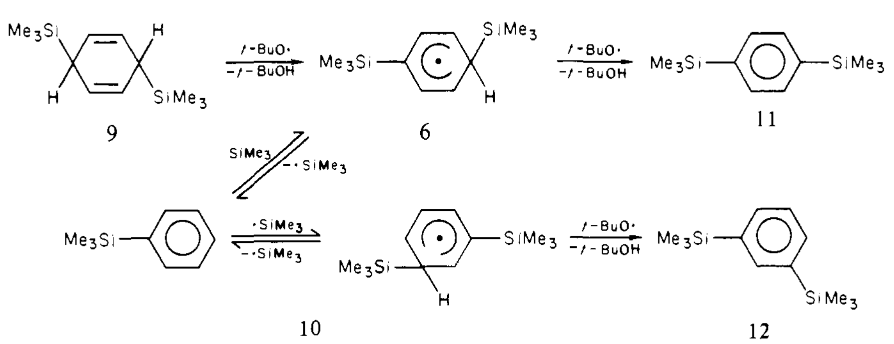


15



16

Scheme IV



produced in the reaction at high temperatures, while the yield of **10** amounted only to 1% in the reaction at 0 °C.

The reaction pathways of primary radical **6** may be represented as shown in Scheme IV.

These results indicate that the spontaneous elimination of a trimethylsilyl radical from **6** is much preferred at high temperatures to the hydrogen abstraction to afford **11**, while the former reaction is not important at low temperatures.

The actual intermediacy of the trimethylsilyl radical for the reaction to give **10** was proved by spin-trapping experiments. When a mixture of **9**, di-*tert*-butyl peroxyoxalate, and 1,1-di-*tert*-butylethylene as a spin-trap was warmed up in an ESR cavity at 40 °C, the silyl-radical adduct (**14**) was detected by ESR with high signal intensity. The hfsc's of **14** were 15.6 G for two β-methylene protons and 0.35 G for 18 protons of two *tert*-butyl groups, in good agreement with those reported by Griller and Ingold.[24]

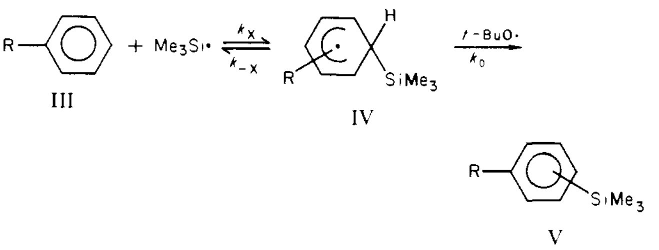
$$t\text{-BuOOC(=O)C(=O)OOBu-}t \xrightarrow{\Delta} 2\,t\text{-BuO}\cdot + 2CO_2$$
$$t\text{-BuO}\cdot + \mathbf{9} \rightarrow \mathbf{6}$$
$$\mathbf{6} \rightarrow \mathbf{10} + Me_3Si\cdot \tag{9}$$
$$Me_3Si\cdot + (t\text{-Bu})_2C{=}CH_2 \rightarrow \underset{\mathbf{14}}{(t\text{-Bu})_2\dot{C}\text{-}CH_2SiMe_3}$$

On the Reversibility of Free-Radical Addition of Group 4B Radicals on Aromatics. Although various free-radical aromatic substitution reactions have been reported, no decisive evidence for the reversibility in the addition step by carbon-centered radicals has been found up to date.[15] On the other hand, Eaborn et al. have suggested the reversible addition of a silyl radical to benzene on the basis of the temperature dependence of the yields for the reaction of bis(trimethylsilyl)mercury with benzene.[25] They also reported that essentially no addition of a germyl radical occurred to aromatics.[25b] Our results described above have clearly demonstrated that the addition of the trimethylsilyl radical to benzene is reversible and that the unimolecular fragmentation of the adduct becomes faster at elevated temperatures than the competitive hydrogen abstraction by *tert*-butoxy radicals.

On the basis of the difference of C–M bond energies among C–C, C–Si, and C–Ge bonds, Jackson has recently interpreted the remarkable difference among the features of the group 4B radical aromatic substitution reactions.[26] From the point of view of the structures of the adduct radicals revealed by the ESR study, one can point out factors influencing the reversibility in homolytic aromatic substitution with a group 4B radical.

(i) The extent of the σ–π conjugation between substituted methylene pseudo-π orbitals and the pentadienyl π system is suggested to increase in the order 6-Me_3Ge > 6-Me_3Si ≫ 6-Me_3C, which is in good agreement with the observed order for the ease of the fragmentation reaction of the 6-substituted cyclohexadienyl radicals. Effective σ–π conjugation may result in the lowering of the C–M σ bond order due to electron delocalization from the bonding orbital.

Scheme V



$$d(V)_x/dt = k_a(IV)_x(t\text{-BuO}\bullet)$$
$$(V)_x/(V)_{x'} = (IV)_x/(IV)_{x'} \approx (k_x/k_{-x})/(k_{x'}/k_{-x'})$$

(ii) Analysis of the ESR spectra for various 6-substituted cyclohexadienyl radicals has indicated the significant out-of-plane deformation of the carbon framework for silyl- and germyl-substituted radicals. A 6-(trimethylgermyl)cyclohexadienyl radical, whose 6-substituent is a better leaving group than that of a 6-(trimethylsilyl)cyclohexadienyl radical, has a more distorted structure. We can imagine from these results that the structure of the transition state for Me_3Ge addition to benzene may resemble a produced 6-(trimethylgermyl)cyclohexadienyl radical. Thus the group 4B radical may approach vertically to the benzene π plane to afford a σ complex with the 6-substituent in the pseudoaxial position of the ring.

Finally we will discuss our previous study on the directive effects and relative reactivities in free-radical aromatic silylation.[27] In the report the reversibility of the silyl radical addition was not taken into account. Since our present study indicated that the rate-determining step should be the hydrogen-abstraction step rather than addition of the silyl radical, the product distribution should be determined by the relative concentration of isomeric silyl-substituted cyclohexadienyl radicals. The observed Hammett relationship between log (k/k_H) and σ constants should be understood as the relationship between log K_x ($K_x = k_x/k_{-x}$) and σ (Scheme V).

Although such modification is necessary, the essential features of conclusions that the silyl radicals are nucleophilic in nature, the addition process is exothermic, and the transition state may resemble the intermediate radical (IV) can be conserved. Hyperconjugative electron donation by the 6-trimethylsilyl group in IV should increase the negative charge on the cyclohexadienyl ring; IV may be stabilized by an electron-withdrawing substituent on the ring.

Experimental Section

Materials. Cyclohexa-1,4-diene was prepared by Birch reduction[28] or by treating 3,6-bis(trimethylsilyl)cyclohexa-1,4-diene with potassium in carbitol.[29] 3-(Trimethylgermyl)-,[30] 3-deuterio-6-(trimethylgermyl)-,

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[24] (a) Griller, D.; Ingold, K. U. *J. Am. Chem. Soc.* **1973**, *95*, 6458. (b) *Ibid.* **1974**, *96*, 6715.

[25] (a) Eaborn, C.; Jackson, R. A.; Pearce, R. *J. Chem. Soc., Chem. Commun.* **1967**, 920. (b) Bennett, S. W.; Eaborn, C.; Jackson, R. A.; Pearce, R. *J. Organomet. Chem.* **1971**, *28*, 59.

[26] Jackson, R. A. *J. Chem. Soc., Chem. Commun.* **1974**, 573.

[27] Sakurai, H.; Hosomi, A. *J. Am. Chem. Soc.* **1971**, *93*, 1709.

[28] Giovannini, E.; Wegmüller, H. *Helv. Chim. Acta* **1959**, *42*, 1142.

[29] Dunoguès, J.; Calas, R.; Ardoin, N. *J. Organomet. Chem.* **1972**, *43*, 127.

3,6-bis(trimethylgermyl)-, and 3-*tert*-butyl-6-(trimethylsilyl)cyclohexa-1,4-dienes were prepared by the general method of Eaborn et al., where the corresponding 1,4-disubstituted benzenes were reduced electrolytically in methylamine in the presence of LiCl.[30]

3-Deuterio-6-(trimethylgermyl)cyclohexa-1,4-diene: NMR (60 MHz, CCl_4) δ 0.22 (s, 9), 2.48 (m, 1), 2.72 (m, 1), 5.59 (m, 4); MS *m/e* 199 (M^+). The deuterium content was determined as 86% by MS analysis.

3-*tert*-Butyl-6-(trimethylsilyl)cyclohexa-1,4-diene. The reduction of 1-*tert*-butyl-4-(trimethylsilyl)benzene gave a mixture of two isomeric cyclohexadienes, the title compound and 1-*tert*-butyl-4-(trimethylsilyl)-cyclohexa-1,4-diene (1:0.9 determined by NMR). NMR of the former (60 MHz, CCl_4): δ 0.08 (s, 9), 0.96 (s, 9), 2.32 (m, 1), 2.57 (m, 1), 5.68 (m, 4). NMR of the latter (60 MHz, CCl_4): δ 0.12 (s, 9), 1.10 (s, 9), 2.73 (m, 4), 5.54 (m, 1), 6.06 (m, 1). The mixture was used satisfactorily for ESR experiments.

3,6-Bis(trimethylgermyl)cyclohexa-1,4-diene. The electrolytic reduction of 1,4-bis(trimethylgermyl)benzene afforded 31% of the title compound: bp 65–90 °C (7 mmHg); NMR (60 MHz, CCl_4) δ 0.21 (s, 18), 2.52 (m, 2), 5.42 (br s, 4); MS m/e 314 (M^+). The GLC analysis indicated the presence of two isomers with a ratio of 69/31 which may be assigned to the cis-trans isomers.

3,6-Bis(trimethylsilyl)cyclohexa-1,4-diene was prepared from benzene, Me_3SiCl, and lithium in THF.[31] From the mixture with 1,4-bis(trimethylsilyl)benzene, the desired product was separated by TLC, mp 50–51 °C (lit. mp 50–51 °C). The purified material was used for both ESR and the product studies of the reaction with di-*tert*-butyl peroxide.

ESR Spectroscopy. ESR spectra were recorded with Varian E-12 equipment (9.5-GHz frequency, 3300-G magnetic field, and field modulation 100 KHz) and are calibrated with the anthracene cation radical in concentrated H_2SO_4.[32] Photolyses were carried out in a cavity of the ESR spectrometer with a 500-W Ushio Super-high-pressure mercury lamp. Temperatures were controlled by a Varian's variable temperature accessory and calibrated with a Cu–constantan thermocouple.

Reaction of 3,6-Bis(trimethylsilyl)cyclohexa-1,4-diene and Di-*tert*-butyl Peroxide. Thermal reaction: A mixture of 3,6-bis(trimethylsilyl)cyclohexa-1,4-diene (0.464 mmol) and DTBP (0.464 mmol) was sealed in a Pyrex glass under argon and was heated in an oil bath at 130 ± 10°C for 6.5 h.

Photoreaction: A mixture of 3,6-bis(trimethylsilyl)cyclohexa-1,4-diene (0.454 mmol) and DTBP (0.473 mmol) in *n*-hexane (1 mL) in a quartz tube was photolyzed by a high-pressure mercury lamp for 3.5 h at 0 °C.

The products were analyzed on a Hitachi K-53 GLC with an Apiezon L (30%, 2 m) or a SE 30 (20%, 2 m) column.

Acknowledgment. We thank Toshiba Silicone Co., Ltd., for gifts of chlorosilanes.

Registry No. 1a, 79585-24-3; **1b**, 79585-26-5; **1c**, 79585-25-4; **2**, 12169-67-4; **3**, 87088-28-6; **4**, 87088-27-5; **5**, 87088-29-7; 6, 63470-25-7; **7**, 86472-63-1; **8**, 87012-82-6; **9**, 18090-43-2; 3-deuterio-6-(trimethylgermyl)cyclohexa-1,4-diene, 87012-81-5; 1-*tert*-butyl-4-(trimethylsilyl)-cyclohexa-1,4-diene, 87012-83-7; *cis*-3,6-bis(trimethylgermyl)cyclohexa-1,4-diene, 87012-84-8; *trans*-3,6-bis(trimethylgermyl)cyclohexa-1,4-diene, 87012-85-9.

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S_N2 Deprotection of Synthetic Peptides with a Low Concentration of HF in Dimethyl Sulfide: Evidence and Application in Peptide Synthesis[1]

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Abstract: An S_N2 deprotection reaction for synthetic peptides was observed when the weak base dimethyl sulfide was used as a diluent for HF. Kinetic studies of the deprotection of *O*-benzylserine revealed that there was a sharp changeover in mechanism from $A_{AL}1$ to $A_{AL}2$ when the concentration of HF in dimethyl sulfide was below 55%. The changeover in mechanism was also found in the deprotection of *O*-benzyltyrosine. At higher HF concentrations (>55%), the $A_{AL}1$ cleavage mechanism, which generates carbonium ions, led to significant 3-benzyltyrosine side product. However, at low HF concentrations, the side product was minimal as a result of an $A_{AL}2$ cleavage mechanism in which carbonium ions are not formed. A sharp increase of side product was seen when the HF concentration reached the critical changeover concentration. The HF–dimethyl sulfide reagent was also found to reduce methionine sulfoxide to methionine and, in the presence of a thiol, to deprotect N^i-formyltryptophan to tryptophan. Both of these reactions were also dependent on the concentration of HF and were optimal at low concentrations. Furthermore, deprotection of aspartic and glutamic acid side chain benzyl esters at the low HF concentration also minimized the $A_{AC}1$ mechanism and the accompanying acylation side reactions. A practical mixture for the S_N2 deprotection reaction was found to be HF–dimethyl sulfide–*p*-cresol (25:65:10 v/v). For the deprotection of Trp(For)-containing peptides, the reagent was adjusted to HF–dimethyl sulfide–*p*-cresol–*p*-thiocresol (25:65:7.5:2.5 v/v) so that the N^i-formyl could be removed concomitantly with other protecting groups. The low-acidity function, S_N2 reaction was also effective for solid-phase peptide synthesis. The same protecting groups were removed as in solution, and in addition the bond holding the peptide to the resin support was cleaved. For more resistant anchoring bonds and protecting groups a combined low–high HF procedure was developed, in which most of the precursors of harmful carbonium ions are removed by a S_N2 mechanism before the final strong-acid, S_N1, step begins. The new deprotection procedure was tested on three synthetic model peptides, methionine-enkephalin, bovine growth hormone fragment (128–131), and C-terminal pentagastrin amide, and was found to provide efficient deprotection and significant reduction in the level of alkylation side reactions, the rearrangement to aspartimide, and the acylation of aromatic scavengers by glutamic acid.

The chemical synthesis of peptides, whether in solution or in solid phase, requires a final step in which all protecting groups and polymeric supports are removed.[2] For this purpose, many methods have been developed, all aiming for a method with

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