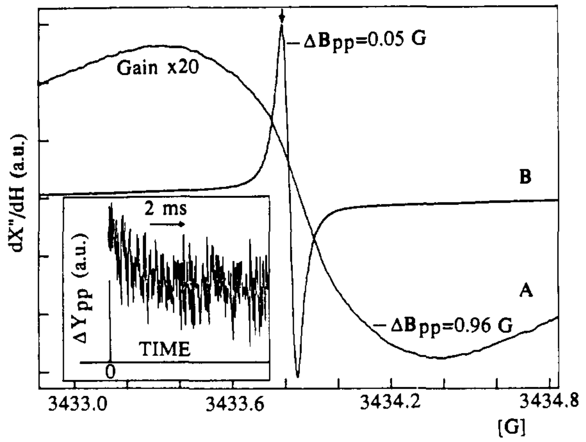

Figure 1. ESR spectra of a buffer solution of PcLi crystals when (A) air exposed and (B) degassed. Arrow indicates ESR position for time-resolved measurement. Inset: Time-resolved changes in PcLi signal amplitude (peak height) related to oxygen evolution in PSII membranes. The trace represents an averaged response after 250 laser pulses separated with 0.2-s dark intervals. Laser pulse at time 0. Time constant: 0.01 ms. For details, see Figure 2.

only weak contact in the lattice and forming channels coaxial with the 4-fold axis into which oxygen freely diffuses without complexation or charge transfer.[5]

In the absence of oxygen, the PcLi ESR signal can be saturated at low microwave power ($P_{1/2}$ = 2.6 mW), while in air-saturated solution, this increases to above our detection limit (>200 mW). This is instantaneous and reversible. Thus the effect arises from the increased spin relaxation rate of the conduction electron spins in PcLi upon collision with oxygen.

The 20-fold broadening of the unsaturated PcLi signal is almost 10 times larger than the broadening observed upon air saturation of the nitroxide molecule perdeuterio[^{15}N]tempone. This increased sensitivity is one of the advantages of the method. The area of the signal is constant at different oxygen concentrations, indicating chemical stability. A plot of ESR signal amplitude at different oxygen concentrations was prepared for calibration (not shown). In the present work, we used nonsaturating microwave power and oxygen concentration changes that were in the linear region of the calibration standards.

The PcLi radical was quite stable in the buffer for at least 2 months. In the PSII membrane mixture, no amplitude change of the ESR signal of PcLi was observed in the dark nor upon illumination until an exogenous electron acceptor (DCBQ) was added to enable reoxidation of the PSII plastoquinone acceptors. No oxygen production was observed in the absence of DCBQ, as monitored polarographically. This shows that the PcLi radical is chemically stable under illumination and in the presence of PSII. This chemical stability is a major advantage over the soluble nitroxide spin probe.

When a series of saturating, single-turnover laser flashes was exposed to dark-adapted PSII membranes, a period-four oscillation in the signal amplitude of PcLi was observed (Figure 2). The changes in the signal amplitude after each flash are plotted in the inset. This is 0 on the first two flashes and maximum on the third, seventh, and 11th flashes, corresponding to the familiar pattern of oxygen formation from the water oxidizing complex.[11] The method described here gives reliable results for oxygen concentrations in the range 0–0.2 mM. The sensitivity of the method is $\Delta[O_2] = 3 \times 10^{-7}$ μmol (for S/N = 1 at 0.5 mg/mL PcLi and 1-s response time). We have been able to use this method effectively for measurement of oxygen in the gas phase, in aqueous suspensions, and in direct contact with nonaqueous membrane samples.

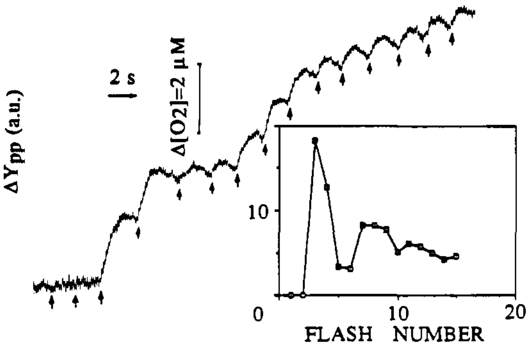

Figure 2. Changes in PcLi ESR signal amplitude (high field derivative peak) after illumination at 300 K of PSII membranes with a series of single-turnover laser flashes separated by 2-s dark intervals. Arrows indicate consecutive laser flashes. PSII membranes were kept in the dark for at least 10 min prior to flash excitation. The reaction medium contained 50 mM Mes-NaOH (pH 6.0), 15 mM $MgCl_2$, 20 mM NaCl, 1 mM DCBQ, 0.5 mg/mL PcLi, and 1 mg/mL chlorophyll as PSII membranes. Excitation source: Nd:YAG laser with a pulse duration of 20 ns, pulse energy of 75 mJ, and λ = 532 nm (MY32, Molectron Corp.). Microwave power: 1 mW. Modulation amplitude: 0.02 G. Time constant: 0.04 s. Inset: plot of the signal amplitude change vs. the flash number.

Time resolution of the signal, as given in Figure 1 (inset), reveals that under repetitive flashes a transient decrease in the PcLi signal can be resolved having a half-life of 1–2 ms. This signal appears only on resonance with the PcLi ESR signal and is abolished by treatments that inactivate oxygen production. These kinetics match those reported for the detection of oxygen at a Pt rate electrode when poised at the reduction potential suitable for oxygen detection.[2,12]

Acknowledgment. We thank Mr. Richard Hutchins for technical assistance and Dr. Peter Gast for advice. This research was supported by the National Science Foundation through Grant DCB89-14017.

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A Versatile Protecting Group for 1,2-Dicarba-*closo*-dodecaborane(12) and the Structure of a Silylcarborane Derivative

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The incorporation of the icosahedral $1,2\text{-}C_2B_{10}H_{12}$ carborane moiety into ever more complex organic structures has recently become of great importance. This rapid development of carborane chemistry derives from a renewed interest[1a] in the cytotoxic boron-neutron capture reaction $^{10}B(n,\alpha)^7Li$, as the basis of a binary method for cancer therapy (BNCT), and the recent discovery of radiometallacarborane reagents of unprecedented stability suitable for radiomedical application as immunoconjugates.[1b] Unfortunately, the synthesis of very valuable mono-C-substituted $1,2\text{-}C_2B_{10}H_{12}$ species is now based upon the two synthesis methods of limited utility exemplified below.

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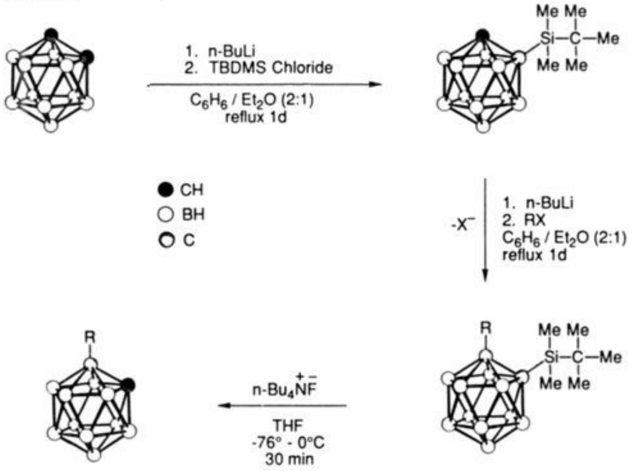
(1) (a) Hawthorne, M. F. *Pure Appl. Chem.* **1991**, *63*(3), 327 and references therein. (b) Hawthorne, M. F.; Varadarajan, A.; Knobler, C. B.; Chakrabarti, S.; Paxton, R. J.; Beatty, B. G.; Curtis, F. L. *J. Am. Chem. Soc.* **1990**, *112*, 5365.

Scheme I



The first method (eq 1) utilizes a terminal alkyne, RC≡CH, in which the substituent group, R, is limited to alkyl, alkenyl, aryl, and a paucity of groups that contain the alkylcarboxylate function (L = donor ligand such as Et_2S).[2]

$$RC{\equiv}CH + B_{10}H_{12}L_2 \rightarrow 1\text{-R-}1,2\text{-}C_2B_{10}H_{11} + 2L + H_2 \qquad (1)$$

The second method (eq 2) requires the monolithiation of $1,2\text{-}C_2B_{10}H_{12}$ (**1**) at carbon, followed by the use of the resulting monolithiocarborane as a nucleophile.[3] This sequence of reactions is complicated by the facile disproportionation of the monolithio species which leads to dominant and undesired di-C-substituted products or exocyclic species in the case of bifunctional electrophiles. While this second method is potentially the more convenient source of the desired carborane derivatives, to our knowledge no group suitable for the selective protection of a single carborane carbon atom in a lithiation sequence is known. Herein we describe a versatile protecting group for **1** that achieves this goal: *tert*-butyldimethylsilyl (TBDMS).

$$\begin{tikzcd}
1,2\text{-}C_2B_{10}H_{12} \arrow[r, "BuLi", "-BuH"'] & 1\text{-Li-}1,2\text{-}C_2B_{10}H_{11} \arrow[r, leftrightharpoons] \arrow[d, "RX"', "-LiX"'] & 1/2\ 1,2\text{-}Li_2\text{-}1,2\text{-}C_2B_{10}H_{10} + 1/2\ 1,2\text{-}C_2B_{10}H_{12} \arrow[d, "RX"', "-LiX"'] \\
 & 1\text{-R-}1,2\text{-}C_2B_{10}H_{11} & 1/2\ 1,2\text{-}R_2\text{-}1,2\text{-}C_2B_{10}H_{10}
\end{tikzcd} \qquad (2)$$

Reaction of **1** with 1 equiv of *n*-BuLi at 0 °C in 2:1 C_6H_6/Et_2O established the equilibrium (2). The monolithio component of this equilibrium reacts quantitatively with 1 equiv of TBDMS chloride at 35 °C to produce **2** in 99% yield (Scheme I). To monolithio **2** formed from **2** and 1.1 equiv of *n*-BuLi in 2:1 C_6H_6/Et_2O was added 0.5 equiv of 1,2-bis(bromomethyl)benzene. After 24 h at 35 °C, **3** was obtained in 74% yield. Complete retention of the silyl group was observed. Deprotection of **3** with $n\text{-}Bu_4N^+F^-$ in THF (−76 to 0 °C) for 20 min afforded **4** (71% overall).

Colorless parallelepipeds of **3** suitable for single-crystal X-ray analysis[4] were grown from an acetone solution. The molecular structure of **3** is presented in Figure 1. Examination of the structure confirms incorporation of the silyl protecting group adjacent to the *o*-xylyl bridge. The molecule adopts a structure that most likely serves to minimize steric repulsions between the bulky silyl groups. This feature is reflected by normal Si–C single bond distances, essentially tetrahedral geometry at silicon, and the lack of structural distortions of the carborane cage geometry.

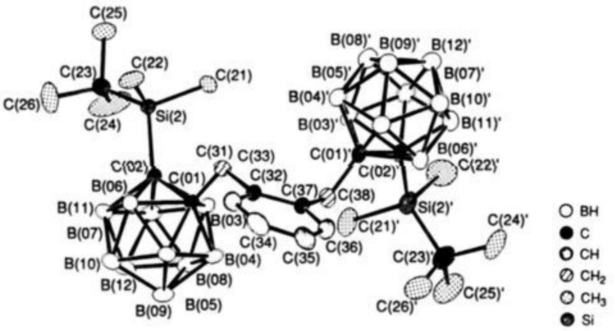
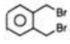
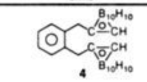
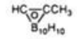
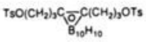
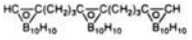
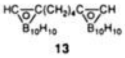
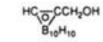


Figure 1. ORTEP representation of **3** showing the numbering scheme. All hydrogen atoms were removed for clarity. Elipsoids were drawn at 0.2 probability. Interatomic distances in Å: Si(2)–C(02) 1.951 (4), C(01)–C(02) 1.714 (6), Si(2)′–C(02)′ 1.956 (5), C(01)′–C(02)′ 1.707 (7).

Table I. Protected and Deprotected *closo*-$1,2\text{-}C_2B_{10}H_{12}$ Derivatives

Substrate (RX)	Protected Product (RTBDMS)	Protected Product Yield	Deprotected Product (RH)	Deprotected Product Yield
	3	74%	 **4**	94%
CH_3I	5	86%	 **10**	80%
$n\text{-}C_4H_9Br$	6	80%	 **11**	90%
	7	75%	 **12**	94%
$Br(CH_2)_4Br$	8	70%	 **13**	92%
ClC(O)OMe	9	93%	 **14**[a]	88%

[a] The reaction was carried out in THF with 1.4 equiv of $LiAlH_4$.

From Table I it can be seen that the lithio derivative of **2** reacts in good yield with a variety of mono- and difunctional electrophiles under mild conditions to form the corresponding silylated products. Efficient desilylation produces the desired C-substituted and C-bridged carborane derivatives, thus providing a far superior route to these materials. Specifically, an inefficient synthesis of **4**, which employed $1\text{-HOCH}_2\text{-}1,2\text{-}C_2B_{10}H_{11}$ as the starting material, required eight steps.[5] The exocyclic ring derivative was the only product observed when the lithiocarborane–dilithiocarborane equilibrium mixture (reaction 2) was used in a separate attempt to prepare **4** from 1,2-bis(bromomethyl)benzene.[6] Other protecting groups such as Me_3Si and PhS were attached to **1**, but were easily displaced by base (*n*-BuLi) in the subsequent step. It is interesting to note that *tert*-butyldiphenylsilyl chloride did not function as a silylation reagent, presumably due to steric constraints. The TBDMS group presents the proper balance of steric requirements that allows the selective monosilylation of **1** and retention of the C–Si bond in **2** during subsequent reactions.

The utility of the protected silylcarborane is illustrated in the development of functionalized precursors of bridged carborane chelating systems employed for the complexation of radiometal ions (Venus flytrap clusters), and their subsequent conjugation to monoclonal antibodies.[1b,7]

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[4] Crystal data for **3**: $C_{24}H_{58}B_{20}Si_2$; space group *Pbca* with $a = 14.9627$ (4) Å, $b = 16.8350$ (4) Å, $c = 32.5970$ (8) Å, $V = 7893$ Å^3, and $Z = 8$. Data collected on a Syntex $P\bar{1}$ diffractometer at 25 °C with Cu Kα ($\lambda = 1.5418$ Å). A 2θ range from 0 to 115° gave 5408 unique data. The structure was solved by direct methods (SHELX86) and refined by least-squares and Fourier techniques using 313 variables against 3172 data for which $F^2 > 3\sigma(F^2)$, to give $R = 6.00\%$, $R_w = 7.30\%$, and GOF = 2.00.

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We have described a versatile protecting group (TBDMS) for 1,2-$C_2B_{10}H_{12}$ that allows the efficient synthesis of monosubstituted and linked carboranes. The generality of the method coupled with the high yields obtained offers a valuable new tool for organic transformations on carborane cages. As shown previously, the silyl substituent on carborane cages provides unique reactivity, crystal growth and cage stability.[8] Work that extends to other areas of carborane chemistry is currently in progress.

Acknowledgment. We thank the National Institutes of Health for support of this research under Grant CA43904 and for an NIH MARC predoctoral fellowship (Grant GM11586) for F.A.G. We also thank the National Science Foundation for a postdoctoral fellowship (Grant NSF-CHE 90-01819) for S.E.J. We also thank Lai-Ling Ng and Carolyn Knobler for assistance.

Supplementary Material Available: Tables of bond distances and angles and positional and thermal parameters for **3**, details of the crystallographic data collection for **3**; experimental data on the preparation of **2–14**, and collection and reduction of X-ray data and solution and refinement of the structure of **3** (18 pages); table of observed and calculated structure factors for **3** (19 pages). Ordering information is given on any current masthead page.

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Silicon-Promoted Nef Reaction by a γ-Effect

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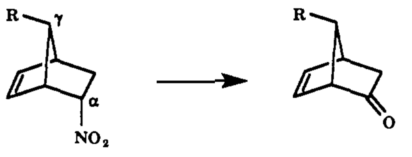
The γ-effect of silicon[1] results from the interaction between the back lobes of the Si–C_γ bond and the developing p orbital at the C_α position in a silicon-containing species. Studies on the solvolysis of γ-silyl-substituted compounds provide solid evidence to show the existence of the γ-effect.[2-8] Few examples, however, have demonstrated the use of this effect in synthesis.[9] We report herein the first systematic application of the silicon γ-effect to an organic reaction: a γ-trimethylsilyl group can assist nitro compounds to be converted to ketones under mild conditions.

Many methods have been developed for performance of the Nef reaction.[10] Nevertheless, some nitro compounds fail to be degraded to ketones under most conditions employed, such as the conversion of 5-nitrobicyclo[2.2.1]hept-2-enes **1** and **2** to the corresponding ketones **4** and **5**, respectively (Scheme I). The major products isolated are a cyclic hydroxamic ester and a lactone.[11-14] A compound possessing the skeleton of **1** would provide an ideal example to show the feasibility of the γ-silicon-promoted Nef reaction. Accordingly, we synthesized γ-trimethylsilyl nitro compound **3** by following Ranganathan's procedure.[15]

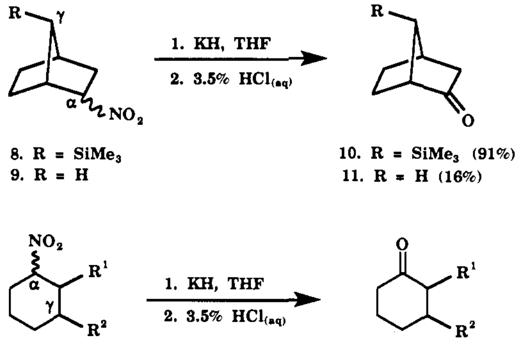
Scheme I



1. R = H
2. R = CH$_2$OMe
3. R = SiMe$_3$

4. R = H
5. R = CH$_2$OMe
6. R = SiMe$_3$ (64%)

Scheme II



8. R = SiMe$_3$
9. R = H

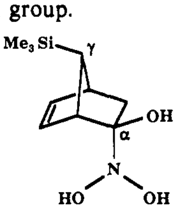
10. R = SiMe$_3$ (91%)
11. R = H (16%)

12. R^1 = H, R^2 = SiMe$_3$
13. R^1 = R^2 = H
14. R^1 = CH$_2$SiMe$_3$, R^2 = H
15. R^1 = Me, R^2 = H

16. R^1 = H, R^2 = SiMe$_3$ (87%)
17. R^1 = R^2 = H (8%)
18. R^1 = CH$_2$SiMe$_3$, R^2 = H (85%)
19. R^1 = Me, R^2 = H (18%)

We treated nitro compound **3** with 1.5 equiv of KH in THF at 0 °C–room temperature for 3 h and then with 3.5% aqueous HCl. After workup and purification, ketone **6** was obtained in 64% yield.

In comparison with failure of the Nef reaction for **1** and **2**, the successful conversion of **3** to **6** must be attributed to the Me_3Si group. We believe that the route from **3** to **6** involves the hydrated intermediate **7**,[16] in which the Me_3Si group is anti to the trihydroxyl moiety $HOCN(OH)_2$. Thus the silicon-promoted conversion must result from the γ-effect, not from the steric congestion caused by the Me_3Si group.



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[*] Research fellow of the Alfred P. Sloan Foundation (1986–1990).

[†] The Johns Hopkins University.

[‡] Address correspondence to this author at National Tsing Hua University and Academia Sinica.

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