0.82) at pH 6 along with the corresponding percent fluorescence intensity increase (>145%) could then be obtained.[17] Similarly, values were determined at pH 6 for the binding of **1** to ATP (log K_{eq} = 4.2, 79%), citrate (log K_{eq} = 2.3, 97%), sulfate (log K_{eq} = 1.6, 114%), acetate (log $K_{eq} \leq 0.6$, >98%), and dimethyl phosphate (log $K_{eq} \leq 0.5$, >66%). As an indication that even larger fluorescence enhancements are likely with structurally modified conjugate probes, we have observed a 6-fold CHEF effect for the binding of citrate to anthrylbis(polyamine) **2** (Figure 3); however, calculations indicate a binding event of more complex stoichiometry that is under study.

The present work demonstrates that intracomplex protonation of a quenching nitrogen leads to CHEF effects in aqueous solution in the same way that metal ion chelation does. We believe our results suggest a general and heretofore undescribed method for the chromogenic "signalling" of anion binding. Since the origin of the effect can be rationalized at the molecular level, a structural basis exists for the design of conjugate probes for ionic and hydrogen-bonding guests. Given the almost limitless synthetic approaches to nitrogen-containing hosts,[18] the fabrication of useful analytic tools seems likely to result.

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(17) Binding constants were determined by using the computer program ENZFITTER, available from Elsevier-BIOSOFT, 68 Hills Road, Cambridge CB2, 1LA, United Kingdom.

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Chiral Organosilicon Compounds in Synthesis. Highly Enantioselective Synthesis of Arylcarbinols[1]

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Because of the usefulness of organosilicon compounds in organic synthesis, it is not surprising that considerable attention has recently been focused on the use of chiral organosilicon compounds for enantioselective synthesis.[1-11] One approach is to utilize organosilanes where the silicon atom is the chiral center, usually the 1-naphthylphenylmethylsilyl group.[2-7] The alternative approach is to use organosilicon compounds with the chirality located at a site attached to, but removed, from silicon. A number of groups,[8-11] including our own,[1] have taken up this approach because of the greater structural variety that can be incorporated into the chiral moiety. Chiral auxiliaries derived from optically active natural products[1,8,9,11] or by resolution[10] have been used. However, it is fair to say that the stereoselectivity obtained from either approach has been modest so far.

We report here our recent results, which show that highly enantioselective synthesis of arylcarbinols can be achieved by alkylation of chiral organosilicon compounds. It is our expectation that the approach may have general applicability.

The chiral organosilicon compound **1** was prepared from dimethyl(chloromethyl)benzylsilane (**2**)[12] and (*S*)-(+)-2-(methoxymethyl)pyrrolidine (**3**) (Scheme I). Treatment of **1** with *sec*-butyllithium in THF gave the carbanion **4**, which on quenching with methyl iodide gave the alkylated product **5a** in good yield. As is evident from ^{1}H NMR and subsequent transformations (vide

Scheme I

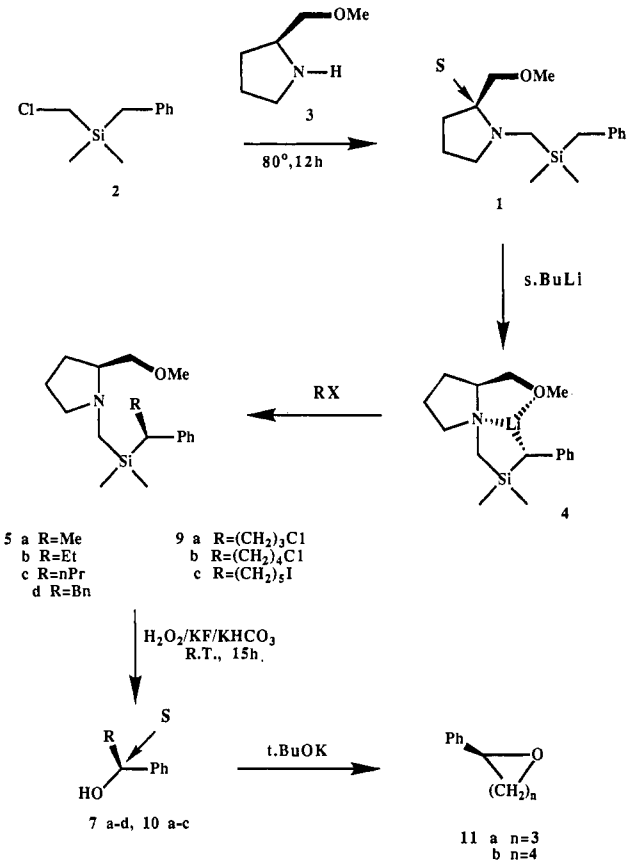

Table I. Alkylation of Carbanion **4** with Alkyl Halide RX According to Scheme I

RX	product	yield,[a] %	$[\alpha]^{20}_D$ (*c* 1, $CDCl_3$), deg	de (NMR),[b] %
MeI	**5a**	86	-98	>95
nPrI	**5c**	82	-73	>95
EtI	**5b**	78	-81	>95
$PhCH_2Cl$	**5d**	58	-4	>95
$I(CH_2)_5I$	**9c**	55	-43	>95
$Cl(CH_2)_3Br$	**9a**	61	-49	>95
$Cl(CH_2)_4Br$	**9b**	64	-59	>95

[a] Yield after flash chromatography. [b] ^{1}H NMR showed only one diastereomer.

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(12) Compound **2** was prepared from the reaction of benzylmagnesium chloride and dimethyl(chloromethyl)chlorosilane in 95% yield. It has the following physical characteristics: bp 120-124 °C (40 mmHg); ^{1}H NMR (in $CDCl_3$, 200 MHz) δ 7.20 (s, 5 H), 2.78 (s, 2 H), 2.27 (s, 2 H), 0.15 (s, 6 H).

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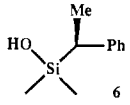
Table II. Oxidation of **5** or **9** To Give Alcohols **7** or **10**

R	product	yield,[a] %	$[\alpha]_D$ (c 1, $CDCl_3$), deg	lit. $[\alpha]_D$	% ee GC[e]
Me	**7a**	91	-39	-41.3[b]	98.5
nPr	**7c**	90	-45	-48.6[b]	>99.5
Et	**7b**	92	-44	-47.6[c]	99.0
$PhCH_2$	**7d**	82	-14	-56.1[d]	*f*
$I(CH_2)_5$	**10c**	84	-21		
$Cl(CH_2)_3$	**10a**	89	-33		
$Cl(CH_2)_4$	**10b**	87	-32		

[a] After flash chromatography. [b] Reported values for Aldrich. [c] See: Yoshioka, M.; Kawakita, T.; Ohno, M. *Tetrahedron Lett.* **1989**, *30*, 1657-1660. [d] See: Berti, G.; Bottari, F.; Ferrarini, P. L.; Macchia, B. *J. Org. Chem.* **1965**, *30*, 4091-4096. [e] The % ee was determined by GC according to ref 17. [f] The % ee of **7d** was determined by ^1H NMR using $Eu(tfc)_3$ to be better than 95%. We are unable at the present time to account for the discrepancy between the ^1H NMR determination and the literature $[\alpha]_D$ values.

infra), compound **5a** was formed as a mixture of diastereomers (75:25, 50% de). *However, when the same reaction was carried out in ether as solvent, compound* ***5a*** *was obtained as a single diastereomer.* Since the ^1H NMR signals of the Si-Me of the two diastereomers are clearly separable (δ = 0.057 and -0.081 for the major diastereomer and δ = 0.002 and -0.034 for the minor one) at 200 MHz, the diastereomeric excess must be better than the detection limit of NMR. similar alkylation of the carbanion **4** in ether with several alkyl halides gave the corresponding alkylated products **5** in good yield (Table I), again in high diastereomeric excess according to ^1H NMR.

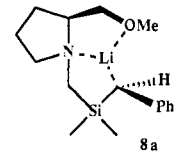
The usefulness of organosilicon compounds in synthesis is due in large part to the ease by which the silyl group can be replaced under electrophilic substitution conditions and can thus be considered as a latent functional group.[13] However, in the case of an alkylsilane where electrophilic substitution has to occur at a saturated carbon, the presence of one or more electronegative groups such as halogen or oxygen (or its equivalent) on the silyl moiety is often required to facilitate the reaction.[14,15] Recently we found, however, that (aminomethyl)silanes can be readily oxidized to the corresponding silanols.[16] Indeed, when **5a** was treated with H_2O_2, oxidative cleavage of the aminomethyl carbon-silicon bond occurred to give silanol **6** together with phe-



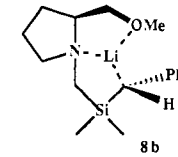
6

nylethanol (**7a**). If the oxidation was carried out with H_2O_2 and $KHCO_3$ for a longer period (15 h), complete conversion of **5a** via **6** into (*S*)-(-)-phenylethanol (**7a**) took place. Similar oxidation of **5b,c** gave the corresponding arylcarbinols **7**, again in good yield. In all cases, the arylcarbinols have the *S* configuration. For compound **7c**, the enantiomeric excess was found to be better than 99.5%, the detection limit of the capillary gas chromatographic method.[17]

We attribute the stereochemical results in the following manner. The carbanion **4** is most likely to have the lithium ion coordinated to both the nitrogen and the oxygen atoms of the pyrrolidine ligand as in **8a** or **8b**. Similar internal chelation has been suggested for



8a



8b

other silyl carbanions.[18] Of the two diastereomeric structures, **8a** is likely to be preferred because the more bulky phenyl group is placed exo to the bicyclic system. The electrophile RX reacts with **8a** presumably with retention of stereochemistry in a S_E-type reaction, to give **5** with the *S* configuration at the benzylic carbon. Since it is well established that oxidative cleavage of the carbon-silicon bond occurs with retention of stereochemistry,[14] *S*-arylcarbinol **7** is obtained as the final product.

Alkylation of the carbanion **4** with dihalides can be selectively controlled at the monoalkylation stage to give compounds **9**, again with the same high diastereoselectivity (Table I). Subsequent oxidation of **9** gave the halo alcohols **10** (Table II). Either **9** or **10** can be manipulated further by functional-group transformations. An example is the conversion of the halo alcohols **10a,b** under basic conditions to the optically active cyclic ethers **11a,b**.

The present results demonstrate that highly stereoselective reaction can be achieved with chiral organosilicon compounds. Since the chemistry of α-silyl carbanions[19] as well as the electrophile substitution reactions of organosilicon compounds[13] have been extensively utilized in organic synthesis, we expect that chiral organosilicon compound **1** and similar reagents will find application in enantioselective synthesis.

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Synthesis, Structure, and Reactivity of Substituted Niobocene Acyl Compounds

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The migratory insertion reaction of alkylcarbonyl metal compounds is one of the most fundamental reactions in organometallic chemistry.[2] An interesting comparison arises in the group V metals, since vanadocene systems readily form acyls via this route[3] while niobium and tantalum analogues[4] do not (eq 1 and 2).[5]

$$Cp_2VMe + 2CO \rightarrow Cp_2V(CO)(COMe) \quad (1)$$

$$Cp_2NbMe + CO \rightarrow Cp_2Nb(CO)(Me) \quad (2)$$

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