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AN EFFECT OF SILICON SUBSTITUTION REMOTE FROM REACTIVE SITE

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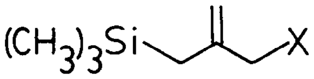
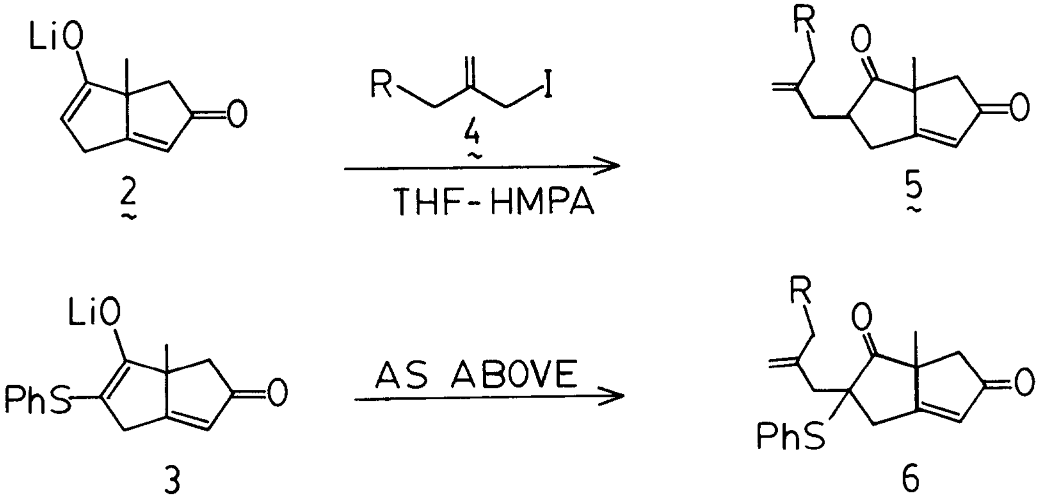
ABSTRACT: The source of a rate retardation of the trimethylsilyl substituent in an alkylation reaction is probed.

The increasing importance of silanes in mediating C-C bond formation, especially allylsilanes,[1] has led to the search for convenient methods for introduction of such functionality. In this regard, we noted the particular utility of bifunctional reagents like 1[2] which, in the case of **1** X=I, served

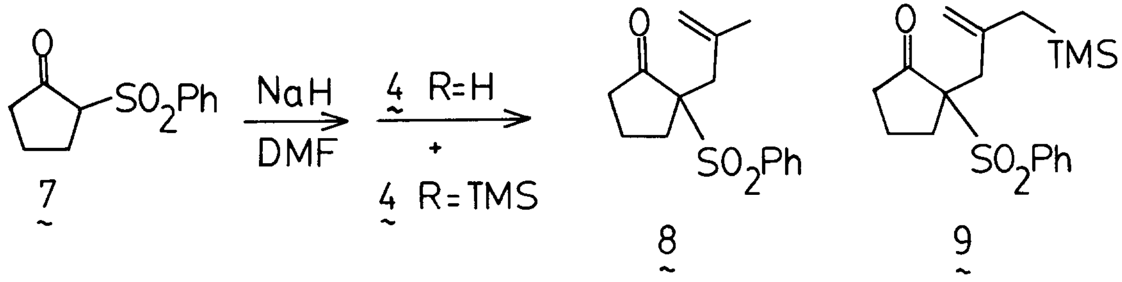


1 X=OH, OAc, OMs, I

as an excellent alkylating agent towards the anions of β-ketosulfones in a novel three carbon intercalation.[3] We were, therefore, quite surprised when supposedly more reactive anions like 2 or 3[4] failed to react successfully

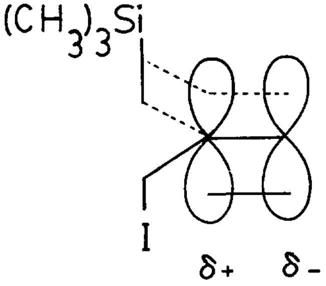


with **4** (R=TMS)[5] but behaved normally towards **4** (R=H)[6] to give **5** and **6**, R=H. To verify the above implication that **4** (R=H) is more reactive than **4** (R=TMS), we performed an internal competition between these two alkyl iodides for a deficiency of the sodium salt of the β-ketosulfone **7**. The mixture of alkylated



products was isolated in 88% yield in a 10:1 ratio of **8**:**9**,[7] confirming the inhibitory effect of the trimethylsilyl group even though it is quite remote from the carbon undergoing displacement. Thus, the failure of **2** and **3** to be alkylated with **4** (R=TMS) stems from the thermal lability of these enolates. The sluggishness in the rate of alkylation with **4** (R=TMS) is sufficient to permit their thermal decomposition at a rate faster than C-C bond formation.

Two sources of this remote effect of the TMS group can be proposed - (1) electronic, (2) steric. The former can arise from a hyperconjugative type of interaction of silicon with the double bond (e.g. **I**) whose net effect would



I

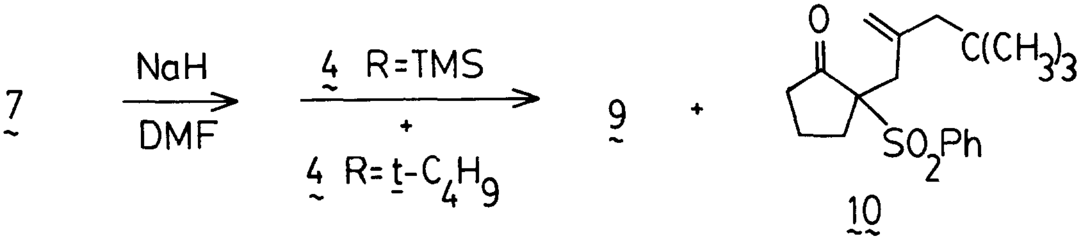
increase the polarization of the double bond. By increasing the electropositive nature of the olefinic carbon adjacent to the center undergoing displacement, a rate retardation in the S$_N$2 displacement would result.[8] ^{13}C NMR shifts seem to confirm this polarization (see Table). The difference in the olefinic ^{13}C shifts can be taken as a measure of the olefin polarization.[9]

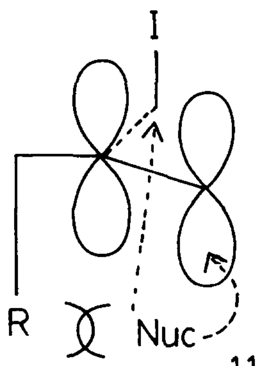
TABLE. ^{13}C NMR Shifts

compound	$\delta C(1)$	$\delta C(2)$	$\Delta[\delta C(2)-\delta C(1)]$
4 R=H	113.9	142.1	28.2
4 R=t-C_4H_9	117.8	144.9	27.1
4 R=TMS	111.8	144.4	21.6

When replacing H by alkyl substituents in **4**, a decrease in this polarization would be expected.[10] Indeed, in the carbon analog for TMS, ie. (CH$_3$)$_3$C, this trend is noted. On the other hand, a totally opposite trend is observed for the TMS compound, an observation in accord with the enhanced polarization as shown in **10**.

To evaluate steric effects, a competitive alkylation was performed between **4** (R=TMS) and **4** (R=*t*-C$_4$H$_9$)[11] for a deficiency of the anion of **7** as before. This time **9** dominated over **10** by 2.5:1 (86% yield). This result is in accord with steric effects being the major contributor to the lower reactivity of **4** (R=TMS). The fact that TMS is effectively smaller than t-C$_4$H$_9$ due to the longer C-Si bond length compared to a C-C bond length accounts for the slightly higher reactivity of **4** (R=TMS) over **4** (R=*t*-C$_4$H$_9$). Thus, while a change in ground state polarization in **4** (R=TMS) appears to be real, steric and not electronic effects appear to be the major source of the rate retardation. Exactly how such a remote group can have such a steric effect on the rate of alkylation remains only speculative at the moment. For example, due to the expected preferred conformations of the leaving group and the R group, the latter must experience a 1,3-type diaxial-like interaction either with the incoming nucleophile as in **11** (via either a S$_N$2 or S$_N$2' reaction) or with the leaving group as in **12**.





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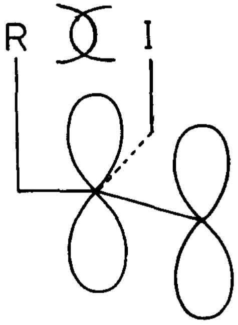

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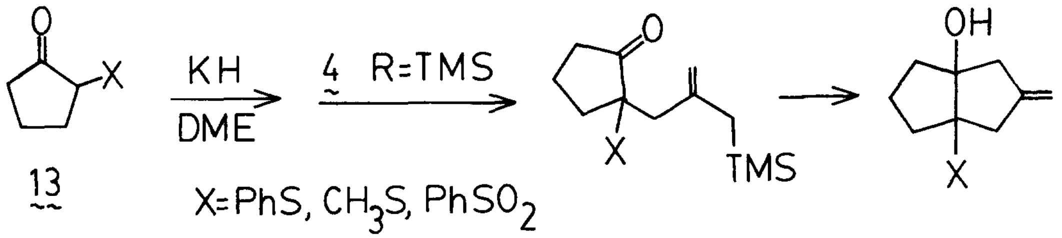
It should not be misconstrued that **4** (R=TMS) is not a useful alkylating agent. With thermally stable nucleophiles such as the anions from **13**, excellent yields (72-90%) of the desired alkylation products are obtained and



(1)

permit the cyclopentane annulation as shown in equation 1.[12] Even in the case of **2**, stabilization of the enolate by addition of trimethylstannyl iodide produces a modest yield (20%) of the alkylation product **5** (R=TMS).

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7. A control experiment verified that **9** does not protodesilylate under these conditions.
8. S_N2' alkylation could also be retarded by the increased negative charge on C_1.
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11. Compound **4** (R=t-C_4H_9) was prepared from 2,4,4-trimethyl-1-pentene by the following series of steps: (1) mCPBA, $NaHCO_3$, CH_2Cl_2, rt; (2) LDA, Et_2O, rt; (3) MsCl, Et_3N, CH_2Cl_2, 0°C; (4) NaI, acetone, rt.
12. Cf reference 3. Also see Hosomi, A.; Shirabata, A., Sakurai, H. *Tetrahedron Lett*. **1978**, 3043.

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