CHEMISTRY LETTERS, pp. 1807-1810, 1993.

Prediction of Structural Effects of Trialkylsilyl Groups on Reactivity toward Nucleophilic Displacement at Silicon

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A quantitative method of predicting reactivities of trialkylsilyl groups relative to Me_3Si toward nucleophilic displacement at silicon has been established on the basis of statistical analyses of the rates of solvolysis for a comprehensive series of chlorosilanes in aqueous dioxane.

Despite extensive use of triorganochlorosilanes in organic synthesis, there have been established no empirical methods to predict structural effects of silyl groups on reactivity toward nucleophilic displacement at silicon.[1,2] We previously presented a quantitative scale of reactivity for a comprehensive series of triorganosilyl groups, defined as the logarithmic rates of solvolysis ($\log k_{rel}$) for corresponding chlorosilanes relative to trimethylchlorosilane in 89 mol% aqueous dioxane at 25 °C (Table 1).[3]

$$R^1R^2R^3SiCl \xrightarrow[\text{aq. dioxane}]{k} R^1R^2R^3SiOH$$

$$\log k_{rel} = \log k\,(R^1R^2R^3SiCl)\,/\,k\,(Me_3SiCl)$$

We here show that the reactivity of any trialkylsilyl group on this scale can be readily and quantitatively predicted on the basis of three empirical relationships given by Eqs. 1-3, where $S(R)$ denotes the structural effect of a group R at silicon, defined as $\log k_{rel}$ for RMe_2SiCl.

$$S(RCH_2) = 0.20\,S(R) - 0.57 \qquad (1)$$

$$S(R^1R^2R^3C) = S(R^1CH_2) + 1.6\,S(R^2CH_2) + 4.0\,S(R^3CH_2) \qquad (2)$$

$$\log k_{rel}\,(R^1R^2R^3Si) = S(R^1) + 1.15\,S(R^2) + 1.35\,S(R^3) \qquad (3)$$

In Eqs. 2 and 3, the structural effect of an alkyl group R^i in $R^1R^2R^3C$ or $R^1R^2R^3Si$ is assumed to be largest with R^1 and smallest with R^3, *i. e.*, $|S(R^1)| > |S(R^2)| > |S(R^3)|$.

The structural effect of alkyl groups of the type RCH_2 exhibits a linear response to $S(R)$, as shown in Fig. 1, affording the relationship given by Eq. 1 [r (correlation coefficient) = 0.992 for R = Me, Et, n-Pr, i-Pr, and t-Bu]. Since the variation in the electronic effect of alkyl groups is very small, Eq. 1 reveals that the steric effect is transmitted through a methylene bridge with a fall-off factor of 0.20. Points for H, Ph, and $SiMe_3$ groups in Fig. 1 do not fit the correlation line; this deviation is ascribable to their anticipated electronic effects, which are transmitted through a CH_2 group in a different manner from that for the steric effect.

From Eq. 1, the structural effect for any n-alkyl group can be predicted using a single structural constant, *S*(Me), which is zero by definition, *e. g.*, *S*(Et) = 0.20*S*(Me) - 0.57 = -0.57, *S*(n-Pr) = 0.20*S*(Et) - 0.57 = -0.68, and so on (No. 2 - 7 in Table 1).

The variation in the *S*(R) values for Et, i-Pr, and t-Bu groups, *i.e.*, *S*($MeCH_2$) : *S*(Me_2CH) : *S*(Me_3C) = 1.0 : 2.6 : 6.6, suggests that the structural effect of an alkyl group of the type, $R^1R^2R^3C$, can be described by Eq. 2 as a sum of contributions from each β–sub-group; Eq. 2 holds for alkyl groups including Et, i-Pr, t-Bu, n-Pr, s-Bu, Et_2CH, and (i-Pr)Me_2C (r = 0.992). Using the *S* values of n-alkyl groups calculated from Eq. 1, we can estimate the structural effects of secondary and tertiary alkyls from Eq. 2 (No. 8 - 14); *e. g.*, *S*(i-Pr) = 2.6*S*(Et) = -1.48, *S*(s-Bu) = *S*(n-Pr) + 1.6*S*(Et) = -1.59, *S*(t-Bu) = 6.6*S*(Et) = -3.76, etc.. The *S* (RCH_2) values, where R is a secondary or tertiary alkyl, are then calculated from Eq. 1 (No. 15, 16), *e. g.*, *S*(neopentyl) = 0.20 x (-3.76) - 0.57 = -1.32. Thus, the structural effects of alkyl groups of any type can be assessed from Eqs. 1 and 2 just starting from the single constant, *S*(Me) = 0 (No. 2 - 23), e. g., *S*[(t-Bu)EtMeC] = *S*(neopentyl) + 1.6 *S*(n-Pr) + 4.0 *S*(Et) = -4.69. The predicted *S* values agree with those observed within 0.1 log *k* units in most cases.

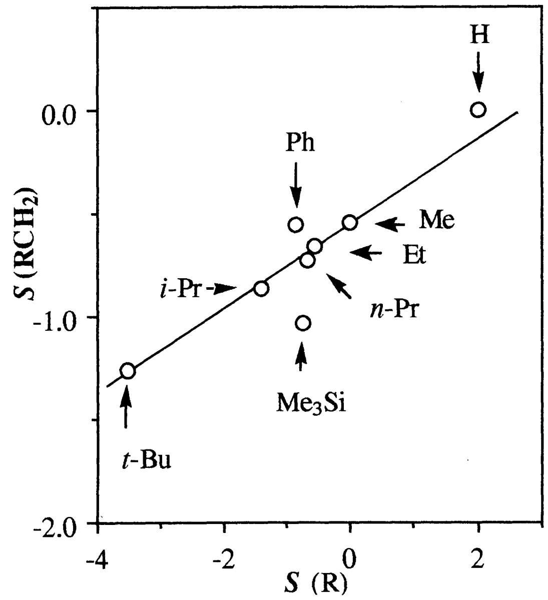

Fig. 1. *S*(RCH_2) *vs*. *S*(R).

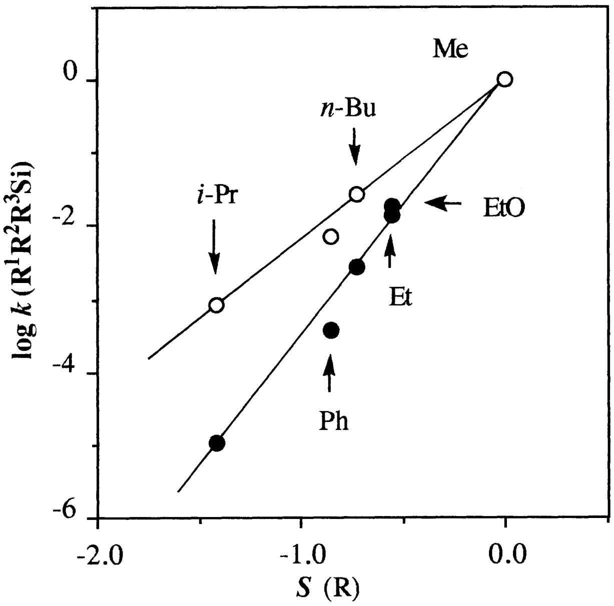

Fig. 2. log k_{rel} *vs*. *S*(R) for R_2MeSi (○) and R_3Si groups (●).

As Fig. 2 shows, the reactivities of the two series of chlorosilanes, $R_2MeSiCl$ and R_3SiCl, are both in proportion to *S*(R) with slopes of 2.15 and 3.50, respectively, suggesting that reactivities of $R^1R^2R^3Si$ groups can be described by Eq. 3, which holds for Me_3Si, Et_3Si, $(n\text{-}Bu)_2MeSi$, $(n\text{-}Bu)_3Si$, $(i\text{-}Pr)_2MeSi$, and $(i\text{-}Pr)_3Si$ (r = 0.997). This relationship shows that the α–alkyl effect is not exactly but approximately additive; the coefficients reflect a gradual increase in sensitivity to the steric effect for the successive replacement of the first, the second, and the third methyl group in Me_3Si with other alkyl substituents.

Table 1. Prediction of Reactivities for Various Silyl Groups

		$\log k_{\text{rel}}$				$\log k_{\text{rel}}$	
Silyl group (No.)		Obsd a)	Cacld b)	Silyl group (No.)		Obsd a)	Calcd b)
for RMe_2Si groups				(i-Pr)Me_2CO	30	-1.975 c)	-1.92
R = H	1	1.990	2.85	CF_3CH_2O	31	0.759	
Me	2	0.00	0.00	C_6H_5O	32	-0.599	
Et	3	-0.547	-0.57	Me_3SiO	33	-0.859	
n-Pr	4	-0.662	-0.68	C_6H_5	34	-0.852	
n-Bu	5	-0.730	-0.71	p-$NO_2C_6H_4$	35	0.093	
n-C_6H_{13}	6	-0.730	-0.71	p-MeC_6H_4	36	-0.925	
n-$C_{18}H_{37}$	7	-0.830	-0.71	$PhCH_2$	37	-0.560	
i-Pr	8	-1.421	-1.48	Me_3Si	38	-0.743	
s-Bu	9	-1.478	-1.60	Me_3SiCH_2	39	-1.032	
Et_2CH	10	-1.714	-1.77				
c-C_6H_{11}	11	-1.589		*for $R^1R^2R^3Si$ groups*			
t-Bu	12	-3.507	-3.76	(n-Bu)$_2$MeSi	40	-1.560	-1.53
$EtMe_2C$	13		-3.87	(n-Bu)$_3$Si	41	-2.567	-2.49
Et_3C	14		-4.49	Et_3Si	42	-1.869	-2.00
i-$PrCH_2$	15	-0.858	-0.87	(i-Pr)$_2$MeSi	43	-3.066	-3.18
t-$BuCH_2$	16	-1.265	-1.32	(t-$BuCH_2$)$_3$Si	44		-4.62
(i-Pr)MeCH	17		-1.78	(i-Pr)$_3$Si	45	-4.968	-5.18
(t-Bu)MeCH	18		-2.23	t-Bu(i-Pr)EtSi	46		-6.23
(i-Pr)$_2$CH	19		-2.26	t-Bu(i-Pr)$_2$Si	47		-7.46
(t-Bu)$_2$CH	20		-3.43	(t-Bu)$_2$MeSi	48	-7.825	-8.08
(i-Pr)Me_2C	21	-3.988	-4.06	(t-Bu)$_3$Si	49		-13.16
(t-Bu)Me_2C	22		-4.51	(EtO)$_3$Si	50	-1.724	-1.96
(t-Bu)EtMeC	23		-4.69	(t-BuO)$_3$Si	51		-6.34
MeO	24	-0.342	-0.34	Ph_2MeSi	52	-2.157	-1.83 d)
EtO	25	-0.559	-0.56				-2.00 e)
n-PrO	26	-0.693	-0.61	Ph_3Si	53	-3.438	-2.98 d)
t-$BuCH_2O$	27	-0.886	-0.85				-3.62 e)
i-PrO	28	-0.801	-0.92	(t-Bu)Ph_2Si	54	-6.889	-5.89 d)
t-BuO	29	-1.628	-1.81				-6.53 e)

a) Data taken from Ref. 3. b) Calculated from Eqs. 1-4 using a single constant, S(Me) = 0. c) Determined in this work. d) Calculated from Eq. 3 using an observed *S*(Ph) value of -0.852. e) Calculated from Eq. 3 using *S*(Ph) values of -0.85, -1.0, and -1.2 for the phenyl group as R^1, R^2, and R^3, respectively.

Since the S value of any alkyl group can be calculated from Eqs. 1 and 2, the reactivities of trialkylsilyl groups of the general type, $R^1R^2R^3Si$, are now predictable from Eq. 3 (No. 40 - 49), *e. g.*, log k_{rel} for a chlorosilane, (t-Bu)(i-Pr)EtSiCl, is calculated to be S(t-Bu) + 1.15S(i-Pr) + 1.35S(Et) = -6.23. The agreement between the predicted and observed reactivities is quite satisfactory. For example, di(t-butyl)methylchlorosilane solvolyzed $10^{-7.83}$ times less rapidly than did trimethylchlorosilane in 89 mol% aqueous dioxane at 25 °C, in excellent agreement with the prediction ($10^{-8.08}$) despite a marked difference in reactivity between the two chlorosilanes.

Although the strict application of the present method should be confined to trialkylsilyl groups, it seems interesting from a practical point of view to extend its applicability to alkoxy- or phenyl-substituted silyl groups, such as $(EtO)_3Si$ and $(t\text{-Bu})Ph_2Si$. The structural effects for a series of alkoxyl groups, S(RO), were found to be linearly correlated with S(R), affording Eq. 4 (r = 0.991 for R in RO; Me, Et, n-Pr, t-$BuCH_2$, i-Pr, t-Bu, and i-$PrMe_2C$); consequently, the reactivities of alkoxy-substituted silyl groups are also predictable using S(R) values calculated from Eqs. 1 - 3 (No. 24-30, 50, 51). Noteworthy is the fact that the alkoxy-substituents (RO) at silicon are as effective as or slightly more effective in reducing the reactivity of silyl groups toward S_N2-type reactions than the corresponding alkyls (RCH_2), contrary to our expectation from electronegative nature of oxygen relative to carbon, and a small steric size of the alkoxy group relative to the corresponding alkyl.[4] For instance, $(t\text{-BuO})_3SiCl$ is predicted to be one order of magnitude less reactive than $(t\text{-BuCH}_2)_3SiCl$ or $(i\text{-Pr})_3SiCl$ (No. 51 *vs.* 44 or 45).

$$S(RO) = 0.39\, S(R) - 0.34 \qquad (4)$$

As anticipated from the deviation of the phenyl group in Fig. 2, the application of Eq. 3 to Ph_2MeSi, Ph_3Si, and $(t\text{-Bu})Ph_2Si$ groups using the observed S(Ph) value of -0.852 leads to the predicted reactivities significantly higher than those found (No. 52 - 54). The discrepancy would mainly be associated with the structural feature that the phenyl group is thin but wide in shape. The effective size of such a group would probably increase with increasing steric crowding around it; therefore, it seems reasonable to set different values for S(Ph) depending on whether the phenyl group acts as R^1, R^2 or R^3 ($|S(R^1)| > |S(R^2)| > |S(R^3)|$). The reactivities for these phenyl-substituted silyl groups are well predictable, when values of -0.85, -1.0, and -1.2 are respectively used as $S(R^1)$, $S(R^2)$, and $S(R^3)$ for the phenyl group.

Financial support by the Nippon Oil & Co., Ltd. is gratefully acknowledged.

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(Received May 17, 1993)