Likewise was prepared the (*R*)-(+) isocyanate, (*R*)-**1** from (*S*)-MTPA, and the specific rotation was as follows: $[\alpha]^{25}_{D}$ +41.4° (*c* 3.81 g in 100 mL, benzene).

1-[(1-Naphthyl)ethyl]-3-[α-methoxy-α-(trifluoromethyl)-benzyl]urea (2). Into a solution of 85 mg of (*S*)-1-(1-naphthyl)ethylamine in 1 mL of benzene was added a solution of 120 mg of (*S*)-**1** in 1 mL of benzene, and the reaction mixture was allowed to stand until white crystals separated out. The crystals were collected and recrystallized from benzene to give an analytical sample: mp ca. 150 °C; ^{1}H NMR 1.485 (d, CH_3), 3.554, 3.560 (each s, OCH_3);[12] ^{13}C NMR 22.12 (CCH_3), 45.29 (*C*H), 51.37, 51.40 (OCH_3),[12] 154.37 (*C*=O).

Anal. Calcd for $C_{22}H_{21}N_2O_2F_3$ (402.2): C, 65.69; H, 5.27; N, 6.96. Found: C, 66.04; H, 5.31; N, 6.77.

A sample for NMR analysis was prepared by mixing 5 mg of (*S*)-1-(naphthyl)ethylamine and 8 mg of **1** in 0.6 mL of $CDCl_3$ in an NMR sample tube. Both the ^{1}H and ^{19}F NMR spectra were identical with those obtained above for the pure sample of (*S,S*)-**2** except for the presence of a signal at 3.3 ppm (OCH_3 of **1**) in the former and at −6.67 (CF_3 of **1**) in the latter.

Other NMR samples of urea derivatives were prepared in the same way.

Acknowledgment. We are indebted to Professor T. Nakai at Tokyo Institute of Technology for his kind advice in taking fluorine NMR and to the Ministry of Education for the financial help in purchasing the NMR spectrometer.

Registry No. (*S*)-**1**, 114693-11-7; (*R*)-**1**, 114693-12-8; **2**, 114693-15-1; (*R*)-(+)-MTPA (hydrazide), 114693-13-9; (*S*)-MTPA (hydrazide), 114693-14-0; (*RS*)-$CH_3CH_2CH(NH_2)CH_3$, 33966-50-6; (*R*)-$CH_3CH_2CH(CH_3)CH_2NH_2$, 36272-22-7; (*S*)-$CH_3CH_2CH(CH_3)CH_2NH_2$, 34985-37-0; (*RS*)-$(CH_3)_2CHCH(NH_2)CH_3$, 110509-11-0; (*R*)-$PhCH(NH_2)CH_3$, 3886-69-9; (*S*)-$PhCH(NH_2)CH_3$, 2627-86-3; (*R*)-CH_3CH(1-Naph)NH_2, 3886-70-2; (*S*)-CH_3CH(1-Naph)NH_2, 10420-89-0; (*R*)-$CH_3CH_2CH(OH)CH_3$, 14898-79-4; (*S*)-$CH_3CH_2CH(OH)CH_3$, 4221-99-2; (*RS*)-$(CH_3)_3CCH(OH)CH_3$, 20281-91-8; (*S*)-$PhCH(OH)CH_3$, 1445-91-6; (*R*)-$PhCH(OH)CH_2CH_3$, 1565-74-8; (*S*)-$PhCH(OH)CH_2CH_3$, 613-87-6; (*RS*)-2-methylazetidine, 52730-18-4; (*R*)-2-(phenylimino)-6-methyltetrahydro-1,3-oxazine, 114693-16-2; (*S*)-2-(phenylimino)-6-methyltetrahydro-1,3-oxazine, 114693-17-3; (*R*)-2-(phenylimino)-6-methyltetrahydro-1,3-thiazine, 114693-18-4; (*S*)-2-(phenylimino)-6-methyltetrahydro-1,3-thiazine, 114693-19-5.

(12) Such an NMR nonequivalence of OCH_3 was also observed in the ureas derived from 1-phenylethylamine (Table I, entry 4), 2-(phenylimino)-6-methyltetrahydro-1,3-oxazine (entry 7) and thiazine (entry 8).

Linear Electric Field Effects on ^{13}C NMR Shifts in Saturated Aliphatic Frameworks: Scope and Limitations[1]

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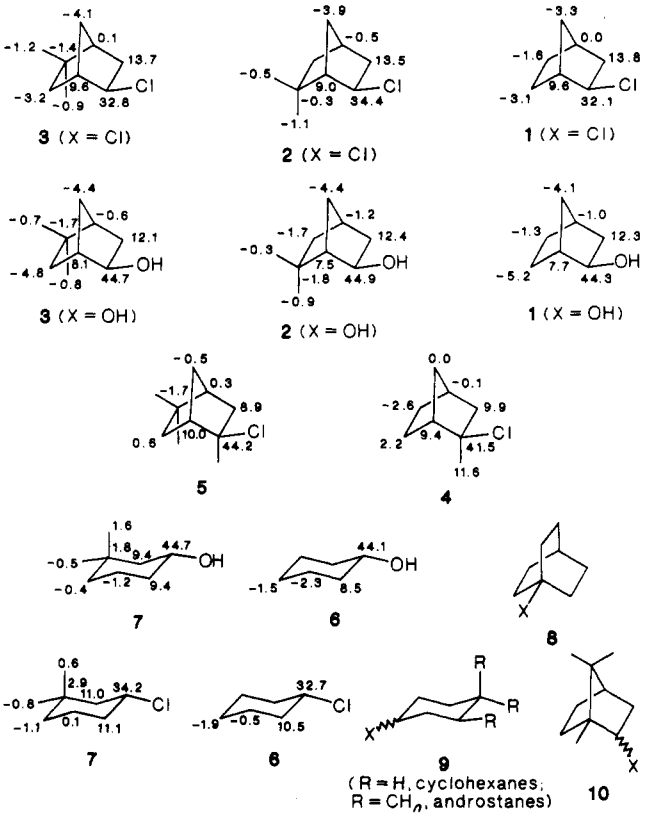
Introduction

The transmission of polar substituent effects through aliphatic bonds is one of the rare cases of a common basis for organic reaction as well as of NMR shielding mechanisms. Local electron density variations by through-space field or by inductive through bond substituent effects and their influence on chemical rates and equilibria have been in the focus of many physical-organic studies[2] but have been to a lesser degree scrutinized with respect to their visibility in NMR screening constants. ^{13}C NMR shifts[3] are known to be particularly sensitive to such electron density variations and do often show intuitively expected patterns in similar compounds. Related electric field as well as inductive effects have been studied widely with unsaturated but not so much with saturated systems.[4] In the present paper ^{13}C NMR shielding variations are observed in newly prepared norbornane derivatives and are compared to related aliphatic frameworks; at the same time we try to explore the possibilities of classical linear electric field calculations in such systems.

Chart I. Substituent-Induced Shielding Values (in ppm) Relative to the Parent Hydrocarbon



Substituent Effects on ϑ-Positions. The significance of linear electric through-space field effects (LEF) has been first pointed out for protons[5] as well as later for heavier nuclei,[6] including ^{13}C.[7] We have shown that the C-ϑ-shift variations in 12 substituted cyclohexanes[8a] can be de-

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Table I. Substituent-Induced Shielding (SIS) on ϑ-C Atoms and Calculated Charge Variations Δq[a]

	X		obsd C	F		Cl		Br		I			
				SIS	Δq	SIS	Δq	SIS	Δq	SIS	Δq	m	r
cyclohexane	eq	9	CH_2[b]	−2.5	−3.4	−2.2	−3.0	−2.45	−2.7	−2.05	−2.0	470	0.965
	ax	9	CH_2[b]	−2.0	−3.4	−1.45	−3.0	−1.55	−2.7	−1.25	−2.0	380	0.981
androstane	3-eq	9	qC[c]	−0.8	−2.6	−1.0	−2.2	−0.95	−2.1	−1.0	−1.7	370	0.88
isobornane	2-exo	10	9-CH_3[d] (anti)			+0.5	+1.5	+0.6	+1.45			370 (av)	
bornane	2-endo	10	8-CH_3[d]			−0.7	−3.8	−1.1	−3.1			280 (av)	
	2-endo	10	9-CH_3[d]			+1.2	+2.7	+1.2	+2.5			460 (av)	
6,6-dimethylnorbornane	2-exo	2	endo-CH_3[d]	−0.7	−0.40	−1.1	−3.2	−1.15	−3.2			270	0.89
	2-exo	2	exo-CH_3[d]	−0.6	+2.5	−0.5	+2.3	−0.4	+2.0			f	
bicyclo[2.2.2]octane	1	8	CH[e]	+0.1	−11	−0.9	−10	−1.5	−9	−2.7	−8	(X = I; m = 340)[f]	

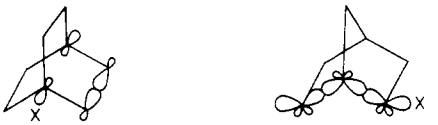
[a] SIS in ppm, Δq in 10^{-3} elementary charge units, both relative to X = H; calculational procedures and parametrization, ref 8, 9; m refers to sensitivity (ppm/e) obtained from linear regression (with correlation coefficient r) if more than two values are available, otherwise from average. [b] SIS values ref 11. [c] SIS values ref 8b. [d] SIS values, this work. [e] SIS values ref 12; for C-4 in **8** anisotropy contributions (ppm) were calculated as follows: X = F, −0.78; X = Cl, −0.71; X = Br, −0.83; X = I −1.05. [f] No correlation.

scribed with a point pole approximation of the inducing Cα–X dipole.[8] Our calculational procedure, which is used in the present paper with some recent modifications,[9] contrasts to the one proposed by Batchelor[7b] by an explicit evaluation of all polarized bonds around the observed carbon atom, since a symmetry-based uniform LEF = 0 for quaternary C-atoms[7b] exists only at so large distances from Cα–X that the whole effect almost vanishes there.[8a,b] The results from the earlier cyclohexanoid systems[8] are in Table I put together with the ones obtained with new compounds comprising mostly bicyclo[2.2.1] derivatives (Chart I).

A severe limitation for LEF calculations has been noted already with olefinic compounds, which usually show good correlations only if the polarized double bond lies in or close to the plane dissecting the inducing Cα–X dipole,[8c] which happens to be the case for several systems analyzed earlier.[10] The newly prepared 5,5- and 6,6-dimethylnorbornanes **3** and **2** as well as some related compounds such as **4** or **7** provide examples in which the observed ϑ-CH_3 is also less symmetric with respect to Cα–X than ϑ-CH_2 in cyclohexanes[8a,11] or ϑ-Cq (C-10) in 3α/β-X androstanes[8b] **9**.

Table I contains also LEF calculations on bridgehead-substituted bicyclo[2.2.2]octanes **8**, besides additional results with bornane derivatives (**9**, **10**). On the basis of measurements with **8** and qualitative arguments, Wiberg, Pratt, and Bailey[12] have claimed that the field effect is not a major contributor. However, LEF calculations based on MM2[13]-optimized realistic geometries show that the replacement of the Cα–H dipole by the Cα–H_al dipole of opposite sign *does* generate an electron flow toward C both in the C–C as well as in the C–H bonds accumulating an electron density increase at Cϑ between 8 (for X = I) and 11 (for X = F) charge units (10^{-3} electron charge units, see Table I).

Chart II



Obviously, only the experimental SIS (substituent-induced shift) for X = I is in line with this LEF contribution (Table I). What could be the mechanism which must counteract the LEF toward increased shielding from X = Br to X = F? We have calculated the anisotropy contributions which were made responsible by Wiberg et al.[9] and find them quite insufficient to explain the observed SIS decline from X = I to X = F (see footenote *e* in Table I). However, bicyclo[2.2.2]octane bridgehead-substituted compounds are ideally suited for a hyperconjugative charge transfer from Cα–X via *three* parallel Cβ–Cγ bonds toward the again parallel Cϑ–H bond (Chart II), and this contribution is known to increase sharply with small nuclei such as X = F.[14]

A related reasoning holds for the exo-methyl carbon in the 6,6-dimethylnorbornanes **2**, which show deshielding SIS of up to +2.5 ppm, again with X = F at the extreme (Table I). Here, all bonds intervening between X and C have an almost ideal planar "W" disposition for an orbital interaction which is well-known from the corresponding spin-spin coupling (Scheme 2). The endo-methyl carbon atoms in **2**, on the other hand, lack this special disposition and show a relatively good agreement between calculated LEF and observed SIS (Table I).

In summary, LEF calculations can reproduce experimental SIS even on saturated ϑ-carbon atoms fairly well if (a) nonlongitudinal contributions along the polarized bonds are either small or cancel (as is the case for the symmetric disposition of Cα–X and Cϑ–R) and if (b) "nonclassical" through-bond contributions (Chart II) will not prevail. It should be noted that the salient test for the LEF analysis is not so much the observation of linear correlations but the correctness of the sensitivity, or the SIS:Δq ratio obtained. In view of the difficulties involved with the selection of point charges, of the reaction field, and of the calculational procedures,[15] it is gratifying that with predictable exceptions the observed sensitivities lie in the range of 250–450 ppm per elementary charge unit (Table I), which comes close enough to the generally assumed[3,4] value of ~200 ppm/charge.

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(15) See, e.g.: Schneider, H.-J.; Schmidt, G. *J. Chem. Soc., Perkin Trans. 2* **1985**, 2027.

Table II. ^{13}C NMR Shifts in 5,5- and 6,6-Dimethylbicyclo[2.2.1]heptanes[a]

	Me position	X	chem shifts C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
2	6,6	H[b]	48.1	25.1	36.9	48.1	47.2	36.9	38.7	31.7 (exo)	27.3 (endo)	
2	6,6	2-exo-F[c]	53.10	93.04	*d*	*d*	45.17	34.50	*d*	31.13	26.58	
2	6,6	2-exo-Cl	57.10	59.54	38.35	47.56	44.83	36.60	34.84	31.20	26.19	
2	6,6	2-exo-Br	57.42	50.83	38.84	47.97	44.94	37.14	35.32	31.30	26.16	
2	6,6	2-exo-OH	55.64	70.03	37.54	46.90	45.53	35.06	34.25	31.43	26.39	
2	6,6	2-exo-OAc	52.78	73.83	35.01*	46.80	45.30	35.34	34.77*	30.47	26.52	
3	5,5	H[b]	38.8	28.7	25.1	48.1	36.9	47.2	38.7	31.7 (exo)	27.3 (endo)	
3	5,5	2-exo-F	44.13	94.90	*d*	*d*	34.50	*d*	*d*	31.13	26.30	
3	5,5	2-exo-Cl	48.4	61.53	38.78	48.20	35.49	44.00	34.56	30.48	26.40	
3	5,5	2-exo-Br	48.68	52.32	39.06	48.68	35.15	44.85	34.87	30.50	26.40	
3	5,5	2-exo-OH	46.93	73.44	37.18	47.46	35.18	42.44	34.28	31.00	26.52	
3	5,5	2-exo-OAc	43.94	76.24	34.87	47.19	35.34	41.86	34.77	30.47	26.52	
5	5,5,2	exo-H[b]	44.2	33.2	35.,7	49.5	37.4	39.5	38.9	*e*	*e*	*e*
5	5,5,2	2-exo-Cl	54.2	77.4	44.6	49.8	35.7	40.2	38.4	28.5* (2)	31.6 (exo)	25.9*(endo)
5	5,5,2	2-exo-OH	50.9	76.1	42.0	48.4	35.7	39.8	36.6	36.1(2)	31.9 (exo)	25.0 (endo)
5	5,5,2	endo-H[b]	45.5	35.4	35.2	48.6	37.1	46.3	35.0	*e*	*e*	*e*
5	5,5,2	2-endoOH	50.2	75.3	41.1	48.8	35.5	38.0	32.0	31.1* (2)	31.9* (exo)	26.0 (endo)

[a] In ppm vs internal TMS in 10–30% $CDCl_3$ solutions at 300 ± 10 K; * denotes exchangeable signals. [b] Data from ref 22; carbon numbering adjusted to the other entries. [c] J_{CF} at C2, 178 Hz, at C6, <2 Hz. [d] Signals (in mixtures of the fluorides) not clearly visible. [e] Data not available.

Substituent Effects in α- to γ-Positions. These SIS values (Table II) will be discussed only briefly for the new compounds and compared to findings with known[3] related frameworks (Chart I).

γ-Effects have been shown to be almost inaccessible to classical shielding calculations at the present time [8a,d], with the possible exception of "steric" effects of alkyl groups.[3a,15–17] Polar substituents X not only exert through-bond effects in addition to LEF but also are too close to Cγ for a homogenous LEF application.[8a,d] The observed failure of LEF estimations to predict experimental SIS, e.g., on syn and anti γ carbon atoms in 7-substituted norbornanes[11] is therefore no argument against LEF contributions, which here also can be masked by orbital mixing, e.g., within an again almost planar "W" arrangement F–C7–C1–C2 anti-γ H2. Two observations deserve comment: (a) the anti-γ-SIS—which with 2-substituted norbornanes is *shielding* even with less electronegative and "small" substituents such as Cl compared, e.g., to F—becomes almost zero if the observed γ-carbon is quaternary (Chart I, Table I, **2** vs **1** or **3**). This observation, which is also made with corresponding cyclohexanes (**7**[8d] vs **6**) is another case against the hyperconjugative charge-transfer explanation[18] for first row substituents. (b) The syn-γ-effects seen with the 2-exo-substituted bicyclo[2.2.1]heptanes **2–5** at C7 are consistently enhanced if additional geminal dimethyl groups are present (**3** vs **2**, **5** vs **4**). This is to be expected from the buttressing and stiffening effects of the *gem*-dimethyl groups, which should bring C7 closer to the C2–X substituent.

β-Effects observed in **2–5** show as usual[3a,12] little dependence on additional remote methyl group substitution. Interestingly, the α-SIS are *not* really independent of the number of existing γ-gauche orientations,[3a] as illustrated by the SIS differences between **2** and **1** or **3** and even **7** and **6**. It is also remarkable that methyl groups in ϑ-position even within the fairly rigid norbornane framework can lead to α-SIS differences of up to 2.7 ppm (**5** vs **4**).

Experimental Section

NMR spectra were obtained at 22.62 MHz with Bruker HX 90 and WH 90 systems at ambient temperature in chloroform-d_3 10–30% solutions with TMS as internal reference; digital resolution was usually ±0.02 ppm. Line assignments were secured by SFORD experiments if necessary.

5,5- and 6,6-Dimethylbicyclo[2.2.1]hept-2-yl Compounds 3 and 2 were obtained similar to described procedures by electrophilic additions to camphenilene (5,5-dimethylbicyclo-[2.2.2.1]hept-2-ene).[19] In general agreement with earlier observations[19] the additions went smoothly exo without rearrangement (a Wagner–Meerwein isomerization would be degenerate), however, with little or no preference for **3** over **2**; the ^{13}C NMR spectra were taken in mixtures. Thus, reaction of 1 g (0.01 mol) camphenilene in 5 mL of carbon disulfide (dried over molecular sieve) at −78 °C with HBr for 10 min or with HCl for 20 min after removal of excess HBr/HCl by an air stream at room temperature and after workup with aqueous $NaHCO_3$ yielded the bromides in a ratio of **3**:**2** = 57:43 (^1H, ^{13}C NMR): ^1H NMR [**2**, X = Br] 0.92, 0.98 (Me), 4.47 ppm, [**3**, X = Br] 0.97, 1.00 (Me), 3.38 ppm. Fractionation over a 20-cm Vigreux column brought no significant **2**:**3** (X = Br) ratio change, $bp_{0.15}$ 29 °C. The chloride ratio was 53:47 = **3**:**2**: ^1H NMR [**2** X = Cl] 0.93–1.00 (Me, overlapping) 4.32 ppm, [**3**, X = Cl] 0.93–1.00 (Me, overlapping), 3.8 ppm. Treatment with HCl at 0 °C in nitromethane, saturated with triethylbenzylammonium chloride, yielded a ratio of **3**:**2** = 67:33.

Reaction with HF in $CFCl_3$ at −78 °C for 1 h and further HF for 0.5 h at 0 °C (2.2 g, 0.018 mol, of olefin with 0.8 g + 0.35 g = 0.06 mol of HF) yielded only 60% fluorides with **3**:**2** = 67:33, with 10% unreacted educt and 30% polymers. Chromatography on alumina (neutral, 50 cm/2.5 cm, cyclohexane) allowed only purification to ~80% but no isomer separation. ^1H NMR [**2**, X = F] 0.9–1.0 (Me, overlapping), 4.88 (J_{HF} = 56 Hz), [**3**, X = F] 0.92–1.0 (Me), 4.46 (J_{HF} 55 Hz). In order to secure the regioisomer structure and NMR signals the alcohol **3** (X = OH) was treated with HBr in CCl_4 under reflux for 1.5 h, yielding **3** (X = Br) in >95% purity (^{13}C NMR). Reaction of this bromide (1.2 g, 6 mMol) with silver fluoride (1.5 g, 12 mmol) in 5 mL of nitromethane yielded impure yet preferentially **3** (X = F).

Acetates 2 and 3 (X = OOCMe) were obtained as described by McGreer;[17a] reduction with $LiAlH_4$ in ether yielded the alcohols.

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Alcohols 2 and 3[18] **(X = OH)** were prepared from the acetates (see above) or directly from acetoxymercuration following the standard procedure[19] in 55% yeld; the alcohols (**3:2** = 50:50) were separated on a alumina (neutral) column (200 cm/3 cm, with dichloromethane): ^{1}H NMR [**2**, X = OH] 0.97 (2 Me), 4.13 ppm, [**3**, X = OH] 0.90, 0.97 (Me), 3.63 ppm.

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The Use of Organosilicon Esters for the Synthesis of Alkyl Phosphonofluoridates

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Introduction

The alkyl methylphosphonofluoridates are an important class of highly toxic compounds. In order to minimize the safety hazards associated with preparing these esters, simple high yield syntheses are highly desirable. The method that is usually employed to prepare these compounds involves the reaction of an alcohol with methylphosphonic difluoride (**1**) in the presence of an HF acceptor such as an alkyl amine.[1] Another reaction that is sometimes used to prepare the alkyl methylphosphonofluoridates involves the controlled addition of an alcohol to an equimolar mixture of **1** and methylphosphonic dichloride dissolved in refluxing methylene chloride.[2] Both of these methods suffer from the necessity of controlling the addition of the alcohol in order to moderate the heat from the reaction and from the workup procedures that are necessary to obtain pure products that are free from a solvent or an ammonium fluoride salt.

In the chemistry of organosilicon compounds, the reactions in which Si–F bonds are formed are usually highly exothermic. In reactions in which silicon tetrafluoride is formed, the Si–F bond energy[3] of 160 kcal/mol provides the driving force for these reactions. In view of the affinity of silicon for fluorine, and the lability of the fluorine atoms of **1**, it seemed logical to investigate the potential reactivity of alkoxy-substituted silanes with **1**. It seemed reasonable to suppose that a ligand exchange reaction with P–F systems might occur by a simple redistribution mechanism.

Results and Discussion

We found that **1** reacts with the tetraalkoxysilanes **2a–c** to give the alkyl methyphosphonofluoridates **3a–c** together with the dialkyl methylphosphonates **4a–c** and silicon tetrafluoride (eq 1). The difluoride **1** also undergoes an

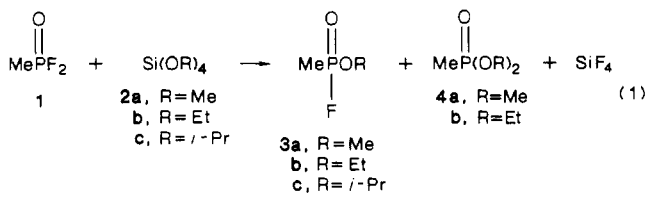


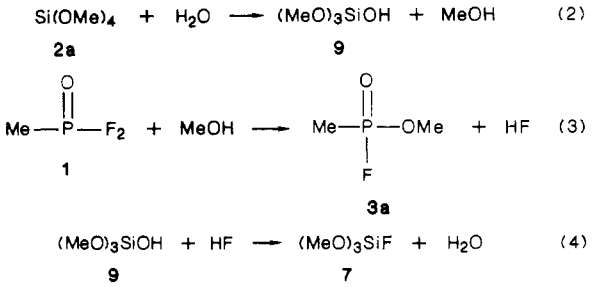
Table I. Reactions of 1 with the Alkoxysilanes

alkoxysilane	ratio[a]	reactn time	products (% yield)[b]
2a	1:3	15 min	**3a** (79), **4a** (19)[c]
2a	1:1	20 h	**4a** (>95)
2a + 7 + 8	1:1[d]	4 min	**3a** (80), 1 (20)
2a + H_2O[e]	1:4	15 s	**3a** (92), **4a** (6)
2b	1:4	1.5 h	**3b** (81)[f]
2c	1:4	48	**3c** (85)
2c + H_2O[g]	1:4	15 s	**10** (90)
2c + H_2O[h]	1:4	4 min	**3c** (60), **10** (19), 1 (20)
5	1:3	10 min	**3a** (80), **4a** (10), 1 (10)
6	1:1	5 days	**3a** (86), **4a** (5)

[a] Molar ratio of alkoxysilane to **1**. [b] Product yields by ^{1}H NMR. [c] Product yield by ^{31}P NMR. [d] Equimolar ratio of total methoxy groups to **1**. [e] Equimolar ratio of H_2O and **2a**. [f] Isolated yield after distillation. [g] Equimolar ratio of H_2O and **1**. [h] Equimolar ratio of H_2O and **2c**.

exchange reaction with trimethoxysilane (**5**) as well as with trimethylmethoxysilane (**6**) when a catalytic amount of a KF-saturated acetonitrile solution containing 1% (w/v) 18-crown-6 is employed. In order to further explore the reaction between **1** and **2a**, the synthesis of the fluorinated methoxysilane intermediates was attempted. A mixture consisting of 20% **2a**, 56% trimethoxyfluorosilane (**7**), and 23% dimethoxydifluorosilane (**8**) was obtained upon treating **2a** with antimony trifluoride. Trifluoromethoxysilane should also have been formed, but it reportedly[4] disproportionates to give **2a** and silicon tetrafluoride. From these experiments (Table I) it is evident that the fluorinated methoxysilanes are more reactive toward the exchange reaction with **1** than is **2a**.

As part of our attempts to determine the mechanism of this reaction, a number of potential catalysts were screened. Among the reagents tested for catalytic activity were potassium fluoride/18-crown-6, pyridine–HF, boron trifluoride etherate, triethylamine, and methanol. In these trials a 4:1 molar ratio of **1** to **2a** was employed, because the end of the reaction could be visualized by the emission of SiF_4. In all cases, instead of increasing the rate of reaction, the presence of the potential catalysts delayed the emission of SiF_4 (end of reaction) from 15–20 min (absence of added catalyst) to 25–40 min. In these experiments it was noted that a rise in the reaction temperature to 55–65 °C occurs simultaneously with the emission of SiF_4. The presence of water, however, causes a marked acceleration in the rate of the reaction. A possible mechanism that would account for these results is suggested in eq 2–4.



In this mechanism, methanol is produced by the hydrolysis of **2a** (eq 2) and reacts with **1** to give **3a** and HF (eq 3). The HF dehydrates trimethoxysilanol (**9**) that is formed in eq 2, resulting in the regeneration of H_2O and the formation of **7** (eq 4). The fluorosilane **7** then reacts with water and continues this cycle until SiF_4 is formed.

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(4) Noskov, V. G.; Kalinina, L. N.; Englin, M. A. *Zh. Obshch. Khim.* **1972**, *42*, 2028.