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Enhanced Nucleophilic Fluorination and Radiofluorination of Organosilanes Appended with Potassium-Chelating Leaving Groups

Mohammed H. Al-huniti^a, Shuiyu Lu^b, Victor W. Pike^{b,*}, and Salvatore D. Lepore^{a,*}

^aDepartment of Chemistry, Florida Atlantic University, Boca Raton, Florida 33431

^bMolecular Imaging Branch, National Institute of Mental Health, National Institutes of Health, Bethesda, MD 20892-1003

Abstract

Here we aimed to explore the feasibility of enhancing the fluorination of organosilanes by appending potassium-chelating groups to the substrates. For this purpose, eight organosilanes were prepared in which a linear or cyclic leaving group, with putative potassium-chelating ability, was attached covalently to a congested silicon atom via an ether linkage to serve as a potential nucleophilic assisting leaving group (NALG). Organosilicon-NALGs with expected strong potassium-chelating capability enhanced reactions with potassium fluoride in acetonitrile to produce organofluorosilanes without any need to separately add phase transfer reagent. Similar rate enhancements were also observed with cyclotron-produced [¹⁸F]fluoride ion ($t_{1/2} = 109.7$ min, $\beta^+ = 97\%$) in the presence of potassium carbonate in MeCN-0.5% H₂O. This study found that metal-chelating NALG units can accelerate fluorination and radiofluorination reactions at sterically crowded silicon atoms.

Keywords

chelating leaving group; fluoroorganosilane; fluorine-18; fluorination; radiofluorination

1. Introduction

We have shown that the appendage of particular metal-chelating leaving groups to substrates is capable of facilitating nucleophilic substitution reactions, where the halide nucleophile originates from a metal salt^[1] or titanium(IV) complex.^[2] We dubbed such groups as ‘nucleophile assisting leaving groups’ (NALGs), arguing that the observed rate enhancements afforded by these new nucleofuges are primarily due to stabilizing interactions between substrates and metal-nucleophile pairs to lower transition state energies.^[3] More recently, we have applied NALGs to expedite the formation of C-¹⁸F bonds in potential radiotracers for molecular imaging with positron emission tomography (PET).^[4]

The exploitation of organosilanes as superb [¹⁸F]fluoride ion acceptors has emerged as an interesting strategy for the rapid introduction of cyclotron-produced no-carrier-added (NCA) fluorine-18 ($t_{1/2} = 109.7$ min; $\beta^+ = 97\%$) into potential PET radiotracers.^[5] Nevertheless, [¹⁸F]organofluorosilanes have not yet been widely used in PET because of certain shortcomings, such as susceptibility to Si-¹⁸F bond hydrolysis *in vivo*, and high lipophilicity.

*Corresponding authors: pikev@mail.nih.gov and slepore@fau.edu.

Recently, however progress has been made to reduce metabolic instability by incorporating bulky *iso*-propyl or *tert*-butyl groups near the silicon atom,^[6] and to reduce overall lipophilicity by introducing charged or hydrophilic groups at an aromatic linker.^[7] Moreover, small molecule [¹⁸F]organofluorosilanes have been developed as labeling synthons^[8] for preparing macromolecular PET radiotracers, especially peptides and proteins. Low molecular weight [¹⁸F]organosilanes are also now appearing as PET radiotracers.^[9]

Existing techniques for the radiofluorination of organosilyl groups require forcing conditions, which include an acidic reaction medium, elevated temperature and polar solvent (e.g., DMSO). For example, the radiofluorinations of some ethoxysilanes were recently achieved with a solution of [¹⁸F]fluoride ion[−]-quaternary ammonium salt in 2% acetic acid-DMSO at 90 °C for 23 minutes.^[10,11] In most radiofluorination reactions, K⁺-kryptofix 2.2.2 (K⁺-K 2.2.2), K⁺-18-crown-6 or another bulky cation is used as a necessary phase transfer agent^[12]. Such phase transfer complexes react slowly with organosilanes, especially if the silicon atom is bonded to bulky organic groups for the purpose of ultimately avoiding rapid hydrolysis *in vivo*.^[6] Alternative radiolabeling by ¹⁸F/¹⁹F exchange reactions, either in labeling synthons^[13] or preformed macromolecular substrates,^[6a,8b] does not have wide utility because the resultant PET radiotracers have low specific activity.

Here we aimed to explore the utility of NALGs for enhancing the fluorination and radiofluorination of organosilanes. We found that organosilanes that bear a linear or cyclic leaving group with expected strong potassium-chelating ability, enhance fluorination reactions with potassium fluoride or radiofluorination with NCA [¹⁸F]fluoride ion in the presence of potassium carbonate. The NALG strategy appears valuable for preparing non-radioactive organofluorosilanes but requires further development to be useful for preparing NCA PET radiotracers in adequate amounts due to the limited solubility of NCA [¹⁸F]fluoride ion in the absence of separate phase transfer agent.

2. Results and Discussion

2.1. Fluorination with potassium fluoride

2.1.1. Fluorination in the absence of 18-crown-6—Our initial experiments to investigate the effect of metal-chelating leaving groups on the yields of fluorinations of organosilanes used non-radioactive potassium fluoride (Table 1). Except where noted, all reactions were conducted with 0.1 M organosilane substrate at room temperature in acetonitrile-*d*₃ (1.0 mL) with potassium fluoride as the limiting reagent (0.5 eq) in the absence of any separate phase transfer agent. Under these conditions potassium fluoride was initially in a suspension, but became completely dissolved after 10 to 15 minutes. Substrate **1**, containing a linear oligoether moiety and consequently a potential potassium-chelating leaving group, failed to give detectable amounts of the desired organofluorosilane product **9** after 30 minutes. However, in the presence of excess potassium fluoride (4 eq), substrate **1** was quantitatively converted into **9** after 6 hours. Under identical conditions, substrate **2**, containing a linear leaving group expected to be incapable of potassium chelation, yielded no **9** and remained inert even after 6 hours.

We next examined substrates **3–5** and **6–8**. The silicon atoms in these substrates are variously congested with alkyl and phenyl groups and carry one of three types of alkoxide leaving group. Gratifyingly, substrate **3**, containing a metal-chelating hydroxymethyl-18-crown-6 leaving group, reacted with potassium fluoride in anhydrous acetonitrile-*d*₃ to give *tert*-butyldiphenylsilyl fluoride (TBDPSF, **10**) in 59% yield after 30 min and in quantitative yield after 2.3 hours. By contrast, compound **4**, containing a linear methoxy triethylene oxide leaving group, failed to give any of the organofluorosilane **10** at 30 minutes. Not

surprisingly, substrate **5**, possessing a simple methoxy leaving group, also gave no measurable organofluorosilane, even after 6 hours. Similarly, substrate **6** gave **11** in 79% yield in 30 minutes, but **7** and **8** did not give any measurable organofluorosilane **11** under the same conditions.

2.1.2. Fluorination in the presence of 18-crown-6—In view of the preceding results, the reactivity of substrates **1–8** towards fluoride ion in the presence of an added phase transfer agent 18-crown-6 (18-C-6) was also assessed. Remarkably, only substrates **3** and **6** gave no yield of fluorinated product, in stark contrast to the high yield obtained in the absence of 18-C-6 described above. Here the added 18-C-6 presumably chelated all available potassium ion, but this complex was unable to react effectively at the sterically crowded silicon center (i.e., any NALG effect was negated). Other substrates gave similar results. Substrates **4** and **5** gave organofluorosilane **10** in low (10%) and moderate (33%) yields with the assistance of 18-C-6. Substrates **7** and **8** needed the assistance of 18-C-6 to produce organofluorosilane **11** in good yields (72 and 77%, respectively).

2.2. Radiofluorination with [^{18}F]fluoride ion in the presence of potassium carbonate

2.2.1. Radiofluorination in the absence of K 2.2.2—For the radiofluorination of substrates **3–5** in the absence of K 2.2.2, the substrate was dissolved first in the desired solvent. The solution was then transferred to a V-vial that contained NCA ‘anhydrous potassium [^{18}F]fluoride’, prepared by drying cyclotron-produced aqueous [^{18}F]fluoride ion in the presence of potassium carbonate through conventional additions and azeotropic removals of acetonitrile. In anhydrous acetonitrile, **3** gave 70–80% decay-corrected radiochemical yield (RCY) based on the radioactivity that entered liquid phase. However, the drying of [^{18}F]fluoride ion in the absence of phase transfer agent resulted in less than 5% dissolution of the starting radioactivity in acetonitrile for this reaction. The radiofluorination of **4** and **5** gave only trace amounts of radioactive product. Again, in both cases, only very low proportions of starting activity (~1%) were solubilized for reaction.

Inclusion of a low concentration of water (0.5% v/v) in the solvent increased the dissolution of [^{18}F]fluoride ion from 4 to 31%. However, further increase in water content (up to 5% v/v), although increasing the solubilization of [^{18}F]fluoride ion, also reduced its reactivity, thereby reducing overall RCY. Therefore, to compare the reactivity of each organosilane-NALG, radiofluorination was carried out under identical conditions of 1.8 mM K_2CO_3 in acetonitrile containing 0.5% water at room temperature (Figure 1). Radiofluorination of **3** for just 2 minutes gave [^{18}F]**10** in a moderate yield from solubilized [^{18}F]fluoride ion (35%). However, thereafter the yield gradually decreased showing that product was degrading.

Substrates **4** and **5** were not so reactive under these conditions; each gave [^{18}F]**10** in less than 5% yield after 45 minutes. Hence, the organosilicon-NALG having a cyclic crown ether component (**3**), rather than a linear oligoether component (**4** and **5**), was clearly most effective for promoting radiofluorination. This finding accords with results from the non-radioactive fluorination reactions.

We suspected that [^{18}F]**10** was labile to base. Lowering the concentration of potassium carbonate from 1.8 mM to 0.36 mM in the radiofluorination of **3** reduced decomposition of product and led to 50% yield in 20 minutes at room temperature (Figure 1). To our knowledge, this is the fastest silicon radiofluorination ever reported without the use of a phase transfer agent, such as K 2.2.2. The yields of [^{18}F]**10** from **4** and **5** improved slightly to near 10% when the concentration of potassium carbonate was reduced.

The effect of base concentration on the radiofluorination of **6** was somewhat different. The substrate and the product, [^{18}F]**11**, were much more stable to high base concentration. Radiofluorination of **6–8** in the absence of K 2.2.2 was performed in acetonitrile containing 0.5% water, but using an optimally high K_2CO_3 concentration (9 mM; Figure 1). The highest yield (45%) for this substrate group was obtained from **6**. Yields for **7** and **8** were 33 and 30% for 45-min reaction time, respectively. Thus, once again, a substrate containing a cyclic crown ether as NALG unit (**6**) appeared most reactive.

2.2.2. Radiofluorination in the presence of K 2.2.2—In order to establish the effect of potassium-chelating leaving group on the reactivity of compounds **3–8** towards NCA radiofluorination, reactions were also conducted in the presence of anhydrous K 2.2.2/ K^{18}F in acetonitrile, at room temperature (Figure 2). In these experiments, K 2.2.2 was in molar excess over K^+ (1.8:1). An aliquot of reaction mixture was quenched in MeCN- H_2O (1:1 v/v) and then analyzed with reversed phase radio-HPLC.

[^{18}F]*tert*-Butyldiphenylsilyl fluoride ([^{18}F]**10**) was obtained from substrates **3–5**. Yields from starting [^{18}F]fluoride ion peaked after 20 minutes. [^{18}F]Biphenyldiisopropylsilyl fluoride ([^{18}F]**11**) was obtained from substrates **6–8**. Yields from **7** and **8** reached plateaus at about 45 minutes whereas the yield from **6** always slowly increased. Reactions in borosilicate glass or polypropylene vials gave identical results. The highest yields were obtained for the substrates **5** and **8**, featuring not a metal-chelating leaving group but a methoxy unit (Figure 2). These results mirror those obtained with non-radioactive potassium fluoride. They may be understood on the basis that K 2.2.2 likely chelates K^+ more effectively than the leaving groups thereby preventing close interaction of potassium ion with substrate. The larger metal-chelating groups might also impart some steric hindrance under these conditions.

2.3. Mechanistic considerations

We postulate that the 18-C-6- CH_2O - leaving group enhances the reaction rate, at least in part, by positioning the fluoride ion near to its silicon target (entropic advantage). The reaction then proceeds through the well-established pentacoordinate silicon anion intermediate (Scheme 1).^[14] This anionic intermediate is likely stabilized by a potassium cation positioned nearby due to chelating interactions with the chelating leaving group. Others have shown that an 18-C-6/ K^+ counter ion is capable of stabilizing pentacoordinate silicon anion.^[15] Computational studies suggest that the pentacoordinate silicon atom prefers to distribute negative charge to its substituents^[16] thus we expect stabilizing ionic interactions with the oxygen of the leaving group.

3. Conclusions

Our findings, especially with compounds having leaving groups containing crown ether units (substrates **3** and **6**), demonstrate that potassium-chelating units enhance fluoride substitution at silicon centers. However, this reactivity was undermined in NCA radiochemistry by the difficulty of solubilizing NCA K^{18}F in the reaction solvent. This problem needs to be surmounted in future work. We also suspect that different linkers connecting a crown ether moiety to a silicon center can be found to maximize metal involvement in the transition state for faster fluorination.

4. Experimental

4.1. General procedure for silylation of alcohols

In an oven-dried vial under argon atmosphere, alcohol (1.0 mmol) was dissolved in dichloromethane (5 mL) to which was added imidazole (2.0 mmol). This solution was then stirred in an ice-bath for 10 min. Silyl chloride (2.0 mmol) was then added and the reaction was allowed to warm to rt. After completion, volatiles were removed under reduced pressure and the crude mixture was purified with silica gel chromatography using hexanes/EtOAc as eluent.

4.2. General procedure for fluorination

In an oven-dried vial purged with argon, silyl ether (0.10 mmol) was dissolved in anhydrous acetonitrile- d_3 (0.1 M solution, 1.0 mL) and stirred at rt for 5 min. Finely powdered anhydrous potassium fluoride (0.5 mmol) was then added to the stirred solution resulting initially in a suspension and then a homogeneous mixture after 10 - 15 min. After KF addition, the reaction was stirred at room temperature for 30 min (overall time) and then directly analyzed by ^1H -NMR. Percent conversion to silyl fluoride product was calculated based on the limiting reagent KF using the proton integration of an alkyl (^tBu and ^iPr) group present on silicon in both starting material and product.

4.2.1. 2-Methyl-2-phenyl-3,6,9,12-tetraoxa-2-silatridecane (1)—Yield = 61%. ^1H NMR (400 MHz, CDCl_3): δ 7.58–7.56 (m, 2H), 7.37–7.34 (m, 3H), 3.74 (t, J = 5.2 Hz, 2H), 3.63–3.61 (m, 6H), 3.55–3.52 (m, 4H), 3.36 (s, 3H), 0.38 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 138.0, 133.7, 129.8, 128.0, 72.6, 72.1, 70.8, 70.8, 70.7, 62.6, 59.2, –1.5. MS calc. for $\text{C}_{15}\text{H}_{26}\text{O}_4\text{Si}$ $[\text{M}+\text{H}]^+$: 299.17. Found: 299.61.

4.2.2. (Heptyloxy)dimethyl(phenyl)silane (2)—Yield = 71%. ^1H NMR (400 MHz, CDCl_3): δ 7.62–7.61 (m, 2H), 7.42–7.40 (m, 3H), 3.62 (t, J = 6.6, 2H), 1.56 (m, 2H), 1.29 (m, 8H), 0.91 (t, J = 6.7, 3H), 0.41 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 138.3, 133.7, 129.8, 128.0, 63.4, 32.9, 32.1, 29.4, 26.0, 22.9, 14.4, –1.5. APCI-TOF-MS calc. for $\text{C}_{15}\text{H}_{26}\text{OSi}$ $[\text{M}+\text{H}]^+$: 251.1826. Found: 251.1825.

4.2.3. ((1,4,7,10,13,16-Hexaoxacyclooctadecan-2-yl)methoxy)-(tert-butyl)diphenylsilane (3)—Yield = 97%. ^1H NMR (400 MHz, CDCl_3): δ 7.67 (m, 4H), 7.39–7.32 (m, 6H), 3.65 (m, 25H), 1.04 (s, 9H). ^{13}C -NMR (100 MHz, CDCl_3): δ 135.5, 135.4, 133.3, 133.3, 129.5, 127.5, 127.5, 79.9, 71.0, 70.7, 70.5, 70.6, 70.6, 70.5, 70.5, 70.5, 70.4, 69.9, 63.3, 26.6, 19.1. ESI-HRMS calc. for $\text{C}_{29}\text{H}_{44}\text{O}_7\text{Si}$ $[\text{M}+\text{Na}]^+$: 555.2749. Found: 555.2754.

4.2.4. 13,13-Dimethyl-12,12-diphenyl-2,5,8,11-tetraoxa-12-silatetradecane (4)—Yield = 74%. ^1H -NMR (400 MHz, CDCl_3): δ ppm 7.70–7.67 (m, 4H), 7.42–7.36 (m, 6H), 3.81 (t, J = 4 Hz, 2H), 3.67–3.52 (m, 10H), 3.37 (s, 3H), 1.05 (s, 9H). ^{13}C -NMR (100 MHz): δ 135.8, 133.9, 129.8, 127.9, 72.7, 72.2, 71.0, 70.9, 70.8, 63.6, 59.3, 27.0, 19.4. ESI-HRMS Calc. for $\text{C}_{23}\text{H}_{34}\text{O}_4\text{Si}$ $[\text{M}+\text{Na}]^+$: 425.2119. Found: 425.2126.

4.2.5. tert-Butyl(methoxy)diphenylsilane (5)—Yield = 84%. ^1H NMR (400 MHz, CDCl_3): δ 7.74–7.73 (m, 4H), 7.47–7.43 (m, 6H), 3.57 (s, 3H), 1.08 (s, 9H). ^{13}C NMR (CDCl_3 , 150.92 MHz, 25 °C): δ 135.7, 133.7, 129.8, 127.9, 52.4, 27.0, 19.4. CI-HRMS Calc. for $\text{C}_{17}\text{H}_{22}\text{OSi}$ $[(\text{M}+\text{H})-\text{CH}_3\text{OH}]^+$: 239.1256. Found: 239.1251.

4.2.6. ((1,4,7,10,13,16-Hexaoxacyclooctadecan-2-yl)methoxy)-([1,1'-biphenyl]-4-yl)diisopropylsilane (6)—Yield = 68%. ^1H NMR (400 MHz, CDCl_3): δ

7.61–7.27 (m, 6H), 7.47–7.43 (m, 2H), 7.37–7.35 (m, 1H), 3.86–3.63 (m, 25H), 1.33–1.27 (m, 2H), 1.08–1.03 (m, 12H). ^{13}C -NMR (100 MHz, CDCl_3): δ 141.8, 141.0, 135.1, 132.9, 128.7, 127.3, 127.1, 126.3, 80.2, 71.6, 70.9, 70.8, 70.7, 70.7, 70.6, 70.6, 70.6, 70.5, 70.1, 63.7, 17.4, 17.3, 12.0. ESI-HRMS calc. for $\text{C}_{31}\text{H}_{48}\text{O}_7\text{Si}$ $[\text{M}+\text{Na}]^+$: 583.3062. Found: 583.3078.

4.2.7. 12-([1,1'-Biphenyl]-4-yl)-12-isopropyl-13-methyl-2,5,8,11-tetraoxa-12-silatetradecane (7)—Yield = 91%. ^1H NMR (400 MHz, CDCl_3): δ 7.65–7.58 (m, 6H), 7.47–7.43 (m, 2H), 7.37–7.35 (m, 1H), 3.94 (t, J = 5.6 Hz, 2H), 3.69 (m, 8H), 3.35 (m, 2H), 3.37 (s, 3H), 1.34–1.26 (m, 2H), 1.09 (d, J = 7.6 Hz, 6H), 1.04 (m, J = 7.6 Hz, 6H). ^{13}C -NMR (100 MHz, CDCl_3): δ 141.8, 141.0, 135.1, 128.2, 127.3, 127.1, 126.2, 72.6, 71.9, 70.8, 70.7, 70.6, 63.3, 59.0, 17.4, 17.3, 12.02. ESI-HRMS calc. for $\text{C}_{25}\text{H}_{38}\text{O}_4\text{Si}$ $[\text{M}+\text{Na}]$: 453.2432. Found: 453.2447.

4.2.8. [1,1'-Biphenyl]-4-yl diisopropyl(methoxy)silane (8)—Yield = 90%. ^1H NMR (400 MHz, CDCl_3): δ 7.64–7.60 (m, 6H), 7.46–7.43 (m, 2H), 7.37–7.35 (m, 1H), 3.64 (s, 3H), 1.37–1.29 (m, 2H), 1.10 (d, J = 7.2 Hz, 6H), 1.05 (d, J = 7.2 Hz, 6H). ^{13}C -NMR (100 MHz, CDCl_3): δ 141.6, 141.0, 135.1, 132.7, 128.7, 127.3, 127.1, 126.3, 52.1, 17.5, 17.3, 11.95. CI-HRMS calc. for $\text{C}_{19}\text{H}_{26}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 299.1831. Found: 299.1844.

4.2.9. [1,1'-Biphenyl]-4-yl fluorodiisopropylsilane (11)—Yield = 81%. ^1H -NMR (400 MHz, CDCl_3): δ 7.67–7.56 (m, 6H), 7.48–7.41 (m, 2H), 7.39–7.32 (m, 1H), 1.37–1.25 (m, 2H), 1.12–1.05 (m, 12H). ^{13}C -NMR (100 MHz, CDCl_3): δ 141.5, 134.9, 134.3, 134.3, 129.0, 128.8, 127.7, 127.5, 127.3, 127.1, 127.0, 126.5, 126.1, 17.8, 17.6, 16.7 (d, $J_{\text{C-F}}$ = 2 Hz), 16.5, 13.8, 12.2 (d, $J_{\text{C-F}}$ = 14 Hz). CI-HRMS calc. for $\text{C}_{18}\text{H}_{23}\text{FSi}$ $[\text{M}+\text{H}]^+$: 287.1631. Found: 287.1635.

4.3. Radiochemistry

Cyclotron-produced NCA ^{18}F fluoride ion (30–100 mCi) in ^{18}O water (60–250 μL) was mixed with stock $\text{K}_2\text{CO}_3/\text{K}$ 2.2.2 (0.7 μmol and 2.6 mmol in 9:1 MeCN: H_2O mixture) or aqueous K_2CO_3 (0.1–3.6 μmol), then dried by four cycles of azeotropic evaporation with acetonitrile (0.65 mL for each addition) at 110 $^\circ\text{C}$ using a robot-based automation module.^[17] All reactions were performed at room temperature. For radiochemical studies with K 2.2.2, substrate (1 μmol) and anhydrous $^{18}\text{F}^-/\text{K}^+$ K 2.2.2 in MeCN (200 μL) were added to a glass vial to form a clear solution. For radiochemical studies without K 2.2.2, substrate (1 μmol) was dissolved in the MeCN containing H_2O (0.5–5%, v/v, 200 μL), and the solution transferred to the V-vial that contained dried K^{18}F . For both types of experiment, an aliquot (10 μL) of reaction mixture was sampled at a designated time and quenched in a mixture of $\text{H}_2\text{O}:\text{MeCN}$ (1:1, v/v, 500 μL). A portion of the quenched aqueous solution (20 μL) was injected onto a reverse phase HPLC (Luna, C18, 10 μm , 250 $\times$ 4 mm) for analysis with UV-absorbance (254 nm) and radioactivity detectors. The mobile phase was a mixture of 25 mM aqueous ammonium formate (A) and MeCN (B), initially with B at 40% for 2 min, and then increased to 90% over 1 min. Flow rate was 2 mL/min. Product identity was confirmed by coelution with authentic non-radioactive compound. RCY (%) was calculated as the ratio of the peak area of the product to the sum of peak areas of all radio-peaks. No decay correction was performed because the time lapse between the two radio-peaks was small (around 10 min).

Supplementary Material

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Acknowledgments

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jfluchem.2013.12.005>.

Figure 1.

RCYs versus time for the radiofluorinations of substrates **3–8** in the presence of the stated concentration of K_2CO_3 in acetonitrile containing 0.5% water at rt (in the absence of K 2.2.2). Substrate concentration was 5 mM.

Figure 2.

RCYs versus time for the radiofluorinations of **3–8** in the presence of K_2CO_3 and K 2.2.2 in anhydrous acetonitrile at rt. Substrate concentration was 5 mM; K_2CO_3 concentration was 3.6 mM.

Scheme 1.

Likely mechanism for rate enhancement in silicon fluorination using a crown ether leaving group

Table 1

Fluorination of organosilanes with diverse alkoxide leaving groups.

$\begin{array}{c} \text{R}^1 \quad \text{R}^1 \\ \diagdown \quad \diagup \\ \text{R}-\text{Si}-\text{LG} \end{array} \xrightarrow[\text{rt, 30 min}]{\text{KF (0.5 eq), MeCN-}d_3}$		$\begin{array}{c} \text{R}^1 \quad \text{R}^1 \\ \diagdown \quad \diagup \\ \text{R}-\text{Si}-\text{F} \end{array}$	$\begin{array}{ll} \text{R} = & \text{R}^1 = \\ \text{Ph} & \text{Me} \\ \text{tBu} & \text{Ph} \\ \text{4-biphenyl} & \text{tPr} \end{array}$	
1,2 3-5 6-8		9 10 11		
entry	substrate	product	conversion (%) [*]	
			alone	18-C-6
1		9	0	20 [†]
2		9	0	13
3		10	59	0
4		10	0	10
5		10	0	33
6		11	79	0
7		11	0	72

entry	substrate	product	conversion (%) [*]	
			alone	18-C-6
8	8	11	0	77

^{*} All fluorinations were carried out at 0.1 M substrate conc. in anhydrous acetonitrile-*d*₃ (1.0 mL) at room temperature. Percent conversion, based on potassium fluoride as limiting reagent, was measured with ¹H-NMR.

[†] In the presence of excess potassium fluoride (4 eq), substrate **1** was quantitatively converted into **9** after 6 hours.