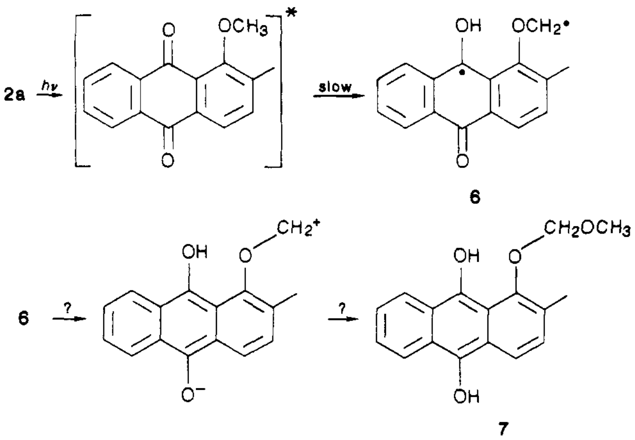
2878 J. Org. Chem. 1988, 53, 2878-2880

Scheme I



terestingly, there are reports in the literature that anthracyclines are unstable in the presence of visible[7] and ultraviolet light,[8] although products from these photolyses have not been identified. Demethylation does not occur if the anthraquinone is reduced to its corresponding anthrahydroquinone prior to irradiation. 1-Methoxy-2-methyl-9,10-dihydroxyanthracene, prepared by the electrochemical reduction of **2a**, was recovered quantitatively after exposure to the xenon chloride eximer laser for relatively long periods (>20 min).

To probe the mechanism of this photodemethylation, the deuteriated anthraquinone **2d** was prepared. With either a tungsten lamp or the 308 nm laser, a quantum yield of 0.0080 was obtained. This compares to a value of 0.020 for **2a**, giving a k_H/k_D ratio of 2.5, which is within the range of values for a reaction that exhibits a primary hydrogen isotope effect.

These preliminary results suggest the partial mechanism in Scheme I. The isotope study supports a 1,6-H atom transfer from an excited state of **2a** leading to the free radical intermediate **6**. Similar hydrogen atom transfers have been observed in photoexcited naphthoquinones[9] and β-alkoxypropiophenones.[10] One can only speculate how the reaction proceeds beyond this point but primary photoproduct **7** would give the observed products upon workup (e.g., exposure to oxygen and chromatographic separation on silica gel). One possible pathway to **7** could involve an intramolecular electron transfer to form a zwitterion followed by methanol capture. The observation that **4** reacts much more slowly than **2a** supports an electron-transfer step since an anthraquinone containing two methoxy groups would be more difficult to reduce. Also, the failure of **5** to demethylate cleanly is consistent with its inability to undergo intramolecular hydrogen transfer. Efforts thus far, however, to isolate the presumably air- and acid-sensitive anthrahydroquinone **7** have been unsuccessful. Work is in progress aimed at further elucidating the mechanism and determining the scope of this photodemethylation reaction.

Acknowledgment. We are indebted to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Research Corporation. R.L.B. thanks Calvin College for a Calvin Research Fellowship (1986–1987).

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Synthesis of (α-Hydroxyalkyl)trialkylsilanes via a Reverse Brook Rearrangement

Summary: The transmetalation and rearrangement of [α-((trialkylsilyl)oxy)alkyl]trialkylstannanes have been achieved, providing a method for the direct conversion of several aldehydes and cyclohexanone into (α-hydroxyalkyl)trialkylsilanes in reasonable yields.

Sir: The Brook rearrangement,[1] an intramolecular migration of silicon from carbon to oxygen, readily proceeds for (α-hydroxybenzyl)trialkylsilanes with a catalytic amount of base. The stereospecific intramolecular rearrangement is driven forward due to the favorable increase in the thermodynamic bond strength in changing from a C–Si bond to an O–Si bond. The reverse, or anti-Brook rearrangement, the migration of silicon from oxygen to carbon, has been demonstrated for (α-trialkylsilyloxy)benzylic ethers.[2] The "reverse" process requires an excess of base and presumably proceeds due to the stability of the alkoxide anion vs the carbanion. The reverse rearrangement has apparently been limited to silyl ethers that can be deprotonated at the ether carbon to generate the requisite carbanion. Benzylic systems are well-known[2,3] and allylic silyl ethers also readily rearrange upon deprotonation with strong base.[4] There have been no reports of an analogous reverse Brook rearrangement occuring for an aliphatic silyl ether.[5] We would now like to report that the reverse Brook rearrangement can be readily accomplished through the intermediacy of an [α-((trialkylsilyl)oxy)alkyl]trialkylstannane.

α-Alkoxy organostannanes are now well-known as a source of α-alkoxy lithio species[6] and have also provided α-alkoxy organocuprates.[7] The facile transmetalation of Sn to Li is readily accomplished at low temperatures in ethereal solvents. We initially assessed the feasibility of affecting a reverse Brook rearrangement by trans-

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[1] Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77.

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[5] The Brook rearrangement (forward sense) has been carried out in aliphatic systems, see ref 11b and: Hudrlik, P. F.; Hudrlik, A. M.; Kulkarni, A. K. *J. Am. Chem. Soc.* **1982**, *104*, 6809.

[6] (a) Still, W. C. *J. Am. Chem. Soc.* **1980**, *102*, 1201. (b) McGarvey, G. J.; Kimura, M. *J. Org. Chem.* **1985**, *50*, 4655. (c) Sawyer, J. S.; MacDonald, T. L.; McGarvey, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 3376. (d) Duchene, A.; Quintard, J. P. *J. Chem. Soc., Chem. Commun.* **1987**, 29.

[7] (a) Linderman, R. J.; Godfrey, A. *Tetrahedron Lett.* **1986**, *27*, 4553. (b) Linderman, R. J.; Godfrey, A.; Horne, K. *Tetrahedron Lett.* **1987**, *28*, 3911. (c) Hutchinson, D. K.; Fuchs, P. L. *J. Am. Chem. Soc.* **1987**, *109*, 4930.

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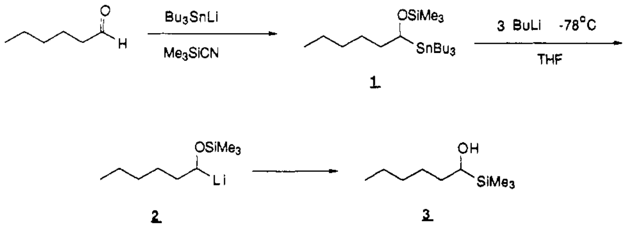
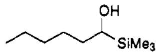
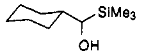
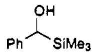
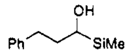
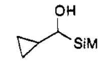
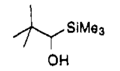
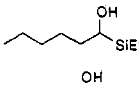
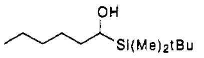
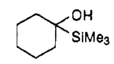
metalation of the [α-((trialkylsilyl)oxy)alkyl]trialkylstannane derived from hexanal and tributylstannyllithium. Attempted silylation of the lithium alkoxide generated by condensation of the tin anion and the aldehyde using trimethylsilyl chloride was unsuccessful. Aqueous quench of the condensation reaction followed by generation of the sodium or potassium alkoxide did not facilitate silyl ether formation. The silylation problem was readily solved by using either trimethylsilyl cyanide[8] or trimethylsilyl triflate as the electrophile. In this fashion [α-((trialkylsilyl)oxy)alkyl]trialkylstannane intermediate **1** was obtained in 70% yield after chromatography. Transmetalation of **1** to the lithio species **2** was attempted using 1.2 equiv of *n*-butyllithium in THF at −78 °C; however, only the starting material **1** was recovered from the reaction. Using 3 equiv of *n*-butyllithium resulted in transmetalation and rearrangement at −78 °C within 15 min. The (α-hydroxyalkyl)trimethylsilane **3** was obtained in 80% yield after chromatography. The two-step process had occurred in 56% overall yield from hexanal. The method could be simplified further by avoiding chromatographic purification at the intermediate step. In this fashion, the silylation reaction was subjected to an aqueous workup, the crude [α-((trialkylsilyl)oxy)alkyl]trialkylstannane product was then taken up in THF and cooled to −78 °C, and 3.0 equiv of *n*-butyllithium was added. The yield of **3** by this procedure is better than the overall yield obtained via an independent synthesis employing an acyl silane intermediate. Several (α-hydroxyalkyl)trimethylsilanes were prepared in 45–65% overall yield by this "one-pot" procedure (see Table I, entries 1–5).

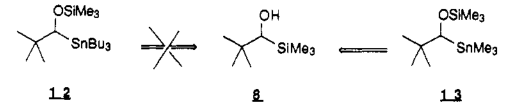


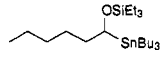
With the standard transmetalation/rearrangement conditions (3.0 equiv of *n*-butyllithium in THF at −78 °C for 15 min), the attempted preparation of the *tert*-butyl-substituted silane **8** from the corresponding stannane **12** did not result in the isolation of any of the (α-hydroxyalkyl)trimethylsilane **8**. Extended reaction times, up to 4 h at −78 °C, or the use of a large excess (4–8 equiv) of *n*-butyllithium were also unsuccessful. Interestingly, the starting stannane **12** could be recovered from the reaction mixture. This recalcitrant behavior of an organostannane toward transmetalation is unusual. The possibility of material loss due to transmetalation without subsequent rearrangement was not a problem since the destannylated silyl ethers or the simple alcohols (effectively a reduction of the starting aldehyde) were not isolated. The conversion of **12** to **8** did proceed sluggishly upon warming the reaction mixture to −20 °C, but complete conversion of **12** to **8** was not achieved. The apparent steric restriction for the transmetalation/rearrangement process at carbon was circumvented by using trimethylstannyllithium in place of tributylstannyllithium for the initial condensation step. Transmetalation of the trimethylstannane derivative **13** using the standard conditions required for rearrangement of **1** to **3** provided clean conversion of **13** to **8** in 49% overall yield.

Table I. (α-Hydroxyalkyl)trialkylsilanes Prepared by a Reverse Brook Rearrangement

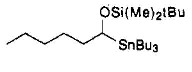
entry	(α-hydroxyalkyl)trialkylsilane	yield, %[a]
1	 **3**	56
2	 **4**	57
3	 **5**	65
4	 **6**	56
5	 **7**	45[b]
6	 **8**	49[b]
7	 **9**	54
8	 **10**	68
9	 **11**	47

[a] Isolated yield after chromatography of crude product. All new compounds exhibited correct spectral and analytical data. [b] Some reduction in yield due to the volatility of the product.





14



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In light of the steric effect at carbon, we also examined the possibility of a steric effect at silicon. The intermediate α-hydroxy stannane generated from the reaction of hexanal and lithium tributylstannylate was quenched with triethylsilyl triflate. Rearrangement of the triethylsilyl ether **14** was then accomplished under the standard transmetalation/rearrangement conditions and the product **9** obtained in 54% overall yield (Table I, entry 7). The *tert*-butyldimethylsilyl ether **15**, prepared by using *tert*-butyldimethylsilyl triflate, did not rearrange under the standard conditions at −78 °C but required 3 h at 0 °C. Nevertheless, the (α-hydroxyalkyl)-*tert*-butyldimethylsilane **10** was obtained in 68% overall yield.

The utility of this procedure for the synthesis of (α-hydroxyalkyl)silanes is further demonstrated by the synthesis of **11** from cyclohexanone. As in the pivaldehyde example (**12** to **8**), rearrangement of 1-((trimethylsilyl)oxy)-1-(tributylstannyl)cyclohexane could not be accomplished even under forcing conditions (4–12 equiv of *n*-BuLi, DME, −20 to 25 °C, 1–12 h). However, by employment of the trimethylstannyl intermediate **16**, the rearrangement product **11** was obtained in 47% overall yield using 3.0 equiv of *n*-butyllithium in THF at −78 °C for 1 h.

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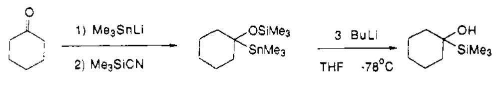
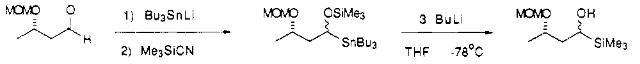
[8] Trimethylsilyl cyanide has been shown to be a very effective silylating agent for hindered alcohols. Mai, K.; Patil, G. *J. Org. Chem.* **1986**, *51*, 3545.



16 11

Our initial results also indicate that this procedure is applicable to the preparation of functionalized (α-hydroxyalkyl)trialkylsilanes. The optically active aldehyde 17[9] was condensed with (tributylstannyl)lithium and the reaction quenched with trimethylsilyl cyanide to produce a diastereomeric mixture of **18**. The crude product **18** was subjected to the standard rearrangement conditions, providing the silane **19** in 37% overall yield from **17** (unoptimized).



17 18 19

The direct synthesis of (α-hydroxyalkyl)trialkylsilanes is not readily accomplished by other methods.[10] In particular, the nucleophilic addition of trialkylsilyl anions to aldehydes or ketones is not synthetically useful.[11] The method described herein also obviates the need for the synthesis of an acyl silane intermediate.[12] Indeed, the oxidation of the (α-hydroxyalkyl)trialkylsilane obtained by the rearrangement process can lead to the synthesis of acyl silanes by means other than the conventional acyl anion approach.[13]

In conclusion, we have reported a method[15] for the successful reverse Brook rearrangement of aliphatic silyl ethers which provides (α-hydroxyalkyl)trialkylsilanes directly from several aldehydes and cyclohexanone in reasonable overall yields. Further experiments using configurationally defined species are in progress to critically assess the stereochemical consequence of this procedure and to further explore the unusual transmetalation behavior observed.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of the research.

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(9) Obtained from polymeric 3-hydroxybutyric acid by the following sequence: (a) depolymerization by the method of Seebach;[14] (b) MOMCl, *i*-PrNEt$_2$, CH$_2$Cl$_2$; (c) LiAlH$_4$, Et$_2$O; (d) ClCOCOCl, DMSO, Et$_3$N.

(10) For an example of the oxidation of a vinyl silane, see: Hudrlik, P. F.; Hudrlik, A. M.; Kulkarni, A. K. *J. Am. Chem. Soc.* **1985**, *107*, 4260.

(11) The addition of Me$_3$SiLi to nonenolizable aldehydes has been reported;[11a] however, the addition of this anion to aldehydes[11b] or ketones[11c] has been problematic. (a) Corey, E. J.; Tius, M. A.; Das, J. *J. Am. Chem. Soc.* **1980**, *102*, 1742. (b) Wilson, S. R.; Hague, M. S.; Misra, R. N. *J. Org. Chem.* **1982**, *47*, 747. (c) Vedejs, E.; Arnest, M. J.; Eustache, J. M.; Krafft, G. A. *J. Org. Chem.* **1982**, *47*, 4384. Additions of PhMe$_2$SiLi have been carried out successfully.[11c–f] (d) Reich, H. J.; Eisenhart, E. K. *J. Org. Chem.* **1984**, *49*, 5282. (e) Reich, H. J.; Eishenhart, E. K.; Olson, R. E.; Kelly, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 7791. (f) Reich, H. J.; Holtan, R. C.; Borkowsky, S. L. *J. Org. Chem.* **1987**, *52*, 314. Acylsilanes (see ref 12 and 13) can be prepared and subsequently reduced by lithium aluminum hydride to provide the (α-hydroxyalkyl)silane; however, this should not be viewed as a direct method.

(12) (a) Brook, A. G.; Duff, J. M.; Jones, P. F.; Davis, N. R. *J. Am. Chem. Soc.* **1967**, *89*, 431. (b) Corey, E. J.; Seebach, D.; Freedman, R. *J. Am. Chem. Soc.* **1967**, *89*, 434. For a review of organosilicon compounds including acylsilanes, see: Magnus, P. D.; Sarkur, T.; Djuric, S. In *Comprehensive Organometallic Chemistry*; Wilkenson, G., Ed.; Pergamon: Oxford, 1982; Vol. 7, Chapter 48.

(13) For other alternative routes to acyl silanes, see, inter alia: (a) Seyferth, D.; Weinstein, R. M. *J. Am. Chem. Soc.* **1982**, *104*, 5534. (b) Murai, S.; Ryu, I.; Iriguchi, J.; Sonoda, N. *J. Am. Chem. Soc.* **1984**, *106*, 2440. (c) Ricci, A.; Degl'Innocenti, A.; Ancillotti, M. *Tetrahedron Lett.* **1986**, *27*, 5985. (d) Kang, J.; Lee, J. H.; Kim, K. S.; Jeong, J. U.; Pyun, C. *Tetrahedron Lett.* **1987**, *28*, 3261. For the oxidation of (α-hydroxy)silanes, see ref 4b and references cited therein.

(14) Seebach, D.; Imwinkelreid, R.; Stucky, G. *Helv. Chim. Acta* **1987**, *70*, 448.

(15) General experimental procedure. (a) Synthesis of [α-((trialkylsilyl)oxy)alkyl]trialkylstannanes: Tributylstannyllithium or trimethylstannyllithium was prepared by published procedures.[6] A tetrahydrofuran solution of the stannyl anion (0.95 equiv, 0.1 M concentration) was cooled to −78 °C, and the aldehyde (1.0 equiv) was added dropwise. The reaction mixture was stirred at −78 °C for 15 min and then quenched at −78 °C by the dropwise addition of the desired trialkylsilyl cyanide or triflate (1.5 equiv). The mixture was allowed to gradually warm to room temperature and then stirred for 1 h. The solution was then diluted with 100 mL of petroleum ether, washed with 20 mL of saturated aqueous sodium chloride solution, and dried over anhydrous sodium sulfate. The solvents were removed under reduced pressure to provide the crude stannyl silyl ether. (b) Reverse Brook rearrangement: The crude stannyl silyl ether was dissolved in 25 mL of dry tetrahydrofuran and cooled to −78 °C (under Ar). A hexane solution of *n*-butyllithium (3.0 equiv) was added dropwise via syringe. The reaction mixture was then allowed to stir at −78 °C for 15 min (or a variation described in the text) and quenched at −78 °C by the rapid addition of 5 mL of water. After warming to room temperature the reaction mixture was worked up by extraction using petroleum ether (as described above). The (α-hydroxyalkyl)trialkylsilane product was purified by flash chromatography on silica gel using 100% hexane to first elute the tetraalkylstannane byproduct, followed by a gradient elution using a 1%, 2%, and then 3% ethyl acetate/hexane system.

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