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Regioselective Preparation of 2,4-, 3,4-, and 2,3,4-Substituted Furan Rings. 1. [1,4] O → C and [1,4] C → O Silyl Migrations of Silyl Ethers and Esters Attached to Furan and Thiophene Rings

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[1,4] O → C and [1,4] C → O rearrangements are described for a variety of furans and thiophenes. Treatment of 3-((silyloxy)methyl)furans and -thiophenes with *n*-BuLi in HMPA provided 2-silylated-3-(hydroxymethyl)furans and -thiophenes in good to excellent yields. The reaction was shown by crossover studies to proceed via an intramolecular [1,4] O → C silyl migration. Silyl esters of 3-furoic acids also underwent an intramolecular [1,4] O → C silyl migration to provide 2-silylated-3-furoic acids in moderate to good yield when treated with a mixture of LDA and HMPA. Finally, the above silyl migrations were shown to be reversible. Treatment of 2-silylated-3-(hydroxymethyl)furans and -thiophenes with NaH in DMF provided 3-((silyloxy)methyl)furans and -thiophenes in excellent yields via a [1,4] C → O silyl migration. The [1,4] C → O silyl migration was also shown to be an intramolecular process by a crossover study.

Of the many disubstituted furan patterns possible, the 3,4-disubstituted system is probably most difficult to prepare since furan rings preferentially lithiate[1] and add electrophiles[2] in the C-2 or C-5 positions. The second most difficult is the 2,4-disubstituted pattern, since 3-substituted furans preferentially lithiate at the C-2 position, thereby providing 2,3-disubstituted furan rings.[1] Since many natural products incorporate furan rings with 3,4-, 2,4-, or 2,3,4-substitution patterns,[3] a need has emerged for developing synthetic routes toward the preparation of furan rings containing these substitution patterns. Some elaborate methods for preparing 3,4-disubstituted furans have been reported. These include Diels−Alder/retro-Diels−Alder chemistry,[4] chemical modifications of 3,4-furandicarboxylic acid,[5] and the synthetic modification of acyclic precursors.[6]

In 1988 we reported the first successful regiospecific C-4 lithiation of a 2,3-disubstituted furan.[7] Thus 2-(*tert*-butyldimethylsilyl)-3-(hydroxymethyl)furan (**3**), prepared by a [1,4] O → C silyl migration of **1**, when treated with 2.2 equiv of *n*-BuLi in DME or THF/HMPA at 0 °C for 1 h, and treated with an electrophile, provided 2-(*tert*-butyldimethylsilyl)-3-(hydroxymethyl)-4-substituted furans (**5**) in good to excellent yield (Scheme 1). Subsequent removal of the C-2 silyl group with tetra-*n*-butylammonium fluoride or via a [1,4] C → O silyl rearrangement (NaH, DMF) provided the corresponding 3,4-disubstituted furans (**7** or **8**) respectively. Thus a direct, high-yielding synthesis of 3,4-disubstituted furans via lithiation has been achieved. A few years later, we showed that silyl esters of 3-furoic acid (**2**) undergo a similar sequence providing 4-substituted-3-furoic acids in good to excellent yields (Scheme 1, see **2** → **4** → **6** → **9**).[8]

In this and the following paper, we provide a full account of our work on the silyl migrations and regioselective lithiations. This paper will provide a full account of (a) the [1,4] O → C silyl rearrangement of 3-((silyloxy)methyl)furans and -thiophenes,[9] (b) the [1,4] O → C silyl migration of silyl esters of 3-furoic acid and 3-thiophenecarboxylic acids;[10] and (c) the [1,4] C → O silyl rearrangement of 2-silylated-3-(hydroxymethyl)-4-substituted furans and thiophenes.[11] The next paper (i.e., part 2) will discuss in detail regioselective lithiations of 2-silylated-3-substituted furan systems.

It was reasoned that a new synthetic pathway to 3,4-disubstituted furans could be possible by employing a carefully modified 2,3-disubstituted furan ring such that lithiation would occur at the C-4 position and not the C-5

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[5] (a) Corey, E. J.; Crouse, D. N.; Anderson, J. E. *J. Org. Chem.* **1975**, *14*, 2140. (b) Schultz, A. G.; Motyka, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 5800. (c) Schultz, A. G.; Motyka, L. A.; Plummer, M. *J. Am. Chem. Soc.* **1986**, *108*, 1056.

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[9] Bures, E. J.; Keay, B. A. *Tetrahedron Lett.* **1987**, *28*, 5965.

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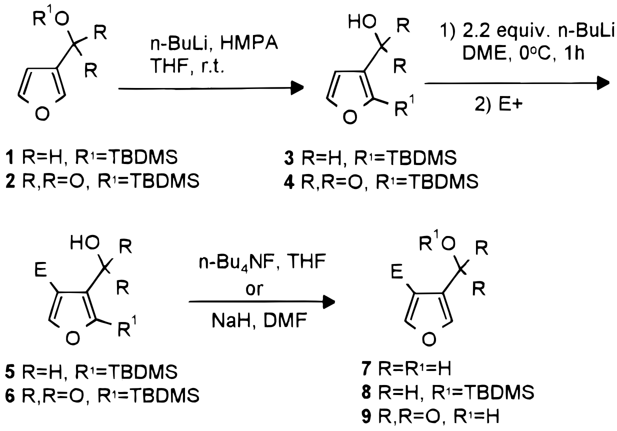
S0022-3263(97)01097-9 CCC: $14.00

Scheme 1

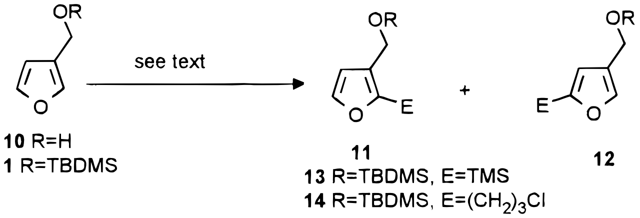


position. Two criteria were necessary for the C-4 lithiation to occur. First, an *ortho*-lithiation director must be present at the C-3 position of the furan ring.[12] In addition, this functional group must be easy to modify for use in the synthesis of natural products. Second, the C-2 position should have a bulky substituent, which is easily attached and removed from the furan ring. The size of this substituent was thought to be essential for a successful C-4 lithiation, since the steric bulk at C-2 would presumably impede lithium coordination with the furan ring oxygen atom, thereby reducing the likelihood of a C-5 lithiation with *n*-BuLi. The system chosen initially to meet the above criteria was 2-(*tert*-butyldimethylsilyl)-3-(hydroxymethyl)furan (**3**) (Scheme 1). The hydroxymethyl group would act as the *ortho*-lithiation director[13] while the bulky silane at C-2 would provide the necessary steric hindrance during the lithiation. Later, we found that the carboxylic acid group was also a good *ortho*-lithiation director in these systems.[8] The silyl group was also chosen since the C−Si bond in arylsilanes and vinylsilanes can be cleaved by protodesilylation or treatment with tetra-*n*-butylammonium fluoride.[14] Thus, removal of the silyl moiety on the furan ring should be a facile process.

[1,4] O → C of Silyl Migrations of Silyl Ethers

Tanis *et al.*[15] and Katsumura *et al.*[16] have reported that treatment of 3-(hydroxymethyl)furan (**10**) with 2.2 equiv of *n*-BuLi in TMEDA (0 °C) or THF (-78 °C, 2 h, 0 °C, 1 h) affords a 4:1 and 9:1 ratio of the 2,3-disubstituted- and 2,4-disubstituted-furans (**11** and **12**), respectively, after quenching the dianions with an electrophile (Scheme 2). In our hands, treatment of the dianion of **10**, formed using Katsumura's conditions, with *tert*-butyldimethylsilyl chloride afforded a 9:1 mixture of compounds **3** and **12** (R = H, E = Si(*t*-Bu)Me$_2$), which could not be easily separated by chromatography or distillation.[17] While investigating alternative methods for preparing **3**, we discovered that **3** could be prepared in good yield via a [1,4] O → C silyl migration.

Scheme 2



Goldsmith *et al.* have reported[18] that 3-((*tert*-butyldimethylsilyl)oxy)methyl)furan (**1**) can be regiospecifically lithiated at C-2 (1 equiv of *n*-BuLi, ether, rt, 6 h) to provide 2-(trimethylsilyl)-3-(((*tert*-butyldimethylsilyl)oxy)methyl)furan (**13**) in good yield (90%) after quenching the anion with trimethylsilyl chloride (Scheme 2). In an unrelated project, we found that treating the C-2 anion of furan **1** with 1-bromo-3-chloropropane afforded the alkylated product **14** in poor yield (28%). However, changing the lithiation conditions (*n*-BuLi, THF, 0 °C, 6 h) and then adding HMPA simultaneously with the electrophile resulted in the isolation of starting material **1** (36%) and a slower running spot by TLC, which was identified as 2-(*tert*-butyldimethylsilyl)-3-(hydroxymethyl)furan (**3**) (55%).[19] Furan **3** was unexpected from this reaction and appeared to be formed by a [1,4] O → C silyl rearrangement.[20] Since a search of the literature (in 1987−88) indicated there were only 5 examples of [1,4] C → O silyl rearrangements,[21] and none involved an initially formed carbanion at an sp^2 center, we investigated this reaction in more detail.[22]

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[12] For excellent reviews on directed *ortho*-lithiation, see: (a) ref 1. (b) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.

[13] For use of a benzylic alcohol moiety as an *ortho*-lithiation director, see: (a) Uemura, M.; Tokuyana, S.; Sakan, T. *Chem. Lett.* **1975**, 1195. (b) Meyer, N.; Seebach, D. *Chem. Ber.* **1980**, *118*, 1304. (b) Panetta, C. A.; Dixit, A. S. *Synthesis* **1981**, 59. (d) Uemura, M.; Take, K.; Tobe, K.; Minani, T.; Hayashi, Y. *Tetrahedron* **1985**, *41*, 5771. (e) Katsuura, K.; Snieckus, V. *Can. J. Chem.* **1987**, *65*, 124. For a synthetic sequence which results in products from the α-lithiation of the benzylic methylene group, see: Katritzky, A. R.; Fan, W.-Q.; Kutagawa, K. *Synthesis* **1987**, 415.

[14] (a) Colvin, E. *Silicon in Organic Synthesis*; Butterworth and Co. Ltd.: London, 1981. (b) Colvin, E. *Silicon Reagents in Organic Synthesis*; Academic Press: London, 1988.

[15] Tanis, S. P.; Head, D. B. *Tetrahedron Lett.* **1984**, *25*, 4451.

[16] Katsumura, S.; Hori, K.; Fujiwara, S.; Isoe, S. *Tetrahedron Lett.* **1985**, *26*, 4625.

[17] Compounds **3** and **12** (R = H, E = Si(*t*-Bu)Me$_2$) required four silica gel columns (EtOAc:petroleum ether, 1:9) to afford compound **3** in 56% isolated yield.

[18] Goldsmith, D.; Liotta, D.; Saindane, M.; Waykole, L.; Bowen, P. *Tetrahedron Lett.* **1983**, *24*, 5835.

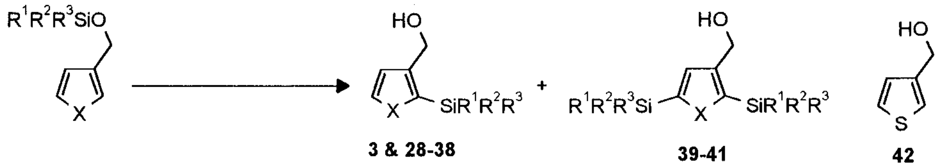
[19] The spectral data of furan **3**, isolated from the reaction involving furan **1** with HMPA, were identical to the major product isolated from reaction of the dianion of compound **10** with *tert*-butyldimethylsilyl chloride.

[20] Oxygen-to-carbon silyl migrations are sometimes referred to as retro[1,*n*]Brook rearrangements, see: (a) Brook, A. G. *J. Am. Chem. Soc.* **1958**, *80*, 1886. (b) Brook, A. G. ; Warner, C. M.; McGriskin, M. E. *J. Am. Chem. Soc.* **1959**, *81*, 981. (c) Brook, A. G. *Pure Appl. Chem.* **1966**, *13*, 215. (d) Brook, A. G.; Pascoe, J. D. *J. Am. Chem. Soc.* **1971**, *93*, 6224. (e) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77. (f) Brook, A. G.; Bassendale, A. R. *Rearrangements in Ground and Excited States*; De Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 2, pp 149−227. (g) Brook, A. G.; Chrusciel, J. J. *Organometallics* **1984**, *3*, 1317 and references therein. For recent references to many [1,*n*] X → Y silyl migrations, see: He, H.-M.; Fanwick, P. E.; Wood, K.; Cushman, M. *J. Org. Chem.* **1995**, *60*, 5905.

[21] (a) Speier, J. L. *J. Am. Chem. Soc.* **1952**, *74*, 1003. (b) Ben,keser, R. A.; Cunico, R. F. *J. Org. Chem.* **1967**, *32*, 395. (c) Evans, D. A.; Takacs, J. M. *J. Am. Chem. Soc.* **1979**, *101*, 371. (d) Hunig, J.; Oller, M. *Chem. Ber.* **1980**, *113*, 3803. (e) Mora, J.; Costa, A. *Tetrahedron Lett.* **1984**, *25*, 3493. (f) Rucker, C. *Tetrahedron Lett.* **1984**, *25*, 4349. For an example in which the proposed mechanism involves a [1,4] O → C silyl migration, see: Karlsson, J. O.; Nguyen, N. V.; Foland, L. D.; Moore, H. W. *J. Am. Chem. Soc.* **1985**, *107*, 3392.

[22] Since 1988, more [1,4] O → C silyl rearrangements have been reported, see: (a) Braun, M. *Agnew. Chem., Int. Ed. Engl.* **1989**, *28*, 896. (b) Satoh, T.; Oohara, T; Ueda, Y.; Yamakawa, K. *J. Org. Chem.* **1989**, *54*, 3130. (c) Kim, K. D.; Magriotis, P. A. *Tetrahedron Lett.* **1990**, *43*, 6137. (d) Wang, K. K.; Liu, C.; Gu, Y. G.; Burnett, F. N. *J. Org. Chem.* **1991**, *56*, 1914. (e) Lautens, M.; Delanghe, P. H. M.; Goh, J. B.; Zhang, C. H. *J. Org. Chem.* **1992**, *57*, 3270. (f) Hoffmann, R. W. Bewersdorf, M. *Tetrahedron Lett.* **1989**, *54*, 3130. (g) Hoffmann, R.; Bruckner, R. *Chem. Ber.* **1992**, *125*, 1471 and 2731. (h) Lautens, M.; Delanghe, P. H. M.; Goh, J. B.; Zhang, C. H. *J. Org. Chem.* **1995**, *60*, 4213. (i) Rücker, C. *Chem. Rev.* **1995**, *95*, 1009.

Table 1. Results of the [1,4] O → C Silyl Migration of Silyl Ethers



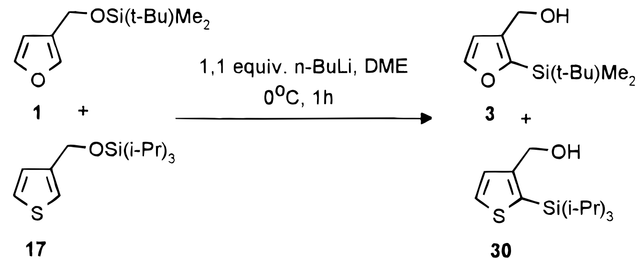
entry	starting material		product(s) (% yield)^{a}
1	**1**	X = O; $R^1 = R^2 =$ Me; $R^3 =$ *t*-Bu	**3** (87)
2	**15**	X = S; $R^1 = R^2 =$ Me; $R^3 =$ *t*-Bu	**28** (87)
3	**16**	X = O; $R^1 = R^2 = R^3 =$ i-Pr	**29** (86)
4	**17**	X = S; $R^1 = R^2 = R^3 =$ i-Pr	**30** (89)
5	**18**	X = O; $R^1 = R^2 =$ Ph; $R^3 =$ *t*-Bu	**31** (87)
6	**19**	X = S; $R^1 = R^2 =$ Ph; $R^3 =$ *t*-Bu	**32** (63)
7	**20**	X = O; $R^1 = R^2 = R^3 =$ *n*-Bu	**33** (85)
8	**21**	X = O; $R^1 = R^2 = R^3 =$ Et	**34** (79)
9	**22**	X = S; $R^1 = R^2 =$ Ph; $R^3 =$ Me	**35** (75)
10	**23**	X = S; $R^1 = R^2 =$ Me; $R^3 =$ i-Pr	**36** (29)^{a} + **23** (11)^{b} + **42** (40)^{b} + **39** (15)^{a}
11	**24**	X = O; $R^1 = R^2 =$ Me; $R^3 =$ i-Pr	**37** (24)^{a} + **24** (15)^{b} + **10** (43)^{b} + **40** (12)^{a}
12	**25**	X = S; $R^1 = R^2 =$ Me; $R^3 =$ Ph	**38** (38)^{a} + **25** (15)^{b} + **42** (25)^{b} + **41** (10)^{b}
13	**26**	X = O; $R^1 = R^2 = R^3 =$ Me	
14	**27**	X = S; $R^1 = R^2 = R^3 =$ Me	

^{a} Isolated yields. ^{b} GC yields.

The silyl rearrangement was optimized by treating compound **1** with 1.1 equiv of *n*-BuLi in THF containing HMPA (1.1 equiv) at −20 °C for 1 h, followed by stirring the reaction mixture at room temperature overnight. Standard workup afforded furan **3** in 87% yield. The reaction is quite general and is not limited to either the *tert*-butyldimethylsilyl group or the furan ring (Table 1). A variety of silyl derivatives (**15**−**22**) undergo the silyl rearrangement in good to excellent yield to provide compounds **28**−**35**, respectively. In addition, the silyl rearrangements occur when a thiophene ring is present (Table 1, entries 2, 4, 6, and 9). Interestingly, the yield of the expected 2,3-disubstituted heterocycles decreased as the steric bulk of the substituents on the silane decreased (Table 1, entries 10−12). Thus the isopropyldimethylsilyl and dimethylphenylsilyl derivatives (**23**−**25**) afforded the expected 2,3-disubstituted heterocycles **36**−**38**, respectively, in yields ranging from 24 to 38%. In addition, 2,5-disilylated-3-(hydroxymethyl)-heterocycles **39**−**41** were formed (10−15%), plus some unreacted starting material (**23**−**25**, 11−15%) and desilylated starting material **10** and **42** (25−43%). The 3-(((trimethylsilyl)oxy)methyl)furan (**26**) and -thiophene (**27**) provided only desilylated starting material under the rearrangement conditions. This was not unexpected since it is well-known that trimethylsilyl ethers are readily cleaved by alkyllithiums.[23]

The appearance of the 2,5-disilylated-3-(hydroxymethyl)-heterocycles (**39**−**41**), when the silyl substituents were either isopropyldimethyl or dimethylphenyl, prompted us to investigate the mechanism of this reaction in more detail. A crossover experiment confirmed that the silyl rearrangement was *intra*molecular in nature (Scheme 3). Thus an equimolar mixture of 3-(((*tert*-butyldimethylsilyl)oxy)methyl)furan (**1**) and 3-(((triisopropylsilyl)oxy)methyl)thiophene (**17**), when treated under the rearrangement conditions, provided an equimolar mixture of furan **3** and thiophene **30**.[24] Analogous *intra*molecular rearrangements have been reported for [1,4] O → C,[21,22] [1,4] O → O,[25a] [1,5] O → O,[25b] and [1,4] C → C[25c] silyl rearrangements.

Scheme 3



The above experiment indicated that the products from the rearrangements of compounds **1** and **15**−**23** were formed by an intramolecular transfer of the silyl moiety from the oxygen atom to the C-2 position of the furan or thiophene ring. This was expected on the basis of the report of Goldsmith *et al.*[18] that the lithiation of furan **1** *in ether* was C-2 regiospecific.[26] Since the above silyl rearrangements were observed *in THF*, we found that the poor yield of compounds **36**−**38** and the formation of the 2,5-disilylated products **39**−**41** could be explained by studying the lithiation of furan **1** in THF in the *absence* of HMPA.

Treatment of furan **1** with *n*-BuLi in THF at −20 °C for 1 h followed by a quench with trimethylsilyl chloride provided a 2:1 ratio (by ^{1}H NMR)[27] of furans **13** and **43** (Scheme 4). Thus, a mixture of C-2 and C-5 monoanions are being formed initially in THF. When furan **1** was treated under the same conditions and HMPA added after 1 h instead of an electrophile, only furan **3** was obtained in 87% yield. The size of the groups on the silicon atom in combination with the initial mixture of C-2 and C-5 anions in THF therefore must be controlling whether the silyl rearrangement occurs cleanly (to give **1** and **15**−**22**) or provides a mixture of products (**23**−**25**).

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[23] Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd Ed.; John Wiley & Sons Inc.: New York, 1991.

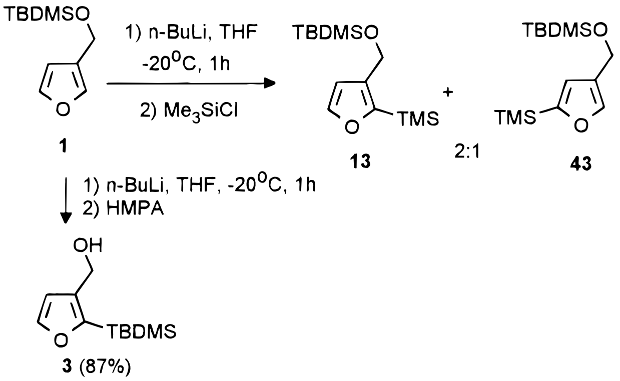
[24] Compounds **1** and **17** were chosen for the crossover study since they were found to rearrange at approximately the same reaction rate.

[25] (a) van Boeckel, C. A. A.; van Aelst, S. F.; Beetz, T. *Recl. Trav. Chim. Pays-Bas.* **1983**, *102*, 415. (b) Torisawa, Y.; Shibasaki, M.; Ikegami, S. *Chem. Pharm. Bull.* **1983**, *31*, 2607. (c) Daney, M.; Lapouyade, R.; Bouas-Laurent, H. *J. Org. Chem.* **1983**, *48*, 5055.

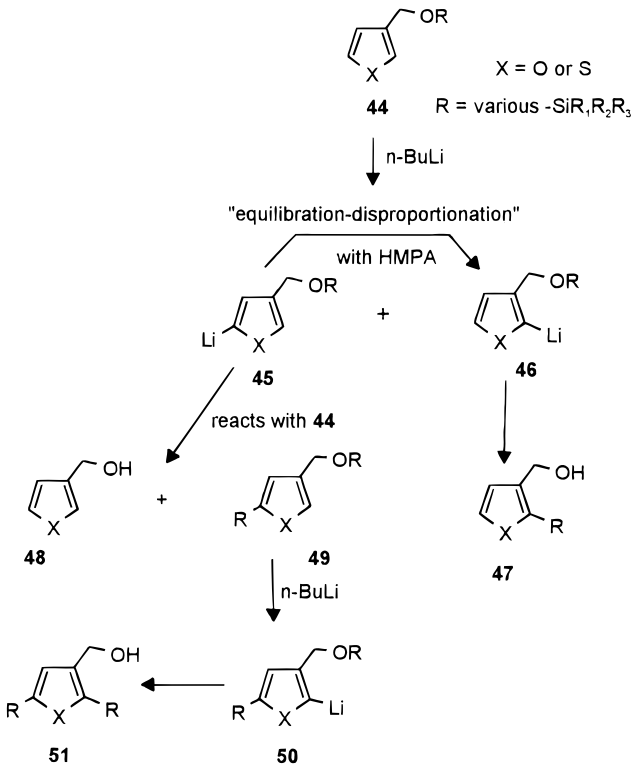
[26] In our hands the lithiation of furan **1** with *n*-BuLi in ether (rt, 6 h) provided a 9:1 mixture of **11**:**12** (Scheme 2: R = *tert*-butyldimethylsilyl; E = Li). The 9:1 ratio was determined by quenching the mixture of anions with MeOD and integrating the furan signals in the ^{1}H NMR spectrum.

[27] Compounds **13** and **43** could not be separated on a silica gel column (petroleum ether:EtOAc (9:1)) or by fractional distillation.

Scheme 4



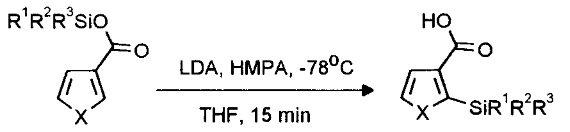
Scheme 5



When the groups attached to the silicon atom are large (entries 1−9, Table 1), the initially formed C-2 anion (**46**, Scheme 5) undergoes an intramolecular silyl rearrangement to form the 2,3-disubstituted heterocycle **47**; however, in the presence of HMPA, the C-5 anion **45** undergoes a "equilibration−disproportionation"[28] to form the C-2 anion **46** faster than the C-5 anion can intermolecularly attack another silyl moiety to form **49**. This process leads to the formation of 2,3-disubstituted furans and thiophenes in excellent yield when the groups attached to silicon are bulky.

When smaller groups are attached to the silicon atom (entries 10−12, Table 1) a different reaction path is taken. The initially formed C-2 anion **46** results in the intramolecular silyl migration to form **47**. The C-5 anion, however, intermolecularly attacks some unreacted starting material **44** to form **49** and desilylated starting material **48**. The remaining *n*-BuLi (which did not lithiate the starting material **44**) then lithiates compound **49** at the C-2 position to form **50**, which rearranges to form the 2,5-disilylated heterocycles **51**. Support for the proposed mechanism came from a crossover study in which an equimolar mixture of furan **24** and thiophene **25**, when treated with *n*-BuLi, provided a complex mixture of 10 products. GC/MS analysis of the mixture revealed the presence of compounds **10**, **24**, **25**, **37**, **38**, **40**, **41**, **42**, 2-(dimethylisopropylsilyl)-5-(dimethylphenylsilyl)-3-(hydroxymethyl)furan (**52**, $M^{•+}$ = 332) and 2-(dimethylphenylsilyl)-5-(dimethylisopropylsilyl)-3-(hydroxymethyl)thiophene (**53**, $M^{•+}$ = 348). The presence of compounds **52** and **53** indicates that an intermolecular transfer of a silyl group is occurring.

Table 2. Results of the [1,4] O → C Silyl Migration of Silyl Esters



entry	starting material		product(s) (% yield)[a]
1	**2**	X = O; $R^1 = R^2$ = Me; R^3 = *t*-Bu	**4** (72)[b]
2	**54**	X = S; $R^1 = R^2$ = Me; R^3 = *t*-Bu	**61** (47)[c]
3	**55**	X = O; $R^1 = R^2 = R^3$ = i-Pr	**62** (56)[b]
4	**56**	X = S; $R^1 = R^2 = R^3$ = i-Pr	**63** (57)[c]
5	**57**	X = O; $R^1 = R^2$ = Ph; R^3 = *t*-Bu	**64** (43)[b]
6	**58**	X = S; $R^1 = R^2$ = Ph; R^3 = *t*-Bu	**65** (64)[c]
7	**59**	X = O; $R^1 = R^2 = R^3$ = *n*-Bu	**66** (51)[b]
8	**60**	X = O; $R^1 = R^2 = R^3$ = Et	**67** (57)[b]

[a] Isolated yields. [b] 3-Furoic acid was also isolated. [c] 3-Thiophene carboxylic acid was also isolated.

In summary, good to excellent yields of 2-silylated-3-(hydroxymethyl)furans and -thiophenes are obtained via [1,4] O → C silyl migrations when the groups on the silicon atom are bulky.

[1,4] O → C Silyl Migration of Silyl Esters

Since Knight *et al.*[29] have reported that 3-furoic acids can be lithiated with 2.2 equiv of LDA at the C-2 position, we became interested to determine if silyl esters would lithiate at the C-2 position and undergo a [1,4] O → C silyl migration. At the time this investigation was started we could not find any examples of silyl esters undergoing a silyl migration. Most of the work reported in the literature dealing with silyl esters has involved studying reduction reactions of silyl esters[30] and using silyl esters as protecting group for carboxylic acids.[31]

Silyl esters **2** and **54**−**60** (Table 2) were prepared by treatment of either 3-furoic or 3-thiophenecarboxylic acid with a silyl chloride (1.2 equiv) and imidazole (1.2 equiv) in DMF at 60 °C for 48 h.[32] Yields of the silyl esters ranged from 60 to 89%. During workup, the contact time with water was minimized by performing fast extractions since most of the silyl esters hydrolyzed to the acid upon prolonged exposure to water.

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(28) (a) Zeigler, F. E.; Fowler, K. W. *J. Org. Chem.* **1976**, *41* 1564. (b) Leonard, N. J.; Bryant, J. D. *J. Org. Chem.* **1979**, *44*, 4612. (c) Ronald, R. C.; Winkle, M. W. *Tetrahedron* **1983**, *39*, 2031. (d) Marsais, F.; Quegwiner, G. *Tetrahedron* **1983**, *39*, 2009.

(29) (a) Knight, D. W.; Nott, A. P. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1125. (b) Knight, D. W. *Tetrahedron* **1979**, *20*, 469.

(30) (a) Corriu, R. J. P.; Lanneau, G. F.; Perrot, M. *Tetrahedron Lett.* **1987**, *28*, 3841. (b) Larson, G. L.; Ortiz, M.; Rodriguez de Roca, M. *Synth. Commun.* **1981**, *11*, 583.

(31) (a) Borgulya, J.; Bernauer, K. *Synthesis* **1980**, 545. (b) Hart, T. W.; Metcale, D. A.; Scheinmann, F. *J. Chem. Soc., Chem. Commun.* **1979**, 156. (c) Corey, E. J.; Kim, C. U. *J. Org. Chem.* **1973**, *38*, 1233.

(32) For the preparation of silyl esters, see: (a) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem.Soc.* **1972**, *94*, 6190. (b) Tacke, R.; Lange, H. *Chem. Ber.* **1983**, *116*, 3685.

Silyl esters **2** and **54**−**60** underwent a [1,4] O → C silyl migration in the presence of LDA to provide 2-silyl-3-hetereocyclic carboxylic acids **4** and **61**−**67**, respectively (Table 2). Thus, the addition of silyl esters **2** (or **54**−**60**) to a mixture of LDA and HMPA (1.2 equiv each) in THF at −78 °C resulted in a migration of the silyl group into the C-2 position of the furan or thiophene ring after approximately 15 min. An acidic workup followed by purification through a silica gel column provided 2-silyl-3-furoic acids (**4**, **62**, **64**, **66**, and **67**) and 3-thiophenecarboxylic acids (**61**, **63**, and **65**) in moderate to good yields (Table 2). 3-Furoic acid and 3-thiophenecarboxylic acid were also isolated from the reaction mixture. The formation of the acids was not unexpected, since it has been reported that nitrogen nucleophiles can attack the silicon atom of silyl esters.[33] Changing the type of base (LHMDS), solvent (ether, DME), additive (TMEDA), and temperature (−78 °C → rt) employed in the reaction did not noticeably improve the yields.

The silyl migration was shown to be an intramolecular process by treating an equimolar mixture of compounds **54** and **55** with an LDA/HMPA mixture in THF; acids **61** and **62** were the only compounds detected (by ^{1}H NMR) and isolated. This result is in accord with the crossover study performed on the silyl ethers (Scheme 3, *vide supra*) and others reported in the literature.[21,22,25]

The above results indicate that 3-substituted silyl esters of furans and thiophenes undergo a [1,4] O → C silyl migration when treated with a mixture of LDA/HMPA in THF at −78 °C to provide 2,3-disubstituted heterocycles in moderate to good yield.

[1,4] C → O Silyl Migrations of 2-Silylated-3-substituted Furans and Thiophenes

With a variety of 2-silylated-3-(hydroxymethyl)furans and -thiophenes in hand, we investigated whether a [1,4] C → O silyl migration would be possible with these systems. The idea of using a [1,4] O → C migration, followed by a lithiation at C-4, and then reprotection of the hydroxymethyl group using the same silyl group that underwent the initial [1,4] O → C migration seemed very attractive as a synthetic method (see Scheme 1). Although some [1,4] C → O silyl migrations had been reported by 1989, none had involved the use of furan and thiophene ring systems.[34] Since 1989, two other examples of [1,4] C → O silyl migrations have been reported.[22h,35]

Treatment of compound **3** with excess NaH (5 equiv) in DMF (1 h, rt) provided an excellent yield of furan **1**, in which the silyl group had apparently migrated from the carbon atom to the oxygen atom (entry 1, Table 3). The ^{1}H and ^{13}C NMR spectra of the product matched the spectra obtained from the silylation of 3-(hydroxymethyl)furan (**10**). The migration was not limited to furan rings or the *tert*-butyldimethylsilyl group; both thiophenes and other silyl groups underwent the migration (entries 1−15, Table 3). Groups present in the C-4 position of the furan ring[36] did not impede the migration and 3,4-disubstituted furans were obtained in excellent yields (entries 16−20, Table 3). A few of the reactions were tried in THF as a solvent and found to take approximately 16 h for completion. Generally the yields are very high for furans and thiophenes in both DMF and THF. The migration was also not limited to primary alcohols since the secondary alcohols **72** and **73** provided migrated products **77** and **78** in 95% and 88% yields, respectively.

Some of the silyl ethers were found to be labile under the conditions of NaH/DMF (entries 12, 14, and 15, Table 3). In these cases, 1 h in DMF provided only 3-(hydroxymethyl)furan (**10**). It was determined that a reductive cleavage of the expected silyl ether had occurred. Thus, compounds **22**, **24**, and **26** were prepared by silylation of **10** and found to be completely desilylated after 1 h in a NaH (5 equiv)/DMF mixture. In an attempt to isolate the corresponding silyl ethers from the migrations, the reactions with compounds **35** and **37** were stopped after 5 min. Silyl ethers **22** and **24** were isolated in good yields, respectively. Therefore the desilylation occurred after the migration was complete. These results indicate that NaH/DMF may be a suitable method for the desilylation of diphenylmethylsilyl- and dimethylisopropylsilyl groups.[37]

Since the above migrations were completed within 5 min when performed in DMF, we reinvestigated the reaction with compounds **3** and **28** and found that migrated products **1** and **15** were obtained in 93% and 85% yields, respectively, after only 5 min. In fact, TLC indicated that the reaction of compound **3** was complete within a few seconds.[38] Since the time of the reaction varied greatly between THF and DMF, we performed the migration with furan **3** in diethyl ether and DME (Table 4). The reaction was complete after 30 min in DME[39] (entry 2, Table 4) and did not proceed in diethyl ether after stirring at rt for 7 days (entry 4, Table 4).[40] The addition of excess DMF to the ether solution (after 7 days), however, resulted in a rapid silyl migration to form furan **1** in 92% yield (entry 4, Table 4). Reducing the amount of NaH to catalytic quantities in DMF slowed down the reaction, but it was still complete after 15 min (entry 5, Table 4).

Various counterions were employed in the migration of furan **3** (Table 4). Potassium ions[41] gave similar results as sodium ions (compare entries 3 and 6), and when NaOH was used instead of NaH, the migration occurred in DMF after 1 h, producing a mixture of silyl ether **1** and desilylated material **10** (entry 7, Table 4). The use of magnesium or lithium cations in THF resulted in no migration; however, if excess DMF was added after

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(33) (a) Hudrlik, P. F.; Feasley, R. *Tetrahedron Lett.* **1972**, 1781. (b) Gornowicz, G. A.; West, R. *J. Am. Chem. Soc.* **1968**, *90*, 4478. (c) Sommer, L. H.; Parker, G. A.; Frye, C. L. *J. Am. Chem. Soc.* **1964**, *86*, 3280. (d) Anderson, H. H.; Fischer, H. *J. Org. Chem.* **1954**, *19*, 1296.

(34) (a) Woodbury, R. P.; Rathke, M. W. *J. Org. Chem.* **1979**, *43*, 1947. (b) Isobe, M.; Kitamura, M.; Goto, T. *Tetrahedron Lett.* **1979**, *20*, 3465. (c) Matsuda, I.; Murata, S.; Izumi, Y. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2389. (d) Matsuda, I.; Murata, S.; Ishii, Y. *J. Chem. Soc., Perkin Trans. 1* **1979**, 26. (e) Isobe, M.; Kitamura, M.; Goto, T. *Tetrahedron Lett.* **1980**, *21*, 4727. (f) Fleming, I.; Floyd, C. D. *J. Chem. Soc., Perkin Trans. 1* **1981**, 969. (g) Takeda, T.; Naito, S.; Ando, K.; Fujiwara, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 967. (h) Brook, A. G.; Chrusciel, J. J. *Organometallics* **1984**, *3*, 1317. (i) Isobe, M.; Ichikawa, Y.; Funabashi, Y.; Mio, S.; Goto, T. *Tetrahedron* **1986**, *42*, 2863.

(35) Tietze, L. F.; Feissler, H.; Gewert, J. A.; Jakobi, U. *Synlett* **1994**, 2863.

(36) The preparation of compounds **69**−**73** is discussed in the following paper in this issue; see ref 55.

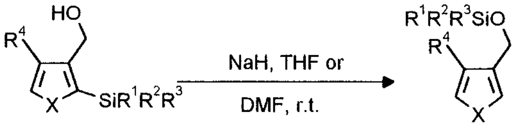
(37) For an example of a reductive desilylation using NaH/HMPA, see: Shekani, M.S.; Kahn, K. M.; Mahmood, K. *Tetrahedron Lett.* **1988**, *29*, 6161.

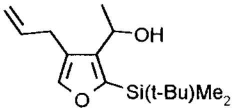
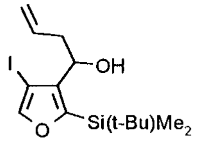
(38) Although the silyl migration is finished within a few seconds, we did not go back and repeat all the examples in Table 3. All migrations performed since our initial report with excess NaH in DMF have been finished with a few seconds, so we have no reason to doubt that all the examples in Table 3 would be complete within a few seconds.

(39) The reaction time of 56 h in DME for this reaction in our initial communication was an error and all reactions done to date in DME have been complete within 0.5 h.

(40) Other [1,4] C → O migrations using sodium ions in diethyl ether have been reported not to proceed. See 34f.

Table 3. Results of the [1,4] C → O Silyl Migration of Silyl Ethers



Entry	Starting Material		Product, Time (% Isolated Yield)	
			DMF	THF
1	**3**	X=O; R^1=R^2=Me; R^3=*t*-Bu; R^4=H	**1**, 1h (88)	**1**, 16h (86)
2			**1**, 5 min (93)	
3	**28**	X=S; R^1=R^2=Me; R^3=*t*-Bu; R^4=H	**15**, 1h (76)	**15**, 16h (89)
4			**15**, 5 min (85)	
5	**29**	X=O; R^1=R^2=R^3=i-Pr; R^4=H	**16**, 1h (89)	**16**, 16h (86)
6	**30**	X=S; R^1=R^2=R^3=i-Pr; R^4=H	**17**, 1h (86)	**17**, 16h (90)
7	**31**	X=O; R^1=R^2=Ph; R^3=*t*-Bu; R^4=H	**18**, 1h (89)	**18**, 16h (91)
8	**32**	X=S; R^1=R^2=Ph; R^3=*t*-Bu; R^4=H	**19**, 1h (88)	**19** 16h (93)
9	**33**	X=O; R^1=R^2=R^3=*n*-Bu; R^4=H	**20**, 1h (75)	**20**, 16h (81)
10	**34**	X=O; R^1=R^2=R^3=Et; R^4=H	**21**, 1h (81)	--
11	**35**	X=S; R^1=R^2=Ph; R^3=Me; R^4=H	**22**, 5 min (91)	**10**, 16h (95)
12			**10**, 1h (92)	
13	**37**	X=O; R^1=R^2=Me; R^3=i-Pr; R^4=H	**24**, 5 min (88)	**10**, 16h (92)
14			**10**, 1h (89)	
15	**68**	X=O; R^1=R^2= R^3=Me; R^4=H	**10**, 1h (96)	**10**, 16h (91)
16	**69**	X=O; R^1=R^2=Me; R^3=*t*-Bu; R^4=CHO	**74**, 5 min (88)	--
17	**70**	X=O; R^1=R^2=Me; R^3=*t*-Bu; R^4=CH_2CHCH_2	--	**75**, 16h (83)
18	**71**	X=O; R^1=R^2=Me; R^3=*t*-Bu; R^4=Sn(*n*-Bu)$_3$	**76**, 5 min (98)	--
19	**72**		**77**, 5 min (95)	--
20	**73**		**78**, 5 min (88)	--

1 d at rt, migrated product **1** was isolated in excellent yields (entries 8–10, Table 4). The results with (a) various counterions (b) the rate enhancement observed with sodium ions on changing the solvent from ether to THF to DME to DMF, and (c) the addition of DMF to either the ether solution containing sodium ions or the THF solution containing Mg or Li ions can be rationalized on the degree of ion pair dissociation. A similar argument has been proposed to explain the effect of counterions on the rate of oxy-Cope reactions[42] and other reactions.[43–45] The enhanced ion pair dissociation has been related to the polarity of the solvent;[46] the more polar the solvent, the more ion pair dissociation occurs and thus the reaction rate increases.[47]

An alternative explanation for the rate increase observed in more polar solvents is that the solvent is activating the silicon atom to attack by the oxygen atom by forming a pentavalent intermediate with the solvent. Rate enhancements in the nucleophilic displacement reactions at silicon have been reported in the presence

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(41) KH was not used in DMF since it is known to reduce DMF, see: Brown, C. A. *J. Org. Chem.* **1974**, *39*, 3913.

(42) (a) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 5765. (b) Magnera, T. F.; Caldwell, G.; Sunner, J.; Ikuta, S.; Kebarle, P. *J. Am. Chem. Soc.* **1984**, *106*, 6140.

(43) Reichardt, C. *Solvent Effects in Organic Chemistry*; Verlag Chemie: New York, 1988; pp 232–239.

(44) (a) Kolodziejski, W. *J. Mol. Struct.* **1987**, *159*, 335. (b) Stevenson, G. R.; Hajhim, R. T. *J. Phys. Chem.* **1986**, *90*, 3217. (c) Szwarc, M. *Ions and Ion Pairs in Organic Reactions*; Wiley and Sons: New York, 1974; Vol. 2, p 386.

(45) For theoretical calculations on Li^+, Na^+, and K^+ interactions with solvents, see: Portmann, P.; Marvizumi, T.; Welti, M.; Badertscher, M.; Neszmelyi, A.; Simon, W.; Pretsch, E. *J. Chem. Phys.* **1987**, *87*, 493. For theoretical calculations on BF_3 affinities for some solvents, see: Rauk, A.; Hunt, I. R.; Keay, B. A. *J. Org. Chem.* **1994**, *59*, 6808. For theoretical calculations on proton affinities with solvents, see: Yamabe, S.; Hiraa, K.; Wasada, H. *J. Chem. Phys.* **1992**, *96*, 10261.

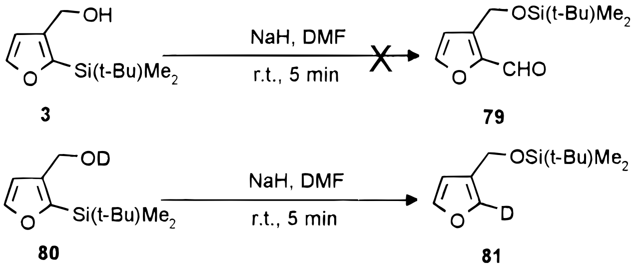
(46) (a) See ref 43, pp 17–25. (b) Maria, P.-C.; Gal, J.-F. *J. Phys. Chem.* **1985**, *89*, 1296 and references therein.

Table 4. Effect of Various Solvents and Bases on the [1,4] C → O Silyl Migration of Furan 3

entry	base	solvent	time	product (% yield)
1	5 equiv of NaH	DMF	seconds	**1** (88)
2	5 equiv of NaH	DME	0.5 h	**1** (96)
3	5 equiv of NaH	THF	16 h	**1** (80)
4	5 equiv of NaH	Et_2O	7 d [DMF][a]	S.M. [**1** (88)][b]
5	1 mol % of NaH	DMF	15 min	**1** (92)
6	5 equiv of KH	THF	2 d	**1** (61)
7	5 equiv of NaOH	DMF	1 h	**1** (64) + **10** (23)
8	1 equiv of vinyl-MgBr	THF	1 d [DMF][a]	S.M. [**1** (85)][b]
9	1 equiv of MeLi	THF	1 d [DMF][a]	S.M. [**1** (89)][b]
10	1 equiv of *n*-BuLi	THF	1 d [DMF][a]	S.M. [**1** (88)][b]

[a] After stirring at rt for the time shown excess DMF was added. [b] Product and yield after excess DMF was added to the solution. S.M. = starting material.

Scheme 6



of DMF, DMSO, or HMPA.[48] An activation of the silicon atom by the formation of a pentavalent intermediate with the solvent has been proposed. A similar effect may be occurring with the more polar solvents DMF and DME versus THF and diethyl ether.

We were initially surprised to find that furan **79** was not formed when the [1,4] C → O silyl migration was performed in anhydrous DMF (Scheme 6), since it is well-known that aryl carbanions can be quenched with dry DMF to provide aldehydes.[1] We also tried to trap any incipient C-2 carbanion with iodomethane. Thus, a solution of furan **3** in THF containing 2 equiv of MeI was treated with *excess* NaH and stirred at rt. After 8 h furan **1** was isolated in 87% yield; ^{1}H NMR indicated that neither 2-methyl-3-(((*tert*-butyldimethylsilyl)oxy)methyl)furan nor 2-(*tert*-butyldimethylsilyl)-3-(methoxymethyl)furan had formed.

To understand further what was happening during the migration, the mechanism of this reaction was investigated. A crossover study with an equimolar mixture of furan **3** and thiophene **30** (NaH, DMF) only provided furan **1** and thiophene **17**, indicating the migration is an intramolecular process. Since aldehyde **79** was not formed during the migrations performed in DMF, the question arose as to the source of the proton which is being transferred to the C-2 position of the furan ring. To prove that the proton source was indeed the hydroxyl hydrogen atom of unrearranged starting material, the following experiment was conducted. Furan **80** was prepared by treating alcohol **3** with excess D_2O in DME. The solution of D_2O, furan **80**, and DME was passed through a plug of Na_2SO_4 directly into a solution of *excess* NaH in DMF. Workup after 5 min gave the C-2 deuterated silyl ether **81** exclusively (Scheme 6). Since deuterium was incorporated at C-2 of the furan ring, the rate of the silyl migration must be faster than the rate of proton abstraction from the hydroxyl group by NaH. Similar results have been reported with other C → O silyl migrations.[20f,22h] This deuteration study suggests why aldehyde **79** was not formed when the migration was done in DMF. The reaction of any incipient species at C-2 of the furan ring is expected to be protonated by the unreacted alcohol faster than undergoing a reaction with either MeI or DMF.

A cyclic intermediate having a pentavalent silicon atom may also be involved in the reaction, and its formation may be enhanced by the presence of good electron pair donor solvents. Intermediates involving pentavalent silicon atoms have been postulated in other intramolecular [1,*n*] silyl migrations[20f,34f,49] and have been shown to be viable intermediates through *ab initio* level calculations.[50] Such an intermediate could also account for the nonreactivity with electrophiles (DMF and MeI) other than protons in this reaction.[51]

Conclusions

We have shown that [1,4] O → C and [1,4] C → O silyl migrations are facile reactions with 3-substituted furans and thiophenes and proceed in good to excellent yields with silanes containing bulky substituents. Both silyl ethers and silyl esters undergo these rearrangements.

The next paper describes the C-4 and C-5 regiospecific lithiations of various 2-silylated-3-substituted furans and illustrates how 3,4-disubstiuted-, 2,4-disubstituted, and 2,3,4-trisubstituted furan rings can be prepared.

Experimental Section

^{1}H and ^{13}C NMR spectra were run at 300 or 200 MHz and 75 or 50 MHz, respectively, and in $CDCl_3$ as a solvent unless otherwise noted. Elemental analyses were performed by either Guelph Chemical Laboratories, Guelph, Ontario, Canada, or by Ms. Dorothy Fox at the University of Calgary. *tert*-Butyldimethylsilyl chloride was supplied from the Lithium Corporation of America (now FMC), Gastonia, NC. All solvents were dried and distilled prior to use. The oil from the NaH was removed by three successive washes with anhydrous diethyl ether. The remaining ether was removed under a high vacuum (4 h, rt). Flash column chromatography was performed using E. Merck silica gel (230−400 mesh A.S.T.M.) by the method developed by Still *et al.*[52]

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(47) Although refs 43−46 indicate that solvent polarity can be related to sodium ion solvation, Abraham and Liszi have reported the ionic solvation free energies for Na and K ions in DMF, THF, and DME. Although the free energy change for Na and K ions was more negative for DMF (−97.3 kcal/mol for Na ions and −79.5 kcal/mol for K ions), when compared to the values for THF and DME (see below), the free energy change for sodium ions in THF (−94.3 kcal/mol) was more negative than that with DME (−92.5 kcal/mol), while with K ions, the values were about the same (−73.3 kcal/mol in THF vs −73.1 kcal/mol in DME). These results indicate that the observed rate enhancements may be due to a combination of factors, see: Abraham, M. H.; Liszi, J. *J. Chem. Soc., Faraday Trans. 1* **1978**, 1604.

(48) Bassindale, A. R.; Taylor, P. G. Reaction Mechanisms of Nucleophilic Attack at Silicon. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley and Sons: New York, 1989; Part 1, Chapter 13, pp 839−892.

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(51) ^{29}Si NMR indicated that a pentavalent silicon atom does not form in d_{10}-diethyl ether when furan **3** was treated with excess NaH (*i.e.* an upfield shift of the ^{29}Si signal was not observed). This does not preclude, however, that a pentavalent intermediate was involved in the migration when excess DMF was added (entry 4, Table 4). The reaction in the presence of DMF was too fast to observe any intermediates by NMR.

3-(Hydroxymethyl)furan (10). To a stirred mixture of lithium aluminum hydride (7 g, 184 mmol) and dry diethyl ether (100 mL) at 0 °C was added 3-furoic acid (20 g, 178 mmol) over a 30 min period. After being stirred for 6 h at rt, the solution was cooled to 0 °C and treated dropwise with water (7 mL), 15% aqueous NaOH (7 mL), and water (21 mL). The solution was filtered through Celite and the solvent evaporated *in vacuo* to leave an oil which was purified by distillation to afford **10** (13.5 g, 77%) as an oil: bp 98−100 °C/20 Torr (lit.[53] bp 79−80 °C/17 Torr); IR (neat) 3390 cm^{-1}; ^1H NMR δ 2.80 (bs, 1H, exchanges with D_2O), 4.45 (s, 2H), 6.37 (d, 1H, J = 1.1 Hz), 7.34 (m, 2H); ^{13}C NMR δ 56.2, 109.7, 125.0, 139.8, 143.3; MS *m/e* 98 (M^+).

3-(Hydroxymethyl)thiophene (42). To a stirred mixture of lithium aluminum hydride (4.5 g, 117 mmol) and dry diethyl ether (60 mL) at 0 °C was added 3-thiophenecarboxaldehyde (12 g, 107 mmol) over a 30 min period. After being stirred 6 h at rt, the solution was cooled to 0 °C and treated dropwise with water (4.5 mL), 15% aqueous NaOH (4.5 mL), and water (13.5 mL). The solution was filtered through Celite and the solvent evaporated *in vacuo* to leave an oil which was purified by distillation to afford **42** (10.1 g, 83%) as an oil: bp 95−98 °C/20 Torr (lit.[54] bp 86−88 °C/10 Torr); IR (neat) 3347 cm^{-1}; ^1H NMR δ 4.51 (s, 2H), 4.70 (s, 1H, exchanges with D_2O), 7.1−7.3 (m, 3H); MS *m/e* 114 (M^+).

General Procedure 1: Silylation of an Alcohol. To a solution of imidazole (84 mmol) in DMF (20 mL) at 0 °C was added appropriate silyl chloride (40 mmol). After 10 min the alcohol (40 mmol) was added and the mixture stirred 12 h at rt. Saturated sodium chloride (20 mL) and diethyl ether (20 mL) were added, and the ether layer was separated, dried (Na_2SO_4), and removed *in vacuo* to leave an oil. The oil was purified by distillation.

3-(((*tert*-Butyldimethylsilyl)oxy)methyl)furan (1). Using general procedure 1, compound **1** was prepared in 95% yield: bp 106−109 °C/20 Torr; IR (neat) 1063 cm^{-1}; ^1H NMR δ −0.04 (s, 6H), 0.81 (s, 9H), 4.54 (s, 2H), 6.42 (d, 1H, J = 1.1 Hz), 7.51−7.55 (m, 2H); ^{13}C NMR δ −2.9, 18.2, 25.8, 57.5, 109.7, 125.9, 139.4, 143.1; MS *m/e* 212 (M^+). Anal. Calcd for $C_{11}H_{20}O_2Si$: C, 62.21; H, 9.49. Found: C, 62.34; H, 9.43.

General Procedure 2: [1,4] O → C Silyl Migration. A solution of freshly distilled silylated alcohol (3.3 mmol) and HMPA (3.6 mmol, dried over CaH_2, distilled and stored over molecular sieves) in dry THF (10 mL) was cooled to −78 °C under argon and treated with *n*-BuLi (1.43 mL of 2.5 M in hexanes, 3.6 mmol). The solution was allowed to come to rt over 6 h and stirred at rt overnight. Saturated ammonium chloride was added and the solution extracted with diethyl ether. The organic layer was washed three times with saturated copper sulfate and dried (Na_2SO_4), and the solvent was removed *in vacuo* to afford after distillation a 2-silylated-3-hydroxymethyl heterocycle.

2-(*tert*-Butyldimethylsilyl)-3-(hydroxymethyl)furan (3). Using general procedure 2, compound **3** was prepared in 87% yield: bp 75−78 °C/0.02 Torr; IR (KBr) 3319, 1070 cm^{-1}; ^1H NMR δ 0.01 (s, 6H), 0.89 (s, 9H), 1.5 (bs, 1H, exchanges with D_2O), 4.57 (s, 2H), 6.46 (d, 1H, J = 1.8 Hz), 7.57 (d, 1H, J = 1.8 Hz); ^{13}C NMR δ −5.7, 18.1, 25.7, 57.1, 110.5, 135.9, 146.7, 155.0; MS *m/e* 212 (M^+). Anal. Calcd for $C_{11}H_{20}O_2Si$: C, 62.21; H, 9.49. Found: C, 62.27; H, 9.47.

General Procedure 3: Preparation of Silyl Esters 2 and 54−60. A mixture of either 3-furoic acid or 3-thiophenecarboxylic acid (1.0 equiv), silyl chloride (1.2 equiv), and imidazole (2.5 equiv) in DMF (2 mL/g of acid) were heated at 60 °C for 48 h. The reaction mixture was cooled to rt, ether (2 mL/g of acid) was added, and the organic phase was washed with a saturated brine solution (3 × 4 mL). The organic phase was dried (Na_2SO_4), filtere,d and removed *in vacuo* to provide the silyl esters which were purified by distillation.

***tert*-Butyldimethylsilyl 3-Furoate (2).** Compound **2** was prepared in 84% yield according to general procedure 3 using 3-furoic acid (1.2 g, 10.7 mmol): bp 40−45 °C/0.08 Torr; IR (NaCl) 1713, 1163 cm^{-1}; ^1H NMR δ 0.35 (s, 6H), 0.97 (s, 9H), 6.72 (d, 1H, *J* = 1.8 Hz), 7.41 (t, 1H, J = 1.8 Hz), 7.97 (d, 1H, *J* = 1.8 Hz); ^{13}C NMR δ −4.9, 17.6, 25.5, 110.0, 121.0, 143.6, 148.0, 162.9; MS *m/e* 226 (M^+), 169 (M^+ − *t*-Bu); HRMS calcd for $C_7H_9O_3Si$ 169.0321, found 169.0325.

General Procedure 4: [1,4] O → C Silyl Migration of Silyl Esters 2 and 54−60. To a mixture of LDA (1.2 equiv) and HMPA (1.2 equiv) in THF (1 mL/mmol) at −78 °C was added the silyl ester (1.0 equiv) in THF (1 mL/mmol). After 15 min at −78 °C, chloroform was added and the mixture transferred to a separatory funnel. HCl (5 mL of 10%) was added, the separatory funnel was shaken vigorously, and the aqueous layer was removed as fast as possible to prevent decomposition of the furan ring. The chloroform layer was dried (Na_2SO_4), filtered, and removed to leave an oil. Chromatography on silica gel provided 2-silylated 3-carboxylic acid of furan or thiophene.

2-(*tert*-Butyldimethylsilyl)-3-furoic Acid (4). Compound **4** was prepared in 72% yield according to general procedure 4 starting with compound **2** (0.31 g, 0.91 mmol). 3-Furoic acid was also recovered from the mixture (12%). Column chromatography: petroleum ether:EtOAc (20:1); mp 83−88 °C; IR (KBr) 3250−2250 (br), 1685, 1293 cm^{-1}; ^1H NMR δ 0.37 (s, 9H), 0.97 (s, 9H), 6.80 (d, 1H, *J* = 1.8 Hz), 7.63 (d, 1H, *J* = 1.8 Hz); ^{13}C NMR δ −5.9, 18.0, 26.7, 111.0, 128.0, 146.5, 168.0, 170.3; MS *m/e* 169 (M^+ − *t*-Bu). Anal. Calcd for $C_{11}H_{18}O_3Si$: C, 58.37; H, 8.02. Found: C, 58.61; H, 8.15.

General Procedure 5: [1,4] C → O Silyl Migration of Compounds 3, 28−35, 37, and 68−73. To a solution of an alcohol (0.27 mmol) in DMF or THF (5.4 mL) at rt was added NaH (1.36 mmol), and the mixture was stirred for the time shown in Table 3. Ether (6 mL) was added followed by the slow addition of a saturated brine solution (*CAUTION*: violent evolution of H_2). The ether layer was separated, washed with saturated brine (6×'s, only when DMF was used), and dried (Na_2SO_4). The ether was removed *in vacuo* to leave an oil which was distilled.

Compounds **3**, **28**−**34**, and **68** provided compounds **1**, **15**−**21**, and **10**, respectively. Compounds **35** and **37** provided compounds **22** (or **10**) and **24** (or **10**), respectively. The spectral data from **1**, **10**, and **15**−**22** matched those reported above. The migration of compound **71** has been reported previously.[7b]

4-(((*tert*-Butyldimethylsilyl)oxy)methyl)-3-furaldehyde (74). General migration procedure 5 was performed on furan **69**[55] (0.1 g, 0.42 mmol) for 5 min to produce, after distillation, furan **74** as a clear colorless liquid in 88% yield: bp 60−63 °C/0.05 mmHg (air bath); IR (KBr) 1680 cm^{-1}; ^1H NMR δ 0.08 (s, 6H), 0.90 (s, 9H), 4.83 (s, 2H), 7.41 (d, 1H, *J* = 1.4 Hz), 7.99 (d, 1H, *J* = 1.4 Hz), 9.91 (s, 1H); ^{13}C NMR δ −5.5, 18.3, 25.8, 57.8, 125.6, 126.4, 142.0, 152.7, 185.1; MS *m/e* 182 (M^+ − *t*-Bu). Anal. Calcd for $C_{12}H_{20}O_3Si$: C, 59.96; H, 8.39. Found: C, 60.12; H, 8.36.

4-(((*tert*-Butyldimethylsilyl)oxy)methyl)-2-deuteriofuran (81). To a solution of furan **80** (0.13 g, 0.59 mmol) in DME (0.2 mL) was added D_2O (53 uL). After 15 min the solution was passed through a plug of sodium sulfate directly into DMF (5 mL) containing excess NaH. After 5 min the mixture was worked up according to general procedure 5 to produce, after distillation, furan **81** as a clear colorless liquid in 82% yield: bp 61−63 °C/0.03 mmHg (air bath); IR (neat) 1082 cm^{-1}; ^1H NMR δ 0.07 (s, 6H), 0.90 (s, 9H), 4.58 (s, 2H), 6.35 (d, 1H, *J* = 1.4 Hz), 7.35 (d, 1H, *J* = 1.4 Hz); ^{13}C NMR δ −5.3, 18.0, 25.9, 57.4, 109.6, 125.7, 139.3 (three lines equal intensity), 143.0; MS *m/e* 156 (M^+ − *t*-Bu).

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Supporting Information Available: Complete spectral data for **15**−**25**, **28**−**40**, **54**−**60**, **61**−**67**, **75**, **77**, and **78** (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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