Pergamon

Tetrahedron, Vol. 53, No. 10, pp. 3497-3512, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00083-5

Regiospecific Synthesis of Polysubstituted Furans From Silylated Furans : Expedient Syntheses of Rosefuran†

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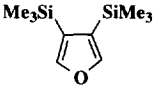
Abstract: By utilizing a sequence of regiospecific lithiation-alkylation, *ipso*-iodination, boroxine formation, Sonogashira cross-coupling, nickel-catalyzed cross-coupling and Suzuki cross-coupling reactions, several methods have been developed for the syntheses of 2,3-disubstituted furans, 2,4-disubstituted furans, 2,3,4-trisubstituted furans and 2,3,5-trisubstituted furans. Our approach uses as the key theme trimethylsilyl groups as both blocking groups as well as *ipso*-directing groups. The advantage of this program is aptly illustrated by two expedient syntheses of rosefuran (**9c**).

INTRODUCTION

Furan rings are found in many naturally occurring molecules, either in fully unsaturated forms or in reduced or partly reduced frameworks.[1] Polysubstituted furans, moreover, also play a major role as key precursors in organic synthesis.[2] Synthetically, it has long been recognized that regioselective introduction of carbon substituents into a furan ring is by no means trivial. For this reason, practical methods for procuring polysubstituted furans usually involve acyclic precursors.[3] There are several recent reports in the literature on the synthesis of 2,3-disubstituted furans,[4] 2,4-disubstituted furans,[5] 3,4-disubstituted furans,[6] 2,3,4-trisubstituted furans,[3,7] 2,3,5-trisubstituted furans[8] as well as 2,3,4,5-tetrasubstituted furans,[9] which generally requires multi-step procedures and/or inaccessible starting materials.



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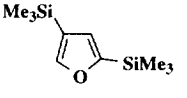

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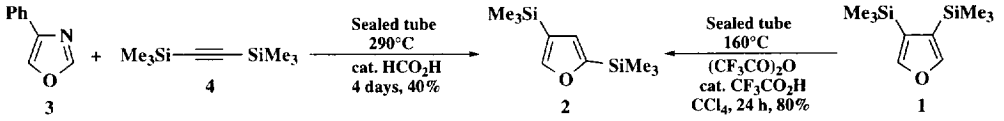
In our previous work, we have demonstrated the use of Diels-Alder and retro Diels-Alder reactions to form 3,4-bis(trimethylsilyl)furan (**1**),[6c] which now serves as a building block for the regiospecific synthesis of 3,4-disubstituted furans.[6bc] During the preparation of **1**, certain amount of 2,4-bis(trimethylsilyl)furan (**2**) was always identified as a chromatographically inseparable mixture with **1**. It is noteworthy that **2** has been prepared previously in a small quantity by a photo-rearrangement of 2,5-bis(trimethylsilyl)furan.[10]

Employing trimethylsilyl groups as blocking groups and/or as *ipso*-directing groups,[11] it was anticipated that 2,4-bis(trimethylsilyl)furan (**2**) should also serve as a building block for the preparation of polysubstituted furans. We report herein a modified preparation of **2** so that it can be obtainable in a larger quantity and in a better yield. With a sufficient amount of **2** in hand, we have achieved in a straightforward mode the regiospecific synthesis of 2,3-disubstituted furans and 2,3,5-trisubstituted furans. 2,4-Disubstituted furans and 2,3,4-trisubstituted furans have also been realized utilizing a similar routine.

RESULTS AND DISCUSSION

(a) Preparation of 2,4-bis(trimethylsilyl)furan (2).

In order to put to test our goal of utilizing **2** as a building block of polysubstituted furans, it was of paramount importance that **2** should be obtained in relatively large amounts and in a reliable way. We reasoned that the rearrangement of **1**[6c] to **2** was of an acid-catalyzed nature. As such, it is similar to the rearrangement mechanism of 1,2-bis(trimethylsilyl)benzene to 1,3-bis(trimethylsilyl)benzene.[12] In support of this argument, we eventually discovered that the sealed tube thermal reaction at 290°C between 4-phenyloxazole (**3**)[13] and bis(trimethylsilyl)acetylene (**4**) in the presence of a catalytic amount of formic acid gave pure **2** in 40% yield (Scheme 1).



Scheme 1

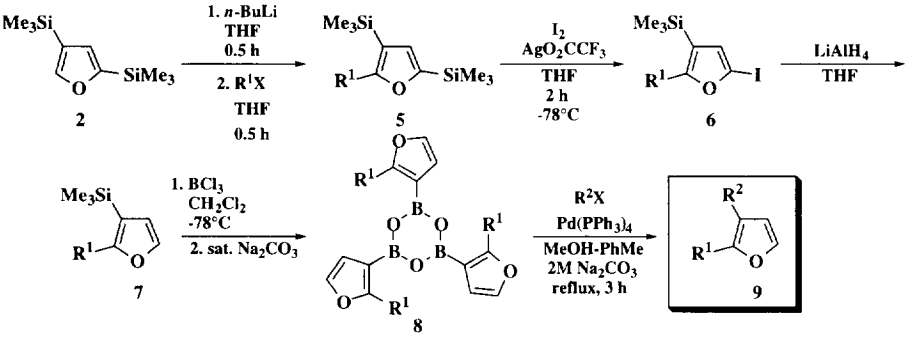
After many unfruitful trials, furan **1**[6c] was also converted eventually to **2** in a good yield on heating at 160°C in a sealed tube with trifluoroacetic anhydride (containing a minute amount of trifluoroacetic acid due to moisture) in CCl_4 as solvent (Scheme 1). It is believed that the driving force for the rearrangement of a trimethylsilyl group from C-3 to C-2 of **1** is due to the sterically unfavorable orientation of the two trimethylsilyl groups at C-3 and C-4. The mechanism[12] may proceed through a series of silicon-directed *ipso*-protonation, migration of the trimethylsilyl group involving pentavalent silicon cation intermediate[14] and deprotonation.

The ^1H NMR spectrum of **2** shows two one-proton singlets at δ 6.60 and 7.54, and is in agreement with the general proton absorption trend established for furan α- and β-protons.[15] There are also two nine-proton singlets for the two trimethylsilyl groups at δ 0.20 and 0.25.

(b) Synthesis of 2,3-trisubstituted furans: Rosefuran (9c) syntheses.

It is well-known that lithiation takes place readily at C-2 and C-5 positions of furan due to the electron-withdrawing character of the oxygen atom.[16] Such avenue was first explored by treating **2** consecutively with *n*-BuLi and organohalides. In this manner, several carbon substituents were introduced to the unsubstituted α-position of **2**. The results are summarized in Scheme 2 and in Table 1. Here in these lithiation-substitution reactions, the C-2 trimethylsilyl group befittingly functioned as a blocking group, rendering isolation of trisubstituted furans **5**. As can be seen in Scheme 2, the α-trimethylsilyl group of **5** preferentially underwent

regiospecific *ipso*-iodination[17] to give iodides **6** which were not purified and were reduced with lithium aluminum hydride to provide 2-substituted-3-trimethylsilylfurans **7**. On reaction with BCl_3, the remaining β-trimethylsilyl group was converted to boroxines **8**, which, via Suzuki reactions, eventually gave 2,3-disubstituted furans **9** (Scheme 2).[6bc,18]



Scheme 2

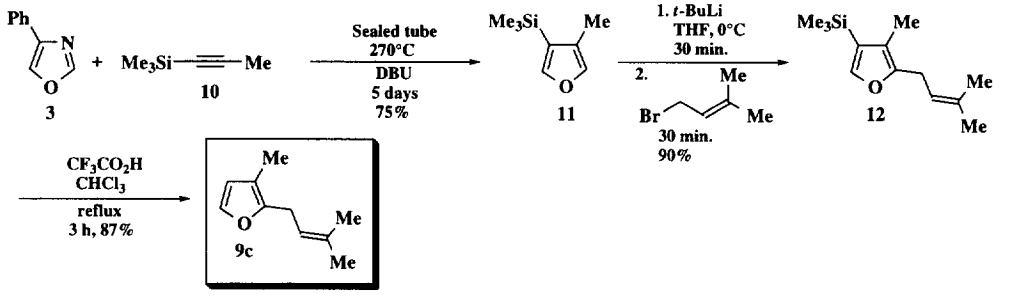
Table 1

Entry	R^1X	R^1	Yield of 5	Yield of 6	Yield of 7 from 5	R^2X	R^2	Yield of 9 from 7
a	$PhCH_2Br$	$PhCH_2$-	82%	74%	61%	3,4-$(OCH_2O)C_6H_3CH_2Br$	3,4-$(OCH_2O)C_6H_3CH_2$-	24%
b	2-naphthyl-CH_2Br	2-naphthyl-CH_2-	61%	-	56%	-	-	-
c	Me_2C=$CHCH_2Br$	Me_2C=$CHCH_2$-	85%	-	42%	Me_2SO_4	Me-	22%
d	*n*-$C_6H_{13}Br$	*n*-C_6H_{13}-	81%	-	38%	$PhCH_2Br$	$PhCH_2$-	42%
e	Me_2SO_4	Me-	83%	-	53%	-	-	-
f	3,5-$Me_2C_6H_3CH_2Br$	3,5-$Me_2C_6H_3CH_2$-	46%	90%	-	-	-	-

After completing the synthesis of two 2,3-disubstituted furans **9a** and **9d**, this procedure was also employed to the synthesis of rosefuran (**9c**), the essence of one of the most prized fragrance, namely oil of rose. Since its first reported synthesis in 1968,[19] there have been over ten recorded syntheses of this molecule.[20] However, most of the syntheses of **9c** either generated a mixture of **9c** and its isomer or gave unsatisfactory overall yields. As can be seen from Entry c in Table 1, our own method afforded rosefuran (**9c**) from **2** also only in an overall yield of 11%. The ^1H NMR spectrum of **9c** shows two singlets locating at δ 1.60 (6H) and 2.19 (3H) which correspond to the C-2 allylic methyl protons and the C-3 methyl protons. The allylic methylene protons and the furan protons at C-4 and C-5 exhibit three doublets at δ 3.27 (2H, J = 6.7 Hz), 6.15 (1H, J = 1.8 Hz) and 7.21 (1H, J = 1.8 Hz), respectively. The multiplet of the allylic vinyl proton appears at between δ 5.22-5.28 (1H). All other physical data of **9c** are identical to those of literature reports.[19,20]

Having prepared **9c** from **2** in a disappointingly low overall yield, we considered as one of the possible modification of the original tactics the deployment of 3-methyl-4-trimethylsilylfuran (**11**) as a precursor. In our earlier work, furan **11** has been obtained from the thermal reaction between 4-phenyloxazole (**3**) and trimethylsilylpropyne (**10**).[21] This preparation was repeated and upgraded to give **11** in a slightly better yield (75%) and in a larger scale. The preparation of **11** and its conversion to rosefuran **9c** are illustrated in Scheme 3. After several experimentation, *t*-BuLi was finally chosen to deprotonate the less hindered C-2 proton, resulting in, after quenching with prenyl bromide, the generation of 2-prenyl-3-methyl-4-trimethylsilylfuran

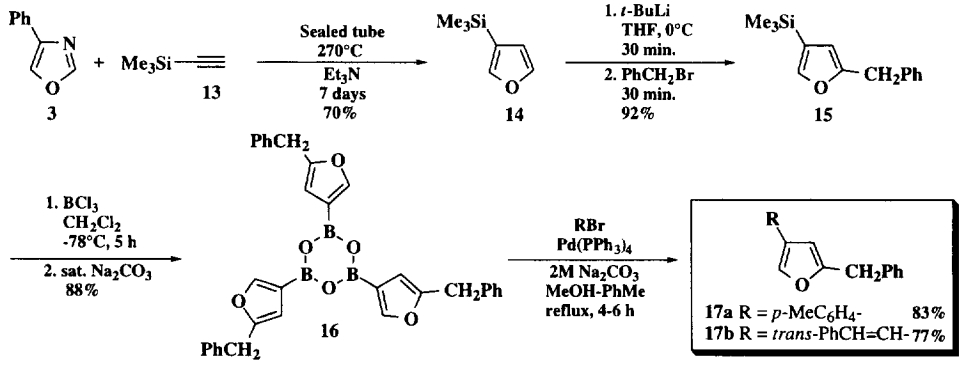
(**12**) as a single isomer. Other bases such as *n*-BuLi furnished only chromatographically inseparable mixtures of regio-isomers. Subsequent protodesilylation with trifluoroacetic acid in $CHCl_3$ at refluxing temperature removed the trimethylsilyl group to afford rosefuran (**9c**) in an overall yield of 61% from **3** and **10** (Scheme 3). The structure of **9c** prepared in this way is supported by both elemental analysis and spectrometric data as compared to literature reports.[19,20]



Scheme 3

(c) Synthesis of 2,4-disubstituted furans.

From our synthetic strategy of rosefuran (**9c**) using **11** as a building block, it was believed that 3-trimethylsilylfuran (**14**) could be significant for the realization of 2,4-disubstituted furans. Again, furan **14** was successfully prepared from 4-phenyloxazole (**3**) and trimethylsilylacetylene (**13**) (Scheme 4). Our aforementioned assumption was evidenced by the formation in a good yield of only one regio-isomer **15** by allowing **14** to react consecutively with *t*-BuLi and benzyl bromide (Scheme 4). Boroxine **16** was obtained from **15** via well-established procedures.[6bc] Suzuki reaction of **16** provided two 2,4-disubstituted furans **17a** and **17b** in satisfactory yields.

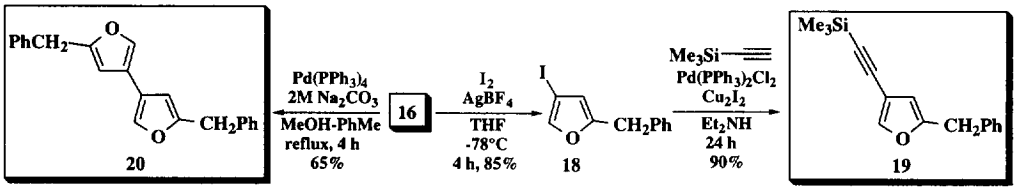


Scheme 4

The ^1H NMR spectrum of **17a** exhibits two doublets at δ 7.13-7.16 (2H, J = 7.7 Hz) and 7.31-7.34 (2H, J = 7.7 Hz) which are the absorptions of the two pairs of symmetrical protons of the C-4 tolyl group. The tolyl-methyl group show a singlet at δ 2.33 (3H), so are the benzylic protons at δ 3.99 (2H). The furan C-3 and C-5 protons give signals at δ 6.29 (1H) and 7.58 (1H), respectively. The other aromatic protons appear as a

multiplet at δ 7.24-7.31. In the ^{1}H NMR of **17b**, the *trans*-vinylic protons show signals at δ 6.63-6.88 (2H, J = 16.1 Hz). The furan C-3 and C-5 protons provide two singlets at δ 6.20 (1H) and 7.36 (1H), respectively. The benzylic protons absorb at δ 3.90 and the aromatic protons of the two phenyl rings afford a multiplet at δ 7.14-7.33 (10H). The formula of **17a** and **17b** are also confirmed by mass spectral analyses and correct elemental analyses.

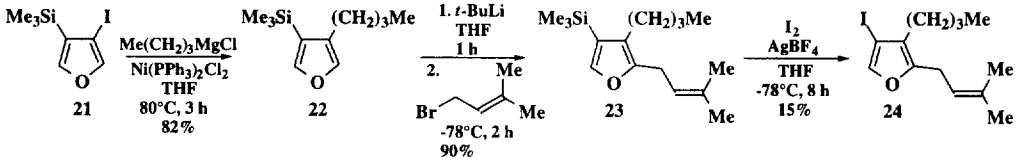
Another way in which boroxine **16** can be converted was the formation of iodide **18** via a regiospecific iodination reaction.[17,22] Thus, treatment of **16** with iodine in the presence of silver tetrafluoroborate afforded iodofuran **18** in a good yield. A standard Sonogashira reaction[23] converted **18** to the alkynylfuran **19** in excellent yield (Scheme 5). In line with our recent finding,[6b] in the absence of an organohalide under the normal Suzuki reaction, self-coupling of boroxine **16** took place to generate the bifuran **20** (Scheme 5).



Scheme 5

(d) Synthetic studies of a 2,3,4-trisubstituted furan

Having introduced regiospecifically substituents to several silylated furans in a stepwise manner, we would like to also attempt the synthesis of 2,3,4-trisubstituted furans. By virtue of the steric hindrance of the bulky trimethylsilyl group, we anticipated that 3-alkyl-4-trimethylsilylfuran should undergo lithiation at C-2 regioselectively. Thus, 3-*n*-butyl-4-trimethylsilylfuran (**22**) was chosen as the building block. Furan **22** could be prepared either by the Diels-Alder and retro Diels-Alder procedure[21] starting from 4-phenyloxazole (**3**) and trimethylsilyl-1-hexyne, or by a nickel-catalyzed cross-coupling reaction[17a,24] between 4-iodo-3-trimethylsilylfuran (**21**)[17a] and *n*-butylmagnesium chloride (Scheme 6). Expectedly, C-2 lithiation and alkylation were accomplished in a regiospecific manner when **22** was treated consecutively with *t*-BuLi and prenyl bromide, affording the 2,3,4-trisubstituted furan **23** in a good yield (Scheme 6). Subsequent *ipso*-iodination of **23** provided furan **24** whose yield was a meager 15%. Because of this low yield step, **24** has not been converted further, though it is believed that this route is potentially serviceable for the realization of 2,3,4-trisubstituted furans.

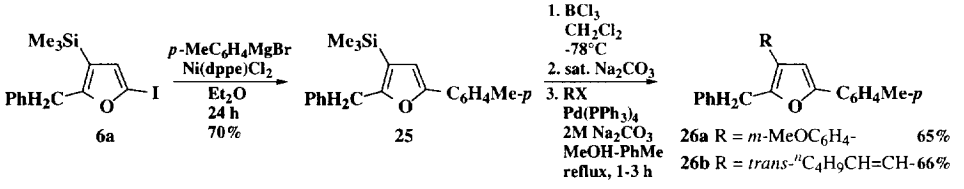


Scheme 6

(e) Synthesis of 2,3,5-trisubstituted furans

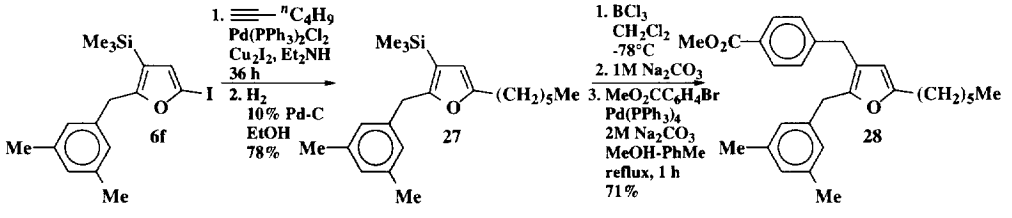
In the present study, it is clear that various polysubstituted furans are obtainable from silylated furans via a combination of regiospecific reactions. It was thus of interest to put to assess the practical viability of

this approach to the synthesis of 2,3,5-trisubstituted furans. Starting from the known iodide **6a**, nickel-catalyzed cross-coupling reaction with a Grignard reagent furnished furan **25**, which on treatment with BCl_3 gave as expected the boroxine which was not purified and was transformed via the standard Suzuki reaction[18] to give either **26a** or **26b** in acceptable yields. The structure of **26a** was substantiated by its ^1H NMR spectrum which shows two doublets at δ 7.16-7.19 and 7.55-7.58 (4H, J = 8.2 Hz) which are due to the two pairs of symmetrical C-5 tolyl protons. The methyl protons of the C-5 tolyl group appear as a singlet at δ 2.35. The methoxy and the benzylic protons show absorptions at δ 3.76 (3H) and 4.20 (2H), respectively. The remaining nine aromatic protons give rise to a multiplet at δ 6.81-7.33. The structure of **26a** is also supported by its mass spectrum which show M^+ at *m/e* 354. In the ^1H NMR spectrum of **26b**, the terminal methyl protons of the C-3 hexenyl group show a triplet at δ 0.89-0.95 (3H, J = 7.0 Hz) and the other aliphatic protons absorb at δ 1.26-1.46 (4H) and 2.14-2.22 (2H) as multiplets. The methyl protons of the C-5 tolyl group and the C-2 benzylic protons display two singlets at δ 2.34 (3H) and 4.05 (2H), respectively. The C-3 vinylic protons resonance at δ 5.89-6.00 (1H) and 6.20-6.27 (1H) as two sets of multiplets. The C-4 furan proton provides a singlet at δ 6.69, whose absorption region is typical of a furan β-proton. There is also an AA'XX' system for the C-5 tolyl group locating at δ 7.13-7.16 (2H, J = 8.2 Hz) and 7.49-7.53 (2H, J = 8.2 Hz). The other aromatic protons afford a multiplet at δ 7.20-7.33 (5H). The composition of **26b** is also confirmed by an elemental analysis.



Scheme 7

Utilizing the Sonogashira reaction,[23] iodide **6f** afforded an acetylene intermediate which was hydrogenated directly to furan **27**. Further conversion of **27** gave the 2,3,5-trisubstituted furan **28** (Scheme 8). The ^1H NMR spectrum of **28** indicates the presence of the hexyl protons in the region δ 0.83-2.54. The protons of the C-2 mesityl group exhibit a singlet at δ 2.24 (6H). The two sets of benzylic protons at C-2 and C-3 show two singlets at δ 3.72 (2H) and 3.84 (2H), respectively. The benzoate methyl affords a singlet at δ 3.89 (3H) and the aromatic protons of the C-2 benzyl group show two typical singlets at δ 6.74 (2H) and 6.82 (1H). An AA'XX' system for the C-3 benzyl group is also found to locate at δ 7.18-7.94 (4H, J = 8.3 Hz).



Scheme 8

EXPERIMENTAL SECTION

Melting points were measured on a Reichert Microscope apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker Cryospec WM 250 spectrometer, using $CDCl_3$ as solvent. Proton (250.13 Hz) chemical shifts are reported relative to $CHCl_3$ at δ 7.26 and tetramethylsilane at δ 0.00. Coupling constants are reported in Hz. NMR spectrometric terms are reported by using the following abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet. Mass spectra were obtained with a VG Micromass 7070F spectrometer and were determined at an ionizing voltage of 70 eV, relevant data were tabulated as *m/e*. Elemental analyses were performed at Shanghai Institute of Organic Chemistry, The Chinese Academy of Sciences.

Unless otherwise stated, all reactions were carried out in oven-dried glassware. THF was distilled from sodium benzophenone ketyl. CH_2Cl_2 was distilled from CaH_2. All solutions were evaporated under reduced pressure with a rotary evaporator. Flash chromatography was performed using E. Merck silica gel 60 (230-400 mesh). The plates used for thin-layer chromatography (TLC) were E. Merck silica gel 60 F_{254} (0.25 mm thickness) percoated on aluminum plates, and they were visualized under short (254 nm) UV light.

Reagents were purchased from commercial suppliers and were used without further purification. $Pd(PPh_3)_4$, $Pd(PPh_3)_2Cl_2$, $Ni(PPh_3)_2Cl_2$ were purchased from Aldrich Chemical Company and were used as received.

2,4-Bis(trimethylsilyl)furan (2).[10]

(a) From 4-phenyloxazole (3) and bis(trimethylsilyl)acetylene (4). A mixture of **3** (30 g, 0.15 mol), **4** (15 g, 0.15 mol) and formic acid (2 mL, 0.05 mol) was placed in a tube (thickness: 2 mm; diameter: 40 mm; length: 200 mm). The tube was sealed and heated at 290°C for 5 days to give a dark mixture. Vacuum distillation (62°C, 0.5 mmHg) of the mixture gave a colorless liquid. Column chromatography on silica gel (180 g, hexanes) afforded **2** as a colorless oil (29.6 g, 40%). ^{1}H NMR δ 0.20 (s, 9H), 0.25 (s, 9H), 6.59 (s, 1H), 7.53 (s, 1H); MS *m/e* 212 (M^+). The spectral and physical data are identical with those reported in the literature.[10]

(b) From 3,4-bis(trimethylsilyl)furan (1). A solution of **1**[6c] (8 g, 0.04 mol) in CCl_4 (30 mL) was placed in a tube (thickness: 2 mm; diameter: 25 mm; length: 200 mm). To this solution was added trifluoroacetic anhydride (4 mL, 8.0 mmol) via a syringe. The tube was sealed and was heated to 160°C for 24 h. The resulting mixture was evaporated to give a brown oil which was purified by chromatography on a silica gel column (150 g, hexanes) to afford **2** as a colorless oil (6.4 g, 80%). The physical and spectrometric data are identical with those of an authentic sample prepared previously.

General Procedure for the Preparation of 5.

(a) 2-Benzyl-3,5-bis(trimethylsilyl)furan (5a). To a stirred solution of **2** (1.32 g, 6 mmol) in anhyd. THF (24 mL) was added *n*-BuLi (1M solution in hexane, 6.5 mL, 6.5 mmol) through a syringe under nitrogen. The mixture was stirred for 30 min. Benzyl bromide (1.06 g, 6 mmol) in anhyd. THF (10 mL) was added dropwise to the mixture which became light yellow in color immediately. The resulting mixture was left stirring for another 30 min and was then poured into Et_2O (40 mL) and washed with water (3 x 30 mL). The crude product after evaporation was purified by chromatography on a silica gel column (50 g, hexanes) to give **5a** as a colorless oil (1.54 g, 82%). ^{1}H NMR δ 0.23 (s, 9H), 0.28 (s, 9H), 4.10 (s, 2H), 6.58 (s, 1H), 7.18-7.34 (m, 5H); MS *m/e* 302 (M^+). Anal. Calcd for $C_{17}H_{26}OSi_2$: C, 67.48; H, 8.66. Found: C, 67.51; H, 8.48.

(b) 2-(2-naphthylmethyl)-3,5-bis(trimethylsilyl)furan (5b). Furan **5b** was prepared from **2** (2.2 g, 10 mmol) in anhyd. THF (30 mL), *n*-BuLi (11 mmol), 2-naphthylmethyl bromide (2.2 g, 10 mmol) in anhyd. THF (15 mL). Chromatography of the product on silica gel (70 g, hexanes) gave **5b** as a colorless oil (2.15 g, 61%). ^{1}H NMR δ 0.17 (s, 9H), 0.20 (s, 9H), 4.56 (s, 2H), 6.64 (s, 1H), 7.17-7.31 (m, 7H); MS *m/e* 352 (M^+). Anal. Calcd for $C_{21}H_{28}OSi_2$: C, 71.53; H, 8.00. Found: C, 71.24; H, 8.29.

(c) 2-(Prenyl)-3,4-bis(trimethylsilyl)furan (5c). Furan **5c** was prepared from **2** (1.5 g, 7.1 mmol) in anhyd. THF (30 mL), *n*-BuLi (7.4 mmol) and prenyl bromide (10.6 g, 7.1 mmol) in anhyd. THF (10 mL). Chromatography of the product on silica gel (50 g, hexanes) gave **5c** as a colorless oil (1.69 g, 85%). ^{1}H NMR δ 0.22 (s, 9H), 0.25 (s, 9H), 1.71 (s, 6H), 3.39 (d, 2H, J = 6.8 Hz), 5.23-5.27 (m, 1H), 6.48 (s, 1H); MS *m/e* 280 (M^+). Anal. Calcd for $C_{15}H_{28}OSi_2$: C, 64.22; H, 10.06. Found: C, 64.32; H, 9.79.

(d) 2-(*n*-Hexyl)-3,4-bis(trimethylsilyl)furan (5d). Furan **5d** was prepared from **2** (1 g, 4.7 mmol) in anhyd. THF (40 mL), *n*-BuLi (5 mmol) and *n*-hexyl bromide (2.31 g, 5 mmol) in anhyd. THF (10 mL). Chromatography of the product on silica gel (50 g, hexanes) gave **5d** as a colorless oil (1.12 g, 81%). ^{1}H NMR δ 0.14 (s, 9H), 0.16 (s, 9H), 0.78-0.83 (t, 3H, J = 6.6 Hz), 1.18-1.22 (m, 5H), 1.50-1.58 (m, 3H), 2.55-2.61 (t, 2H, J = 7.5 Hz), 6.40 (s, 1H); MS *m/e* 296 (M^+). Anal. Calcd for $C_{16}H_{32}OSi_2$: C, 64.79; H, 10.88. Found: C, 64.42; H, 10.84.

(e) 2-Methyl-3,4-bis(trimethylsilyl)furan (5e). Furan **5e** was prepared from **2** (1.76 g, 8 mmol) in anhyd. THF (30 mL), *n*-BuLi (8.5 mmol) and dimethyl sulfate (1 g, 8 mmol) in anhyd. THF (10 mL). Chromatography of the product on silica gel (50 g, hexanes) gave **5e** as a colorless oil (1.5 g, 83%). ^{1}H NMR δ 0.24 (s, 9H), 0.26 (s, 9H), 2.07 (d, 3H, J = 0.6 Hz), 6.74 (s, 1H); MS *m/e* 226 (M^+). Anal. Calcd for $C_{11}H_{22}OSi_2$: C, 58.34; H, 9.79. Found: C, 58.38; H, 9.86.

(f) 2-(3,5-Dimethylbenyl)-3,4-bis(trimethylsilyl)furan (5f). Furan **5f** was prepared from **2** (0.6 g, 2.8 mmol) in anhyd. THF (12 mL), *n*-BuLi (2.8 mmol) and 3,5-dimethylbenzyl bromide (0.4 g, 2 mmol) in anhyd. THF (5 mL). Chromatography of the product on silica gel (50 g, hexanes) gave **5e** as a colorless oil. ^{1}H NMR δ 0.32 (s, 9H), 0.35 (s, 9H), 2.37 (s, 6H), 4.10 (s, 2H), 6.65 (s, 1H), 6.90 (s, 2H), 6.92 (s, 1H); MS *m/e* 330 (M^+). Anal. Calcd for $C_{19}H_{30}OSi_2$: C, 69.02; H, 9.14. Found: C, 69.12; H, 9.00.

General Procedure for the Preparation of 7.

(a) 2-Benzyl-3-trimethylsilyl-5-iodofuran (6a) and 2-benzyl-3-trimethylsilylfuran (7a). Furan **5a** (0.47 g, 1.6 mmol) was mixed with silver trifluoroacetate (0.78 g, 3.5 mmol) in anhyd. THF (10 mL). After all the silver salt had dissolved, the reaction flask was cooled to -78°C. The mixture was stirred under nitrogen for 5 min and then iodine (0.4 g, 1.6 mmol) in anhyd. THF (10 mL) was added dropwise in a period of 30 min. After stirring for one more hour, the resulting suspension was filtered through a bed of Celite to give a light yellowish solution which was diluted with saturated sodium metabisulfite ($Na_2S_2O_5$) solution (20 mL) and Et_2O (20 mL). The organic layer was separated, dried over $MgSO_4$ and evaporated to yield a yellow oil. Purification of this oil by silica gel column chromatography (30 g, hexanes) afforded **6a** as a colorless oil (0.41 g, 74%). ^{1}H NMR δ 0.25 (s, 9H), 4.07 (s, 2H), 6.46 (s, 1H), 7.18-7.35 (m, 5H); MS *m/e* 356 (M^+). Anal. Calcd for $C_{14}H_{17}IOSi$: C, 47.20; H, 4.81. Found: C, 47.32; H, 4.63. $LiAlH_4$ (49 mg, 1.3 mmol) was added in one portion to a stirred solution of **6a** (830 mg, 2.3 mmol) in anhyd. THF (10 mL) under nitrogen at room temperature. The suspension was stirred for 10 h. After that the reaction mixture was cooled in an ice bath and water (5 mL) was added very slowly to destroy the unreacted $LiAlH_4$. The resulting solution was further diluted with water (10 mL) and was extracted with Et_2O (15 mL). The organic layer was separated, dried over

$MgSO_4$ and evaporated to give a crude product which was purified by silica gel column chromatography (60 g, hexanes) to afford **7a** as a colorless oil (441 mg, 82%). ^1H NMR δ 0.24 (s, 9H), 4.02 (d, 2H, J = 1.7 Hz), 6.29-6.30 (t, 1H, J = 1.9 Hz), 7.14-7.27 (m, 5H), 7.34 (t, 1H, J = 1.9 Hz); MS *m/e* 224 (M^+). Anal. Calcd for $C_{14}H_{18}OSi$: C, 72.99; H, 7.87. Found: C, 72.78; H, 7.65.

Alternatively, furan **7a** was also obtained directly without purification and identification of **6a**. Thus, after stirring for one hour after the addition of iodine to the solution containing **5a** and silver trifluoroacetate as mentioned above, $LiAlH_4$ (0.17 g, 4.6 mmol) was added. The mixture was stirred at room temperature for 18 h. After work-up as mentioned above, the crude product was chromatographed on a silica gel column (30 g, hexanes) to afford **7a** as a colorless oil (0.16 g, 56%). The physical and spectrometric data of **7a** are identical to those of a sample prepared previously.

(b) 2-(2-Naphthylmethyl)-3-trimethylsilylfuran (**7b**). Furan **7b** was prepared from **5b** (1.1 g, 3 mmol), silver trifluoroacetate (1.66 g, 7.5 mmol) in anhyd. THF (15 mL) and iodine (0.82 g, 3.2 mmol) in anhyd. THF (10 mL). Without isolation of **6b**, $LiAlH_4$ (0.35 g, 9 mmol) was added. Usual work-up and chromatography on a silica gel column (50 g, hexanes) afforded **7b** as a colorless oil (0.59 g, 56%). ^1H NMR δ 0.13 (S, 9H), 4.66 (s, 2H), 6.82 (d, 1H, J = 1.8 Hz), 7.47-7.54 (m, 8H); MS *m/e* 280 (M^+). Anal. Calcd for $C_{18}H_{20}OSi$: C, 77.09; H, 7.19. Found: C, 76.85; H, 6.87.

(c) 2-Prenyl-3-trimethylsilylfuran (**7c**). Furan **7c** was prepared from **5c** (0.7 g, 2.5 mmol), silver trifluoroacetate (1.38 g, 6.25 mmol) in anhyd. THF (15 mL) and iodine (0.67 g, 2.6 mmol) in anhyd. THF (10 mL). Without isolation of **6c**, $LiAlH_4$ (0.29 g, 7.5 mmol) was added. Usual work-up and chromatography on a silica gel column (50 g, hexanes) afforded **7c** as a colorless oil (0.22 g, 42%). ^1H NMR δ 0.25 (s, 9H), 1.72 (s, 6H), 3.39 (d, 2H, J = 6.8 Hz), 5.23-5.27 (m, 1H), 6.23 (d, 1H, J = 1.8 Hz), 7.31 (d, 1H, J = 1.8 Hz); MS *m/e* 208 (M^+). Anal. Calcd for $C_{12}H_{20}OSi$: C, 69.17; H, 9.67. Found: C, 69.78; H, 9.61.

(d) 2-(*n*-Hexyl)-3-trimethylsilylfuran (**7d**). Furan **7d** was prepared from **5d** (0.5 g, 1.7 mmol), silver trifluoroacetate (0.93 g, 4.23 mmol) in anhyd. THF (10 mL) and iodine (0.53 g, 1.79 mmol) in anhyd. THF (10 mL). Without isolation of **6d**, $LiAlH_4$ (0.19 g, 5 mmol) was added. Usual work-up and chromatography on a silica gel column (45 g, hexanes) afforded **7d** as a colorless oil (0.14 g, 38%). ^1H NMR δ 0.22 (s, 9H), 0.85-0.91 (t, 3H, J = 6.5 Hz), 1.25-1.35 (m, 6H), 1.56-1.65 (m, 2H), 2.60-2.66 (t, 2H, J = 7.5 Hz), 6.24 (d, 1H, J = 1.7 Hz), 7.32 (d, 1H, J = 1.7 Hz); MS *m/e* 224 (M^+). Anal. Calcd for $C_{13}H_{24}OSi$: C, 69.58; H, 10.78. Found: C, 68.97; H, 10.84.

(e) 2-Methyl-3-trimethylsilylfuran (**7e**). Furan **7e** was prepared from **5e** (0.34 g, 1.5 mmol), silver trifluoroacetate (0.81 g, 3.8 mmol) in anhyd. THF (8 mL) and iodine (0.39 g, 1.5 mmol) in anhyd. THF (5 mL). Without isolation of **6e**, $LiAlH_4$ (0.17 g, 4.5 mmol) was added. Usual work-up and chromatography on a silica gel column (30 g, hexanes) afforded **7e** as a colorless oil (0.12 g, 53%). ^1H NMR δ 0.21 (s, 9H), 2.37 (s, 3H), 6.36 (d, 1H, J = 2.5 Hz), 7.39 (d, 1H, J = 2.5 Hz); MS *m/e* 154 (M^+). HRMS calcd. for $C_8H_{14}OSi$: 154.0808. Measured: 154.0816.

General Procedure for the Preparation of 2,3-Disubstituted Furans 9.

(a) 2-Benzyl-3-[3,4-(methylenedioxy)benzyl]furan (**9a**). To a stirred solution of **7a** (0.2 g, 0.8 mmol) in CH_2Cl_2 (20 mL) at -78°C under nitrogen was added BCl_3 (1M solution in CH_2Cl_2, 1.22 mL, 1.22 mmol) through a syringe. The solution was left stirring for 5 h. The resulting mixture was poured into sat. Na_2CO_3 solution (5 mL) and was extracted with Et_2O (10 mL). The ethereal layer was dried over $MgSO_4$ and evaporated to give the crude boroxine **8a** which was chromatographed on a silica gel column (20 g, Et_2O:hexanes 1:2) to give a yellowish solid **8a**. To **8a** was immediately added 3,4-(methylenedioxy)benzyl

chloride (70 mg, 0.4 mmol) and $Pd(PPh_3)_4$ (20 mg, 0.02 mmol) in MeOH (6 mL) and toluene (6 mL). The solution was heated to dissolve the palladium catalyst and then 2M Na_2CO_3 solution (2 mL) was added in one portion. The mixture was refluxed for 3 h. After that the solution was allowed to cool to room temperature, poured into water (10 mL) and extracted with Et_2O (10 mL). The ethereal solution was dried over $MgSO_4$ and evaporated. Chromatography of the crude residue on a silica gel column (10 g, hexanes) afforded **9a** as a colorless oil (20 mg, 24%). ^1H NMR δ 3.58 (s, 2H), 3.88 (s, 2H), 5.82 (s, 2H), 6.07 (d, 1H, J = 1.8 Hz), 7.19 (d, 1H, J = 1.8 Hz), 6.51-6.54 (m, 2H), 6.61-6.64 (m, 1H), 7.07-7.23 (m, 5H); MS *m/e* 292 (M^+). Anal. Calcd for $C_{19}H_{16}O_3$: C, 78.06; H, 5.52. Found: C, 77.81; H, 5.61.

(b) Rosefuran (9c). Rosefuran (**9c**) was prepared from **7c** (0.5 g, 2.4 mmol) in CH_2Cl_2 (30 mL) and BCl_3 (4.8 mmol). After quenching in sat. Na_2CO_3 (10 mL), the crude boroxine **8c** obtained was purified on a silica gel column (30 g, Et_2O:hexanes 1:2) to give yellowish solid, which was allowed to react with Me_2SO_4 (0.91 g, 7.2 mmol) and $Pd(PPh_3)_4$ (0.28 g, 0.24 mmol) in a mixture of MeOH (10 mL), toluene (10 mL) and 2M Na_2CO_3 (3 mL). Usual work-up and chromatography on a silica gel column (30 g, *n*-pentane) afforded rosefuran (**9c**) as a colorless oil (0.79 g, 22%). ^1H NMR δ 1.60 (s, 6H), 2.19 (s, 3H), 3.27 (d, 2H, J = 6.7 Hz), 5.22-5.28 (br t, 1H, J = 7.8 Hz), 6.15 (d, 1H, J = 1.8 Hz), 7.21 (d, 1H, J = 1.8 Hz). The physical and spectrometric data of **9c** are identical to those reported.[19,20]

(c) 2-(*n*-Hexyl)-3-benzylfuran (9d). Furan **9d** was prepared from **7d** (0.5 g, 2.2 mmol) in CH_2Cl_2 (30 mL) and BCl_3 (2.46 mmol). After quenching in sat. Na_2CO_3 (13 mL), the crude boroxine **8d** obtained was purified on a silica gel column (35 g, Et_2O:hexanes 1:2) to give a yellowish solid, which was allowed to react with benzyl bromide (1.14 g, 6.7 mmol) and $Pd(PPh_3)_4$ (0.26 g, 0.22 mmol) in a mixture of MeOH (10 mL), toluene (10 mL) and 2M Na_2CO_3 (4 mL). Ususal work-up and chromatography on a silica gel column (30 g, hexanes) afforded **9d** as a colorless oil (0.23 g, 42%). ^1H NMR δ 0.81-0.83 (br s, 3H), 1.21 (s, 4H), 1.50 (s, 4H), 2.50-2.53 (t, 2H, J = 7.5 Hz), 3.83 (s, 2H), 5.83 (d, 1H, J = 1.8 Hz), 7.13-7.24 (m, 6H); MS *m/e* 242 (M^+). Anal. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.91; H, 9.38.

3-Methyl-4-trimethylsilylfuran (11).

4-Phenyloxazole (**3**) (21.8 g, 0.15 mol) and trimethylsilylpropyne (**10**) (16.8 g, 0.15 mol) were mixed in a tube (thickness: 2 mm; diameter: 40 mm; length: 200 mm) to which anhyd. DBU (2.3 g, 0.2 mol) was added. The tube was sealed and was heated at 270°C for 5 days to give a dark brown mixture. Vacuum distillation (85-90°C, 0.2 mmHg) of this mixture gave a colorless liquid. Further purification of this liquid on a silica gel column (150 g, *n*-pentane) afforded **11** as a colorless oil (17.3 g, 75%). ^1H NMR δ 0.26 (s, 9H), 2.08 (d, 3H, J = 0.8 Hz), 7.26 (m, 2H); MS *m/e* 154 (M^+). The spectrometric data of **11** are identical with an authentic sample prepared previously.[21]

2-Prenyl-3-methyl-4-trimethylsilylfuran (12).

To a stirred solution of **11** (1.0 g, 6.5 mmol) in anhyd. THF (50 mL) at 0°C under nitrogen was added *t*-BuLi (1.6M in pentane, 4.3 mL, 6.8 mmol) through a syringe. After the mixture had been stirred for 30 min, prenyl bromide (0.97 g, 6.5 mmol) in anhyd. THF (20 mL) was added dropwise, and the mixture turned light yellow in color immediately. The resulting mixture was left stirring for another 30 min, poured into Et_2O (45 mL) and washed with water (30 mL). After evaporation, the residue was chromatographed on a silica gel column (50 g, hexanes) to give **12** as a colorless oil (1.3 g, 90%). ^1H NMR δ 0.20 (s, 9H), 1.70 (s, 6H), 2.00 (d, 3H, J = 5.1 Hz), 3.24-3.27 (d, 2H, J = 7.0 Hz), 5.21-5.27 (m, 1H), 7.10 (s, 1H); MS *m/e* 222 (M^+). Anal. Calcd for $C_{13}H_{22}OSi$: C, 70.21; H, 9.97. Found: C, 70.78; H, 9.65.

Rosefuran (9c).

A mixture of **12** and trifluoroacetic acid (26 mg, 0.2 mmol) in $CHCl_3$ (30 mL) was heated under reflux for 3 h. After that it was poured into ice water (20 mL) and extracted with Et_2O (2 x 15 mL). The combined ethereal extract was dried over $MgSO_4$ and evaporated. The residue was purified by column chromatography on silica gel (30 g, *n*-pentane) to give **9c** as a colorless oil (0.29 g, 87%). The physical and spectrometric data are identical to a sample prepared previously and also to those reported in the literature.[19,20]

3-Trimethylsilylfuran (14).

4-Phenyloxazole (**3**) (36.3 g, 0.25 mol) and trimethylsilylacetylene (**13**) (24.5 g, 0.25 mol) were mixed in a tube (thickness: 2 mm; diameter: 50 mm; length: 200 mm) to which anhyd. Et_3N (2.5 g, 30 mmol) was added. The tube was sealed and was heated at 270°C for 7 days to give a dark brown mixture. Vacuum distillation of the resulting mixture gave a colorless liquid (b.p. 50-52°C, 1 mmHg). Further purification of the compound on a silica gel column (200 g, *n*-pentane) afforded **14** as a colorless oil (24.5 g, 70%). ^1H NMR δ 0.10 (s, 9H), 6.21 (q, 1H, J = 2.5 Hz), 7.19 (q, 1H, J = 2.2 Hz), 7.33 (t, 1H, J = 5.2 Hz). Anal. Calcd for $C_7H_{12}OSi$: C, 59.94; H, 8.62. Found: C, 60.04; H, 8.72.

2-Benzyl-4-trimethylsilylfuran (15).

To a stirred solution of **14** (12 g, 85.7 mmol) in anhyd. THF (150 mL) at 0°C under nitrogen was added *t*-BuLi (1.6M solution in pentane, 58.8 mL, 94 mmol) through a syringe. The mixture was stirred for 30 min and benzyl bromide (10.2 mL, 85.7 mmol) in anhyd. THF (20 mL) was added dropwise. The resulting mixture was left stirring for another 30 min and was diluted with Et_2O (150 mL) and washed with water (3 x 150 mL). After evaporation, the residue was chromatographed on a silica gel column (150 g, hexanes) to afford **15** as a colorless oil (18.1 g, 92%). ^1H NMR δ 0.11 (s, 9H), 3.90 (s, 2H), 5.89 (d, 1H, J = 0.8 Hz), 7.16-7.25 (m, 6H); MS *m/e* 230 (M^+). Anal. Calcd for $C_{14}H_{18}OSi$: C, 72.99; H, 7.88. Found: C, 72.36; H, 7.73.

Tris(2-benzylfuran-4-yl)boroxine (16).

To a stirred solution of **15** (10 g, 43.5 mmol) in anhyd. CH_2Cl_2 (400 mL) was added BCl_3 (1M solution in CH_2Cl_2, 18 mL, 18 mmol) under nitrogen at -78°C. After stirring for 5 h at -78°C the reaction was quenched with sat. Na_2CO_3 (50 mL) and the mixture was extracted with Et_2O (3 x 100 mL). The ethereal solution was dried over $MgSO_4$ and evaporated. The residue was chromatographed on a silica gel column (200 g, Et_2O:hexanes 1:1) to give **16** as white solids (7.03 g, 88%), m.p. 148-149°C. ^1H NMR δ 4.03 (s, 6H), 6.06 (q, 3H, J = 3.9 Hz), 7.28-7.39 (m, 18H); MS *m/e* 552 (M^+). Anal. Calcd for $C_{33}H_{27}O_6B_3$: C, 71.80; H, 4.93. Found: C, 71.81; H, 5.16.

General Procedure for the Preparation of 17.

(a) 2-Benzyl-4-(*p*-tolyl)furan (17a). A stirred mixture of **16** (0.20 g, 0.36 mmol), *p*-bromotoluene (0.18 g, 1.1 mmol), 2M Na_2CO_3 (5 mL) and $Pd(PPh_3)_4$ (40 mg, 0.03 mmol) in a mixed solvent of MeOH-toluene (1:1, 30 mL) was heated under reflux for 4 h. After that it was poured into ice water (30 mL) and extracted with Et_2O (3 x 20 mL). The combined ethereal solution was dried over $MgSO_4$ and evaporated. The residue was purified by chromatography on a silica gel column (30 g, hexanes) to give **17a** as white solids (0.22 g, 83%), m.p. 102-103°C. ^1H NMR δ 2.33 (s, 3H), 3.99 (s, 2H), 6.29 (d, 1H, J = 1.0 Hz), 7.13-7.16 (d, 2H, J = 7.7 Hz), 7.24-7.31 (m, 5H), 7.31-7.34 (d, 2H, J = 7.7 Hz), 7.58 (s, 1H); MS *m/e* 248 (M^+). Anal. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49. Found: C, 87.40; H, 6.72.

(b) 2-Benzyl-4-(*trans*-2-styryl)furan (17b). Furan **17b** was prepared by heating a mixture of **16** (0.1 g, 0.2 mmol), *trans*-β-bromostyrene (0.17 g, 0.9 mmol), 2M Na_2CO_3 (5 mL) and $Pd(PPh_3)_4$ (120 mg, 0.1 mmol) in MeOH-toluene (1:1, 20 mL) for 6 h. Usual work-up and chromatography on a silica gel column (20

g, hexanes) gave **17b** as colorless needles (0.11 g, 77%), m.p. 114-115°C. ^{1}H NMR δ 3.90 (s, 2H), 6.20 (s, 1H), 6.63-6.88 (ABq, 2H, J = 16.1 Hz), 7.14-7.33 (m, 10H), 7.36 (s, 1H); MS *m/e* 260 (M^+). Anal. Calcd for $C_{19}H_{16}O$: C, 87.66; H, 6.20. Found: C, 87.81; H, 6.16.

2-Benzyl-4-iodofuran (18).

To a solution of **16** (1.0 g, 1.8 mmol) in anhyd. THF (150 mL) at -78°C under nitrogen was added silver tetrafluoroborate (0.88 g, 4.5 mmol). The mixture was stirred for 5 min to ensure complete dissolution. Iodine (1.4 g, 5.4 mmol) in anhyd. THF (30 mL) was added dropwise and the resulting mixture was stirred at -78°C for 4 h. Then the resulting suspension was filtered through a bed of Celite to give a light yellow solution which was diluted with 3M $Na_2S_2O_5$ solution (30 mL) and Et_2O (30 mL). The ethereal layer was separated, dried over $MgSO_4$ and evaporated to give a residue. Purification of this residue on a silica gel column (60 g, hexanes) afforded **18** as a yellow oil (1.31 g, 85%). ^{1}H NMR δ 3.84 (s, 2H), 5.97 (s, 1H), 7.09-7.23 (m, 6H); MS *m/e* 284 (M^+). Anal. Calcd for $C_{11}H_9IO$: C, 46.51; H, 3.19. Found: C, 46.55; H, 3.00.

2-Benzyl-4-(trimethylsilylethynyl)furan (19).

A mixture of **18** (0.15 g, 0.53 mmol), trimethylsilylacetylene (**13**) (0.22 mL, 1.59 mmol), $Pd(PPh_3)_2Cl_2$ (38 mg, 0.05 mmol) and copper(I) iodide (100 mg, 0.05 mmol) in Et_2NH (30 mL) was stirred at room temperature for 24 h under nitrogen. The solvent was then evaporated and the residue was chromatographed on a silica gel column (30 g, hexanes) to give **19** as a colorless oil (120 mg, 90%). ^{1}H NMR δ 0.19 (s, 9H), 3.90 (s, 2H), 6.03 (d, 1H, J = 0.8 Hz), 7.17-7.31 (m, 5H), 7.50 (s, 1H); MS *m/e* 254 (M^+). Anal. Calcd for $C_{16}H_{18}OSi$: C, 75.54; H, 7.13. Found: C, 75.98; H, 6.72.

2,2'-Bis(benzyl)-4,4'-bifuran (20).

A mixture of **16** (0.30 g, 0.54 mmol) and $Pd(PPh_3)_4$ in MeOH-toluene (1:1, 20 mL) wa stirred for 5 min. To this mixture was then added 2M Na_2CO_3 (4 mL) and the mixture was refluxed for 4 h. After that it was allowed to cool to room temperature and water (50 mL) was added. The resulting mixture was extracted with Et_2O (3 x 30 mL). The ethereal solution was dried over $MgSO_4$ and evaporated. The residue was chromatographed on a silica gel column (40 g, hexanes) to afford **20** as colorless crystals (170 mg, 65%), m.p. 82-84°C. ^{1}H NMR δ 4.04 (s, 4H), 6.17 (s, 2H), 7.30-7.44 (m, 10H), 7.50 (s, 2H); MS *m/e* 314 (M^+). Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.93; H, 5.55.

3-(*n*-Butyl)-4-trimethylsilylfuran (22).[17a,21]

To a solution of **21**[17a] (130 mg, 0.5 mmol) and $Ni(PPh_3)_2Cl_2$ (17 mg, 0.025 mmol) in anhyd. THF (20 mL) was added *n*-butylmagnesium chloride (2M solution in anhyd. THF, 0.4 mL, 0.8 mmol). The mixture was heated at 80°C for 3 h. Filtration of the resulting mixture was followed by evaporation of the filtrate. The residue was extracted with hexanes (15 mL) to remove the insoluble materials. Evaporation of hexanes gave the product which was chromatographed on a silica gel column (30 g, hexanes) to give **22** as a colorless oil (80 mg, 82%). ^{1}H NMR δ 0.09 (s, 9H), 0.79 (t, 3H, J = 7.2 Hz), 1.23 (m, 2H), 1.42 (m, 2H), 1.49 (m, 2H), 7.09 (s, 2H). The physical and spectrometric data of **22** are identical to those of an authentic sample.[17a]

2-Prenyl-3-(*n*-butyl)-4-trimethylsilylfuran (23).

To a stirred solution of **22** (0.5 g, 2.6 mmol) in anhyd. THF (50 mL) under nitrogen at -78°C was added *t*-BuLi (1.6M solution in pentane, 1.75 mL, 2.8 mmol) through a syringe. The mixture was stirred for 1 h. After that prenyl bromide (0.33 mL, 2.81 mmol) in anhyd. THF (20 mL) was added dropwise to the mixture. The resulting mixture was left stirring for another 2 h and was then poured into Et_2O (45 mL). After washing with water (3 x 30 mL), the organic solution was evaporated to give a residue. Chromatography of this residue on a silica gel column (50 g, hexanes) gave **23** as a colorless oil (1.3 g, 90%). ^{1}H NMR δ 0.22 (s,

9H), 0.90-0.95 (t, 3H, J = 7.0 Hz), 1.31-1.47 (m, 4H), 1.71 (d, 6H, J = 0.8 Hz), 2.32-2.38 (t, 2H, J = 6.9 Hz), 3.26-3.29 (d, 2H, J = 7.0 Hz), 5.22-5.28 (td, 1H, J = 5.7, 5,7, 1.4 Hz), 7.11 (d, 1H, J = 4.8 Hz); MS *m/e* 264 (M^+). Anal. Calcd for $C_{16}H_{28}OSi$: C, 72.66; H, 10.67. Found: C, 72.84; H, 10.53.

2-Prenyl-3-(*n*-butyl)-4-iodofuran (24).

To a solution of **23** (50 mg, 0.2 mmol) in anhyd. THF (30 mL) under nitrogen at -78°C was added silver tetrafluoroborate (70 mg, 0.5 mmol). The mixture was stirred for 5 min to ensure complete dissolution. Then iodine (50 mg, 0.2 mmol) in anhyd. THF (8 mL) was added dropwise, and the resulting mixture was stirred at -78°C for 8 h. After that the resulting suspension was filtered through a bed of celite to give a yellow solution which was diluted with 3M $Na_2S_2O_5$ solution (30 mL) and Et_2O (30 mL). The organic layer was separated, dried over $MgSO_4$ and evaporated to give a yellow oil, which was purified by column chromatography on a silica gel (30 g, hexanes) to give **24** as a colorless oil (9 mg, 15%). ^1H NMR δ 0.90-0.95 (t, 3H, J = 7.0 Hz), 1.33-1.50 (m, 4H), 1.71 (d, 6H, J = 0.6 Hz), 2.32-2.38 (t, 2H, J = 7.0 Hz), 3.26-3.29 (d, 2H, J = 6.7 Hz), 5.22-5.25 (br t, 1H, J = 7.2 Hz), 7.12 (s, 1H); MS *m/e* 318 (M^+). Anal. Calcd for $C_{13}H_{19}IO$: C, 49.07; H, 6.02. Found: C, 48.91; H, 4.91.

2-Benzyl-3-trimethylsilyl-5-(*p*-tolyl)furan (25).

p-Tolylmagnesium bromide was prepared by refluxing 4-bromotoluene (1.0 g, 5.8 mmol) with a large excess of magnesium (0.5 g, 20.5 mmol) in anhyd. Et_2O (10 mL). This Grignard reagent was added through a syringe to a stirred solution of **6a** (0.25 g, 0.68 mmol) and [1,2-bis(diphenylphosphino)propane]nickel(II) dichloride (42 mg, 0.07 mmol) in anhyd. Et_2O (5 mL) under nitrogen at room temperature. After stirring for 24 h, the resulting mixture was poured into sat. NH_4Cl solution (10 mL) and was extracted with Et_2O (10 mL). The organic layer was separated, dried over $MgSO_4$ and evaporated. The residue was chromatographed on a silica gel column (80 g, hexanes) to afford **25** as a colorless oil (160 mg, 70%). ^1H NMR δ 0.24 (s, 9H), 2.32 (s, 3H), 4.07 (s, 2H), 6.51 (s, 1H), 7.12-7.15 (d, 2H, J = 8.2 Hz), 7.21-7.29 (m, 6H), 7.48-7.52 (d, 2H, J = 8.2 Hz); MS *m/e* 320 (M^+). Anal. Calcd for $C_{21}H_{24}OSi$: C, 78.69; H, 7.55. Found: C, 78.80; H, 7.38.

General Procedure for the Preparation of 26.

(a) 2-Benzyl-3-(*m*-anisyl)-5-(*p*-tolyl)furan (26a). To a stirred solution of **25** (0.15 g, 0.4 mmol) in CH_2Cl_2 (30 mL) under nitrogen at -78°C was added BCl_3 (1M solution in CH_2Cl_2, 0.6 mL, 0.6 mmol) via a syringe. After stirred at -78°C for 3 h, the mixture was poured into sat. Na_2CO_3 (20 mL) and was extracted with Et_2O (20 mL). After separation, the organic layer was dried over $MgSO_4$ and evaporated to give the crude boroxine which was not purified further. To this boroxine was added 3-bromoanisole (0.12 mL, 1 mmol), $Pd(PPh_3)_4$ (0.14 g, 0.1 mmol), MeOH (10 mL) and toluene (10 mL). The solution was heated to dissolve all palladium catalyst and then 2M Na_2CO_3 solution (5 mL) was added. The mixture was refluxed for 3 h and then diluted with water (15 mL) and Et_2O (15 mL). The ethereal layer was separated, dried over $MgSO_4$ and evaporated to furnish a brownish oil, which was chromatographed on a silica gel column to give **26a** as a colorless oil (0.11 g, 65%). ^1H NMR δ 2.35 (s, 3H), 3.76 (s, 3H), 4.20 (s, 2H), 6.76 (s, 1H), 6.81-7.03 (m, 3H), 7.16-7.19 (d, 2H, J = 8.2 Hz), 7.21-7.33 (m, 6H), 7.55-7.58 (d, 2H, J = 8.2 Hz); MS *m/e* 354 (M^+). Anal. Calcd for $C_{25}H_{22}O_2$: C, 84.72; H, 6.26. Found: C, 84.56; H, 6.33.

(b) 2-Benzyl-3-(*trans*-hexen-1-yl)-5-(*p*-tolyl)furan (26b). Furan **26b** was prepared from **25** (116 mg, 0.4 mmol) in CH_2Cl_2 (10 mL) and BCl_3 (1M solution in CH_2Cl_2, 0.5 mmol). After purification by silica gel column chromatography (30 g, Et_2O:hexanes 1:1), the boroxine obtained was refluxed for 1 h with *trans*-1-iodo-1-hexene (147 mg, 0.7 mmol), $Pd(PPh_3)_4$ (20 mg, 0.02 mmol) and 2M Na_2CO_3 (2 mL) in MeOH (7 mL), and toluene (7 mL). Usual work-up and chromatography on silica gel column (20 g, hexanes) gave **26b**

as a colorless oil (67 mg, 66%). ^{1}H NMR δ 0.89-0.95 (t, 3H, *J* = 7.0 Hz), 1.26-1.46 (m, 4H), 2.14-2.22 (q, 2H, *J* = 6.7 Hz), 2.34 (s, 3H), 4.05 (s, 2H), 5.89-6.01 (m, 1H), 6.20-6.27 (d, 1H, *J* = 16.7 Hz), 6.69 (s, 1H), 7.13-7.16 (d, 2H, *J* = 8.2 Hz), 7.20-7.33 (m, 5H), 7.49-7.52 (d, 2H, *J* = 8.2 Hz); MS *m/e* 330 (M^+). Anal. Calcd for $C_{24}H_{26}O$: C, 87.23; H, 7.93. Found: C, 87.36; H, 7.56.

2-(3,5-Dimethylbenzyl)-3-trimethylsilyl-5-iodofuran (6f).

Furan **5f** (404 mg, 1.2 mmol) was mixed with silver trifluoroacetate (0.55 g, 2.5 mmol) in anhyd. THF (10 mL) under nitrogen. After all the silver salt had dissolved, the reaction mixture was cooled to -78°C and iodine (314 mg, 1.2 mmol) in anhyd. THF (10 mL) was added in a period of 30 min. After stirring for 1 h, the resulting suspension was filtered through a bed of Celite to give a light yellowish solution. Dilution of this solution with $Na_2S_2O_5$ solution (20 mL) was followed by extraction with Et_2O(20 mL). The ethereal solution was dried over $MgSO_4$ and evaporated to furnish a yellow oil which was purified by column chromatography on a silica gel column (30 g, hexanes) to give **6f** as a colorless oil (426 mg, 90%) which decomposed gradually on prolonged standing at room temperature. ^{1}H NMR δ 0.21 (s, 9H), 2.27 (s, 6H), 3.95 (s, 2H), 6.42 (s, 1H), 6.77 (s, 2H), 6.85 (s, 1H). Furan **6f** was used in the following step without further purification.

2-(3,5-Dimethylbenzyl)-3-trimethylsilyl-5-(*n*-hexyl)furan (27).

To a stirred mixture of **6f** (180 mg, 0.5 mmol), $Pd(PPh_3)_2Cl_2$ (128 mg, 0.2 mmol) and copper(I) iodide (100 mg, 0.5 mmol) in Et_2NH (5 mL) under nitrogen at room temperature was added 1-hexyne (1.0 g, 12.7 mmol) through a syringe. The mixture was left stirring for 36 h and was followed by evaporation. The black residue was chromatographed on a silica gel column (30 g, hexanes) to give a colorless oil which was hydrogenated over a catalytic amount of 10% Pd-C in absolute EtOH (12 mL) for 18 h. The resulting mixture was filtered through a bet of Celite and evaporated. The crude product was purified by silica gel column chromatography (30 g, hexanes) to give **27** as a colorless oil (126 mg, 78%). ^{1}H NMR δ 0.20 (s, 9H), 0.84-0.89 (t, 3H, *J* = 6.8 Hz), 1.26-1.59 (m, 8H), 2.26 (s, 6H), 2.52-2.58 (t, 2H, *J* = 7.6 Hz), 3.89 (s, 2H), 5.86 (s, 1H), 6.78 (s, 2H), 6.83 (s, 1H); MS *m/e* 342 (M^+). Anal. Calcd for $C_{22}H_{34}OSi$: C, 77.13; H, 10.00. Found: C, 77.72; H, 10.07.

2-(3,5-Dimethylbenzyl)-3-(*p*-methoxycarbonylbenzyl)-5-(*n*-hexyl)furan (28).

To a solution of **27** (62 mg, 0.2 mmol) in CH_2Cl_2 (9 mL) was added BCl_3 (1M solution in CH_2Cl_2, 0.2 mL, 0.2 mmol) through a syringe. The solution was stirred for 30 min and was poured into 1M Na_2CO_3 (15 mL) and Et_2O (20 mL). The ethereal solution was separated, dried over $MgSO_4$ and evaporated to give the crude boroxine, which was purified by chromatography on a silica gel column (20 g, Et_2O:hexanes 1:2). The boroxine obtained was immediately mixed with $Pd(PPh_3)_4$ (15 mg, 0.01 mmol), *p*-methoxycarbonylbenzyl bromide (44 mg, 0.2 mmol) in MeOH (5 mL) and toluene (5 mL). This mixture was heated to dissolve the palladium catalyst and then 2M Na_2CO_3 (3 mL) was added. The resulting mixture was refluxed for 1 h and was then cooled to room temperature and diluted with water (15 mL) and Et_2O (15 mL). The ethereal solution was separated, dried over $MgSO_4$ and evaporated to give a brownish yellow residue which was purified on a silica gel column (20 g, Et_2O:hexanes 1:20) to yield **28** as a colorless oil (54 mg, 71%). ^{1}H NMR δ 0.83-0.89 (t, 3H, *J* = 6.8 Hz), 1.26-1.61 (m, 8H), 2.24 (s, 6H), 2.48-2.54 (t, 2H, *J* = 7.6 Hz), 3.72 (s, 2H), 3.84 (s, 2H), 3.89 (s, 3H), 5.72 (s, 1H), 6.74 (s, 2H), 6.82 (s, 1H), 7.18-7.22 (d, 2H, *J* = 8.3 Hz), 7.90-7.94 (d, 2H, *J* = 8.3 Hz); MS *m/e* 418 (M^+). Anal. Calcd for $C_{28}H_{34}O_3$: C, 80.35; H, 8.19. Found: C, 80.35; H, 8.21.

Acknowledgement. The financial support from the Research Grants Council (CUHK 296/94P) is gratefully acknowledged.

References and Notes

† Dedicated to Professor Fabian Gerson on the occasion of his formal retirement from an outstanding academic career, in commemoration of a long-standing collaboration which spanned over two decades.

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(*Received in Japan* 16 *December* 1996; *accepted* 20 *January* 1997)