was stirred under O_2 for another day. The reaction mixture was diluted with 10% HCl and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with water (10 mL), dried, and evaporated. The remaining DMF was removed by dissolving the crude mixture in ether, washing the resulting solution with water, drying the solution, and evaporating the solvent to leave pure **14** (7.8 mg, 95%). Further purification could be achieved by preparative TLC (silica gel, 1:2:7 CH_2Cl_2/ether/hexanes), mp 159–161 °C (sealed tube): IR (film, cm^{-1}) 2940, 1715, 1395, 1160; ^1H NMR (300 MHz, C_6D_6) δ 3.48 (br s, 6 H), 3.27 (br s, 10 H), 2.97 (br s, 3 H), 2.17 (s, 2 H), 1.63 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 206.0, 76.8, 73.3, 67.23, 67.16, 67.0, 66.9, 57.0, 30.2; MS m/z calcd (M^+) 316.1827, obsd 316.1805.

ESR Spectroscopic Studies. A Bruker ER-420 X-band spectrometer equipped with a variable temperature unit was used. Data acquisition and spectral simulations were performed on a DEC PDP-11/34 computer.

ESR samples were prepared in 4-mm o.d. quartz tubes, degassed by three freeze–pump–thaw cycles, and sealed under vacuum. Typically, the samples were composed of 2–3 mg of highly purified precursor (**5** or **8**), 10–50 μL of initiator (DTBP, Me_6Sn_2, Et_3SiH), and 0.5–1 mL of solvent (cyclopropane or fluorobenzene). Radicals were generated by direct UV photolysis of the samples with the filtered (UG–5; Schott) output of a 1000-W high-pressure Hg/Xe lamp (Hanovia 977B-1). The g values were determined with the aid of a home-built device, using the digital readout from a frequency counter and a gauss meter.

Matrix-isolation experiments were carried out using an Air Products closed-cycle helium cryostat CV 202. Most of the experimental setup has been described elsewhere.[45] The sample of **5** was evaporated in a vacuum of 10^{-6} mbar at ca. 220 °C; sodium was evaporated at ca. 260 °C. A DDHBr/argon ratio of 1:100 was employed.

AM1/PM3-UHF calculations were performed using the SCAMP 4.20 package[46] on a MicroVax GPX-II workstation. Graphical output was produced by the PERGRA program.[47]

Acknowledgment. This research was supported by the National Institutes of Health (Grant AI-11490 to LAP).

(46) SCAMP, Erlangen Molecular Orbital Package, Version 4.20 (based on AMPAC 1.0 and MOPAC 4.0), Universität Erlangen, Germany. We thank Dr. T. Clark for a copy of this program.

(47) Sustmann, R.; Sicking, W. Universität-GH Essen, Germany, 1990.

Rearrangement of Dimethyl(furylmethyl)ammonium and Dimethyl(thienylmethyl)ammonium *N*-Methylides. Isolation and Reaction of Nonaromatic Intermediates

Takeshi Usami, Naohiro Shirai, and Yoshiro Sato*

Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467, Japan

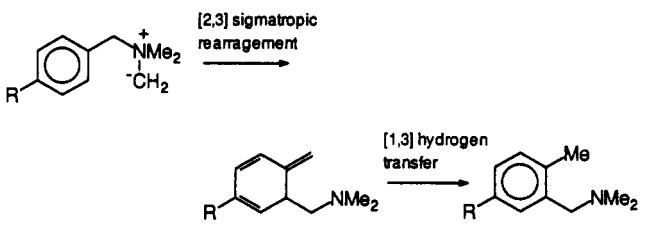
Received May 20, 1992

3-[(Dimethylamino)methyl]-2-methylene-2,3-dihydrofuran (**5o**) and 2-[(dimethylamino)methyl]-3-methylene-2,3-dihydrofuran (**12o**) and their thiophene analogues **5s** and **12s** were prepared in high yields by fluoride-ion induced desilylation of *N,N*-dimethyl-*N*-[(trimethylsilyl)methyl](2-furylmethyl)ammonium (**3o**) and -(3-furylmethyl)ammonium iodides (**10o**) and their thienylmethyl analogues **3s** and **10s**. Compound **5s** or **12s** was successfully converted to 3-[(dimethylamino)methyl](2-thienylmethyl)lithium (**23s**) or 2-[(dimethylamino)methyl](3-thienylmethyl)lithium (**26s**), which reacted with aldehydes to give [(dimethylamino)methyl](2-hydroxyalkyl)thiophenes **25s** or **27s**, respectively.

Introduction

N,N-Dialkylbenzylammonium *N*-methylides rearrange to *N,N*-dialkyl-2-methylbenzylamines (Sommelet–Hauser rearrangement) and/or *N,N*-dialkyl-2-phenylethylamines (Stevens rearrangement).[1] The Sommelet–Hauser rearrangement is the main path from the ylide having an electron-donating or weak electron-releasing substituent on the benzene ring.[2a,b,g] This rearrangement proceeds by a [2,3] sigmatropic rearrangement followed by a [1,3] hydrogen transfer via an intermediate, 6-[(dialkylamino)methyl]-5-methylene-1,3-cyclohexadienes (conjugated triene compounds) (Scheme I). The stability of the conjugated triene compounds increases with the increasing electron-releasing ability of the substituents;[2b,d-f] e.g., 6-[(dimethylamino)methyl]-2-methoxy-5-methylene-1,3-cyclohexadiene was stable at room temperature.[2b] This result seems to suggest that the rearrangement of ylides to an electron-rich aromatic ring may stop at the intermediate compound.

Scheme I



Paul and Tchelitcheff[3] reported that treatment of trimethyl(3-furylmethyl)ammonium or trimethyl(3-thienylmethyl)ammonium salt with sodium amide in liquid ammonia gave 3-methyl-2-[(dimethylamino)methyl]furan or -thiophene (Sommelet–Hauser rearrangement product), but no product was obtained from a similar treatment of

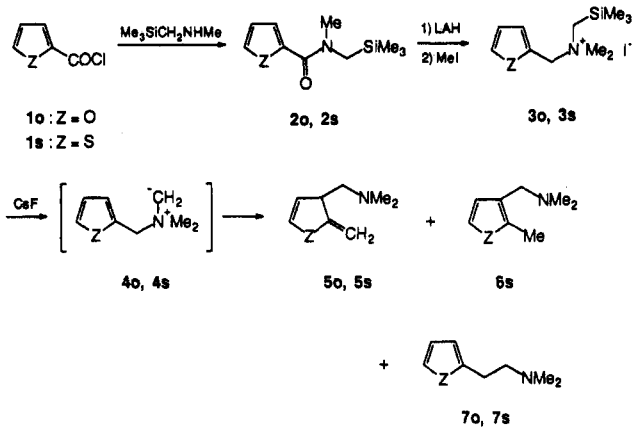
(1) (a) Pine, S. H. *Org. React. (N.Y.)* **1970**, *18*, 403. (b) Lepley, A. R.; Giumanini, A. G. *Mechanisms of Molecular Migrations*; Thyagarajan, B. S., Ed.; Wiley-Interscience: New York, 1971; Vol. 3, p 297.

(2) (a) Nakano, M.; Sato, Y. *J. Org. Chem.* **1987**, *52*, 1844. (b) Shirai, N.; Watanabe, Y.; Sato, Y. *J. Org. Chem.* **1990**, *55*, 2767. (c) Shirai, N.; Sumiya, F.; Sato, Y.; Hori, M. *J. Org. Chem.* **1989**, *54*, 836. (d) Machida, Y.; Shirai, N.; Sato, Y. *Synthesis*, **1991**, 117. (e) Kitano, T.; Shirai, N.; Sato, Y. *Synthesis*, **1991**, 996; *Chem. Pharm. Bull.* **1992**, *40*, 768. (f) Okazaki, S.; Shirai, N.; Sato, Y. *J. Org. Chem.* **1990**, *55*, 334. (g) Tanaka, T.; Shirai, N.; Sugimori, J.; Sato, Y. *J. Org. Chem.*, in press.

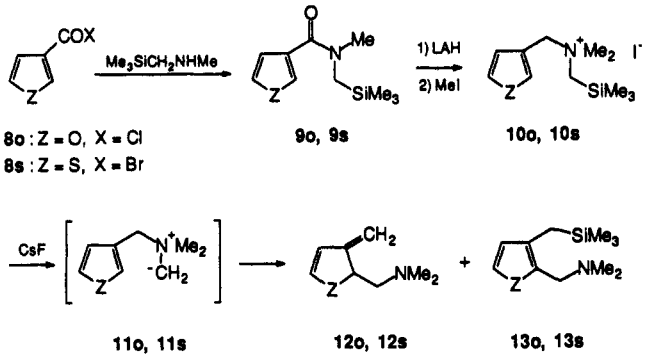
(3) Paul, R.; Tchelitcheff, S. *Bull. Soc. Chim. Fr.* **1968**, 2134.

0022-3263/92/1957-5419$03.00/0

Scheme II



Scheme III



the (2-furylmethyl)ammonium or (2-thienylmethyl)ammonium analogue. We examined the chemical behavior of (furylmethyl)ammonium and (thienylmethyl)ammonium *N*-methylides produced by the fluoride-induced desilylation reaction.[4]

Results and Discussion

N,N-Dimethyl-*N*-[(trimethylsilyl)methyl](2-furylmethyl)ammonium iodide (**3o**) and a 3-thienylmethyl analogue (**3s**) were synthesized starting from 2-furoyl or 2-thiophenecarbonyl chloride (**1o** or **1s**) via *N*-methyl-*N*-[(trimethylsilyl)methyl]-2-furanamide (**2o**) or -2-thiophenecarboxamide (**2s**), respectively (Scheme II). *N,N*-Dimethyl-*N*-[(trimethylsilyl)methyl](3-furylmethyl)ammonium or -(3-thienylmethyl)ammonium iodide (**10o**, **10s**) was prepared from 3-furoyl chloride (**8o**) or 3-thiophenecarbonyl bromide (**8s**) in a manner similar to the preparation of **3o** and **3s** (Scheme III).

The reaction of **3o** with cesium fluoride in HMPA at room temperature gave selectively 3-[(dimethylamino)methyl]-2-methylene-2,3-dihydrofuran (**5o**) which is a [2,3] sigmatropic rearrangement product of intermediate ylide (**4o**), accompanied by small amounts of 2-[2-(dimethylamino)ethyl]furan (**7o**, Stevens rearrangement product) (entries 1–3 in Table I). Although the total yields of both products increased after prolonged stirring, isomerization of **5o** to a Sommelet–Hauser product **6o** was not observed.[5] A similar reaction of **3s** proceeded more quickly to give 3-[(dimethylamino)methyl]-2-methylene-2,3-dihydrothiophene (**5s**) and 2-[2-(dimethylamino)ethyl]thiophene (**7s**) (entry 4), and a small portion of **5s** isomerized to 3-[(dimethylamino)methyl]-2-methylthiophene (**6s**) after 24 h of stirring (entry 5).

Table I. Reaction of *N,N*-Dimethyl-*N*-[(trimethylsilyl)methyl](2-furylmethyl)-ammonium (3o) and -(2-thienylmethyl)ammonium Iodides (3s) with CsF

entry	3	Z	reaction time (h)	total yield (%)	ratio[a] 5:6:7
1	o	O	0.5	36	91:0:9
2	o	O	24	67	90:0:10
3	o	O	48	83	90:0:10
4	s	S	0.5	85	92:0:8
5	s	S	24	85	84:8:8

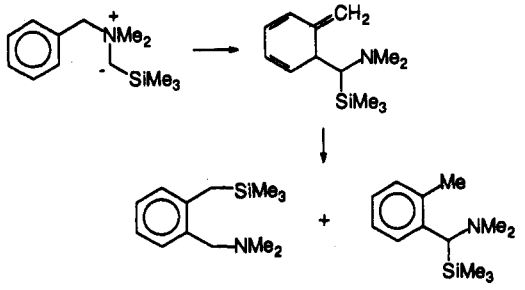
[a] Determined from the proton ratios of ^{1}H NMR.

Table II. Reaction of *N,N*-Dimethyl-*N*-[(trimethylsilyl)methyl](3-furylmethyl)-ammonium (10o) and -(3-thienylmethyl)ammonium Iodides (10s) with CsF

entry	10	Z	reaction time (h)	total yield (%)	ratio[a] 12:13
1	o	O	0.5	27	96:4
2	o	O	24	60	95:5
3	o	O	48	73	96:4
4	s	S	0.5	48	94:6
5	s	S	1	72	90:10
6	s	S	24	71	92:8

[a] Determined from the proton ratios of ^{1}H NMR.

Scheme IV



The reactions of **10o** and **10s** also gave selectively [2,3] sigmatropic rearrangement products **12o** and **12s**, respectively (Table II). The formation of the corresponding Sommelet–Hauser products and Stevens products were not observed in these reactions; however, a new type of by-product, 2-[(dimethylamino)methyl]-3-[(trimethylsilyl)-methyl]furan (**13o**) and a thiophene analogue **13s** were formed.

We reported previously that the ylide produced by treatment of *N,N*-dimethyl-*N*-[(trimethylsilyl)methyl]-benzylammonium iodide with *n*-butyllithium in THF initially rearranged to 6-(dimethylamino)[(trimethylsilyl)-methyl]-5-methylene-1,3-cyclohexadiene and then was subsequently converted to *N,N*-dimethyl-2-[(trimethylsilyl)methyl]benzylamine and *N,N*-dimethyl-2-methyl-α-(trimethylsilyl)benzylamine (Sommelet–Hauser product) (Scheme IV).[6]

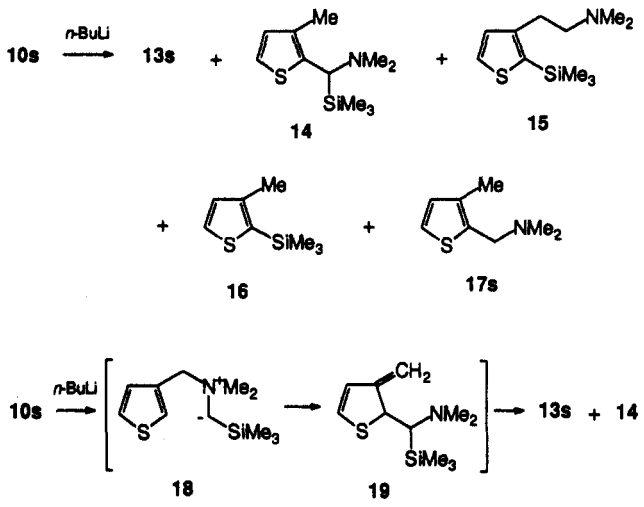
A similar treatment of **10s** with *n*-butyllithium gave **13s** (40%) and 3-methyl-2-[(dimethylamino)(trimethylsilyl)-methyl]thiophene (**14**, 17%, Sommelet–Hauser product) accompanied by 3-[2-(dimethylamino)ethyl]-2-(trimethylsilyl)thiophene (**15**, 20%), 3-methyl-2-(trimethylsilyl)thiophene (**16**, 2%), and 2-[(dimethylamino)-methyl]-3-methylthiophene (**17s**, 8%) (Scheme V). Thus,

(4) For a review of desilylation of α-silyl onium salts, see: Vedejs, E.; West, F. G. *Chem. Rev.* **1986**, *86*, 941.

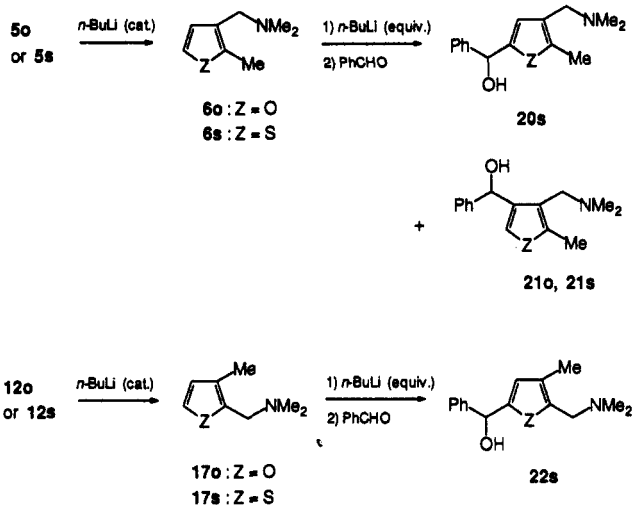
(5) Padwa, A.; Gasdaska, R. *Tetrahedron* **1988**, *44*, 4147. In the fluoride-induced desilylation of *S*-methyl-*S*-[(trimethylsilyl)methyl]-2-(furylmethyl)sulfonium trifluoromethanesulfonate, the presence of 2-methylene-3-[(methylthio)methyl]-2,3-dihydrofuran was detected in the crude product by NMR, but this compound readily isomerized to 2-methyl-3-[(methylthio)methyl]furan.

(6) Sato, Y.; Yagi, Y.; Kato, M. *J. Org. Chem.* **1980**, *45*, 613.

Scheme V



Scheme VI



a ylide **18** was converted to **13s** and **14** probably via a Sommelet–Hauser intermediate **19**. Because the aromatization of **19** to **14** accelerates in the presence of a strong base,[2d,e-g] the yield of **13s** may increase in a nonbasic media. In the reaction **10o** or **10s** with cesium fluoride, a small amount of **18** (or a furan analogue) may be generated from a reaction of **10o,s** and **11o,s**.

Compounds **5o**, **5s**, **12o**, and **12s** were stable oils in inactive gases and purified by distillation under reduced pressure without appreciable isomerization. The addition of a catalytic amount of *n*-butyllithium (0.05 mol %) to their ether solutions resulted in quick conversion to the corresponding Sommelet–Hauser rearrangement products **6o**, **6s**, **17o**, and **17s** in high yields, respectively.

Lithiation of *N,N*-dialkyl-2-methylbenzylamines with *n*-butyllithium occurs selectively on the 2-methyl groups to give 2-[(dialkylamino)methyl]benzyllithiums.[7] However, treatments of **6o** with *n*-butyllithium followed by quenching with benzaldehyde gave 3-[(dimethylamino)-methyl]-4-(α-hydroxybenzyl)-2-methylfuran (**21o**, 29%), and treatment of **6s** afforded 3-[(dimethylamino)-methyl]-5-(α-hydroxybenzyl)-2-methylthiophene (**20s**, 59%) and 4-(α-hydroxybenzyl)thiophene analogue (**21s**, 24%) (Scheme VI). When **17o** and **17s** were similarly treated, the former gave only a complex mixture but the latter afforded 2-[(dimethylamino)methyl]-5-(α-hydroxybenzyl)-3-methylthiophene (**22s**, 85%). Thus, the lithiation of **6o,s** and **17o,s** occurs on the aromatic rings but not on the *o*-methyl groups.

(7) Vaulx, R. L.; Jones, F. N.; Hauser, C. R. *J. Org. Chem.* **1964**, *29*, 1387.

Scheme VII

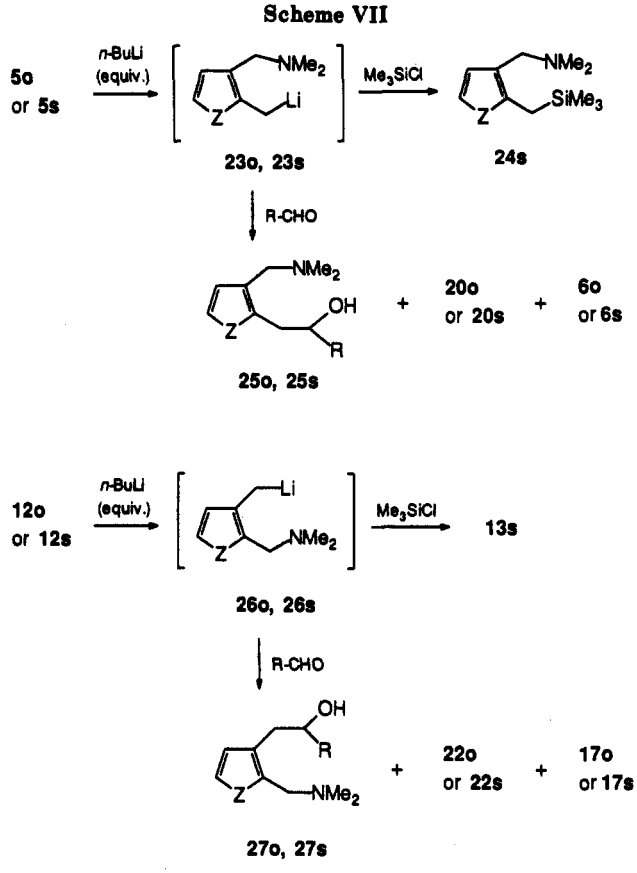


Table III. Treatment of 5o and 5s with 1 equiv of *n*-BuLi Followed by Aldehydes

entry	starting compd		R	solvent/ temp (°C)	total yield (%)	ratio[a] 25s:20s:6s
1	5s	a	Ph	Et_2O/−78	88	87:0:13
2	5s	a	Ph	Et_2O/−20	83	67:17:16
3	5s	a	Ph	THF/−78	87	84:6:10
4	5s	a	Ph	THF/−20	84	0:86:14
5	5s	b	C_8H_{17}	Et_2O/−78	88	73:0:27
6	5s	c	c-C_6H_{11}	Et_2O/−78	87	74:0:26
7	5s	d	*t*-Bu	Et_2O/−78	84	74:0:26 (25o:20o:6o)
8	5o	a	Ph	Et_2O/−78	28	0:0:100

[a] Determined from the proton ratios of ^1H NMR.

When **5s** or **12s** was added to an equimolar amount of *n*-butyllithium in ether and then the reaction was quenched with chlorotrimethylsilane, 3-[(dimethylamino)methyl]-2-[(trimethylsilyl)methyl]thiophene (**24s**, 79%) or **13s** (83%) was obtained (Scheme VII). Thus, **5s** and **12s** were successfully converted to thienylmethyllithium **23s** and **26s**, respectively. However, similar treatment of **5o** and **12o** gave complicated mixtures of many products, and we were unable to confirm the presence of the expected [(trimethylsilyl)methyl]furan derivatives.

Reaction of **23s** with benzaldehyde gave 3-[(dimethylamino)methyl]-2-(2-hydroxy-2-phenylethyl)thiophene (**25sa**) in high yield at −78 °C in ether or THF (entries 1, 3 in Table III). The formation of **20s** increased at −20 °C (entries 2, 4). A similar treatment of **12s** gave 2-[(dimethylamino)methyl]-3-(2-hydroxy-2-phenylethyl)-thiophene (**27sa**) (entries 1–4 in Table IV). The optimum

Table IV. Treatment of 12o and 12s with 1 equiv of *n*-BuLi Followed by Aldehydes

entry	starting compd		R	solvent/ temp (°C)	total yield (%)	ratio[a] 27s:22s:17s
1	12s	a	Ph	Et_2O/-78	86	38:0:62
2	12s	a	Ph	Et_2O/-20	86	85:0:15
3	12s	a	Ph	THF/-78	86	57:29:14
4	12s	a	Ph	THF/-20	83	18:59:23
5	12s	b	C_8H_{17}	Et_2O/-20	81	89:0:11
6	12s	c	c-C_6H_{11}	Et_2O/-20	88	85:0:15
7	12s	d	*t*-Bu	Et_2O/-20	89	75:0:25 (27o:22o:17o)
8	12o	a	Ph	Et_2O/-20	86	38:32:30

[a] Determined from the proton ratios of ^1H NMR.

result was obtained at −20 °C in ether (entry 2). Reaction of other aldehydes with **5s** was carried out at −78 °C in ether (entries 5–7 in Tables III) and with **12s** at −20 °C (entries 5–7 in Table IV) to give the corresponding 2- or 3-(2-hydroxyalkyl)thiophene derivatives **25sb–25sd** and **27sb–27sd**.

Treatment of **12o** with *n*-BuLi followed by quenching with benzaldehyde gave a mixture of **17o**, **22o**, and **27o** (entry 8 in Table IV), and treatment of **5o** afforded mixtures of **6o** and many unidentified products (entry 8 in Table III). The use of ethylmagnesium bromide instead of *n*-butyllithium in the reaction with **5s** or **12s** gave no corresponding thienylmethylmagnesium bromides.

Experimental Section

All reactions were carried out in N_2. HMPA was dried by distillation under reduced pressure from sodium prior to use. Ether and THF were distilled from Na benzophenone ketyl. CsF was dried over P_2O_5 at 170 °C under reduced pressure. ^1H NMR spectra were recorded at 100, 270, or 400 MHz. All melting points and boiling points are uncorrected. Butyllithium, 15% in hexane, was purchased from Kanto Chemical Co. Ltd. Tokyo.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-2-furanamide (2o).** A mixture of 2-furoyl chloride (**1o**, 10.2 g, 77.9 mmol) and *N*-methyl(trimethylsilyl)methylamine (9.0 g, 76.7 mmol) in 10% NaOH (100 mL) was stirred at room temperature for 1 h. The mixture was poured into water (150 mL) and extracted with EtOAc. The extract was dried ($MgSO_4$) and concentrated under reduced pressure. Distillation of the residue gave **2o** (14.9 g, 92%) (mixture of *s*-*Z* and *s*-*E* isomers (77:23):[8] bp 115–116 °C (0.4 mmHg); IR (film) 1620, 843, 743 cm^{-1}; ^1H NMR ($CDCl_3$, −50 °C) *s*-*Z* δ 0.14 (s, 9 H), 3.14 (s, 2 H), 3.33 (s, 3 H), 6.52 (dd, *J* = 1.7, 3.3 Hz, 1 H), 6.97 (dd, *J* = 0.7, 3.3 Hz, 1 H), 7.55 (dd, *J* = 0.7, 1.7 Hz, 1 H); *s*-*E* δ 0.10 (s, 9 H), 3.11 (s, 2 H), 3.33 (s, 3 H), 6.52 (dd, *J* = 0.7, 3.3 Hz, 1 H), 7.08 (dd, *J* = 0.7, 3.3 Hz, 1 H), 7.52 (dd, *J* = 0.7, 1.7 Hz, 1 H). Anal. Calcd for $C_{10}H_{17}NO_2Si$: C, 56.83; H, 8.11; N, 6.63. Found: C, 56.71; H, 8.35; N, 6.64.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-2-thiophenecarboxamide (2s).** In a manner similar to that described above, a mixture of 2-thiophenecarbonyl chloride (**1s**, 13.7 g, 93.6 mmol) and *N*-methyl(trimethylsilyl)methylamine (10.8 g, 92.1 mmol) in 10% NaOH (100 mL) was treated to give **2s** (20.1 g, 96%): bp 105–107 °C (0.4 mmHg); IR (film) 1620, 850, 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.12 (s, 9 H), 3.12 (s, 2 H), 3.22 (s, 3 H), 7.04 (dd, *J* = 4, 5 Hz, 1 H), 7.32 (dd, *J* = 4, 2 Hz, 1 H), 7.42 (dd, *J* = 5, 2 Hz, 1 H). Anal. Calcd for $C_{10}H_{17}NOSSi$: C, 52.82; H, 7.54; N, 6.16. Found: C, 52.71; H, 7.55; N, 5.94.

***N*,*N*-Dimethyl-*N*-[(trimethylsilyl)methyl](2-furylmethyl)ammonium Iodide (3o).** A mixture of **2o** (14.9 g, 70.5 mmol) and $LiAlH_4$ (6 g, 158 mmol) in ether (200 mL) was heated at reflux for 0.5 h. The reaction was quenched with saturated sodium potassium tartrate and extracted with ether. The ether layer was extracted with 5% H_2SO_4 and water. The combined aqueous extract was made alkaline with 20% NaOH and extracted with ether. The ethereal extract was dried ($MgSO_4$), concentrated, and distilled to give *N*-methyl-*N*-[(trimethylsilyl)methyl](2-furylmethyl)amine (13.1 g, 94%): bp 83–84 °C (10 mmHg); ^1H NMR ($CDCl_3$) δ 0.06 (s, 9 H), 1.91 (s, 2 H), 2.25 (s, 3 H), 3.49 (s, 2 H), 6.17 (dd, *J* = 0.7, 3.3 Hz, 1 H), 6.31 (dd, *J* = 2.0, 3.3 Hz, 1 H), 7.37 (dd, *J* = 0.7, 2.0 Hz, 1 H). Anal. Calcd for $C_{10}H_{19}NOSi$: C, 60.86; H, 9.70; N, 7.10. Found: C, 60.88; H, 9.75; N, 7.18.

N-Methyl-*N*-[(trimethylsilyl)methyl](2-furylmethyl)amine (13.1 g, 66.5 mmol) and MeI (55 g, 390 mmol) in MeCN (100 mL) was heated at 50 °C for 0.5 h. The solvent was evaporated, and the residue was recrystallized from a mixture of EtOAc and MeOH to give **3o** (22.1 g, 98%): mp 188–190 °C; ^1H NMR ($CDCl_3$) δ 0.35 (s, 9 H), 3.38 (s, 8 H), 5.08 (s, 2 H), 6.50 (dd, *J* = 1.8, 3.3 Hz, 1 H), 7.08 (dd, *J* = 0.7, 3.3 Hz, 1 H), 7.55 (dd, *J* = 0.7, 1.8 Hz, 1 H). Anal. Calcd for $C_{11}H_{22}INOSi$: C, 38.94; H, 6.54; N, 4.13. Found: C, 38.66; H, 6.50; N, 3.74.

***N*,*N*-Dimethyl-*N*-[(trimethylsilyl)methyl](2-thienylmethyl)ammonium Iodide (3s).** In a manner similar to that described for **3o**, a mixture of **2s** (13 g, 59 mmol) and $LiAlH_4$ (5 g, 132 mmol) in Et_2O (200 mL) was treated to give *N*-methyl-*N*-[(trimethylsilyl)methyl](2-thienylmethyl)amine (12 g, 93%): bp 59–60 °C (2 mmHg); ^1H NMR ($CDCl_3$) δ 0.07 (s, 9 H), 1.43 (s, 2 H), 2.25 (s, 3 H), 3.65 (s, 2 H), 6.8–7.0 (m, 2 H), 7.20 (dd, *J* = 2.0, 5.0 Hz, 1 H). Anal. Calcd for $C_{10}H_{19}NSSi$: C, 56.28; H, 8.97; N, 6.56. Found: C, 56.43; H, 9.25; N, 6.49.

A solution of *N*-methyl-*N*-[(trimethylsilyl)methyl](2-thienylmethyl)amine (17.3 g, 81.1 mmol) and MeI (69.1 g, 487 mmol) in MeCN (100 mL) was heated and worked up to give **3s** (28.2 g, 98%): mp 165–166 °C (EtOAc/MeOH); ^1H NMR ($CDCl_3$) δ 0.35 (s, 9 H), 3.38 (s, 6 H), 3.40 (s, 2 H), 5.28 (s, 2 H), 7.15 (dd, *J* = 3.7, 5.1 Hz, 1 H), 7.52 (dd, *J* = 1.1, 5.1 Hz, 1 H), 7.72 (dd, *J* = 1.1, 3.7 Hz, 1 H). Anal. Calcd for $C_{11}H_{22}INSSi$: C, 37.18; H, 6.24; N, 3.94. Found: C, 36.84; H, 6.37; N, 3.63.

Reaction of 3o or 3s with Cesium Fluoride. In a 30-mL flask equipped with a magnetic stirrer and a septum was placed **3o** (680 mg, 2.0 mmol) or **3s** (712 mg, 2.0 mmol) and CsF (1.52 g, 10 mmol). The flask was dried under reduced pressure and was flushed with N_2. HMPA (10 mL) was added to the flask with a syringe and the mixture was stirred at room temperature for the time listed in Table I. The mixture was poured into 1% $NaHCO_3$ and extracted with Et_2O. The ethereal extract was washed with 1% $NaHCO_3$. The ether layer was dried ($MgSO_4$), filtered, and concentrated.

The residue from **3o** was distilled at bp 80 °C (50 mmHg, oven temperature Kugelrohr distillation apparatus) to give a mixture of 3-[(dimethylamino)methyl]-2-methylene-2,3-dihydrofuran (**5o**) and 2-[2-(dimethylamino)ethyl]furan[10] (**7o**). The residue from **3s** was distilled at bp 75 °C (3 mmHg, Kugelrohr) to give a mixture of 3-[(dimethylamino)methyl]-2-methylene-2,3-dihydrothiophene (**5s**), 3-[(dimethylamino)methyl]-2-methylthiophene[11] (**6s**) and 2-[2-(dimethylamino)ethyl]thiophene[12] (**7s**). The mixture was separated on a HPLC column (Merck LiChrosorb NH_2, ether/hexane). The ratio was determined from the proton ratios of ^1H NMR of the distillates (see Table I).

5o: ^1H NMR ($CDCl_3$) δ 2.27 (s, 6 H), 2.35 (dd, *J* = 5.8, 12.0 Hz, 1 H), 2.45 (dd, *J* = 9.1, 12.0 Hz, 1 H), 3.58–3.65 (m, 1 H), 4.19 (dd, *J* = 2.3, 2.3 Hz, 1 H), 4.57 (dd, *J* = 2.3, 3.5 Hz, 1 H), 5.03 (bs, 1 H), 6.46 (dd, *J* = 2.3, 2.3 Hz, 1 H); UV λ_{max}^{hexane} 240 nm (ε 6900). Anal. Calcd for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 68.91; H, 9.61; N, 10.08.

5s: ^1H NMR ($CDCl_3$) δ 2.29 (s, 6 H), 2.35 (dd, *J* = 5.9, 12.1 Hz, 1 H), 2.55 (dd, *J* = 9.5, 12.1 Hz, 1 H), 3.76–3.82 (m, 1 H), 5.18–5.21 (m, 2 H), 5.73 (ddd, *J* = 0.9, 2.7, 6.4 Hz, 1 H), 6.20 (ddd, *J* = 1.7, 1.7, 6.4 Hz, 1 H); UV λ_{max}^{hexane} 237 nm (ε 3500), 264 (ε 2600), 280 nm (ε 2900). Anal. Calcd for $C_8H_{13}NS$: C, 61.89; H, 8.44; N, 9.02. Found: C, 61.53; H, 8.60, N, 8.87.

6s: ^1H NMR ($CDCl_3$) δ 2.22 (s, 6 H), 2.41 (s, 3 H), 3.34 (s, 2

(8) The geometry was assigned according to Caccamese's report,[9] and the ratio was determined from the integrated values of ^1H NMR of the mixture.

(9) Caccamese, S.; Montaudo, G.; Recca, A. *Tetrahedron* **1974**, *30*, 4129.

(10) Skvortsov, N. M.; Buntyakova, N. A.; Stolyarchuk, A. A.; Ivanova, N. I. *Pharm. Chem. J.* **1972**, *6*, 501.

(11) Judd, D. B.; Bardshaw, J.; Clitherow, J. W.; Price, B. J.; Mackinnon, J. W. M.; Hayes, R.; Carey, L. Eur. Pat. Appl. Ep 27,744, 1981.

(12) McFarland, J. W.; Howeres, H. L. Jr. *J. Med. Chem.* **1969**, *12*, 1079.

H), 6.92 (d, J = 5.1 Hz, 1 H), 7.01 (d, J = 5.1 Hz, 1 H).

7o: ^{1}H NMR ($CDCl_3$) δ 2.27 (s, 6 H), 2.35 (dd, J = 5.8, 12.0 Hz, 1 H), 2.45 (dd, J = 9.1, 12.0 Hz, 1 H), 3.58–3.65 (m, 1 H), 4.19 (dd, J = 2.3, 2.3 Hz, 1 H), 4.57 (dd, J = 2.3, 3.5 Hz, 1 H), 5.03 (bs, 1 H), 6.46 (dd, J = 2.3, 2.3 Hz, 1 H).

7s: ^{1}H NMR ($CDCl_3$) δ 2.31 (s, 6 H), 2.61 (t, J = 7.5 Hz, 2 H), 3.01 (t, J = 7.5 Hz, 2 H), 6.82 (dd, J = 1.1, 3.5 Hz, 1 H), 6.91 (dd, J = 3.5, 5.1 Hz, 1 H), 7.13 (dd, J = 1.1, 5.1 Hz, 1 H).

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-3-furanamide (9o).** In a manner similar to that described for **2o**, a mixture of 3-furoyl chloride[13] (**8o**, 9.9 g, 75.8 mmol) and *N*-methyl(trimethylsilyl)-methylamine (9.0 g, 76.7 mmol) in 10% NaOH (100 mL) was treated to give **9o** (15.0 g, 93%) (mixture of *s*-*Z* and *s*-*E* isomers (81:19)):[8] bp 115–116 °C (3 mmHg); IR (film) 1620, 843, 743 cm^{-1}; ^{1}H NMR ($CDCl_3$, −50 °C) *s*-*Z* δ 0.14 (s, 9 H), 3.12 (s, 2 H), 3.21 (s, 3 H), 6.66 (dd, J = 0.7, 1.7 Hz, 1 H), 7.47 (dd, J = 1.7, 1.7 Hz, 1 H), 7.75 (dd, J = 0.7, 0.7 Hz, 1 H); *s*-*E* δ 0.10 (s, 9 H), 3.09 (s, 3 H), 3.11 (s, 2 H), 6.58 (dd, J = 0.7, 1.7 Hz, 1 H), 7.47 (dd, J = 1.7, 1.7 Hz, 1 H), 7.72 (dd, J = 0.7, 0.7 Hz, 1 H). Anal. Calcd for $C_{10}H_{17}NO_2Si$: C, 56.83; H, 8.11; N, 6.63. Found: C, 57.08; H, 8.12; N, 6.39.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-3-thiophenecarboxamide (9s).** In a manner similar to that described for **2o**, a mixture of 3-thiophenecarbonyl bromide[14] and *N*-methyl(trimethylsilyl)methylamine (16.9 g, 144 mmol) in 10% NaOH (100 mL) was treated to give **9s** (21.9 g, 66%): bp 135 °C (1 mmHg); IR (film) 1620, 840, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.14 (s, 9 H), 3.08 (s, 5 H), 7.19 (dd, J = 1.3, 4.6 Hz, 1 H), 7.31 (dd, J = 3.0, 4.6 Hz, 1 H), 7.46 (dd, J = 1.3, 3.0 Hz, 1 H). Anal. Calcd for $C_{10}H_{17}NOSSi$: C, 52.82; H, 7.54; N, 6.16. Found: C, 52.90; H, 7.73; N, 5.95.

***N*,*N*-Dimethyl-*N*-[(trimethylsilyl)methyl](3-furylmethyl)ammonium Iodide (10o).** In a manner similar to that described for **3o**, a mixture of **9o** (14.9 g, 70.5 mmol) and $LiAlH_4$ (6 g, 158 mmol) in ether (200 mL) was treated to give *N*-methyl-*N*-[(trimethylsilyl)methyl](3-furyimethyl)amine (12.7 g, 92%): bp 84–85 °C (10 mmHg); ^{1}H NMR ($CDCl_3$) δ 0.06 (s, 9 H), 1.87 (s, 2 H), 2.21 (s, 3 H), 3.31 (s, 2 H), 6.37 (bd, J = 1.6 Hz, 1 H), 7.31 (dd, J = 1.0, 1.6 Hz, 1 H), 7.37 (dd, J = 1.6, 1.6 Hz, 1 H). Anal. Calcd for $C_{10}H_{19}NOSi$: C, 60.86; H, 9.70; N, 7.10. Found: C, 60.59; H, 9.90; N, 7.07.

A solution of *N*-methyl-*N*-[(trimethylsilyl)methyl](3-furylmethyl)amine (12.7 g, 64.5 mmol) and MeI (46 g, 324 mmol) in MeCN (100 mL) was treated and recrystallized to give **10o** (20.9 g, 95%): mp 138–140 °C (EtOAc/MeOH); ^{1}H NMR ($CDCl_3$) δ 0.32 (s, 9 H), 3.32 (s, 6 H), 3.35 (s, 2 H), 5.02 (s, 2 H), 6.71 (dd, J = 0.7, 1.8 Hz, 1 H), 7.51 (dd, J = 1.8, 1.8 Hz, 1 H), 8.00 (bs, 1 H). Anal. Calcd for $C_{11}H_{22}INOSi$: C, 38.94; H, 6.54; N, 4.13. Found: C, 38.84; H, 6.71; N, 3.90.

***N*,*N*-Dimethyl-*N*-[(trimethylsilyl)methyl](3-thienylmethyl)ammonium Iodide (10s).** In a manner similar to that described for **3o**, a mixture of **9s** (8.1 g, 36 mmol) and $LiAlH_4$ (5 g, 132 mmol) in Et_2O (100 mL) was treated to give *N*-methyl-*N*-[(trimethylsilyl)methyl](3-thienylmethyl)amine (7.06 g, 93%): bp 75–76 °C (4 mmHg); ^{1}H NMR ($CDCl_3$) δ 0.06 (s, 9 H), 1.89 (s, 2 H), 2.20 (s, 3 H), 3.46 (s, 2 H), 7.04 (dd, J = 1.0, 4.6 Hz, 1 H), 7.08 (dd, J = 1.0, 2.6 Hz, 1 H), 7.25 (dd, J = 2.6, 4.6 Hz, 1 H). Anal. Calcd for $C_{10}H_{19}NSSi$: C, 56.28; H, 8.97; N, 6.56. Found: C, 56.10; H, 9.17; N, 6.26.

Treatment of *N*-methyl-*N*-[(trimethylsilyl)methyl](3-thienylmethyl)amine (18.5 g, 86.5 mmol) and MeI (87.8 g, 618 mmol) in MeCN (100 mL) gave **10s** (30.0 g, 98%): mp 188–190 °C (EtOAc/MeOH); ^{1}H NMR ($CDCl_3$) δ 0.32 (s, 9 H), 3.31 (s, 6 H), 3.36 (s, 2 H), 5.14 (s, 2 H), 7.37 (dd, J = 1.3, 5.0 Hz, 1 H), 7.42 (dd, J = 2.9, 5.0 Hz, 1 H), 7.97 (dd, J = 1.3, 2.9 Hz, 1 H). Anal. Calcd for $C_{11}H_{22}INSSi$: C, 37.18; H, 6.24; N, 3.94. Found: C, 37.08; H, 6.49; N, 3.59.

Reaction of 10o or 10s with Cesium Fluoride. In a manner similar to that described for the reaction of **3o** or **3s** with CsF, a mixture of **10o** (680 mg, 2.0 mmol) or **10s** (712 mg, 2.0 mmol) and CsF (1.52 g, 10 mmol) in HMPA (10 mL) was treated at room temperature for the time listed in Table II.

(13) Ingham, C. F.; Massy-Westropp, A. R.; Reynolds, G. D. *Aust. J. Chem.* **1974**, *27*, 1477.
(14) Cheung, Y.-F. *Tetrahedron Lett.* **1979**, *40*, 3809.

The residue from **10o** was distilled at bp 90 °C (3 mmHg, Kugelrohr) to give a mixture of 2-[(dimethylamino)methyl]-3-methylene-2,3-dihydrofuran (**12o**) and 2-[(dimethylamino)-methyl]-3-[(trimethylsilyl)methyl]furan (**13o**). The residue from **10s** was distilled at bp 75–85 °C (3 mmHg, Kugelrohr) to give a mixture of 2-[(dimethylamino)methyl]-3-methylene-2,3-dihydrothiophene (**12s**) and 2-[(dimethylamino)methyl]-3-[(trimethylsilyl)methyl]thiophene (**13s**). Their samples were isolated on a HPLC column (Merck LiChrosorb NH_2 with a mixture of ether and hexane). The yields and ratios are summarized in Table II.

12o: ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 6 H), 2.37 (dd, J = 2.8, 13.4 Hz, 1 H), 2.66 (dd, J = 9.7, 13.4 Hz, 1 H), 4.46–4.47 (m, 1 H), 4.75 (d, J = 3.1 Hz, 1 H), 5.07 (dddd, J = 2.8, 2.8, 2.8, 9.7 Hz, 1 H), 5.57 (d, J = 2.8 Hz, 1 H), 6.75 (bs, 1 H). UV λ_{max}^{hexane} 263 nm (ϵ 10600). Anal. Calcd for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 68.67; H, 9.07; N, 9.98.

13o: ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 1.75 (s, 2 H), 2.25 (s, 6 H), 3.37 (s, 2 H), 6.09 (d, J = 2.0 Hz, 1 H), 7.27 (d, J = 2.0 Hz, 1 H); mass spectrum m/z 211.1395 (M$^+$, calcd for $C_{11}H_{21}NOSi$, 211.1392), 211 (M$^+$, 45), 167 (78), 166 (46), 75 (33), 73 (100).

12s: ^{1}H NMR ($CDCl_3$) δ 2.31 (s, 6 H), 2.46 (dd, J = 3.9, 12.5 Hz, 1 H), 2.71 (dd, J = 11.3, 12.5 Hz, 1 H), 4.38 (m, 1 H), 4.86 (m, 1 H), 5.09 (d, J = 2.8 Hz, 1 H), 6.01 (d, J = 5.9 Hz, 1 H), 6.52 (dd, J = 0.7, 5.9 Hz, 1 H); UV λ_{max}^{hexane} 301 nm (ϵ 11000). Anal. Calcd for $C_8H_{13}NS$: C, 61.89; H, 8.44; N, 9.02. Found: C, 61.82; H, 8.72; N, 8.86.

13s: ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 2.05 (s, 2 H), 2.28 (s, 6 H), 3.46 (s, 2 H), 6.65 (d, J = 5.1 Hz, 1 H), 7.11 (d, J = 5.1 Hz, 1 H). Anal. Calcd for $C_{11}H_{21}NSSi$: C, 58.09; H, 9.31; N, 6.16. Found: C, 58.36; H, 9.29; N, 6.03.

Treatment of 10s with *n*-BuLi. A suspension of **10s** (396 mg, 1.1 mmol) in THF (10 mL) was treated with *n*-BuLi (0.8 mL, 1.3 mmol) according to the reported method[6] to give a mixture (203 mg) of **13s** (40%), 2-[(dimethylamino)(trimethylsilyl)-methyl]-3-methylthiophene (**14**, 17%), 3-[2-(dimethylamino)-ethyl]-2-(trimethylsilyl)thiophene (**15**, 20%), 3-methyl-2-(trimethylsilyl)thiophene (**16**, 2%), and 2-[(dimethylamino)-methyl]-3-methylthiophene (**17s**, 8%). The mixture was separated on a silica gel column (hexane/EtOAc), and the ratios were determined from the integrated values of GLC (5% PEG-20M column) of the mixture.

14: ^{1}H NMR ($CDCl_3$) δ 0.05 (s, 9 H), 2.12 (s, 3 H), 2.30 (s, 6 H), 3.17 (s, 1 H), 6.74 (d, J = 5.0 Hz, 1 H), 7.07 (d, J = 5.0 Hz, 1 H); mass spectrum m/z 227.1145 (M$^+$, calcd for $C_{11}H_{21}NSSi$, 227.1164), 227 (M$^+$, 8), 212 (5), 154 (100).

15: ^{1}H NMR ($CDCl_3$) δ 0.35 (s, 9 H), 2.37 (s, 6 H), 2.56–2.61 (m, 2 H), 2.89–2.94 (m, 2 H), 7.05 (d, J = 4.7 Hz, 1 H), 7.47 (d, J = 4.7 Hz, 1 H); mass spectrum m/z 227.1171 (M$^+$, calcd for $C_{11}H_{21}NSSi$, 227.1164), 227 (M$^+$, 3), 212 (18), 102 (31), 73 (29), 58 (100).

16: ^{1}H NMR ($CDCl_3$) δ 0.34 (s, 9 H), 2.36 (s, 3 H), 6.99 (d, J = 4.6 Hz, 1 H), 7.44 (d, J = 4.6 Hz, 1 H); mass spectrum m/z 170.0577 (M$^+$, calcd for $C_8H_{14}SSi$, 170.0585), 170 (M$^+$, 28), 155 (100).

17s: bp 75 °C (3 mmHg, Kugelrohr) [lit.[3] bp 91–92 °C (20 mmHg)].

Treatment of 5o, 5s, 12o or 12s with a Catalytic Amount of *n*-BuLi. To a solution of freshly distilled **5o** (150 mg, 1.08 mmol), **5s** (227 mg, 1.50 mmol), **12o** (145 mg, 1.04 mmol), or **12s** (227 mg, 1.50 mmol) in ether (10 mL) was added *n*-BuLi (0.05 mol equiv) at −20 °C with stirring for 0.5 h. Water (10 mL) was added, and the mixture was extracted with ether. The extract was dried ($MgSO_4$), concentrated, and distilled to give 3-[(dimethylamino)methyl]-2-methylfuran (**6o**, 129 mg, 86%), 3-[(dimethylamino)methyl]-2-methylthiophene (**6s**, 119 mg, 88%), 2-[(dimethylamino)methyl]-3-methylfuran (**17o**, 126 mg, 87%), and 2-[(dimethylamino)methyl]-3-methylthiophene (**17s**, 119 mg, 88%).

6o: bp 105 °C (140 mmHg, Kugelrohr) [lit.[3] bp 59–60 °C (20 mmHg)]; ^{1}H NMR ($CDCl_3$) δ 2.21 (s, 6 H), 2.25 (s, 3 H), 3.20 (s, 2 H), 6.30 (d, J = 1.7 Hz, 1 H), 7.24 (d, J = 1.7 Hz, 1 H).

17o: bp 120 °C (200 mmHg, Kugelrohr) [lit.[3] bp 62 °C (20 mmHg)].

Treatment of 6o or 17o with Equimolar *n*-BuLi Followed by Benzaldehyde. *n*-BuLi (0.7 mL, 1.2 mmol) was added to a

solution of **6o** or **17o** (139 mg, 1.0 mmol) in ether (10 mL) at 0 °C. After 1 h of stirring, benzaldehyde (127 mg, 1.2 mmol) was added, and stirring was continued for 0.5 h. The reaction was quenched with 10% NaOH (20 mL), and the mixture was extracted with ether. The ether layer was extracted with 10% HCl and water. The combined aqueous extract was made alkaline with 20% NaOH and extracted with ether. The ethereal extract was dried ($MgSO_4$) and concentrated.

Distillation of the residue from **6o** gave 3-[(dimethylamino)-methyl]-4-(α-hydroxybenzyl)-2-methylfuran (**21o**, 49 mg, 29%) and **6o** (31 mg, 33%).

21o: bp 100 °C (0.3 mmHg, Kugelrohr); mp 96–98 °C; IR (KBr) 3120, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.20 (s, 9 H), 2.86, 2.98 (AB-q, J = 12.9 Hz, 2 H), 5.63 (s, 1 H), 7.04 (s, 1 H), 7.22–7.27 (m, 1 H), 7.30–7.34 (m, 2 H), 7.42–7.44 (m, 2 H). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.45; H, 7.81; N, 5.34.

Distillation of the residue from **17o** recovered only unconsumed **17o** (18 mg, 17%).

Treatment of 6s or 17s with Equimolar *n*-BuLi Followed by Benzaldehyde. *n*-BuLi (0.8 mL, 1.3 mmol) was added to **6s** or **17s** (165 mg, 1.1 mmol) in ether (10 mL) and treated in a manner similar to that described above. The residue from **6s** was distilled under reduced pressure to give a mixture (238 mg) of 3-[(dimethylamino)methyl]-5-(α-hydroxybenzyl)-2-methylthiophene (**20s**, 59%) and 3-[(dimethylamino)methyl]-4-(α-hydroxybenzyl)-2-methylthiophene (**21s**, 24%). The components of the mixture were isolated on a silica gel column (hexane/EtOAc), and the ratios were determined from the integrated values of ^1H NMR.

20s: bp 130 °C (0.4 mmHg, Kugelrohr); IR (film) 3400, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.88 (bs, 1 H), 2.20 (s, 6 H), 2.34 (s, 3 H), 3.25 (s, 2 H), 5.94 (s, 1 H), 6.77 (s, 1 H), 7.28–7.45 (m, 5 H). In the ^1H NMR spectrum, 5.3% NOE enhancement was observed at 6.77 ppm (4-H) but not at 3.25 ppm (CH_2N) under irradiation at 5.94 ppm (CHPh). Anal. Calcd for $C_{15}H_{19}NOS$: C, 68.93; H, 7.33; N, 5.36. Found: C, 68.72; H, 7.48; N, 5.36.

21s: mp 78–80 °C; IR (Nujol) 3100, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.59 (bs, 1 H), 2.20 (s, 6 H), 2.37 (s, 3 H), 2.95, 3.15 (AB-q, J = 13.0 Hz, 2 H), 5.73 (s, 1 H), 6.75 (s, 1 H), 7.25–7.43 (m, 5 H). In the ^1H NMR spectrum, 3.0% NOE enhancement at 3.15 ppm (CH_2N) and 5.8% NOE at 6.75 ppm (5-H) were observed under irradiation at 5.73 ppm (CHPh). Anal. Calcd for $C_{15}H_{19}NOS$: C, 68.93; H, 7.33; N, 5.36. Found: C, 69.07; H, 7.57; N, 5.13.

The residue from **17s** was distilled to give 2-[(dimethylamino)methyl]-5-(α-hydroxybenzyl)-3-methylthiophene (**22s**, 244 mg, 85%): bp 140 °C (0.6 mmHg, Kugelrohr); IR (film) 3400, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.57 (bs, 1 H), 2.10 (s, 3 H), 2.23 (s, 6 H), 3.46 (s, 2 H), 5.93 (s, 1 H), 6.57 (s, 1 H), 7.26–7.46 (m, 5 H). In the ^1H NMR spectrum, 8.0% NOE enhancement at 2.10 ppm (3-Me) and 5.0% NOE at 5.93 ppm (CHPh) were observed under irradiation at 6.57 ppm (4-H). Anal. Calcd for $C_{15}H_{19}NOS$: C, 68.93; H, 7.33; N, 5.36. Found: C, 68.89; H, 7.55; N, 5.38.

Preparation of 3-[(Dimethylamino)methyl]-2-[(trimethylsilyl)methyl]thiophene (24s) and 2-[(Dimethylamino)methyl]-3-[(trimethylsilyl)methyl]thiophene (13s). A solution of freshly distilled **5s** or **12s** (155 mg, 1.0 mmol) in ether (8 mL) was slowly added to a solution of *n*-BuLi (0.7 mL, 1.2 mmol) in ether (3 mL) at −78 °C, and then chlorotrimethylsilane (130 mg, 1.2 mmol) was added. After 0.5 h of stirring, 10% NaOH was added and the mixture was extracted with ether. The extract was dried ($MgSO_4$) and concentrated.

Distillation of the residue from **5s** gave a mixture (193 mg) of 3-[(dimethylamino)methyl]-2-[(trimethylsilyl)methyl]thiophene[15] (**24s**, 79%) and **6s** (12%). The ratio was determined from the integrated values of ^1H NMR.

24s: ^1H NMR ($CDCl_3$) δ 0.04 (s, 9 H), 2.21 (s, 6 H), 2.28 (s, 2 H), 3.25 (s, 2 H), 6.90 (d, J = 5.3 Hz, 1 H), 6.92 (d, J = 5.3 Hz, 1 H).

Distillation of the residue from **12s** gave a mixture (195 mg) of **13s** (83%) and **17s** (8%).

Preparation of 3-[(Dimethylamino)methyl]-2-(2-hydroxyalkyl)thiophenes 25s or 2-[(Dimethylamino)-methyl]-3-(2-hydroxyalkyl)thiophenes 27s. General Procedure. In a manner similar to that described above, freshly distilled **5s** or **12s** (155 mg, 1.0 mmol) in ether or THF (8 mL) was slowly added to a solution of *n*-BuLi (0.7 mL, 1.2 mmol) in ether or THF (3 mL) at the temperature listed in Table III or IV, and the mixture was stirred for 0.5 h. Benzaldehyde, 1-nonanal, cyclohexanecarboxaldehyde, or trimethylacetaldehyde (1.2 mmol) was added to the mixture, and stirring was continued for 0.5 h at the listed temperature. The reaction was quenched with 10% NaOH and extracted with ether. The ether layer was extracted with 10% HCl and water. The combined aqueous extract was made alkaline with 20% NaOH and extracted with ether. The ethereal extract was dried ($MgSO_4$), concentrated, and distilled to give a mixture of **25s**, **20s**, and **6s**, or a mixture of **27s**, **22s**, and **17s**. The yields and ratios are summarized in Tables III and IV.

3-[(Dimethylamino)methyl]-2-(2-hydroxy-2-phenylethyl)thiophene (25sa): bp 150 °C (0.7 mmHg, Kugelrohr); IR (film) 3100, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.32 (s, 6 H), 3.09 (dd, J = 8.8, 15.1 Hz, 1 H), 3.21, 3.49 (AB-q, J = 12.5 Hz, 2 H), 3.23 (dd, J = 2.7, 15.1 Hz, 1 H), 4.84 (dd, J = 2.7, 8.8 Hz, 1 H), 6.82 (d, J = 5.1 Hz, 1 H), 7.07 (d, J = 5.1 Hz, 1 H), 7.32–7.40 (m, 5 H). Anal. Calcd for $C_{15}H_{19}NOS$: C, 68.93; H, 7.33; N, 5.36. Found: C, 69.06; H, 7.57; N, 5.24.

3-[(Dimethylamino)methyl]-2-(2-hydroxydecyl)thiophene (25sb): bp 145 °C (0.7 mmHg, Kugelrohr); IR (film) 3100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.2–1.3 (m, 12 H), 1.4–1.5 (m, 2 H), 2.23 (s, 6 H), 2.82 (dd, J = 8.2, 15.0 Hz, 1 H), 3.00 (dd, J = 2.2, 15.0 Hz, 1 H), 3.14, 3.44 (AB-q, J = 12.3 Hz, 2 H), 3.62–3.67 (m, 1 H), 6.80 (d, J = 5.1 Hz, 1 H), 7.07 (d, J = 5.1 Hz, 1 H). Anal. Calcd for $C_{17}H_{31}NOS$: C, 68.63; H, 10.50; N, 4.71. Found: C, 68.53; H, 10.66; N, 4.47.

3-[(Dimethylamino)methyl]-2-(2-cyclohexyl-2-hydroxyethyl)thiophene (25sc): bp 120 °C (0.7 mmHg, Kugelrohr); IR (film) 3100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0–1.9 (m, 11 H), 2.23 (s, 6 H), 2.84 (dd, J = 8.9, 14.8 Hz, 1 H), 2.96 (dd, J = 2.6, 14.8 Hz, 1 H), 3.09, 3.51 (AB-q, J = 12.5 Hz, 2 H), 3.39–3.45 (m, 1 H), 6.79 (d, J = 5.3 Hz, 1 H), 7.07 (d, J = 5.3 Hz, 1 H). Anal. Calcd for $C_{15}H_{25}NOS$: C, 67.37; H, 9.42; N, 5.24. Found: C, 67.54; H, 9.44; N, 5.01.

3-[(Dimethylamino)methyl]-2-(3,3-dimethyl-2-hydroxybutyl)thiophene (25sd): bp 125 °C (2 mmHg, Kugelrohr); IR (film) 3100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (s, 9 H), 2.24 (s, 6 H), 2.70 (dd, J = 10.3, 14.5 Hz, 1 H), 3.01, 3.57 (AB-q, J = 12.5 Hz, 2 H), 3.02 (dd, J = 2.2, 14.5 Hz, 1 H), 3.27 (dd, J = 2.2, 10.3 Hz, 1 H), 6.78 (d, J = 5.1 Hz, 1 H), 7.07 (d, J = 5.1 Hz, 1 H). Anal. Calcd for $C_{13}H_{23}NOS$: C, 64.68; H, 9.60; N, 5.80. Found: C, 64.57; H, 9.69; N, 5.54.

2-[(Dimethylamino)methyl]-3-(2-hydroxy-2-phenylethyl)thiophene (27sa): bp 165 °C (0.8 mmHg, Kugelrohr); IR (film) 3100, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.36 (s, 6 H), 2.88 (dd, J = 8.6, 14.3 Hz, 1 H), 3.07 (dd, J = 2.9, 14.3 Hz, 1 H), 3.32, 3.64 (AB-q, J = 13.6 Hz, 2 H), 4.85 (dd, J = 2.9, 8.6 Hz, 1 H), 6.76 (d, J = 5.1 Hz, 1 H), 7.07 (d, J = 5.1 Hz, 1 H), 7.33–7.37 (m, 5 H). Anal. Calcd for $C_{15}H_{19}NOS$: C, 68.93; H, 7.33; N, 5.36. Found: C, 68.65; H, 7.42; N, 5.24.

2-[(Dimethylamino)methyl]-3-(2-hydroxydecyl)thiophene (27sb): bp 160 °C (1.0 mmHg, Kugelrohr); IR (film) 3200 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 1 H), 1.3–1.4 (m, 12 H), 1.4–1.5 (m, 2 H), 2.27 (s, 6 H), 2.61 (dd, J = 8.4, 14.1 Hz, 1 H), 2.84 (dd, J = 2.4, 14.1 Hz, 1 H), 3.25, 3.63 (AB-q, J = 13.4 Hz, 2 H), 3.63–3.68 (m, 1 H), 6.88 (d, J = 5.1 Hz, 1 H), 7.13 (d, J = 5.1 Hz, 1 H). Anal. Calcd for $C_{17}H_{31}NOS$: C, 68.63; H, 10.50; N, 4.71. Found: C, 68.79; H, 10.72; N, 4.53.

2-[(Dimethylamino)methyl]-3-(2-cyclohexyl-2-hydroxyethyl)thiophene (27sc): bp 160 °C (2.5 mmHg, Kugelrohr); IR (film) 3200 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.1–1.9 (m, 11 H), 2.28 (s, 6 H), 2.60 (dd, J = 9.6, 14.2 Hz, 1 H), 2.80 (dd, J = 2.3, 14.2 Hz, 1 H), 3.15, 3.73 (AB-q, J = 13.5 Hz, 2 H), 3.39–3.45 (m, 1 H), 6.89 (d, J = 5.3 Hz, 1 H), 7.13 (d, J = 5.3 Hz, 1 H). Anal. Calcd for $C_{15}H_{25}NOS$: C, 67.37; H, 9.42; N, 5.24. Found: C, 67.30; H, 9.55; N, 5.19.

2-[(Dimethylamino)methyl]-3-(3,3-dimethyl-2-hydroxybutyl)thiophene (27sd): bp 110 °C (2 mmHg, Kugelrohr); IR (film) 3200 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (s, 9 H), 2.28 (s, 6 H), 2.45 (dd, J = 10.6, 13.9 Hz, 1 H), 2.85 (dd, J = 2.2, 13.9 Hz, 1 H), 3.05, 3.81 (AB-q, J = 13.4 Hz, 2 H), 3.27 (dd, J = 2.2, 10.6 Hz,

(15) Leusen, A. M.; Berg, K. J. *Tetrahedron Lett.* **1988**, *29*, 2689.

1 H), 6.90 (d, J = 5.1 Hz, 1 H), 7.13 (d, J = 5.1 Hz, 1 H). Anal. Calcd for $C_{13}H_{23}NOS$: C, 64.68; H, 9.60; N, 5.80. Found: C, 64.86; H, 9.85; N, 5.66.

Treatment of 12o with Equimolar *n*-BuLi Followed by Benzaldehyde. In a manner similar to that described above, **12o** (128 mg, 0.9 mmol) was treated with *n*-BuLi (0.66 mL, 1.1 mmol) and then benzaldehyde (117 mg, 1.1 mmol) in ether (11 mL) to give a mixture of 2-[(dimethylamino)methyl]-5-(α-hydroxybenzyl)-3-methylfuran (**22o**), 2-[(dimethylamino)methyl]-3-(2-hydroxy-2-phenylethyl)furan (**27o**), and **17o**. Compound **22o** and **27o** were separated on a silica gel column (EtOAc/MeOH). The result is shown in Table IV.

22o: bp 100 °C (0.2 mmHg, Kugelrohr); IR (film) 3330, 1602 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.93 (s, 3 H), 2.20 (s, 6 H), 3.36, 3.39 (AB-q, J = 13.7 Hz, 2 H), 5.78 (s, 1 H), 5.81 (s, 1 H), 7.31–7.37 (m, 3 H), 7.42–7.45 (m, 2 H). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.62; H, 7.83; N, 5.61.

27o: bp 100 °C (0.2 mmHg, Kugelrohr); IR (film) 3350, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.30 (s, 6 H), 2.78 (dd, J = 8.1, 14.7 Hz, 1 H), 2.90 (dd, J = 2.9, 14.7 Hz, 1 H), 3.37, 3.48 (AB-q, J = 13.7 Hz, 2 H), 7.22 (d, J = 1.7 Hz, 1 H), 7.21–7.25 (m, 5 H). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.35; H, 7.98; N, 5.61.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research (No. 04671301) provided by the Ministry of Education, Science and Culture, Japan.

Preparation of New Classes of Aliphatic, Allylic, and Benzylic Zinc and Copper Reagents by the Insertion of Zinc Dust into Organic Halides, Phosphates, and Sulfonates

Carole Jubert[1a] and Paul Knochel*[,1b]

The Willard H. Dow Laboratories, Department of Chemistry, The University of Michigan, Ann Arbor, Michigan 48109

Received June 15, 1992

The insertion of zinc dust into primary alkyl chlorides, bromides, phosphates, and sulfonates in a polar solvent (DMPU, DMA) and in the presence of a catalytic amount of LiI (0.2 equiv) provides new organozinc reagents of the type RZnX (X = Cl, Br, OSO_2R, $OP(O)(OR)_2$) in excellent yields. After the transmetalation to the corresponding copper reagent RCu(CN)ZnX using CuCN·2LiCl, the addition of electrophiles, such as Michael acceptors, affords the desired adducts. Similarly, various new allylic and benzylic zinc reagents were prepared without the formation of any Wurtz-coupling side product and reacted with various electrophiles.

Polyfunctional organozinc and copper reagents are important intermediates in organic synthesis.[2] They react efficiently with various classes of electrophiles[2,3] allowing the construction of highly functionalized molecules without having to use extensively protection–deprotection or functional group interconversion methodologies. They are conveniently prepared by the insertion of zinc dust into alkyl iodides in THF between 25 and 50 °C.[2,3] The less expensive alkyl bromides or chlorides are usually not reactive enough to insert zinc dust and require the use of highly activated zinc metal.[4] We wish to report herein reaction conditions allowing the insertion of zinc dust (Aldrich) to primary alkyl chlorides, bromides, sulfonates, or phosphates **1** (eq 1).

$$\underset{\textbf{1: X = Cl, Br, OMs, OTs, OP(O)(OPh)}_2}{\text{R–X}} \xrightarrow[\text{DMA or DMPU, 40–80 °C, 2–12 h}]{\text{Zn, MI (0.2 equiv), MBr (1.0 equiv)}} \underset{\textbf{2}}{\text{RZnX}} \qquad (1)$$

Thus, the treatment of the primary alkyl bromide with zinc dust in a polar solvent such as *N*,*N*-dimethylacetamide (DMA)[5] or *N*,*N*-dimethylpropyleneurea (DMPU)[6] in the presence of a catalytic amount of an alkali iodide (0.2 equiv) furnishes the corresponding alkylzinc bromide in excellent yields (>85%). Remarkably, the reaction can be extended to the preparation of new alkylzinc chlorides, tosylates, mesylates and diphenylphosphates **2** (RZnX; X

(1) (a) Centre de Recherches, Roussel-Uclaf, 102, 111 route de Noisy, F-92230 Romainville, France. (b) Present address: Philipps-Universität Marburg, Fachbereich Chemie, Hans-Meerwein-Strasse, D-3550 Marburg, Germany.

(2) (a) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390. (b) Knoess, H. P.; Furlong, M. T.; Rozema, M. J.; Knochel, P. *J. Org. Chem.* **1991**, *56*, 5974. (c) Knochel, P.; Rozema, M. J.; Tucker, C. E.; Retherford, C.; Furlong, M.; AchyuthaRao, S. *Pure Appl. Chem.* **1992**, *64*, 361. (d) Tsujiyama, H.; Ono, N.; Yoshino, T.; Okamoto, S.; Sato, F. *Tetrahedron Lett.* **1990**, *31*, 4481. (e) Sörenson, H.; Greene, A. E. *Tetrahedron Lett.* **1990**, *31*, 7597. (f) Tanaka, T.; Bannai, K.; Hazato, A.; Koga, M. Kurozumi, S.; Kato, Y. *Tetrahedron* **1991**, *47*, 1861.

(3) (a) Yeh, M. C. P.; Knochel, P.; Santa, L. E. *Tetrahedron Lett.* **1988**, *29*, 3887. (b) Yeh, M. C. P.; Knochel, P.; Butler, W. M.; Berk, S. C. *Tetrahedron Lett.* **1988**, *29*, 6693. (c) Yeh, M. C. P.; Knochel, P. *Tetrahedron Lett.* **1989**, *30*, 4799. (d) Retherford, C.; Yeh, M. C. P.; Schipor, I.; Chen, H.-G.; Knochel, P. *J. Org. Chem.* **1989**, *54*, 5200. (e) Chen, H.-G.; Gage, J. L.; Barrett, S. D.; Knochel, P. *Tetrahedron Lett.* **1990**, *31*, 1829. (f) Retherford, C.; Knochel, P. *Tetrahedron Lett.* **1991**, *32*, 441. (g) AchyuthaRao, S.; Knochel, P. *J. Am. Chem. Soc.* **1991**, *113*, 5735.

(4) (a) Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1991**, *56*, 1445. (b) The insertion of highly activated copper metal to alkyl chlorides and bromides is also possible: Ebert, G. W.; Rieke, R. D. *J. Org. Chem.* **1984**, *49*, 5280. (c) Rieke, R. D.; Wehmeyer, R. M.; Wu, T.-C.; Ebert, G. W. *Tetrahedron* **1989**, *45*, 443. (d) Ebert, G. W.; Rieke, R. D. *J. Org. Chem.* **1988**, *53*, 4482. (e) Wu, T.-C.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1987**, *52*, 5056. (f) Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1987**, *52*, 5056.

(5) Tamaru, Y.; Ochiai, H.; Nakamura, T.; Tusbaki, K.; Yoshida, Z. *Tetrahedron Lett.* **1985**, *26*, 5559.

(6) (a) Mukhopadhyay, T.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 385. (b) Seebach D.; Beck, A. K.; Mukhopadhyay, T.; Thomas, E. *Helv. Chim. Acta* **1982**, *65*, 1101. (c) Bengtsson, M.; Liljefors, T. *Synthesis* **1988**, 250.

0022-3263/92/1957-5425$03.00/0