

Rearrangement of (Polymethoxybenzyl)ammonium *N*-MethylidesYasuhiro Maeda,<sup>†</sup> Naohiro Shirai,<sup>†</sup> Yoshiro Sato,<sup>\*,†</sup> and Hiroshi Tatewaki<sup>‡</sup>

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Reaction of *N,N*-dimethyl-*N*-[(trimethylsilyl)methyl](polymethoxy-substituted benzyl)ammonium iodides **1a–e** with cesium fluoride gave polymethoxy-substituted 5-[(dimethylamino)methyl]-6-methylene-1,3-cyclohexadienes **3** and **5** ([2,3] sigmatropic rearrangement products). However, these were quickly hydrolyzed to polymethoxytoluenes **8** during the aqueous workup. The pathway of the hydrolysis of **3** and **5** is discussed.

## Introduction

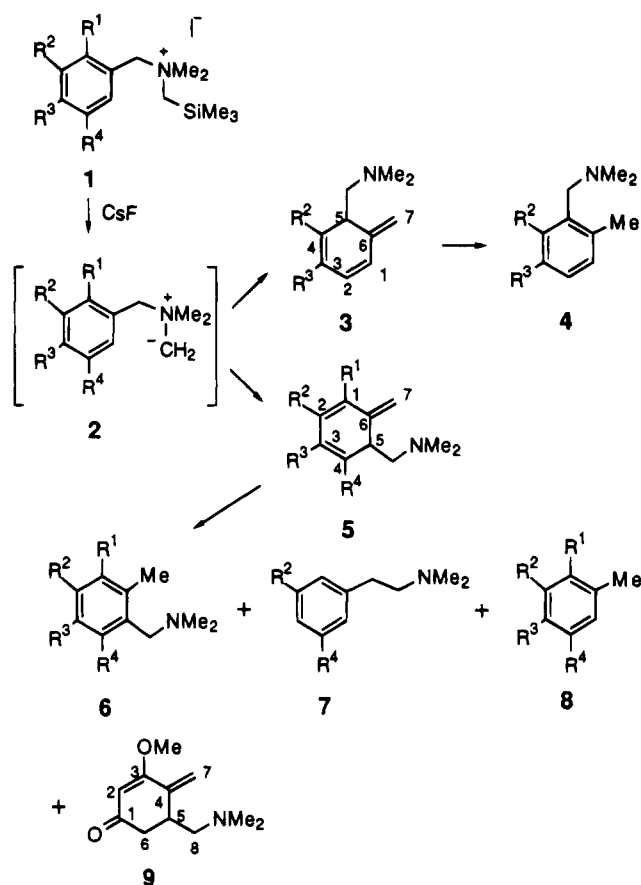
Sommelet–Hauser rearrangement of benzylammonium ylides provides a useful method for selective syntheses of 2-methylbenzylamines.<sup>1</sup> This rearrangement begins with a [2,3] sigmatropic shift giving *isotoluene* intermediates (e.g., **3** and **5** in Scheme 1) and ends with a [1,3] hydrogen shift to give 2-methylbenzylamines (e.g., **4** and **6**).<sup>2</sup> We previously reported from the studies of benzylammonium ylides in non basic media that stability of the *isotoluene* intermediates progressively increases with increase of the electron-donating effect of the substituents on the conjugated triene bonds.<sup>3</sup> For example, 5-[(dimethylamino)methyl]-3-methoxy-6-methylene-1,3-cyclohexadiene (**5f**, R<sup>1</sup> = R<sup>2</sup> = R<sup>4</sup> = H, R<sup>3</sup> = MeO) was stable at room temperature, and its conversion to *N,N*-dimethyl-5-methoxy-2-methylbenzylamine occurred with the aid of a strong base.<sup>3c</sup> Polymethoxy-substituted *isotoluenes* might be more stable than monomethoxy *isotoluenes*. We examined the chemical behavior of *N,N*-dimethyl(polymethoxybenzyl)ammonium *N*-methylides.

## Results and Discussion

Five *N,N*-dimethyl-*N*-[(trimethylsilyl)methyl](polymethoxybenzyl)ammonium iodides **1a–e** were prepared from reaction of the corresponding polymethoxybenzoyl chlorides with *N*-methyl[(trimethylsilyl)methyl]amine followed by reduction with lithium aluminum hydride and quaternization with iodomethane.

Reaction of **1** with cesium fluoride was carried out in HMPA at room temperature and quenched with 1% aqueous sodium bicarbonate<sup>4</sup> after 0.5 h. However, no characteristic signals or absorption indicating the presence of the expected *isotoluene* compounds, except for **1b**, were observed in <sup>1</sup>H NMR and UV spectra of the ethereal

Scheme 1

<sup>†</sup> Faculty of Pharmaceutical Sciences.<sup>‡</sup> Computation Center.<sup>®</sup> Abstract published in *Advance ACS Abstracts*, November 1, 1994.(1) Brasen, W. R.; Hauser, C. R. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. IV, p 585.(2) (a) Pine, S. H. *Org. React. (N.Y.)* **1970**, *18*, 403. (b) Markó, I. E. *Comprehensive Organic Synthesis*, Trost, B. M.; Fleming, I., Ed.; Pergamon Press: Oxford, 1991; Vol. 3, p 913.(3) (a) Shirai, N.; Sumiya, F.; Sato, Y.; Hori, M. *J. Org. Chem.* **1989**, *54*, 836. (b) Okazaki, S.; Shirai, N.; Sato, Y. *J. Org. Chem.* **1990**, *55*, 334. (c) Shirai, N.; Watanabe, Y.; Sato, Y. *J. Org. Chem.* **1990**, *55*, 2767. (d) Kitano, T.; Shirai, N.; Sato, Y. *Synthesis* **1991**, 996. (e) Kitano, T.; Shirai, N.; Sato, Y. *Chem. Pharm. Bull.* **1992**, *40*, 768. (f) Kitano, T.; Shirai, N.; Motoi, M.; Sato, Y. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2851. (g) Tanaka, T.; Shirai, N.; Sugimori, J.; Sato, Y. *J. Org. Chem.* **1992**, *57*, 5034.

(4) Typical workup conditions.

extracts. Distillation of the extracts gave *N,N*-dimethyl-3,4-dimethoxy-2-methylbenzylamine (**6a**, Sommelet–Hauser rearrangement product) and 2,3-dimethoxytoluene (**8a**) from 2,3-dimethoxybenzylammonium salt (**1a**) (entry 1 in Table 1), and *N,N*-dimethyl-2-(3,5-dimethoxyphenyl)ethylamine (**7d**, Stevens rearrangement product) and 3,5-dimethoxytoluene (**8d**) from 3,5-dimethoxybenzylammonium salt (**1d**) (entry 13). The reaction of 3,4-dimethoxybenzylammonium (**1c**) and 3,4,5-trimethoxybenzylammonium salts (**1e**) gave only the corresponding toluene derivatives (**8c** and **8e**) (entries 9, 18). Although the presence of expected 5-[(dimethylamino)methyl]-1,3-dimethoxy-6-methylene-1,3-cyclohexadiene (**5b**) and *N,N*-dimethyl-3,5-dimethoxy-2-methylbenzylamine (**6b**) was confirmed in an ethereal extract of the reaction mixture of 2,4-dimethoxybenzylammonium salt (**1b**) by <sup>1</sup>H NMR spectrum, the yields of both

Table 1. Reaction of *N,N*-Dimethyl(polymethoxybenzyl)ammonium Iodides (1) with CsF

entry	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	reaction		total yield (%)	product ratio <sup>a</sup>					
					condition <sup>b</sup>	time (h)		5	4	6	7	8	
1	1a	OMe	OMe	H	H	A	0.5	68	0		25	0	75
2						A	3	66	0		100	0	0
3						A	48	62	0		100	0	0
4						B	0.5	75	0		100	0	0
5	1b	OMe	H	OMe	H	A	0.5–48	<sup>c</sup> trace	trace		trace	0	0
6						B	0.5	70	29		71	0	0
7						B	3	71	8		92	0	0
8						C	0.5	82	56		44	0	0
9	1c	H	OMe	OMe	H	A	0.5	51	0		0	0	100
10						A	3	62	0	10	0	0	90
11						A	48	56	0	41	15	0	44
12						B	0.5	46	0	44	48	0	8
13	1d	H	OMe	H	OMe	A	0.5	76	0		0	5	95 <sup>d</sup>
14						A	3	67	0		12	5	83 <sup>d</sup>
15						A	48	61	0		97	3	0
16						B	0.5	69	0		97	3	0
17						C	0.5	64	0		94	2	4
18	1e	H	OMe	OMe	OMe	A	0.5	71	0		0	0	100
19						A	3	67	0		8	0	92
20						A	48	61	0		77	0	23
21						B	0.5	68	0		97	0	3
22						C	0.5	76	0		75	0	25

<sup>a</sup> Ratios of the products determined by integration of the <sup>1</sup>H signals in the 500 MHz NMR spectra are considered accurate to within  $\pm 5\%$ . <sup>b</sup> Condition A: The reaction mixture was quenched with 1% NaHCO<sub>3</sub>; B: The reaction was carried out in the presence of 5 mol equivalents of DBU; C: The reaction mixture was quenched with 12 M NaOH. <sup>c</sup> 5-[(Dimethylamino)methyl]-3-methoxy-4-methylene-2-cyclohexen-1-one (**9**, 34%) was yielded. <sup>d</sup> Determined from the integrated values of GLC.

were very low, and 5-[(dimethylamino)methyl]-3-methoxy-4-methylene-2-cyclohexen-1-one (**9**, 34%) was isolated from the aqueous layer after the ether-extraction (entry 5). Thus, neither the expected isotoluene derivatives (**3**, **5**) nor Sommelet–Hauser products (**4**, **6**) were obtained as the main products from **1**, contrary to the result of (monomethoxybenzyl)ammonium *N*-methylides.<sup>3c</sup>

When the reactions were quenched after 3 h or 48 h at room temperature, amounts of **8a,c–e** were decreased and the corresponding amounts of the Sommelet–Hauser products **4c** and **6a,c–e** had been formed (compare entries 1–3, 9–11, 13–15, and 18–20). No change was observed in the reaction of **1b**. These results suggest that **3** and/or **5** initially exist in the reaction mixtures and slowly isomerize to **4** and/or **6**. During the aqueous workup, **3** and/or **5** may be decomposed to **8**, dimethylamine, and formaldehyde.

If this mechanism is correct, when the reaction is carried out in the presence of a strong base (e.g., DBU) or worked up with a strong aqueous base, the products will change to **4** and/or **6** by a base promoted [1,3] hydrogen shift from **3** and/or **5**.<sup>3e</sup> Indeed, the reaction in the presence of DBU (5 mol equivalents) formed **4** and/or **6**, instead of **8** (condition B in Table 1). Quenching with 12 M sodium hydroxide after 0.5 h brought about similar changes in the products (condition C). Thus, the hydrolysis of **3** and **5** was suppressed in concentrated sodium hydroxide and the aromatization was accelerated, though **5b** remained under these conditions (entries 6–8). Reaction of **3** and **5** with hydrogen oxide predominated in 1% sodium bicarbonate.

We were interested in the difference in chemical behavior between monomethoxy- and polymethoxy-substituted isotoluenes in water. We calculated atomic charges and frontier electron densities of **3** and **5** by Gaussian 92 (STO-3G).<sup>5</sup> The atomic charges for **3c–5f** are listed in Table 2. One may find that the negative charges of N and C-7 are quite large for all the molecules and the same is true of C-2 of **5b**, C-3 of **5d**, and C-1 of **5c–e**. At a large distance from the target molecule (**3c**,

Table 2. Atomic Charges in **3** and **5**. Calculation Was Made with Gaussian 92 (STO-3G)

	atomic charges							
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	N
<b>3c</b>	-0.07	-0.07	0.05	0.13	-0.05	0.00	-0.14	-0.28
<b>5a</b>	0.11	0.06	-0.08	-0.06	-0.05	0.00	-0.13	-0.29
<b>5b</b>	0.14	-0.13	0.11	-0.10	-0.05	0.00	-0.12	-0.29
<b>5c</b>	-0.11	0.12	0.10	-0.06	-0.05	0.01	-0.14	-0.29
<b>5d</b>	-0.13	0.14	-0.13	0.15	-0.05	0.01	-0.14	-0.29
<b>5e</b>	-0.12	0.12	0.05	0.13	-0.05	0.01	-0.15	-0.28
<b>5f</b>	-0.05	-0.08	0.11	-0.08	-0.05	0.01	-0.13	-0.29

<sup>a</sup> 5-[(Dimethylamino)methyl]-3-methoxy-6-methylene-1,3-cyclohexadiene (R<sup>1</sup> = R<sup>2</sup> = R<sup>4</sup> = H, R<sup>3</sup> = MeO).

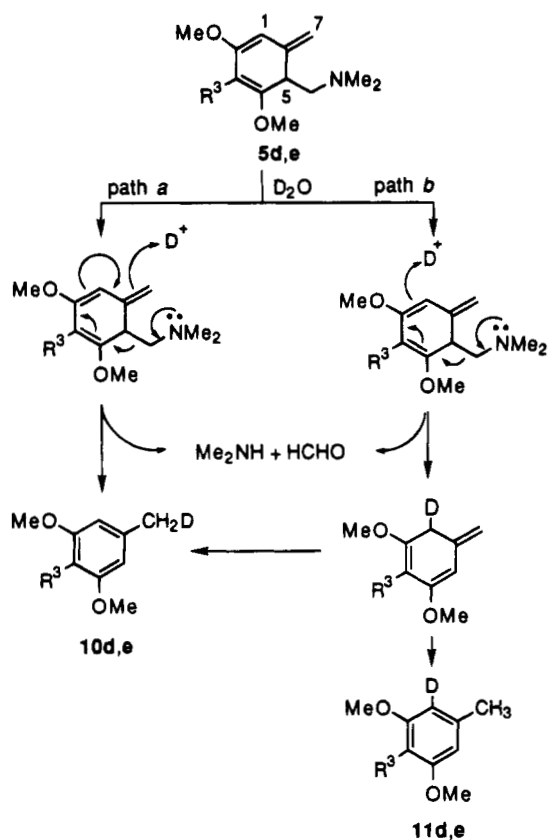
Table 3. Frontier Electron Densities of the HOMO in **3** and **5**. Calculation Was Made with Gaussian 92 (STO-3G)

	frontier electron densities							
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	N
<b>3c</b>	0.32	0.18	0.36	0.33	0.02	0.07	0.28	0.06
<b>5a</b>	0.33	0.44	0.12	0.31	0.02	0.07	0.27	0.04
<b>5b</b>	0.22	0.28	0.21	0.57	0.03	0.05	0.20	0.07
<b>5c</b>	0.42	0.24	0.12	0.27	0.03	0.13	0.45	0.05
<b>5d</b>	0.51	0.23	0.20	0.19	0.02	0.11	0.41	0.04
<b>5e</b>	0.45	0.19	0.24	0.24	0.02	0.09	0.37	0.04
<b>5f</b>	0.26	0.20	0.22	0.48	0.04	0.09	0.31	0.09

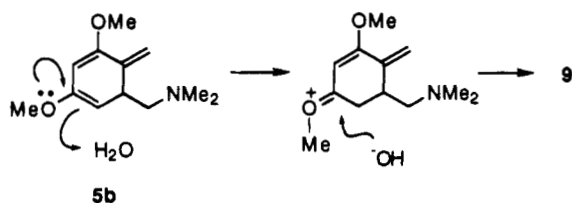
**5a–e**), the proton feels the attracting field generated by negative charges and moves toward the atoms with the negative charges. Table 3 shows the frontier electron densities derived from the HOMO. Near the target molecule, the proton interacts with the frontier electrons in the HOMO. Thus the reactions may proceed at the atoms where the atomic negative charges and frontier electron densities are large. C-7 atoms of **3c**, **5a**, and **5c–e** in Table 3 satisfy what we discussed above. (Compound **5b** where the atomic charges and the frontier

(5) Revision A, Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. Gaussian, Inc., Pittsburgh PA, 1992.

Scheme 2



Scheme 3



electron densities are large will be discussed later). We therefore expect that the protonation occurs at these atoms. In light of the conditions discussed above, competitive reaction may occur at C-1 atom of **5c–e**.

Here we see the competitive reaction at C-7 and C-1. When the reactions of **5d, e** were quenched with deuterium oxide after 0.5 h, the  $^1\text{H}$  NMR and GC-mass spectral analyses of the products indicated the presence of two monodeuterated toluenes **10d, e** and **11d, e** in the ratio of **10d:11d** = 96:4, **10e:11e** = 86:14, respectively. We see in this reaction that C-7 is far more active than C-1. Other higher occupied orbitals as well as the HOMO are sometimes important in chemical reactions. Although we have not shown precise information of other orbital densities and their energies,<sup>6</sup> it indicates that the charge cloud spanned by HOMO and other orbitals around C-7 is more reactive than that around C-1, confirming the path a (**10d, e**) in Scheme 2 is the main route in this reaction.

Dienone **9** may be formed as a result of an electrophilic attack of a proton at the C-4 of **5b** (Scheme 3). In fact, the MO calculation of **5b** showed that the value of the frontier electron density of the HOMO at the C-4 is the largest and the atomic charge is largely negative.

However, from the calculated values of monomethoxy (**5f**) and polymethoxy-substituted isotoluenes (**3c** and **5a–e**), we were able to see no suggestion of difference in their chemical behavior in water.

## Experimental Section

HMPA was dried by distillation from sodium under reduced pressure before use. CsF was dried over  $\text{P}_2\text{O}_5$  at  $180^\circ\text{C}$  under reduced pressure. HMBC (heteronuclear multiple bond correlation spectroscopy) experiment was performed at 125 MHz on a JEOL JNM-A500 spectrometer at  $25^\circ\text{C}$ . Mass spectra were obtained using EI ionization. Aluminum oxide (Merck Aluminumoxide 90, 70–230 mesh), and silica gel (BW-200, Fuji-Davison) were used for column chromatography. All melting points and boiling points are uncorrected.

***N,N*-Dimethyl-*N*-[(trimethylsilyl)methyl]-*N*-(methoxybenzyl)ammonium Iodides 1a–e: General Procedure.** A solution of 2,3-dimethoxybenzoyl, 2,4-dimethoxybenzoyl, 3,4-dimethoxybenzoyl, 3,5-dimethoxybenzoyl, or 3,4,5-trimethoxybenzoyl chloride (83 mmol) and *N*-methyl[(trimethylsilyl)methyl]amine (11 g, 94 mmol) in benzene (80 mL) was stirred with 10% NaOH (80 mL) at room temperature for 0.5 h. The mixture was poured into water (200 mL) and extracted with ether ( $4 \times 100$  mL). The extract was washed with water (400 mL), dried ( $\text{MgSO}_4$ ), and concentrated under reduced pressure. The residue was distilled to give *N*-methyl-*N*-[(trimethylsilyl)methyl]polymethoxybenzamides.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-2,3-dimethoxybenzamide:** yield 91%; bp  $143\text{--}144^\circ\text{C}$  (0.5 mmHg); IR (film) 2950, 1640, 1480, 1270, 1060, and  $860\text{ cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  0.18 (s, 9 H), 2.83 (s, 3 H), 2.85–3.37 (br s, 2 H), 3.85 (s, 3 H), 3.88 (s, 3 H), 6.79 (dd, 1 H,  $J = 1.2, 7.9$  Hz), 6.91 (dd, 1 H,  $J = 1.2, 7.9$  Hz), and 7.07 (t, 1 H,  $J = 7.9$  Hz). Anal. Calcd for  $\text{C}_{14}\text{H}_{23}\text{NO}_3\text{Si}$ : C, 59.75; H, 8.24; N, 4.98. Found: C, 59.56; H, 8.24; N, 5.27.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-2,4-dimethoxybenzamide:** yield 78%; bp  $173^\circ\text{C}$  (0.7 mmHg); IR (film) 2950, 1610, 1210, and  $850\text{ cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  0.15 (s, 9 H), 2.84 (s, 3 H), 2.87–3.62 (br s, 2 H), 3.80 (s, 3 H), 3.81 (s, 3 H), 6.44 (d, 1 H,  $J = 2.2$  Hz), 6.49 (dd, 1 H,  $J = 2.2, 8.2$  Hz), and 7.16 (d, 1 H,  $J = 8.2$  Hz). Anal. Calcd for  $\text{C}_{14}\text{H}_{23}\text{NO}_3\text{Si}$ : C, 59.75; H, 8.24; N, 4.98. Found: C, 59.62; H, 8.19; N, 4.77.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-3,4-dimethoxybenzamide:** yield 89%; bp  $174\text{--}175^\circ\text{C}$  (1 mmHg); mp  $49\text{--}50^\circ\text{C}$ ; IR (KBr) 2950, 1600, 1580, 1260, 1240, 1140, 1020, 860, and  $840\text{ cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  0.15 (br s, 9 H), 3.03 (br s, 3 H), 3.07 (br s, 2 H), 3.89 (s, 3 H), 3.90 (s, 3 H), and 6.84–6.97 (m, 3 H). Anal. Calcd for  $\text{C}_{14}\text{H}_{23}\text{NO}_3\text{Si}$ : C, 59.75; H, 8.24; N, 4.98. Found: C, 59.64; H, 8.21; N, 4.92.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-3,5-dimethoxybenzamide:** yield 87%; bp  $165\text{--}166^\circ\text{C}$  (0.7 mmHg); IR (film) 1600, 1200, 1150, and  $850\text{ cm}^{-1}$ . The presence of (*E*) and (*Z*) isomers was observed on the  $^1\text{H}$  NMR spectrum but the assignment was difficult (isomer-1/isomer-2, 79:21) ( $\text{CDCl}_3$ , 270 MHz)  $\delta$  3.06 (br s, 2 H), 3.78 (s, 6 H), 6.44–6.48 (m, 3 H), isomer-1: 0.14 (br s, 9 H), 2.95 (br s, 3 H); isomer-2: 0.04 (br s, 9 H), 2.89 (br s, 3 H). Anal. Calcd for  $\text{C}_{14}\text{H}_{23}\text{NO}_3\text{Si}$ : C, 59.75; H, 8.24; N, 4.98. Found: C, 59.63; H, 8.15; N, 4.96.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-3,4,5-trimethoxybenzamide:** yield 79%; bp  $178^\circ\text{C}$  (0.9 mmHg); mp  $50\text{--}51^\circ\text{C}$ ; IR (KBr) 1620, 1580, 1420, 1130, 1000, and  $850\text{ cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  0.16 (br s, 9 H), 3.01 (br s, 3 H), 3.08 (br s, 2 H), 3.85 (s, 3 H), 3.87 (s, 6 H), and 6.59 (s, 2 H). Anal. Calcd for  $\text{C}_{15}\text{H}_{25}\text{NO}_4\text{Si}$ : C, 57.85; H, 8.09; N, 4.50. Found: C, 57.73; H, 8.02; N, 4.49.

A mixture of *N*-methyl-*N*-[(trimethylsilyl)methyl]polymethoxybenzamides (72 mmol) and  $\text{LiAlH}_4$  (4.2 g, 111 mmol) in ether (120 mL) was heated at reflux for 3 h. The reaction was quenched with saturated sodium potassium tartrate (400 mL) and extracted with ether ( $4 \times 100$  mL). The extract was dried ( $\text{MgSO}_4$ ), and concentrated under reduced pressure. The residue was distilled to give *N*-methyl-*N*-[(trimethylsilyl)methyl]polymethoxybenzylamines.

(6) More information is reported in the supplementary material.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-2,3-dimethoxybenzylamine:** yield 89%; bp 123–125 °C (0.9 mmHg); IR (film) 2950, 1480, 1250, 1080, and 850 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 0.07 (s, 9 H), 1.96 (s, 2 H), 2.21 (s, 3 H), 3.50 (s, 2 H), 3.81 (s, 3 H), 3.86 (s, 3 H) 6.79–6.83 (m, 1 H), and 7.02 (d, 2 H, *J* = 5.5 Hz). Anal. Calcd for C<sub>14</sub>H<sub>25</sub>NO<sub>2</sub>Si: C, 62.87; H, 9.42; N, 5.24. Found: C, 62.57; H, 9.15; N, 5.30.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-2,4-dimethoxybenzylamine:** yield 91%; bp 124–125 °C (0.7 mmHg); IR (film) 2950, 1610, 1210, and 850 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 270 MHz) δ 0.09 (s, 9 H), 1.96 (s, 2 H), 2.18 (s, 3H), 3.40 (s, 2 H), 3.79 (s, 3 H), 3.80 (s, 3 H), 6.44–6.47 (m, 2 H), and 7.23 (d, 1 H, *J* = 8.6 Hz). Anal. Calcd for C<sub>14</sub>H<sub>25</sub>NO<sub>2</sub>Si: C, 62.87; H, 9.42; N, 5.24. Found: C, 62.65; H, 9.47; N, 4.98.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-3,4-dimethoxybenzylamine:** yield 89%; bp 127–130 °C (1 mmHg); IR (film) 2950, 1510, 1260, 1040, and 850 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 0.06 (s, 9 H), 1.87 (s, 2 H), 2.20 (s, 3 H), 3.37 (s, 2 H), 3.87 (s, 3 H), 3.88 (s, 6 H), 6.80 (s, 2 H), and 6.91 (s, 1 H). Anal. Calcd for C<sub>14</sub>H<sub>25</sub>NO<sub>2</sub>Si: C, 62.87; H, 9.42; N, 5.24. Found: C, 62.83; H, 9.32; N, 5.20.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-3,5-dimethoxybenzylamine:** yield 84%; bp 123–124 °C (0.8 mmHg); IR (film) 1600, 1200, 1150, and 850 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 0.07 (s, 9 H), 1.89 (s, 2 H), 2.21 (s, 3 H), 3.37 (s, 2 H), 3.78 (s, 6 H), 6.34 (t, 1 H, *J* = 2.4 Hz), and 6.51 (d, 2 H, *J* = 2.4 Hz). Anal. Calcd for C<sub>14</sub>H<sub>25</sub>NO<sub>2</sub>Si: C, 62.87; H, 9.42; N, 5.24. Found: C, 62.67; H, 9.29; N, 5.35.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]-3,4,5-trimethoxybenzylamine:** yield 75%; bp 137–140 °C (0.7 mmHg); IR (film) 1590, 1460, 1240, 1130, and 850 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 0.07 (s, 9 H), 1.89 (s, 2 H), 2.23 (s, 3 H), 3.37 (s, 2 H), 3.84 (s, 6 H), 3.86 (s, 3 H), and 6.57 (s, 2 H). Anal. Calcd for C<sub>15</sub>H<sub>27</sub>NO<sub>3</sub>Si: C, 60.57; H, 9.15; N, 4.71. Found: C, 60.31; H, 8.99; N, 4.74.

A solution of *N*-methyl-*N*-[(trimethylsilyl)methyl]poly-methoxybenzylamines (59 mmol) and iodomethane (32.6 g, 229 mmol) in MeCN (50 mL) was stirred at room temperature for 2 h. The solvent was removed, and the residue was recrystallized from acetone to give ammonium iodides (**1a–e**).

***N,N*-Dimethyl-*N*-[(trimethylsilyl)methyl]-2,3-dimethoxybenzylammonium iodide (**1a**):** yield 83%; mp 147–148 °C; IR (KBr) 3000, 1490, 1270, 1260, and 860 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 0.35 (s, 9 H), 3.26 (s, 6 H), 3.55 (s, 2 H), 3.91 (s, 3 H), 3.92 (s, 3 H), 4.93 (s, 2 H), 7.07 (dd, 1 H, *J* = 1.8, 8.0 Hz), 7.16 (t, 1 H, *J* = 8.0 Hz), and 7.40 (dd, 1 H, *J* = 1.8, 8.0 Hz). Anal. Calcd for C<sub>15</sub>H<sub>28</sub>NIO<sub>2</sub>Si: C, 44.01; H, 6.89; N, 3.42. Found: C, 43.73; H, 6.69; N, 3.10.

***N,N*-Dimethyl-*N*-[(trimethylsilyl)methyl]-2,4-dimethoxybenzylammonium iodide (**1b**):** yield 94%; mp 138–139 °C; IR (KBr) 2950, 1610, 1470, 1210, 1040, and 860 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 0.35 (s, 9 H), 3.23 (s, 6 H), 3.47 (s, 2 H), 3.85 (s, 3 H), 3.87 (s, 3 H), 4.77 (s, 2 H), 6.51 (d, 1 H, *J* = 2.4 Hz), 6.57 (dd, 1 H, *J* = 2.4, 8.6 Hz), and 7.68 (d, 1 H, *J* = 8.6 Hz). Anal. Calcd for C<sub>15</sub>H<sub>28</sub>NIO<sub>2</sub>Si: C, 44.01; H, 6.89; N, 3.42. Found: C, 44.04; H, 6.90; N, 3.18.

***N,N*-Dimethyl-*N*-[(trimethylsilyl)methyl]-3,4-dimethoxybenzylammonium iodide (**1c**):** yield 96%; mp 161–162 °C; IR (KBr) 3000, 1520, 1460, 1280, 1250, and 860 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 0.31 (s, 9 H), 3.29 (s, 6 H), 3.37 (s, 2 H), 3.90 (s, 3 H), 3.95 (s, 3 H), 5.05 (s, 2 H), 6.87 (d, 1 H, *J* = 8.3 Hz), 7.17 (dd, 1 H, *J* = 2.0, 8.3 Hz), and 7.44 (d, 1 H, *J* = 2.0 Hz). Anal. Calcd for C<sub>15</sub>H<sub>28</sub>NIO<sub>2</sub>Si: C, 44.01; H, 6.89; N, 3.42. Found: C, 43.91; H, 6.78; N, 3.06.

***N,N*-Dimethyl-*N*-[(trimethylsilyl)methyl]-3,5-dimethoxybenzylammonium iodide (**1d**):** yield 97%; mp 154–155 °C; IR (KBr) 1600, 1210, 1160, 860, and 840 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 270 MHz) δ 0.32 (s, 9 H), 3.34 (s, 6 H), 3.48 (s, 2 H), 3.81 (s, 6 H), 4.97 (s, 2 H), 6.52 (t, 1 H, *J* = 2.3 Hz), and 6.90 (d, 2 H, *J* = 2.3 Hz). Anal. Calcd for C<sub>15</sub>H<sub>28</sub>NIO<sub>2</sub>Si: C, 44.01; H, 6.89; N, 3.42. Found: C, 44.18; H, 6.90; N, 3.23.

***N,N*-Dimethyl-*N*-[(trimethylsilyl)methyl]-3,4,5-trimethoxybenzylammonium iodide (**1e**):** yield 67%; mp 143–145 °C; IR (KBr) 1600, 1340, 1250, 1120, 1010, and 860 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 0.32 (s, 9 H), 3.31 (s, 6 H), 3.40 (s, 2 H), 3.86 (s, 3 H), 3.91 (s, 6 H), 5.08 (s, 2 H), and 7.04

(s, 2 H). Anal. Calcd for C<sub>16</sub>H<sub>30</sub>NIO<sub>3</sub>Si: C, 43.74; H, 6.88; N, 3.19. Found: C, 43.46; H, 6.80; N, 3.00.

**Reaction of 1a–e with CsF: General Procedure. (A).** Ammonium salt **1** (2 mmol) was placed in a 20-mL flask equipped with a magnetic stirrer, a septum, and a test tube connected to the flask by a short piece of rubber tubing. CsF (1.52 g, 10 mmol) was placed in the test tube. The apparatus was dried under reduced pressure and was flushed with N<sub>2</sub>. HMPA (10 mL) was added to the flask with a syringe and then CsF was added from the test tube. The mixture was stirred for the time listed in Table 1 at room temperature, poured into 1% NaHCO<sub>3</sub> (100 mL), and extracted with ether (4 × 50 mL). The extract was washed with water (4 × 100 mL), dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The residue was distilled by Kugelrohr distillation apparatus in the range from 120 to 130 °C (0.5 mmHg) and the distillate was chromatographed on an aluminum oxide column (ether/hexane = 1:1) to give **4**, **6**, **7**, and **8**. The product ratio of the distillate was determined from the integrated values of proton signals in the <sup>1</sup>H NMR spectra or GLC analysis. The results are summarized in Table 1.

***N,N*-Dimethyl-2,3-dimethoxy-6-methylbenzylamine (**4c**):** IR (film) 2950, 1520, 1490, 1290, and 1090 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 2.26 (s, 6 H), 2.33 (d, 3 H, *J* = 0.6 Hz), 3.45 (s, 2 H), 3.81 (s, 3 H), 3.84 (s, 3 H), 6.75 (d, 1 H, *J* = 8.6 Hz), and 6.86 (d, 1 H, *J* = 8.6 Hz). Anal. Calcd for C<sub>12</sub>H<sub>19</sub>NO<sub>2</sub>: C, 68.87; H, 9.15; N, 6.69. Found: C, 68.82; H, 8.94; N, 6.41.

***N,N*-Dimethyl-3,4-dimethoxy-2-methylbenzylamine (**6a**):** IR (film) 2950, 1490, 1280, 1090, and 1020 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 2.22 (s, 6 H), 2.32 (s, 3 H), 3.31 (s, 2 H), 3.78 (s, 3 H), 3.84 (s, 3 H), 6.69 (d, 1 H, *J* = 8.3 Hz), and 6.93 (d, 1 H, *J* = 8.3 Hz). Anal. Calcd for C<sub>12</sub>H<sub>19</sub>NO<sub>2</sub>: C, 68.87; H, 9.15; N, 6.69. Found: C, 68.63; H, 9.01; N, 6.48.

***N,N*-Dimethyl-3,4-dimethoxy-6-methylbenzylamine (**6c**):** IR (film) 2950, 1520, 1460, 1260, 1220, and 1100 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 270 MHz) δ 2.24 (s, 6 H), 2.28 (s, 3 H), 3.31 (s, 2 H), 3.86 (s, 3 H), 3.87 (s, 3 H), 6.66 (s, 1 H), and 6.83 (s, 1 H). Anal. Calcd for C<sub>12</sub>H<sub>19</sub>NO<sub>2</sub>: C, 68.87; H, 9.15; N, 6.69. Found: C, 68.62; H, 9.06; N, 6.42.

***N,N*-Dimethyl-2,4-dimethoxy-6-methylbenzylamine (**6d**):** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 2.22 (s, 6 H), 2.36 (s, 3 H), 3.37 (s, 2 H), 3.78 (s, 3 H), 3.79 (s, 3 H), and 6.31–6.34 (m, 2 H).

***N,N*-Dimethyl-2,3,4-trimethoxy-6-methylbenzylamine (**6e**):** IR (film) 1500, 1480, 1330, 1120, and 1020 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 270 MHz) δ 2.23 (s, 6 H), 2.34 (s, 3 H), 3.34 (s, 2 H), 3.84 (s, 6 H), 3.87 (s, 3 H), and 6.50 (s, 1 H). Anal. Calcd for C<sub>13</sub>H<sub>21</sub>NO<sub>3</sub>: C, 65.25; H, 8.84; N, 5.85. Found: C, 65.22; H, 8.88; N, 5.90.

***N,N*-Dimethyl-2-(3,5-dimethoxyphenyl)ethylamine (**7d**):** IR (film) 1600, 1460, 1200, and 1150 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 270 MHz) δ 2.29 (s, 6 H), 2.50–2.56 (m, 2 H), 2.69–2.75 (m, 2 H), 3.77 (s, 6 H), and 6.30–6.37 (m, 3 H). Anal. Calcd for C<sub>12</sub>H<sub>19</sub>NO<sub>2</sub>: C, 68.87; H, 9.15; N, 6.69. Found: C, 68.62; H, 9.15; N, 6.59.

**2,3-Dimethoxytoluene<sup>8</sup> (**8a**), 3,4-Dimethoxytoluene<sup>9</sup> (**8c**), 3,5-Dimethoxytoluene<sup>10</sup> (**8d**), and 3,4,5-Trimethoxytoluene<sup>11</sup> (**8e**).** The product ratios of **6a:8a**, **4c:6c:8c**, and **6e:8e** were determined from the proton ratios of <sup>1</sup>H NMR spectra. The ratio of **6d:7d:8d** was calculated from the integrated values of GLC analysis (2 m, 5% PEG-20M).

The aqueous layer after the ether-extraction from **1b** was washed with CHCl<sub>3</sub> (4 × 50 mL) and evaporated under reduced pressure. The residue was separated on a silica gel column (CHCl<sub>3</sub>/MeOH = 10:1) to give 5-[(dimethylamino)methyl]-3-

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methoxy-4-methylene-2-cyclohexen-1-one (**9**, 132 mg, 34%): mp 42–43 °C; IR (KBr) 3050, 1655, 1630, 1570, 1380, 1220, 1000, 920, and 885  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 270 MHz)  $\delta$  2.20 (s, 6 H), 2.30 (dd, 1 H,  $J = 8.1, 12.2$  Hz), 2.35 (dd, 1 H,  $J = 7.3, 12.2$  Hz), 2.49 (dd, 1 H,  $J = 5.0, 16.3$  Hz), 2.59 (dd, 1 H,  $J = 5.6, 16.3$  Hz), 2.86–3.00 (m, 1 H), 3.76 (s, 3 H), 5.41 (s, 2 H), and 5.83 (s, 1 H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 67.8 MHz)  $\delta$  38.4, 40.6, 45.7, 55.8, 63.5, 102.5, 116.5, 139.7, 168.8, and 198.6; The structure was confirmed by C-H COSY and HMBC.

UV  $\lambda_{\text{max}}$ , hexane 265 nm ( $\log \epsilon$  4.23);  $m/e$  195 ( $\text{M}^+$ , 3), 151 (3), 137 (4), 123 (6), 109 (9), 91 (10), 77 (17), 69 (18), and 58 (100). Anal. Calcd for  $\text{C}_{11}\text{H}_{17}\text{NO}_2$ : C, 67.66; H, 8.78; N, 7.17. Found: C, 67.40; H, 8.49; N, 7.25.

**Reaction of 1 with CsF in the Presence of DBU: General Procedure.** (**B**). In the same way, CsF (1.52 g, 10.0 mmol) was added to a mixture of **1** (2.0 mmol) and DBU (1.52 g, 10 mmol) in HMPA (10 mL). The mixture was stirred for 0.5 h at room temperature, poured into 1%  $\text{NaHCO}_3$  (100 mL), and extracted with ether (4  $\times$  50 mL). The extract was washed with water (4  $\times$  100 mL), dried ( $\text{MgSO}_4$ ), and concentrated under reduced pressure. The residue (except for **1b**) was distilled by Kugelrohr distillation apparatus to give a mixture of **4**, **6**, **7**, and **8**.

The residue from **1b** was chromatographed on an HPLC column (Nakarai Cosmosil 5NH<sub>2</sub>, 10  $\times$  250 mm). The mobile phase was a mixture of 30% ether in hexane on the initial stage at flow rate of 5 mL/min, increased linearly to 35% in 6 min and then to 50% in 2 min. Fractions of *N,N*-dimethyl-3,5-dimethoxy-2-methylbenzylamine (**6b**) (7.0 min) and 5-(dimethylamino)methyl-1,3-dimethoxy-6-methylene-1,3-cyclohexadiene (**5b**) (8.0 min) were collected. The product ratios were determined from the integrated values of proton signals in the  $^1\text{H}$  NMR spectrum of the mixtures. The results are shown in Table 1.

**5b**: IR (film) 2950, 2770, 1660, 1590, 1200, and 1150  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  2.13 (dd, 1 H,  $J = 5.7, 11.9$  Hz), 2.26 (s, 6 H), 2.48 (dd, 1 H,  $J = 9.5, 11.9$  Hz), 3.29–3.35 (m, 1 H), 3.58 (s, 3 H), 3.65 (s, 3 H), 4.68 (dd, 1 H,  $J = 1.8, 5.1$  Hz), 4.96 (br s, 1 H), 4.99 (dd, 1 H,  $J = 1.8, 3.5$  Hz), and 5.60 (br s, 1 H); UV  $\lambda_{\text{max}}$ , hexane 323 nm ( $\log \epsilon$  3.58). Anal. Calcd for  $\text{C}_{12}\text{H}_{19}\text{NO}_2$ : C, 68.87; H, 9.15; N, 6.69. Found: C, 68.76; H, 9.13; N, 6.95.

**6b**: IR (film) 2950, 1610, 1460, 1200, and 1150  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  2.14 (s, 3 H), 2.24 (s, 6 H), 3.35 (s,

2 H), 3.79 (s, 3 H), 3.80 (s, 3 H), 6.37 (d, 1 H,  $J = 2.5$  Hz), and 6.49 (d, 1 H,  $J = 2.5$  Hz). Anal. Calcd for  $\text{C}_{12}\text{H}_{19}\text{NO}_2$ : C, 68.87; H, 9.15; N, 6.69. Found: C, 68.79; H, 9.15; N, 6.63.

(**C**). The reaction mixture of **1b**, **d**, **e** was vigorously stirred with 12 M NaOH (10 mL) for 10 min, poured into water (90 mL), and extracted with ether (4  $\times$  50 mL). The extract was washed with water (4  $\times$  100 mL), dried ( $\text{MgSO}_4$ ), and concentrated under reduced pressure. The results are shown in Table 1.

(**D**). The reaction mixture of **1d** and **1e** was quenched with  $\text{D}_2\text{O}$  (10 mL) after 10 min, poured into water (90 mL), and extracted with ether (4  $\times$  50 mL). The extract was washed with water (4  $\times$  100 mL), dried ( $\text{MgSO}_4$ ), and concentrated under reduced pressure. Analyses of the residues by GC-mass and  $^1\text{H}$  NMR spectra indicated the presence of 3,5-dimethoxytoluene- $\alpha$ -d<sub>1</sub> (**10d**) and 3,5-dimethoxytoluene-2-d<sub>1</sub> (**11d**), and 3,4,5-trimethoxytoluene- $\alpha$ -d<sub>1</sub> (**10e**) and 3,4,5-trimethoxytoluene-2-d<sub>1</sub> (**11e**).

Mixture of **10d** and **11d**: yield 67%;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 270 MHz)  $\delta$  2.28–2.29 (m, 1.95 H), 3.77 (s, 6 H), and 6.27–6.34 (m, 2.95 H);  $m/e$  154 ( $\text{M}^+ + 1$ , 11), 153 ( $\text{C}_9\text{H}_{11}\text{DO}_2$ ,  $\text{M}^+$ , 100), 152 ( $\text{M}^+ - 1$ , 6), 124 (51), 110 (17), 92 (19), and 78 (13).

Mixture of **10e** and **11e**: yield 68%;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  2.29–2.30 (m, 2.1 H), 3.82 (s, 3 H), 3.84 (s, 6 H), 6.39 (s, 1.9 H);  $m/e$  184 ( $\text{M}^+ + 1$ , 20), 183 ( $\text{C}_{10}\text{H}_{13}\text{DO}_3$ ,  $\text{M}^+$ , 97), 182 ( $\text{M}^+ - 1$ , 9), 168 (98), 140 (100), 135 (59), 125 (57), 110 (50), and 108 (37).

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**Supplementary Material Available:** The orbital energies and frontier electron densities of other orbitals of **3** and **5** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.