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Preparation of Primary Amines by the Alkylation of *O*-Sulfonyloximes of Benzophenone Derivatives with Grignard Reagents

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Primary amines are prepared by the electrophilic amination of Grignard reagents with benzophenone *O*-sulfonyloxime derivatives. 4,4′-Bis(trifluoromethyl)benzophenone *O*-sulfonyloximes react with alkyl Grignard reagents in the presence of a catalytic amount of CuCN in tetrahydrofuran-hexamethylphosphoric triamide to give *N*-alkylimines, which are readily hydrolyzed to primary amines. 3,3′,5,5′-Tetrakis(trifluoromethyl)benzophenone *O*-*p*-tolylsulfonyloxime is arylated to the corresponding *N*-arylimines with aryl Grignard reagents in ether–toluene, and hydrolysis of the resulting imines gives aniline derivatives.

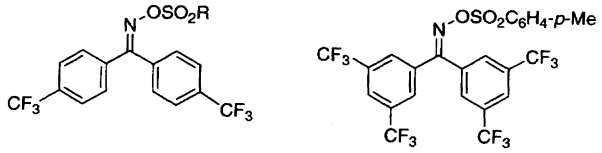
Preparation of primary amines is an important process for the synthesis of nitrogen-containing natural products and biologically active compounds. In general, primary amines are prepared by the reduction of the corresponding nitro compounds[1a] and azides[1b] and also by the alkylation of nucleophilic amination reagents such as phthalimide and trifluoroacetamides.[1b,1c,1d,1e] Though the use of electrophilic amination reagents such as chloramine and *O*-substituted hydroxylamine derivatives has provided another method to prepare primary amines,[2] this method has rarely been employed in organic synthesis.

Recently, one of the authors has reported that the intramolecular substitution reactions on the sp^2 nitrogen atom of oximes proceed by the catalytic use of tetrabutylammonium perrhenate and trifluoromethanesulfonic acid to afford quinolines and azaspirotrienones.[3] Since oximes act as electrophilic amination reagents in this reaction, we have examined the possibility to use oxime derivatives as electrophilic amination reagents of carbon nucleophiles. There have been several reports concerning the alkylation of oxime derivatives with organometallic reagents.[4] Hagopian et al. prepared primary arylamines by the reaction of tetraphenylcyclopentadienone *O*-*p*-tolylsulfonyloxime with large excess amounts of aryllithiums and aryl Grignard reagents, whereas dialkylation proceeded with alkylmetal reagents.[4a] Erdik and Ay reported the reaction of acetone *O*-2,4,6-trimethylphenylsulfonyloxime with aliphatic and aromatic Grignard reagents, which gave primary amines in moderate yield.[4b]

We have examined the alkylation of oxime derivatives and have reported the preliminary results of the preparation of primary alkylamines by the reaction of 4,4′-bis(trifluoromethyl)benzophenone *O*-methylsulfonyloxime with alkyl Grignard reagents and a catalytic amount of CuCN.[5] Primary alkylamines were thus prepared successfully, however, this method could not be applied to the preparation of arylamines. We have developed an alternative method by the reaction of tetrakis(trifluoromethyl)benzophenone *O*-*p*-tolylsulfonyloxime and aryl and alkyl Grignard reagents. In this paper, full accounts of these reactions are reported.

Results and Discussion

Reaction of Benzophenone *O*-Methylsulfonyloxime Derivative and Lithium Dibutylcuprate(I). In order to use oxime derivatives for amination reagents, it is required to choose oxime derivatives which do not usually undergo the Beckmann rearrangement and deprotonation at α-position of imino group. The above consideration suggested to us that we use benzophenone oxime derivatives having electron withdrawing groups, such as 4,4′-bis(trifluoromethyl)benzophenone *O*-methylsulfonyloxime (**1a**), 4,4′-bis(trifluoromethyl)benzophenone *O*-*p*-tolylsulfonyloxime (**1b**), and 3,3′,5,5′-tetrakis(trifluoromethyl)benzophenone *O*-*p*-tolylsulfonyloxime (**2**) (Chart 1). The *O*-sulfonyloximes **1** and **2** were easily prepared from 4,4′-bis(trifluoromethyl)benzophenone (**3**) and 3,3′,5,5′-tetrakis(trifluoromethyl)-benzophenone (**4**) by treatment with hydroxylamine hydrochloride in pyridine and then with methanesulfonyl chloride or *p*-toluenesulfonyl chloride in the presence of triethylamine. Though *O*-sulfonyloximes are generally acid and base sensitive so as to undergo Beckmann rearrangements,[6] **1** and **2** are stable enough to be isolated as crystals.



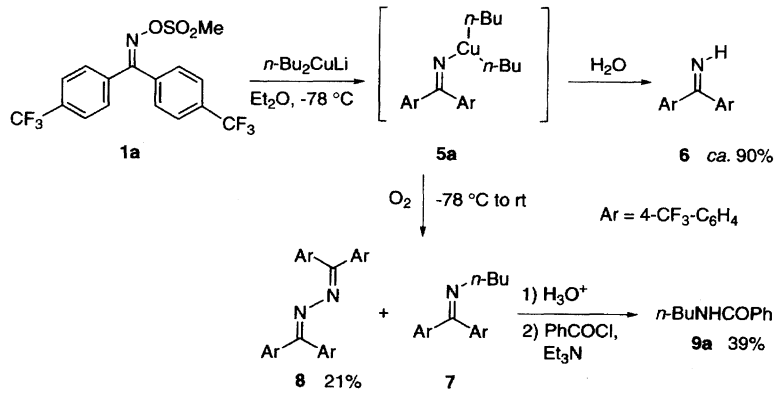
R = Me **1a**
R = *p*-Me-C_6H_4 **1b**

2

Chart 1.

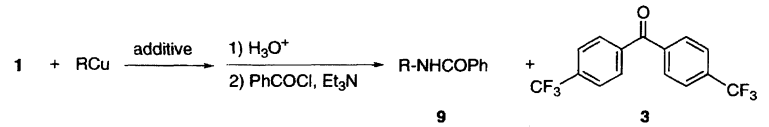
N-Alkylation of **1a** proceeded only very slightly by the reaction with butylmagnesium chloride in THF, and **1a** was recovered. Butyllithium mainly attacked the sulfonyl group of **1a** to afford 4,4′-bis(trifluoromethyl)benzophenone oxime and the reaction was complicated. Though lithium dibutylcuprate(I) smoothly reacted with **1a** at −78 °C, quenching with pH 9 buffer gave only a trace amount of the desired *N*-butylimine **7** and bis(4-trifluoromethylphenyl)methaneimine (**6**) was obtained in about 90% yield.[7] This indicated that the cuprate readily reacted with **1a** at −78 °C to give an *N*-diarylmethaneimino copper intermediate **5a**, which was too stable to cause reductive elimination into the *N*-butylimine **7**. To facilitate the elimination, molecular oxygen was bubbled into the reaction mixture, because alkylaminocoppers are known to afford alkylamines upon exposure to oxygen.[9] Since the imine **7** was easily hydrolyzed during the purification and the resulting butylamine is volatile, **7** was converted to *N*-butylbenzamide (**9a**) by hydrolysis with aq HCl and successive acylation with benzoyl chloride and triethylamine. By the oxidation with O_2, the benzamide **9a** was obtained in 39% yield with 21% yield of 4,4′-bis(trifluoromethyl)benzophenone azine (**8**). When the reaction and the successive oxidation with O_2 were performed in the presence of hexamethylphosphoric triamide (HMPA) or *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), the yield was increased to 61 or 65%, respectively. Use of 1,4-benzoquinone as an oxidizing reagent did not improve the product yield (57%) (Scheme 1).

Reaction of Benzophenone *O*-Sulfonyloximes with Alkylcoppers. In contrast to the reaction with cuprate, the *O*-methylsulfonyloxime **1a** reacted with butylcopper in Et_2O without the oxidation with molecular oxygen, affording *N*-butylbenzamide (**9a**) in 46% yield after the hydrolysis and the acylation with benzoyl chloride (Table 1, Entry 1). The yield of **9a** was increased by addition of polar solvents such as 1,3-dimethyl-2-oxohexahydropyrimidine (DMPU) and TMEDA to 67 and 82%, respectively (Entries 2 and 3). By adding HMPA, the reaction was completed within 30 min to yield **9a** almost quantitatively and 4,4′-bis(trifluoromethyl)benzophenone (**3**) was recovered in 97% yield (Entry 4). The reaction proceeded in THF as well as in Et_2O without forming the azine **8**. The *O*-*p*-tolylsulfonyloxime



Scheme 1. Reaction of the *O*-methylsulfonyloxime **1a** with lithium dibutylcuprate.

Table 1. Reaction of the *O*-Sulfonyloxime **1** with Alkylcoppers[a)]



Entry	**1**	R	Additive	Solvent	Temperature / °C	Time / h	Yield/% Benzamides	**3**
1	**1a**	*n*-Bu	None	Et_2O	−23	0.5	**9a** 46	94
2	**1a**	*n*-Bu	DMPU	Et_2O	−23	1	**9a** 67	81
3	**1a**	*n*-Bu	TMEDA	Et_2O	−23	3	**9a** 82	95
4	**1a**	*n*-Bu	HMPA	Et_2O	−23	0.5	**9a** 97	99
5	**1a**	*n*-Bu	HMPA	THF	−23	0.5	**9a** 97	98
6	**1a**	*n*-Bu	HMPA	THF	−45	1	**9a** 96	99
7	**1a**	*n*-Bu	HMPA	THF	−78	1	**9a** 77	87
8	**1b**	*n*-Bu	HMPA	THF	−23	0.5	**9a** 98	99
9[b)]	**1a**	*n*-Bu	HMPA	THF	−23	0.5	**9a** 92	99
10	**1a**	*s*-Bu	HMPA	THF	−45	1	**9b** 79	94
11	**1a**	*t*-Bu	HMPA	THF	−23	1	**9c** 60	90

a) **1** : RCu : Additive = 1.0 : 1.7 : 8.5. Alkylcoppers were prepared by alkyllithiums and CuI unless otherwise noted. b) Butylcopper was prepared by butylmagnesium chloride and CuBr·LiBr.

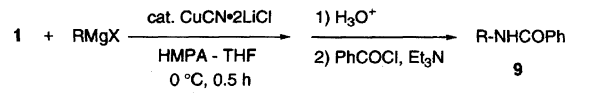
1b could be also employed as an amination reagent (Entry 8), and the Grignard reagent worked well to generate butylcopper (Entry 9). The amination of **1a** proceeded smoothly by employing secondary and tertiary alkylcopper reagents and the corresponding benzamides **9b** and **9c** were obtained in good yield (Entries 10 and 11).

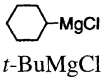
As mentioned, alkylcoppers were found to be more suitable for the alkylation of **1a** than lithium dibutylcuprate(I). As shown in Scheme 2, lithium dibutylcuprate(I) and butylcopper(I) react with **1a** to give aminocopper intermediates **5a** and **5b**, respectively. Probably the reductive elimination of the *N*-butylimine from **5b** proceeds more readily than that from **5a**, because the electron density on the copper atom of the intermediate **5b** is lower than that of **5a**.

Copper-Catalyzed Reaction with Alkyl Grignard Reagents. It is synthetically advantageous to carry out the reaction with a catalytic amount of copper compounds and to use Grignard reagents instead of alkyllithiums. By the use of CuCN·2LiCl, the alkylation proceeded catalytically even with alkyl Grignard reagents. That is, to a THF solution of **1a**, a 0.2 molar amount of CuCN·2LiCl, and HMPA, 1.2 molar amounts of butylmagnesium chloride were added dropwise at 0 °C over 30 min. After the hydrolysis and the acylation, the benzamide **9a** was obtained in 96% yield (Table 2, Entry 1). The copper reagent is essential in this reaction. In the absence of the copper catalyst, the benzamide **9a** was obtained only in 41% yield along with 4,4′-bis(trifluoromethyl)benzophenone *O*-benzoyloxime (**10**) as a side product (Entry 2). Secondary and tertiary alkyl Grignard reagents as well as primary ones reacted with **1a** smoothly (Entries 4—6).

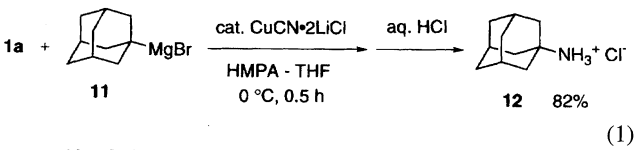
Furthermore, 1-adamantylmagnesium bromide (**11**), a phenethyl Grignard reagent **13**, and 1-norbornylmagnesium chloride (**15**) reacted with the *O*-sulfonyloximes **1** under the above reaction conditions. After the hydrolysis of the crude imines, 1-adamantylammonium chloride (**12**), a dopamine derivative **14**, and 1-norbornylammonium chloride (**16**), which is difficult to prepare by the reaction of 1-norbornyl halide and nucleophilic amination reagents, were obtained in 82, 87, and 96% yield, respectively (Eqs. 1, 2, and 3).

Table 2. CuCN·2LiCl-Catalyzed Reaction of the *O*-Sulfonyloxime **1** with Alkyl Grignard Reagents

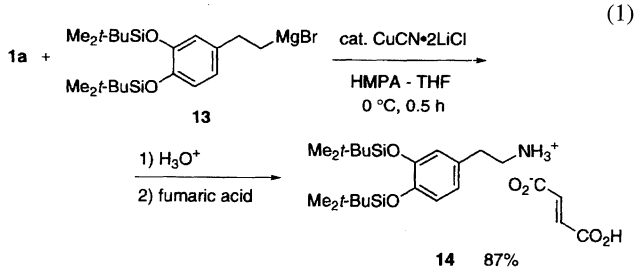


Entry	1	RMgX	Product	Yield/%
1[a]	**1a**	*n*-BuMgCl	**9a**	96
2[b]	**1a**	*n*-BuMgCl	**9a**	41[d]
3[a]	**1b**	*n*-BuMgCl	**9a**	99
4[a]	**1a**	*i*-PrMgBr	**9d**	93
5[a]	**1a**		**9e**	80
6[c]	**1a**	*t*-BuMgCl	**9c**	61

a) **1**:RMgX:CuCN·2LiCl:HMPA = 1.0:1.2:0.2:8.5. b) **1a**:*n*-BuMgCl:HMPA = 1.0:1.2:8.5. c) **1a**:*t*-BuMgCl:CuCN·2LiCl:HMPA = 1.0:1.5:0.5:8.5. d) The *O*-benzoyl oxime **10** was obtained in 27% yield.



(1)



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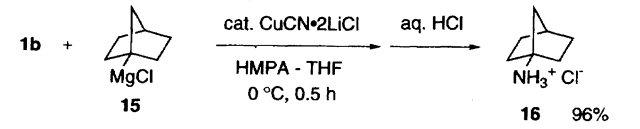
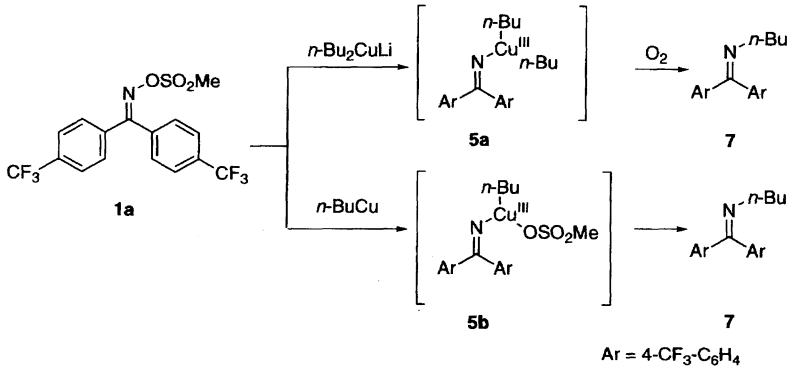


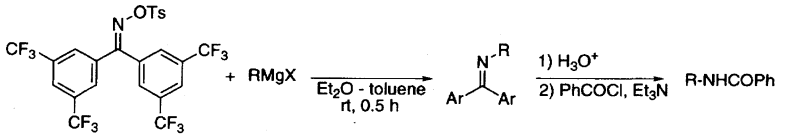
(3)

Reaction between Benzophenone *O*-Sulfonyloximes and Aryl Grignard Reagents. The present catalytic procedure was thus widely applied for the preparation of primary alkylamines, while aniline derivatives could not be prepared successfully. The reaction of the *O*-sulfonyloxime **1a** with phenylmagnesium bromide in the presence of CuCN·2LiCl gave benzanilide (**9f**) only in 7% yield but mainly biphenyl



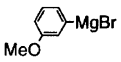
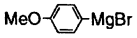
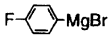
Scheme 2. Mechanism for the reaction of the *O*-methylsulfonyloxime **1a** with lithium dibutylcuprate and butylcopper.

Table 3. Reaction of the *O*-Sulfonyloxime **2** with Grignard Reagents[a)]



2 **18** **9**

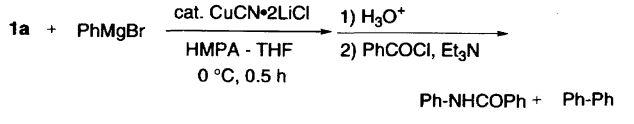
Ar = 3,5-$(CF_3)_2$-C_6H_3

Entry	RMgX	Yield/%			
		18		**9**[c)]	
1	PhMgBr	**18f**	95	**9f**	96
2		**18g**	71	**9g**	72
3		**18h**	94	**9h**	94
4		**18i**	97	**9i**	98
5		**18j**	94	**9j**	86
6		**18k**	90	**9k**	98
7[b)]				**9l**	96
8[b)]	EtMgBr			**9m**	87
9[b)]				**9e**	87
10[b)]	*t*-BuMgCl			**9c**	35

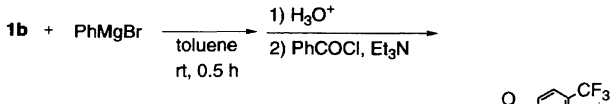
a) **2**:RMgX = 1.0:1.5. b) Imine **18** was not isolated. c) Overall yield from the *O*-sulfonyl oxime **2**.

(Eq. 4).

In the absence of the copper catalyst, **1b** reacted with phenyl Grignard reagent, where a marked solvent effect was observed. Treatment of *O*-*p*-tolylsulfonyl oxime **1b** in toluene with phenylmagnesium bromide prepared in THF afforded benzanilide (**9f**) in 34% yield with 53% recovery of the starting material **1b**. The reaction with phenyl Grignard reagent prepared in ether provided **9f** in better yield (62%), but the Beckmann product **18** was also obtained in 6% yield (Eq. 5).



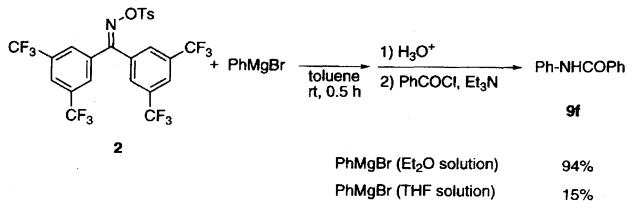
(4)



	9f	**17**
PhMgBr (THF solution)	34%	-
PhMgBr (Et_2O solution)	62%	6%

(5)

To suppress the Beckmann rearrangement, 3,3′,5,5′-tetrakis(trifluoromethylphenyl)benzophenone *O*-*p*-tolylsulfonyloxime **2** was employed as an amination reagent. The *O*-*p*-tolylsulfonyloxime **2** smoothly reacted in toluene with 1.5 molar amounts of phenylmagnesium bromide prepared in ether to afford benzanilide (**9f**) in 96% yield without the formation of any Beckmann rearrangement product. In contrast, phenylmagnesium bromide prepared in THF gave little anilide **9f** (Eq. 6).

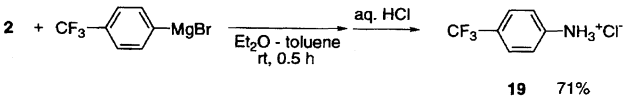


(6)

As shown in Table 3, the reactions of **2** and several Grignard reagents provided anilines and alkyl amines. Methoxyphenyl Grignard reagents reacted smoothly with **2** to afford benzamide derivatives **9** in good yield (Entries 2—4). *p*-Fluorophenyl Grignard reagent also reacted cleanly (Entry 5). In spite of the steric disadvantage, 2,6-dimethylphenylmagnesium bromide afforded an amide **9k** quantitatively (Entry 6). Though *N*-arylimine derivatives are generally labile and decompose by the exposure on silica gel, these *N*-arylimine derivatives **18** are stable enough to be isolated by silica gel column chromatography.

Primary and secondary alkyl Grignard reagents reacted smoothly to give the *N*-alkyl benzamides **9m** and **9e** in good yield, whereas tertiary alkyl Grignard reagent afforded the product **9c** in lower yield (Entries 8—10).

The following equations (Eqs. 7 and 8) illustrate the isolation of primary amines such as *p*-trifluoromethylaniline **19** and 3-phenylpropylamine **20** as hydrochloride salts.



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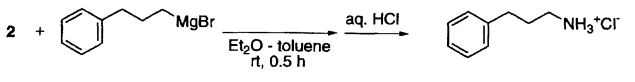

(8)

In conclusion, aliphatic primary amines are prepared by the reaction of 4,4′-bis(trifluoromethyl)benzophenone *O*-sulfonyloximes with primary, secondary, and tertiary alkyl Grignard reagents in the presence of a catalytic amount of CuCN in tetrahydrofuran–HMPA. Anilines and primary-alkyl and secondary-alkyl primary amines are prepared by the reaction of 3,3′,5,5′-tetrakis(trifluoromethyl)-benzophenone *O*-*p*-tolylsulfonyloxime with aryl and alkyl Grignard reagents prepared in ether. In both methods, the use of a slight excess of Grignard reagents is sufficient to prepare these primary amines in good yield.

Experimental

General. ^{1}H NMR (500 MHz) spectra were recorded on Bruker AM 500 and Bruker DRX 500 spectrometers in $CDCl_3$ and DMSO-d_6 using $CHCl_3$ (for ^{1}H, $\delta = 7.24$) and DMSO (for ^{1}H, $\delta = 2.50$) as internal standards. ^{13}C NMR (125 MHz) spectra were recorded on Bruker AM 500 and Bruker DRX 500 spectrometers in $CDCl_3$ and DMSO-d_6 using $CDCl_3$ (for ^{13}C, $\delta = 77.00$) and DMSO-d_6 (for ^{13}C, $\delta = 39.50$) as internal standards. IR spectra were recorded on a Horiba FT 300-S spectrophotometer. High-resolution mass spectra were obtained with a JEOL JMS-SX102A mass spectrometer at an ionization energy of 70 eV. The melting points were uncorrected. Elemental analyses were carried out at The Elemental Analysis Laboratory, Department of Chemistry, Faculty of Science, The University of Tokyo. Flash column chromatography was performed on silica gel (Merck Silica gel 60, and Kanto Chemical Co., Inc. Silica gel 60N (spherical, neutral)) and preparative thin-layer chromatography was carried out using Wakogel B-5F. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were freshly distilled from sodium diphenylketyl under an argon atmosphere. Toluene was freshly distilled from lithium aluminum hydride under an argon atmosphere. Pyridine was distilled from CaH_2. Hexamethylphosphoric triamide (HMPA) was distilled under reduced pressure from CaH_2, and stored over Molecular Sieves 4A. Dichloromethane was distilled from P_2O_5, then from CaH_2, and stored over Molecular Sieves 4A. Alkyllithiums were purchased from Kanto Chemical Co., Inc. and Aldrich Chemical Co., Inc., and were titrated by the literature procedure.[10] Butylmagnesium chloride, isopropylmagnesium bromide, cyclohexylmagnesium chloride, *t*-butylmagnesium chloride, phenylmagnesium bromide, and ethylmagnesium bromide were purchased from Kanto Chemical Co., Inc. and Aldrich Chemical Co., Inc., and were titrated by the literature procedure.[11] 1-Adamantylmagnesium bromide (**11**),[12] 1-norbornylmagnesium chloride (**15**),[13] 2-[3,4-bis-(*t*-butyldimethylsiloxy)phenyl]ethylmagnesium bromide (**13**), 2-methoxyphenylmagnesium bromide, 3-methoxyphenylmagnesium bromide, 4-methoxyphenylmagnesium bromide, 4-fluorophenylmagnesium bromide, 2,6-dimethylphenylmagnesium bromide, 1-naphthylmagnesium bromide, 4-trifluoromethylphenylmagnesium bromide, and 3-phenylpropylmagnesium bromide were prepared according to the references and titrated by the literature procedure.[11]

4,4′-Bis(trifluoromethyl)benzophenone Oxime: After a pyridine solution (380 ml) of 4,4′-bis(trifluoromethyl)benzophenone (**4**)[14,15] (37.9 g, 0.119 mol) and hydroxylammonium chloride (12.4 g, 0.179 mol) was heated to reflux for 30 min, the solvent was removed in vacuo and water was added. The mixture was extracted twice with ethyl acetate, and the combined extracts were washed successively with dil HCl, water, sat. $NaHCO_3$, and brine. The ethyl acetate solution was dried over anhydrous sodium sulfate, and the ethyl acetate was removed in vacuo. Recrystallization of the residual solid from hexane gave 4,4′-bis(trifluoromethyl)-benzophenone oxime (36.8 g, 93%). Colorless needles; mp 153—154 °C; IR (KBr) 3284, 1616, 1408, 1333, 1165, 1130, 1115, 1070, 1005, 933, 845 cm^{-1}; ^{1}H NMR (in $CDCl_3$) $\delta = 7.50$ (2H, d, $J = 8.2$ Hz), 7.55 (2H, d, $J = 8.5$ Hz), 7.59 (2H, d, $J = 8.5$ Hz), 7.73 (2H, d, $J = 8.2$ Hz), 7.90 (1H, s); ^{13}C NMR (in $CDCl_3$) $\delta = 123.81$ (q, $^1J_{CF} = 272.1$ Hz), 123.84 (q, $^1J_{CF} = 272.1$ Hz), 125.41—125.66 (overlapped, m), 128.02, 129.66, 131.55 (q, $^2J_{CF} = 32.9$ Hz), 131.77 (q, $^2J_{CF} = 32.9$ Hz), 135.46, 138.80, 155.97. Anal. Found: C, 54.07; H, 3.02; N, 4.20%. Calcd for $C_{15}H_9F_6NO$: C, 54.07; H, 2.72; N, 4.20%.

3, 3′, 5, 5′- Tetrakis(trifluoromethyl)benzophenone Oxime: After a pyridine solution (45 ml) of 3,3′,5,5′-tetrakis(trifluoromethyl)benzophenone (**3**)[15,16] (4.54 g, 10.0 mmol) and hydroxylammonium chloride (1.04 g, 15.0 mmol) was heated to reflux for 30 min, the solvent was removed in vacuo and water was added. The mixture was extracted twice with ethyl acetate, and the combined extracts were washed successively with dil HCl, water, sat. $NaHCO_3$, and brine. The ethyl acetate solution was dried over anhydrous sodium sulfate, and the ethyl acetate was removed in vacuo. Recrystallization of the residual solid from hexane gave 3, 3′,5,5′-tetrakis(trifluoromethyl)benzophenone oxime (4.33 g, 92%). Colorless prisms; mp 115—117 °C; IR (KBr) 3300, 1625, 1398, 1371, 1286, 1176, 1139, 904, 704, 685 cm^{-1}; ^{1}H NMR (in $CDCl_3$) $\delta = 7.84$ (2H, s), 7.88 (2H, s), 7.93 (1H, s), 8.01 (1H, s); ^{13}C NMR

(in $CDCl_3$) δ = 122.90 (q, $^1J_{CF}$ = 272.8 Hz), 122.92 (q, $^1J_{CF}$ = 273.1 Hz), 123.61—123.98 (overlapped, m), 127.52, 127.54, 129.52, 129.55, 132.40 (q, $^2J_{CF}$ = 33.7 Hz), 132.43 (q, $^2J_{CF}$ = 33.9 Hz), 132.71, 136.98, 153.26. Anal. Found: C, 43.45; H, 1.67; N, 3.06%. Calcd for $C_{17}H_7F_{12}NO$: C, 43.52; H, 1.50; N, 2.99%.

4,4′-Bis(trifluoromethyl)benzophenone *O*-Methylsulfonyloxime (1a): To an ice-cold solution of 4,4′-bis(trifluoromethyl)-benzophenone oxime (1.50 g, 4.50 mmol) and triethylamine (0.547 g, 5.40 mmol) in dichloromethane (25 ml) was slowly added a solution of methanesulfonyl chloride (0.541 g, 4.73 mmol) in dichloromethane (5 ml), and this mixture was stirred at the same temperature for 30 min. After the reaction was quenched with water, the mixture was extracted twice with dichloromethane. The combined extracts were washed with sat. $NaHCO_3$, and the dichloromethane solution was dried over anhydrous sodium sulfate. The dichloromethane was removed in vacuo, and recrystallization of the residual solid from ethyl acetate-hexane gave **1a** (1.80 g, 97%). Colorless needles; mp 93—94 °C; IR (KBr) 1624, 1410, 1377, 1329, 1180, 1134, 1070, 1022, 872, 847, 827, 783, 521 cm^{-1}; ^1H NMR (in $CDCl_3$) δ = 3.27 (3H, s), 7.48 (2H, d, J = 8.2 Hz), 7.64 (2H, d, J = 8.9 Hz), 7.66 (2H, d, J = 8.9 Hz), 7.76 (2H, d, J = 8.2 Hz); ^{13}C NMR (in $CDCl_3$) δ = 36.74, 123.49 (q, $^1J_{CF}$ = 272.7 Hz), 123.51 (q, $^1J_{CF}$ = 272.7 Hz), 125.72—125.86 (overlapped, m), 129.24, 129.44, 132.67 (q, $^2J_{CF}$ = 33.1 Hz), 133.55 (q, $^2J_{CF}$ = 33.3 Hz), 133.72, 163.45. Anal. Found: C, 46.43 H, 2.79; N, 3.57; S, 8.01%. Calcd for $C_{16}H_{11}F_6NO_3S$: C, 46.72; H, 2.70; N, 3.41; S, 7.80%.

4,4′-Bis(trifluoromethyl)benzophenone *O*-*p*-Tolylsulfonyloxime (1b): To an ice-cold solution of 4,4′-bis(trifluoromethyl)-benzophenone oxime (3.35 g, 10.1 mmol) and triethylamine (1.22 g, 12.1 mmol) in dichloromethane (52 ml) was slowly added a solution of *p*-toluenesulfonyl chloride (2.01 g, 10.6 mmol) in dichloromethane (15 ml), and this mixture was stirred at room temperature for 5 h. After the reaction was quenched with water, the mixture was extracted twice with dichloromethane. The combined extracts were washed with sat. $NaHCO_3$, and the dichloromethane solution was dried over anhydrous sodium sulfate. The dichloromethane was removed in vacuo, and recrystallization of the residual solid from ethyl acetate–hexane gave **1b** (4.68 g, 96%). Colorless needles; mp 158—160 °C; IR (KBr) 1603, 1387, 1329, 1180, 1124, 1068, 881, 849, 823, 762, 675, 596, 552 cm^{-1}; ^1H NMR (in $CDCl_3$) δ = 2.46 (3H, s), 7.34—7.41 (4H, m), 7.48 (2H, d, J = 8.1 Hz), 7.59 (2H, d, J = 8.4 Hz), 7.73 (2H, d, J = 8.1 Hz), 7.89 (2H, d, J = 8.2 Hz); ^{13}C NMR (in $CDCl_3$) δ = 21.73, 123.55 (overlapped, q, $^1J_{CF}$ = 272.7 Hz), 125.57—125.77 (overlapped, m), 129.05, 129.07, 129.37, 129.80, 132.16, 132.44 (q, $^2J_{CF}$ = 32.8 Hz), 133.21 (q, $^2J_{CF}$ = 32.6 Hz), 133.87, 145.62, 162.54. Anal. Found: C, 54.08; H, 3.26; N, 3.02; S, 6.68%. Calcd for $C_{22}H_{15}F_6NO_3S$: C, 54.21; H, 3.10; N, 2.87; S, 6.58%.

3,3′,5,5′-Tetrakis(trifluoromethyl)benzophenone *O*-*p*-Tolylsulfonyloxime (2): To an ice-cold solution of 3,3′,5,5′-tetrakis-(trifluoromethyl)benzophenone oxime (2.50 g, 5.33 mmol) and triethylamine (0.647 g, 6.39 mmol) in dichloromethane (35 ml) was slowly added a solution of *p*-toluenesulfonyl chloride (1.07 g, 5.59 mmol) in dichloromethane (15 ml), and this mixture was stirred at room temperature for 3 h. After the reaction was quenched with water, the mixture was extracted twice with dichloromethane. The combined extracts were washed with sat. $NaHCO_3$, and the dichloromethane solution was dried over anhydrous sodium sulfate. The dichloromethane was removed in vacuo, and recrystallization of the residual solid from diisopropyl ether–hexane gave **2** (3.23 g, 97%). White powder; mp 146—147 °C; IR (KBr) 1626, 1597, 1396, 1373, 1284, 1198, 1165, 1137, 906, 810, 717, 687, 580, 547 cm^{-1}; ^1H NMR (in $CDCl_3$) δ = 2.47 (3H, s), 7.40 (2H, d, J = 8.5 Hz), 7.69 (2H, s), 7.76 (2H, s), 7.89 (2H, d, J = 8.5 Hz), 8.00 (1H, s), 8.06 (1H, s); ^{13}C NMR (in $CDCl_3$) δ = 21.76, 122.58 (overlapped, q, $^1J_{CF}$ = 273.0 Hz), 124.90—125.10 (m), 125.27—125.45 (m), 128.42, 128.44, 129.14 (overlapped), 129.99, 131.31, 131.48, 132.74 (q, $^2J_{CF}$ = 34.1 Hz), 132.81 (q, $^2J_{CF}$ = 34.3 Hz), 135.01, 146.34, 159.35. Anal. Found: C, 46.15; H, 2.10; N, 2.29; S, 5.27%. Calcd for $C_{24}H_{13}F_{12}NO_3S$: C, 46.24; H, 2.10; N, 2.25; S, 5.14%.

Bis(4-trifluoromethylphenyl)methaneimine (6): Yellow powder; mp 75—77 °C (hexane); IR (KBr) 3219, 1608, 1570, 1415, 1333, 1207, 1169, 1124, 1070, 1016, 903, 852 cm^{-1}; ^1H NMR (in $CDCl_3$) δ = 7.50 (2H, d, J = 7.9 Hz), 7.67 (2H, d, J = 8.0 Hz), 7.71 (2H, d, J = 7.9 Hz), 7.82 (2H, d, J = 8.0 Hz), 10.67 (1H, s); ^{13}C NMR (in $CDCl_3$) δ = 123.67 (q, $^1J_{CF}$ = 271.5 Hz), 123.83 (q, $^1J_{CF}$ = 272.2 Hz), 125.38, 125.85, 127.78, 129.43, 132.27 (q, $^2J_{CF}$ = 33.1 Hz), 132.80 (q, $^2J_{CF}$ = 32.4 Hz), 140.82, 142.93, 175.87. Anal. Found: C, 57.00; H, 2.99; N, 4.40%. Calcd for $C_{15}H_9F_6N$: C, 56.78; H, 2.86; N, 4.41%.

4,4′-Bis(trifluoromethyl)benzophenone Azine (8): Yellow needles; mp 193—194 °C (ethanol); IR (KBr) 1618, 1556, 1408, 1331, 1161, 1070, 1016, 957, 849, 671 cm^{-1}; ^1H NMR (in $CDCl_3$) δ = 7.42 (4H, d, J = 8.1 Hz), 7.52 (4H, d, J = 8.5 Hz), 7.56 (4H, d, J = 8.5 Hz), 7.72 (4H, d, J = 8.1 Hz); ^{13}C NMR (in $CDCl_3$) δ = 123.77 (overlapped, q, $^1J_{CF}$ = 272.5 Hz), 125.26—125.39 (overlapped, m), 128.83, 129.44, 131.40 (q, $^2J_{CF}$ = 32.7 Hz), 132.22 (q, $^2J_{CF}$ = 32.9 Hz), 138.10, 140.01, 158.94. Anal. Found: C, 56.82; H, 2.72; N, 4.44%. Calcd for $C_{30}H_{16}F_{12}N_2$: C, 56.97; H, 2.55; N, 4.43%.

Typical Procedure for the Reaction of 1 with Alkylcoppers. (Table 1, Entry 4): To a suspension of CuI (63.0 mg, 0.331 mmol) in ether (1.0 ml) was added a hexane solution of butyllithium (1.57 mol dm^{-3}; 0.211 ml, 0.331 mmol) at −40 °C under an argon atmosphere. After the reaction mixture was stirred at the same temperature for 20 min, HMPA (296 mg, 1.65 mmol) was added and the mixture was stirred for 5 min. The resulting solution was warmed to −23 °C, and a solution of **1a** (80.0 mg, 0.194 mmol) in ether (1.0 ml) was added dropwise to the mixture. After the reaction mixture was stirred at the same temperature for 30 min, the mixture was quenched with pH 9 buffer. Inorganic materials were filtered off and organic materials were extracted twice with ether. The combined extracts were washed successively with sat. $NaHCO_3$ and with brine three times, and the ether solution was dried over anhydrous magnesium sulfate. The ether was removed in vacuo, and the crude imine was dissolved in acetone (2 ml) and water (0.5 ml); then 1 M HCl (1 M = 1.00 mol dm^{-3}, 0.292 ml, 0.292 mmol) was added to the solution. After the resulting solution was stirred at room temperature for 30 min, the mixture was cooled to 0 °C. Triethylamine (59.0 mg, 0.583 mmol) was added to the mixture, and a solution of benzoyl chloride (30.1 mg, 0.214 mmol) in acetone (0.5 ml) was added slowly. After the resulting solution was stirred at room temperature for 30 min, the reaction was quenched with water. The mixture was extracted twice with ethyl acetate, and the combined extracts were washed successively with sat. $NaHCO_3$, and brine. The ethyl acetate solution was dried over anhydrous sodium sulfate, and the ethyl acetate was removed in vacuo. The crude materials were purified by thin-layer chromatography (silica gel, hexane : ethyl acetate = 4 : 1) to give *N*-butylbenzamide (**9a**) (33.3 mg, 97%) and benzophenone **3** (61.5 mg, 99%), respectively.

Spectral Data. All of the products are known compounds, and their spectral data are in good agreement with those of authentic samples.

***N*-Butylbenzamide (9a):** Colorless oil; ^{1}H NMR (in $CDCl_3$) δ = 0.92 (3H, t, J = 7.4 Hz), 1.33—1.43 (2H, m), 1.52—1.61 (2H, m), 3.42 (2H, q, J = 6.7 Hz), 6.25 (1H, br s), 7.38 (2H, t, J = 8.1 Hz), 7.45 (1H, t, J = 8.1 Hz), 7.73 (1H, d, J = 8.1 Hz); ^{13}C NMR (in $CDCl_3$) δ = 13.57, 19.96, 31.49, 39.65, 126.81, 128.16, 130.94, 134.66, 167.55.

***N*-*s*-Butylbenzamide (9b):** Colorless needles; ^{1}H NMR (in $CDCl_3$) δ = 0.95 (3H, t, J = 7.4 Hz), 1.21 (3H, d, J = 6.5 Hz), 1.53—1.59 (2H, m), 4.05—4.17 (1H, m), 5.89 (1H, br s), 7.40 (2H, t, J = 7.5 Hz), 7.46 (1H, t, J = 7.5 Hz), 7.73 (1H, d, J = 7.5 Hz); ^{13}C NMR (in $CDCl_3$) δ = 10.35, 20.34, 29.62, 47.00, 126.77, 128.33, 131.06, 134.97, 166.87.

***N*-*t*-Butylbenzamide (9c):** Colorless needles; ^{1}H NMR (in $CDCl_3$) δ = 1.45 (9H, s), 5.93 (1H, br s), 7.39 (2H, t, J = 7.5 Hz), 7.45 (1H, t, J = 7.5 Hz), 7.69 (1H, d, J = 7.5 Hz); ^{13}C NMR (in $CDCl_3$) δ = 28.85, 51.57, 126.66, 128.44, 131.05, 135.90, 166.89.

Typical Procedure for the Copper-Catalyzed Reaction of 1 with Alkyl Grignard Reagents. (Table 2, Entry 1): To a solution of CuCN (17.9 mg, 0.200 mmol) and LiCl (17.0 mg, 0.400 mmol) in THF (4.0 ml) was added a solution of **1a** (411 mg, 1.00 mmol) in THF (6.0 ml) and HMPA (1.48 ml, 8.50 mmol) under an argon atmosphere. The reaction mixture was cooled to 0 °C, and a THF solution of butylmagnesium chloride (0.900 mol dm^{-3}; 1.33 ml, 1.20 mmol) was added dropwise over 30 min. After the reaction mixture was stirred at the same temperature for 30 min, the mixture was quenched with pH 9 buffer. Inorganic materials were filtered off and organic materials were extracted twice with ether. The combined extracts were washed successively with sat. $NaHCO_3$ and with brine three times, and the ether solution was dried over anhydrous magnesium sulfate. The ether was removed in vacuo, and the crude imine was dissolved in acetone (10 ml) and water (2.5 ml); then 1 M HCl (1.50 ml, 1.50 mmol) was added to the solution. After the resulting solution was stirred at room temperature for 30 min, the mixture was cooled to 0 °C. Triethylamine (304 mg, 3.00 mmol) was added to the mixture, and a solution of benzoyl chloride (155 mg, 1.10 mmol) in acetone (2 ml) was added slowly. After the resulting solution was stirred at room temperature for 30 min, the reaction was quenched with water. The mixture was extracted twice with ethyl acetate, and the combined extracts were washed successively with sat. $NaHCO_3$, and brine. The ethyl acetate solution was dried over anhydrous sodium sulfate, and the ethyl acetate was removed in vacuo. The crude materials were purified by flash column chromatography (hexane : ethyl acetate = 14 : 1 → 4 : 1) to give *N*-butylbenzamide (**9a**) (170 mg, 96%).

Spectral Data. All of the products are known compounds, and their spectral data are in good agreement with those of authentic samples.

***N*-Isopropylbenzamide (9d):** Colorless needles; ^{1}H NMR (in $CDCl_3$) δ = 1.23 (6H, d, J = 6.4 Hz); 4.21—4.31 (1H, m), 5.97 (1H, br s), 7.39 (2H, t, J = 7.4 Hz), 7.46 (1H, t, J = 7.4 Hz), 7.72 (2H, d, J = 7.4 Hz); ^{13}C NMR (in $CDCl_3$) δ = 22.77, 41.82, 126.77, 128.42, 131.17, 134.93, 166.67.

***N*-Cyclohexylbenzamide (9e):** Colorless prisms; ^{1}H NMR (in $CDCl_3$) δ = 1.12—1.27 (3H, m), 1.33—1.46 (2H, m), 1.58—1.67 (1H, m), 1.68—1.79 (2H, m), 1.94—2.06 (2H, m), 3.89—4.02 (1H, m), 5.99 (1H, br s), 7.39 (2H, t, J = 7.5 Hz), 7.45 (1H, t, J = 7.5 Hz), 7.72 (2H, d, J = 7.5 Hz); ^{13}C NMR (in $CDCl_3$) δ = 24.88, 25.54, 33.20, 48.64, 126.79, 128.46, 131.19, 135.08, 166.61.

1-Adamantylammonium Chloride (12):[17] To a solution of CuCN (44.8 mg, 0.500 mmol) and LiCl (42.4 mg, 1.00 mmol) in THF (4.0 ml) were added a solution of **1a** (411 mg, 1.00 mmol) in THF (6.0 ml) and HMPA (1.48 ml, 8.50 mmol) under an argon atmosphere. The reaction mixture was cooled to 0 °C, and an ether solution of adamantylmagnesium bromide (0.870 mol dm^{-3}; 1.72 ml, 1.50 mmol) was added dropwise over 30 min. After the reaction mixture was stirred at the same temperature for 30 min, the mixture was quenched with pH 9 buffer. Inorganic materials were filtered off and organic materials were extracted twice with ether. The combined extracts were washed successively with sat. $NaHCO_3$ and with brine three times; then the ether solution was dried over anhydrous magnesium sulfate. The ether was removed in vacuo, and the crude imine was dissolved in acetone (10 ml) and water (2.5 ml); then 1 M HCl (2.00 ml, 2.00 mmol) was added to the solution. After the resulting solution was stirred at room temperature for 30 min, water was added to the mixture and it was washed with ethyl acetate twice. The aqueous solution was removed in vacuo, and recrystallization of the residual solid from aq. ethanol–ether gave **12** (154 mg, 82%). Colorless prisms; ^{1}H NMR (in DMSO-d_6) δ = 1.57 (3H, d, J = 12.1 Hz), 1.62 (3H, d, J = 12.1 Hz), 1.78 (s, 6H), 2.09 (1H, s), 7.96 (3H, br s); ^{13}C NMR (in DMSO-d_6) δ = 28.30, 35.15, 39.82, 50.91.

Methyl 3,4-Bis(*t*-butyldimethylsiloxy)phenylacetate: To an ice-cold solution of 3,4-dihydroxyphenylacetic acid (10.1 g, 60.1 mmol) in methanol (200 ml) was slowly added concd sulfuric acid (2.00 ml, 37.5 mmol), and this mixture was stirred at the same temperature for 10 min. After the reaction mixture was heated to reflux for 1.5 h, the solvent was removed in vacuo and water was added. The mixture was extracted twice with ethyl acetate, and the combined extracts were washed successively with water and brine twice. The ethyl acetate solution was dried over anhydrous sodium sulfate, and the ethyl acetate was removed in vacuo to give methyl 3,4-dihydroxyphenylacetate (10.5 g, 96%).

To an ice-cold solution of methyl 3,4-dihydroxyphenylacetate (10.5 g, 57.6 mmol) and imidazole (19.6 g, 288 mmol) in DMF (75 ml) was added a solution of *t*-butylchlorodimethylsilane (20.0 g, 133 mmol) in DMF (30 ml); this mixture was stirred at the same temperature for 5 min then stirred at room temperature for 2 h. The mixture was quenched with water, and the organic materials were extracted with ether; then the combined extracts were washed successively with water and brine twice. The ether solution was dried over anhydrous magnesium sulfate, and the ether was removed in vacuo. The crude materials were purified by flash column chromatography (hexane : ethyl acetate = 19 : 1) to give methyl 3,4-bis(*t*-butyldimethylsiloxy)phenylacetate (21.2 g, 89%). Pale yellow oil; IR (KBr) 2954, 2933, 2858, 1743, 1511, 1496, 1425, 1294, 1255, 1227, 1155, 1132, 985, 908, 840, 783 cm^{-1}; ^{1}H NMR (in $CDCl_3$) δ = 0.16 (6H, s), 0.17, (6H, s), 0.95 (9H, s), 0.96 (9H, s), 3.47 (2H, s), 3.66 (3H, s), 6.67 (1H, d, J = 8.0 Hz), 6.72 (1H, s), 6.74 (1H, d, J = 8.0 Hz); ^{13}C NMR (in $CDCl_3$) δ = −4.14 (overlapped), 18.41 (overlapped), 25.92 (overlapped), 40.52, 51.88, 120.87, 122.09, 122.11, 126.91, 145.98, 146.70, 172.21. Anal. Found: C, 61.16; H, 9.17%. Calcd for $C_{21}H_{38}O_4Si_2$: C, 61.41; H, 9.33%.

2-[3,4-Bis(*t*-butyldimethylsiloxy)phenyl]ethanol: To an ice-cold solution of methyl 3,4-bis(*t*-butyldimethylsiloxy)phenylacetate (5.00 g, 12.2 mmol) in toluene (50 ml) was added dropwise a hexane solution of diisobutylaluminum hydride (1.00 mol dm^{-3}; 28.0 ml, 28.0 mmol) under an argon atmosphere. After this mixture was stirred at the same temperature for 3 h, the mixture was quenched with sat. potassium sodium tartrate. Inorganic materials were filtered off and organic materials were extracted twice with ethyl acetate. The combined extracts were washed with brine, and the ethyl acetate solution was dried over anhydrous sodium sulfate. The ethyl acetate was removed in vacuo, and the crude materi-

als were purified by flash column chromatography (hexane : ethyl acetate = 9 : 1 → 4 : 1) to give 2-[3,4-bis(*t*-butyldimethylsiloxy)-phenyl]ethanol (4.66 g, quant.). Colorless oil; IR (KBr) 3401, 2954, 2933, 2893, 2860, 1511, 1469, 1421, 1296, 1255, 1225, 908, 841, 783 cm^{-1}; ^1H NMR (in $CDCl_3$) δ = 0.17 (12H, s), 0.96 (18H, s), 1.35 (1H, br t), 2.72 (2H, t, J = 6.5 Hz), 3.73—3.81 (2H, m), 6.63 (1H, d, J = 8.1 Hz), 6.67 (1H, s), 6.74 (1H, d, J = 8.1 Hz); ^{13}C NMR (in $CDCl_3$) δ = −4.11, −4.09, 18.43 (overlapped), 25.93 (overlapped), 38.49, 63.80, 121.04, 121.81, 121.88, 131.28, 145.50, 146.78. Anal. Found: C, 62.78; H, 9.92%. Calcd for $C_{20}H_{38}O_3Si_2$: C, 62.77; H, 10.01%.

1- Bromo- 2- [3, 4- bis(*t*- butyldimethylsiloxy)phenyl]ethane: To a solution of methyl 2-[3,4-bis(*t*-butyldimethylsiloxy)phenyl]-ethanol (4.66 g, 12.2 mmol) and triphenylphosphine (3.51 g, 13.4 mmol) in THF (70 ml) was added a solution of tetrabromomethane (4.85 g, 14.6 mmol) in THF (20 ml) under an argon atmosphere. After this mixture was stirred at room temperature for 10 h, insoluble materials were filtered off and organic solvent was removed in vacuo. The crude materials were purified by flash column chromatography (hexane → hexane : ethyl acetate = 19 : 1) to give 1-bromo-2-[3,4-bis(*t*-butyldimethylsiloxy)phenyl]ethane (2.29 g, 42%). Colorless oil; IR (KBr) 2956, 2933, 2891, 2858, 1510, 1469, 1421, 1296, 1255, 1230, 985, 908, 839, 781 cm^{-1}; ^1H NMR (in $CDCl_3$) δ = 0.16 (6H, s), 0.17 (6H, s), 0.96 (9H, s), 0.97 (9H, s), 3.01 (2H, t, J = 7.8 Hz), 3.48 (2H, t, J = 7.8 Hz), 6.61 (1H, dd, J = 2.1 and 8.1 Hz), 6.65 (1H, d, J = 2.1 Hz), 6.73 (1H, d, J = 8.1 Hz); ^{13}C NMR (in $CDCl_3$) δ = −4.10, −4.07, 18.43 (overlapped), 25.94 (overlapped), 33.22, 38.86, 121.02, 121.49, 121.57, 132.05, 145.81, 146.74. FABHRMS Found: *m/z* 445.1618. Calcd for $C_{20}H_{37}{}^{79}BrO_2Si_2$: M+H, 445.1594.

2-[3,4-Bis(*t*-butyldimethylsiloxy)phenyl]ethylammonium Fumarate (14):[18] To a solution of CuCN (17.9 mg, 0.200 mmol) and LiCl (17.0 mg, 0.400 mmol) in THF (4.0 ml) was added a solution of **1a** (411 mg, 1.00 mmol) in THF (6.0 ml) and HMPA (1.48 ml, 8.50 mmol). The reaction mixture was cooled to 0 °C, and a THF solution of 2-[3,4-bis(*t*-butyldimethylsiloxy)phenyl]ethylmagnesium bromide (0.360 mol dm^{-3}; 3.33 ml, 1.20 mmol) was added dropwise over 30 min. After the reaction mixture was stirred at the same temperature for 30 min, the mixture was quenched with pH 9 buffer. Inorganic materials were filtered off and organic materials were extracted twice with ether. The combined extracts were washed successively with sat. $NaHCO_3$ and with brine three times; then the ether solution was dried over anhydrous magnesium sulfate. The ether was removed in vacuo, and the crude imine was dissolved in acetone (10 ml) and water (3.0 ml); then a solution of oxalic acid dihydrate (189 ml, 1.50 mmol) in water (2 ml) was added to the solution. After the resulting solution was stirred at room temperature for 30 min, the reaction was quenched with sat. $NaHCO_3$. The mixture was extracted twice with ethyl acetate, and the combined extracts were washed with brine. The ethyl acetate solution was dried over anhydrous sodium sulfate, and the ethyl acetate was removed in vacuo. The crude materials were purified by flash column chromatography (hexane : ethyl acetate = 10 : 1→dichloromethane : methanol : triethylamine = 100 : 10 : 1) to give 2-[3,4-bis-(*t*-butyldimethylsiloxy)phenyl]ethylamine (348 mg). The amine was dissolved in ethanol (10 ml), and some fumaric acid (106 mg 0.912 mmol) was added. The ethanol was removed in vacuo, and recrystallization of the residual solid from 2-propanol–ether gave **14** (431 mg, 87%). White powder; mp 166—167 °C; IR (KBr) 2958, 2933, 2893, 1614, 1575, 1512, 1352, 1292, 1255, 1173, 987, 910, 847, 785, 642 cm^{-1}; ^1H NMR (in $CDCl_3$–CD_3OD) δ = 0.09 (12H, s), 0.88 (9H, s), 0.89 (9H, s), 2.71 (2H, t, J = 7.7 Hz), 2.97 (2H, t, J = 7.7 Hz), 6.55—6.59 (2H, m), 6.64 (2H, s), 6.69 (1H, d, J = 8.4 Hz); ^{13}C NMR (in $CDCl_3$–CD_3OD) δ = −4.69, −4.64, 17.96, 18.00, 25.40, 25.43, 32.69, 40.48, 120.98, 121.21 (overlapped), 129.20, 134.77, 145.74, 146.67, 170.15. Anal. Found: C, 57.69; H, 8.42; N, 3.09%. Calcd for $C_{24}H_{43}NO_6Si_2$: C, 57.91; H, 8.71; N, 2.81%.

1-Norbornylammonium Chloride (16):[19] To a solution of CuCN (44.8 mg, 0.500 mmol) and LiCl (42.4 mg, 1.00 mmol) in THF (4.0 ml) was added a solution of **1b** (487 mg, 1.00 mmol) in THF (6.0 ml) and HMPA (1.48 ml, 8.50 mmol) under an argon atmosphere. The reaction mixture was cooled to 0 °C, and an ether solution of norbornylmagnesium chloride (0.303 mol dm^{-3}; 4.95 ml, 1.50 mmol) was added dropwise over 30 min. After the reaction mixture was stirred at the same temperature for 30 min, the mixture was quenched with pH 9 buffer. Inorganic materials were filtered off and organic materials were extracted twice with ether. The combined extracts were washed successively with sat. $NaHCO_3$ and with brine three times; then the ether solution was dried over anhydrous magnesium sulfate. The ether was removed in vacuo, the crude imine was dissolved in acetone (10 ml) and water (2.5 ml); then 1 M HCl (2.00 ml, 2.00 mmol) was added to the solution. After the resulting solution was stirred at room temperature for 30 min, water was added to the mixture and it was washed with ethyl acetate twice. The aqueous solution was removed in vacuo, and recrystallization of the residual solid from 2-propanol–ether gave **16** (141 mg, 96%). White powder; ^1H NMR (in DMSO-d_6) δ = 1.31—1.41 (2H, m), 1.48—1.58 (4H, m), 1.65—1.75 (4H, m), 2.18 (1H, s), 8.53 (3H, br s); ^{13}C NMR (in DMSO-d_6) δ = 29.16, 31.77, 34.72, 40.61, 60.80.

Typical Procedure for the Preparation of Imine 18 by the Reaction of 2 with Grignard Reagents. (Table 3, Entry 1): To a solution of **2** (120 mg, 0.190 mmol) in toluene (3.8 ml) was added dropwise an ether solution of phenylmagnesium bromide (1.20 mol dm^{-3}; 0.237 ml, 0.285 mmol) at room temperature under an argon atmosphere. After the reaction mixture was stirred at the same temperature for 30 min, the mixture was quenched with pH 9 buffer at 0 °C. The mixture was extracted twice with ether, and the combined extracts were washed successively with sat. $NaHCO_3$ and brine. The ether solution was dried over anhydrous magnesium sulfate, and the ether was removed in vacuo. The crude materials were purified by flash column chromatography (hexane : benzene = 5 : 1) to give *N*-{bis[3,5-bis(trifluoromethyl)phenyl]methylidene}aniline (**18f**) (95.2 mg, 95%). Yellow needles; mp 92—93 °C (methanol); IR (KBr) 1630, 1379, 1319, 1286, 1279, 1242, 1182, 1136, 1128, 906, 692 cm^{-1}; ^1H NMR (in $CDCl_3$) δ = 6.62 (2H, d, J = 7.5 Hz), 7.01 (1H, t, J = 7.5 Hz), 7.19 (2H, t, J = 7.5 Hz), 7.53 (2H, s), 7.85 (1H, s), 8.03 (1H, s), 8.15 (2H, s); ^{13}C NMR (in $CDCl_3$) δ = 120.01, 122.67 (q, $^1J_{CF}$ = 272.9 Hz), 122.99 (q, $^1J_{CF}$ = 272.9 Hz), 123.20—123.42 (m), 124.69—124.86 (m), 124.91, 128.94, 129.12, 129.47, 132.21 (q, $^2J_{CF}$ = 34.1 Hz), 132.36 (q, $^2J_{CF}$ = 33.9 Hz), 136.39, 140.12, 149.22, 162.01. Anal. Found: C, 51.98; H, 2.24; N, 2.69%. Calcd for $C_{23}H_{11}F_{12}N$: C, 52.19; H, 2.09; N, 2.65%.

***N*-{Bis[3,5-bis(trifluoromethyl)phenyl]methylidene}(2-methoxyaniline) (18g):** Yellow needles; mp 117—118 °C (methanol); IR (KBr) 1631, 1493, 1375, 1282, 1186, 1138, 1026, 910, 741, 681 cm^{-1}; ^1H NMR (in $CDCl_3$) δ = 3.58 (3H, s), 6.68—6.73 (2H, m), 6.83 (1H, t, J = 6.7 Hz), 6.98 (2H, t, J = 6.7 Hz), 7.58 (2H, s), 7.82 (1H, s), 8.02 (1H, s), 8.18 (2H, s); ^{13}C NMR (in $CDCl_3$) δ = 54.80, 111.12, 120.78, 120.94, 122.74 (q, $^1J_{CF}$ = 272.9 Hz), 122.90—123.15 (m), 122.97 (q, $^1J_{CF}$ = 272.9 Hz), 124.68—124.90 (m), 125.81, 128.61, 128.94, 131.64 (q, $^2J_{CF}$ = 33.7 Hz), 132.24

(q, $^2J_{CF}$ = 33.7 Hz), 137.29, 138.73, 139.69, 147.24, 164.11. Anal. Found: C, 51.54; H, 2.46; N, 2.65%. Calcd for $C_{24}H_{13}F_{12}NO$: C, 51.54; H, 2.34; N, 2.50%.

***N*-{Bis[3,5-bis(trifluoromethyl)phenyl]methylidene}(3-methoxyaniline) (18h):** Yellow prisms; mp 112—113 °C (methanol); IR (KBr) 1633, 1603, 1577, 1481, 1379, 1286, 1281, 1244, 1174, 1132, 1128, 1051, 908, 874, 685 cm^{-1}; ^{1}H NMR (in $CDCl_3$) δ = 3.67 (3H, s), 6.17 (1H, dd, J = 2.1 and 8.0 Hz), 6.23 (1H, t, J = 2.1 Hz), 6.56 (1H, dd, J = 2.1 and 8.0 Hz), 7.08 (1H, t, J = 8.0 Hz), 7.57 (2H, s), 7.87 (1H, s), 8.03 (1H, s), 8.15 (2H, s); ^{13}C NMR (in $CDCl_3$) δ = 55.20, 105.95, 110.66, 112.24, 122.70 (q, $^1J_{CF}$ = 272.9 Hz), 122.98 (q, $^1J_{CF}$ = 273.0 Hz), 123.21—123.46 (m), 124.71—124.98 (m), 128.94, 129.30, 130.00, 132.19 (q, $^2J_{CF}$ = 34.2 Hz), 132.36 (q, $^2J_{CF}$ = 33.7 Hz), 136.42, 140.04, 150.44, 160.59, 162.11. Anal. Found: C, 51.42; H, 2.48; N, 2.63%. Calcd for $C_{24}H_{13}F_{12}NO$: C, 51.54; H, 2.34; N, 2.50%.

***N*-{Bis[3,5-bis(trifluoromethyl)phenyl]methylidene}(4-methoxyaniline) (18i):** Yellow needles; mp 116—117 °C (methanol); IR (KBr) 1610, 1504, 1377, 1284, 1178, 1132, 1032, 906, 847, 706, 683 cm^{-1}; ^{1}H NMR (in $CDCl_3$) δ = 3.73 (3H, s), 6.59 (2H, d, J = 8.8 Hz), 6.73 (2H, d, J = 8.8 Hz), 7.55 (2H, s), 7.88 (1H, s), 8.00 (1H, s), 8.12 (2H, s); ^{13}C NMR (in $CDCl_3$) δ = 55.43, 114.42, 122.29, 122.72 (q, $^1J_{CF}$ = 273.3 Hz), 123.02 (q, $^1J_{CF}$ = 272.9 Hz), 123.11—123.46 (m), 124.40—124.63 (m), 128.75, 129.56, 132.26 (q, $^2J_{CF}$ = 33.8 Hz), 132.36 (q, $^2J_{CF}$ = 34.2 Hz), 136.96, 140.54, 142.12, 157.38, 160.92. Anal. Found: C, 51.57; H, 2.42; N, 2.48%. Calcd for $C_{24}H_{13}F_{12}NO$: C, 51.54; H, 2.34; N, 2.50%.

***N*-{Bis[3,5-bis(trifluoromethyl)phenyl]methylidene}(4-fluoroaniline) (18j):** Yellow needles; mp 95—96 °C (methanol); IR (KBr) 1630, 1606, 1502, 1377, 1284, 1281, 1242, 1190, 1138, 908, 849, 685 cm^{-1}; ^{1}H NMR (in $CDCl_3$) δ = 6.57—6.64 (2H, m), 6.86—6.94 (2H, m), 7.54 (2H, s), 7.89 (1H, s), 8.03 (1H, s), 8.14 (2H, s); ^{13}C NMR (in $CDCl_3$) δ = 116.42 (d, $^2J_{CF}$ = 22.9 Hz), 121.90 (d, $^3J_{CF}$ = 8.2 Hz), 122.65 (q, $^1J_{CF}$ = 273.3 Hz), 122.97 (q, $^1J_{CF}$ = 272.9 Hz), 123.35—123.61 (m), 124.80—125.09 (m), 128.91, 129.41, 132.41 (q, $^2J_{CF}$ = 34.0 Hz), 132.46 (q, $^2J_{CF}$ = 34.2 Hz), 136.67, 140.03, 145.21, 160.10 (d, $^1J_{CF}$ = 245.2 Hz), 162.48. Anal. Found: C, 50.20; H, 1.99; N, 2.83%. Calcd for $C_{23}H_{10}F_{13}N$: C, 50.47; H, 1.84; N, 2.56%.

***N*-{Bis[3,5-bis(trifluoromethyl)phenyl]methylidene}(2,6-dimethylaniline) (18k):** Yellow needles; mp 109—110 °C (methanol); IR (KBr) 1630, 1387, 1373, 1282, 1275, 1246, 1188, 1163, 1147, 1143, 1126, 1111, 1093, 904, 764, 706, 700, 683 cm^{-1}; ^{1}H NMR (in $CDCl_3$) δ = 1.98 (6H, s), 6.86 (1H, t, J = 7.4 Hz), 6.91 (2H, d, J = 7.4 Hz), 7.51 (2H, s), 7.84 (1H, s), 8.05 (1H, s), 8.21 (2H, s); ^{13}C NMR (in $CDCl_3$) δ = 18.19, 122.15 (q, $^1J_{CF}$ = 273.0 Hz), 123.21 (q, $^1J_{CF}$ = 272.9 Hz), 123.59—123.64 (m), 124.44, 124.85—124.91 (m), 124.99, 128.18, 128.42, 128.84, 131.93 (q, $^2J_{CF}$ = 34.0 Hz), 132.41 (q, $^2J_{CF}$ = 33.9 Hz), 161.66. Anal. Found: C, 53.83; H, 2.80; N, 2.69%. Calcd for $C_{25}H_{15}F_{12}N$: C, 53.87; H, 2.71; N, 2.51%

Typical Procedure for the Preparation of Benzamide 9 by the Reaction of 2 with Grignard Reagents. (Eq. 6): To a solution of **2** (632.4 mg, 1.0 mmol) in toluene (20 ml) was added dropwise an ether solution of phenylmagnesium bromide (1.31 mol dm^{-3}; 1.14 ml, 1.50 mmol) at room temperature under an argon atmosphere. After the reaction mixture was stirred at the same temperature for 30 min, the mixture was quenched with pH 9 buffer at 0 °C. The mixture was extracted twice with ether, and the combined extracts were washed successively with sat. $NaHCO_3$ and brine; then the ether solution was dried over anhydrous magnesium sulfate. The ether was removed in vacuo, and the crude imine was dissolved in acetone (10 ml) and water (2.5 ml); then 1 M HCl (2.00 ml, 2.00 mmol) was added to the solution. After the resulting solution was stirred at room temperature for 30 min, the mixture was cooled to 0 °C. Triethylamine (0.55 ml, 4.00 mmol) was added to the mixture, and benzoyl chloride (0.23 ml, 2.00 mmol) was added slowly. After the resulting solution was stirred at room temperature for 30 min, the reaction was quenched with water. The mixture was extracted twice with ethyl acetate, and the combined extracts were washed successively with sat. $NaHCO_3$ and brine. The ethyl acetate solution was dried over anhydrous sodium sulfate, and the ethyl acetate was removed in vacuo. The crude materials were purified by flash column chromatography (hexane : dichloromethane = 40 : 1→10 : 1→hexane : ethyl acetate = 4 : 1) to give benzanilide (**9f**) (188.7 mg, 96%). Colorless prisms; ^{1}H NMR (in $CDCl_3$) δ = 7.14 (1H, t, J = 7.5 Hz), 7.36 (2H, t, J = 7.5 Hz), 7.48 (2H, t, J = 7.4 Hz), 7.54 (1H, t, J = 7.4 Hz), 7.62 (2H, d, J = 7.5 Hz), 7.76 (1H, br s), 7.86 (2H, d, J = 7.4 Hz); ^{13}C NMR (in $CDCl_3$) δ = 120.30, 124.52, 127.02, 128.68, 129.00, 131.74, 134.93, 137.91, 165.88.

Spectral Data. All of the products are known compounds, and their spectral data are in good agreement with those of authentic samples.

2′-Methoxybenzanilide (9g): Colorless needles; ^{1}H NMR (in $CDCl_3$) δ = 3.91 (3H, s), 6.91 (1H, dd, J = 1.4 and 8.0 Hz), 7.01 (1H, dt, J = 1.4 and 8.0 Hz), 7.07 (1H, dt, J = 1.4 and 8.0 Hz), 7.44—7.57 (3H, m), 7.88 (1H, dt, J = 6.9 and 1.8 Hz), 8.52 (1H, dd, J = 1.4 and 8.0 Hz), 8.54 (1H, br s); ^{13}C NMR (in $CDCl_3$) δ = 55.79, 109.93, 119.84, 121.19, 123.83, 127.02, 127.80, 128.71, 131.64, 135.33, 148.13, 165.20.

3′-Methoxybenzanilide (9h): Colorless needles; ^{1}H NMR (in $CDCl_3$) δ = 3.81 (3H, s), 6.69 (1H, dd, J = 2.4 and 8.2 Hz), 7.08 (1H, d, J = 8.2 Hz), 7.24 (1H, t, J = 8.2 Hz), 7.42 (1H, t, J = 2.4 Hz), 7.46 (2H, t, J = 7.8 Hz), 7.53 (1H, t, J = 7.8 Hz), 7.72—7.95 (1H, br), 7.84 (2H, d, J = 7.8 Hz); ^{13}C NMR (in $CDCl_3$) δ = 55.23, 105.90, 110.47, 112.41, 127.00, 128.64, 129.63, 131.72, 134.89, 139.19, 160.13, 165.89.

4′-Methoxybenzanilide (9i): Colorless prisms; ^{1}H NMR (in $CDCl_3$) δ = 3.79 (3H, s), 6.89 (1H, d, J = 6.8 Hz), 7.45 (2H, t, J = 7.3 Hz), 7.49—7.55 (3H, m), 7.75 (1H, br s), 7.85 (2H, d, J = 7.3 Hz); ^{13}C NMR (in $CDCl_3$) δ = 55.46, 114.18, 122.18, 127.00, 128.65, 131.05, 131.60, 135.02, 156.60, 165.59.

4′-Fluorobenzanilide (9j): Colorless prisms; ^{1}H NMR (in $CDCl_3$–CD_3OD) δ = 6.98—7.07 (2H, m), 7.45 (2H, t, J = 7.3 Hz), 7.52 (1H, t, J = 7.3 Hz), 7.55—7.61 (2H, m), 7.83 (2H, d, J = 7.3 Hz); ^{13}C NMR (in $CDCl_3$–CD_3OD) δ = 115.29 (d, $^2J_{CF}$ = 22.3 Hz), 122.42 (d, $^3J_{CF}$ = 8.0 Hz), 127.10, 128.32, 131.62, 134.02. 134.56, 159.39 (d, $^1J_{CF}$ = 243.7 Hz), 166.86.

2′,6′-Dimethylbenzanilide (9k): Colorless needles; ^{1}H NMR (in $CDCl_3$) δ = 2.28 (6H, s), 7.10—7.13 (3H, m), 7.34 (1H, br s), 7.49 (2H, t, J = 7.4 Hz), 7.56 (1H, t, J = 7.4 Hz), 7.91 (2H, d, J = 7.4 Hz); ^{13}C NMR (in $CDCl_3$) δ = 18.45, 127.19, 127.40, 128.25, 128.73, 131.75, 133.86, 134.48, 135.56, 165.89.

***N*-1-Naphtylbenzamide (9l):** Colorless prisms; ^{1}H NMR (in $CDCl_3$) δ = 7.49—7.54 (5H, m), 7.59 (1H, t, J = 7.3 Hz), 7.73 (1H, d, J = 8.3 Hz), 7.88—7.91 (2H, m), 7.98 (2H, d, J = 7.3 Hz), 8.04 (1H, d, J = 6.8 Hz), 8.19 (1H, br s); ^{13}C NMR (in $CDCl_3$) δ = 120.75, 121.33, 125.73, 126.01, 126.10, 126.36, 127.19, 127.50, 128.78, 128.81, 131.90, 132.38, 134.13, 134.79, 165.20.

4-Trifluoromethylaniline Hydrochloride (19):[20] To a solution of **2** (126.5 mg, 0.20 mmol) in toluene (4 ml) was added dropwise an ether solution of 4-trifluoromethylphenylmagnesium bromide (0.89 mol dm^{-3}; 0.34 ml, 0.3 mmol) at room temperature under an argon atmosphere. After the reaction mixture was stirred at the

same temperature for 30 min, the mixture was quenched with pH 9 buffer at 0 °C. The mixture was extracted twice with ether, and the combined extracts were washed successively with sat. $NaHCO_3$ and brine; then the ether solution was dried over anhydrous magnesium sulfate. The ether was removed in vacuo, and the crude imine was dissolved in acetone (2 ml) and water (0.5 ml); then 1 M HCl (0.40 ml, 0.40 mmol) was added to the solution. After the resulting solution was stirred at room temperature for 30 min, the mixture was quenched with sat. $NaHCO_3$. The mixture was extracted twice with ethyl acetate, and the combined extracts were washed with brine. The ethyl acetate solution was dried over anhydrous sodium sulfate, and the ethyl acetate was removed in vacuo. The crude materials were purified by thin-layer chromatography (silica gel, hexane : dichloromethane = 1 : 2) to give 4-trifluoromethylaniline. The aniline was dissolved in ethanol (2 ml), and 1 M HCl (0.40 ml, 0.40 mmol) was added. The ethanol was removed in vacuo to gave **19** (28.1 mg, 71%). White powder; ^{1}H NMR (in DMSO-d_6) δ = 6.90 (2H, d, J = 7.5 Hz), 6.91—7.45 (3H, br s), 7.45 (2H, d, J = 7.5 Hz); ^{13}C NMR (in DMSO-d_6) δ = 117.12, 120.32, 124.48 (q, $^1J_{CF}$ = 271.4 Hz), 126.41—126.80 (m), 141.75—142.05 (m).

3-Phenylpropylamine (20):[21] To a solution of **2** (632.4 mg, 1.0 mmol) in toluene (20 ml) was added dropwise an ether solution of 3-phenylpropylmagnesium bromide (1.25 mol dm^{-3}; 1.20 ml, 1.50 mmol) at room temperature under an argon atmosphere. After the reaction mixture was stirred at the same temperature for 30 min, the mixture was quenched with pH 9 buffer at 0 °C. The mixture was extracted twice with ether, and the combined extracts were washed successively with sat. $NaHCO_3$ and brine; then the ether solution was dried over anhydrous magnesium sulfate. The ether was removed in vacuo, and the crude imine was dissolved in acetone (10 ml) and water (2.5 ml), and 1 M HCl (2.00 ml, 2.00 mmol) was added to the solution. After the resulting solution was stirred at room temperature for 30 min, water was added to the mixture and it was washed with ether twice. The aqueous solution was removed in vacuo to gave **20** (164 mg, 96%). White powder; ^{1}H NMR (in DMSO-d_6) δ = 1.84—1.90 (2H,m), 2.50 (2H, t, J = 7.6 Hz), 2.75 (2H, t, J = 7.6 Hz), 7.18—7.22 (3H, m), 7.30 (2H, t, J = 7.5 Hz), 8.13 (3H, br s); ^{13}C NMR (in DMSO-d_6) δ = 28.63, 31.87, 38.22, 125.95, 128.25, 128.36, 140.90.

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