

# An Efficient Method for the Preparation of Versatile Building Blocks: 1-Substituted 2,2-Dimethoxyethylamine Hydrochlorides

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**Abstract:** A novel method for the preparation of 1-substituted 2,2-dimethoxyethylamine hydrochlorides was developed. The method includes three highly efficient steps: (1) direct use of aqueous  $(\text{MeO})_2\text{CHCHO}$  for the preparation of *N,O*-acetal by condensation with Betti base without acidic catalyst; (2) regioselective alkylations of the *N,O*-acetal with Grignard reagents; and (3) Pd/C catalytic hydrogenolyses of benzylamines in the presence of  $\text{ClCH}_2\text{CHCl}_2$  to directly give the target products as crystalline amine hydrochlorides. The method reported is extremely convenient and highly efficient with wide substrate scopes.

**Key words:** heterocycles, alkylation, N-debenzylation, Betti base, 2,2-dimethoxyethylamines

$\alpha$ -Amino aldehydes **1** (Figure 1) are important precursors in organic synthesis<sup>1</sup> because they hold both the highly reactive amino and formyl groups. Since they are not chemically stable, one of the functional groups needs to be protected for storage and reactions. 2-Amidoacetaldehydes **2** and 2,2-dialkoxyethylamines **3** are two major forms depending on the purpose of the application. In literature, numerous biologically important N-containing heterocycles, such as isoquinolines,<sup>2</sup> imidazoles,<sup>3</sup> pyrazines,<sup>4</sup> azepines,<sup>5</sup> and indoles<sup>6</sup> etc., were prepared efficiently by using the derivatives of **3** as versatile building blocks. In these preparations, substrates **3** usually were introduced into the target molecules by N-alkylation or N-acylation. Then, its formyl group was released by an in situ deprotection of the acetal group under acidic conditions to undergo an intramolecular cyclization.

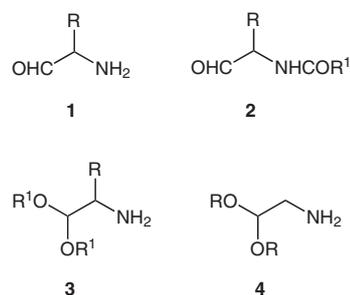


Figure 1

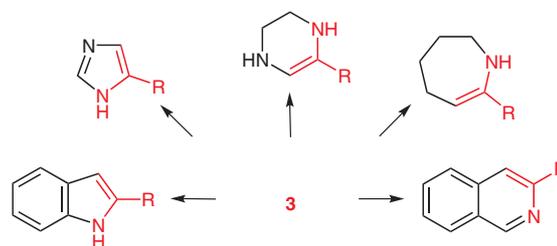
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It is noteworthy that 2,2-dimethoxyethylamine (**4a**, R = Me) and 2,2-diethoxyethylamine (**4b**, R = Et) were most often used for this purpose for two reasons: (a) they are commercially available products; and (b) their deacetylations are much easier than most others. Thus, we may expect that the structural diversity in heterocycle synthesis can be achieved conveniently by replacement of **4a,b** with 1-substituted 2,2-dialkoxyethylamines **3**, which would practically benefit our current projects on chemical biology and drug discovery (Scheme 1).



Scheme 1

Unfortunately, a literature survey indicated that the preparation of **3** remains a challenge. For example, some chiral **3** were prepared from natural  $\alpha$ -amino acids by multi-step synthesis,<sup>7</sup> but the method suffered from tedious operations with poor total yields. In practice, the chirality for **3** is not necessary in most of its heterocycles syntheses (Scheme 1). Although the reductive amination of  $\alpha,\alpha$ -dialkoxy ketones offered a fast protocol,<sup>8</sup> its application was seriously limited because the substrates themselves are not easy to synthesize. In fact, there were only two procedures that deal with the methodology for the preparation of **3** to date. As shown in Figure 2, benzotriazolyl-substituted Mannich base **5**<sup>9</sup> and benzyl substituted *N,O*-acetal **6**<sup>10</sup> were employed as key intermediates in those two procedures, in which the substituents were introduced by treatment of **5** and **6** with Grignard reagents.

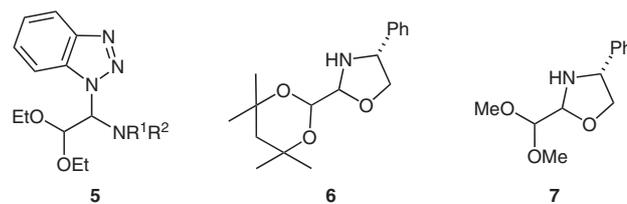
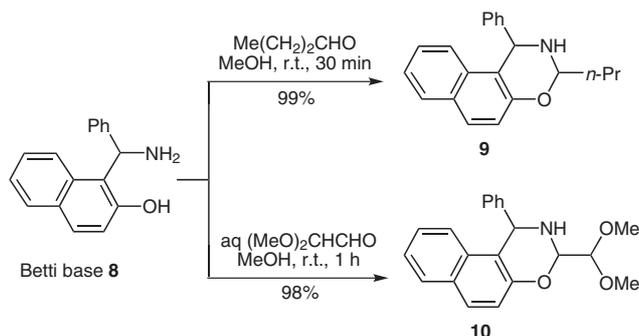


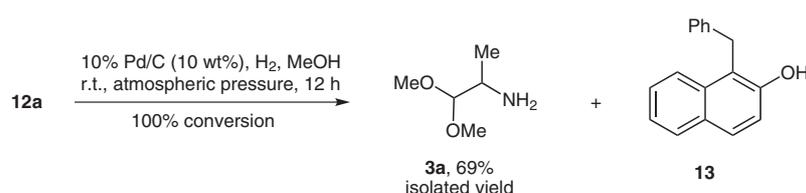
Figure 2

However, when we repeated the former procedure, we found that it was only suitable for *N,N*-disubstituted or *N*-aryl products because Mannich base **5** with  $\text{NH}_2$  or *N*-alkyl groups did not react with Grignard reagents at all. While, according to the latter procedure, we did not obtain the corresponding *N,O*-acetal **7** by the condensation of  $(\text{MeO})_2\text{CHCHO}$  and (*R*)-(-)-2-amino-2-phenylethanol. This result must arise from the fact that  $(\text{MeO})_2\text{CHCHO}$  is available as an aqueous product (60 wt%), which is not suitable for direct use in the preparation of *N,O*-acetals. Herein, we report a novel and general procedure for the preparation of 1-substituted 2,2-dialkoxyethylamine hydrochlorides (**3**-HCl), which is convenient and efficient with wide substrate scope.

Betti base **8** is an 1,3-aminohydroxy compound and easily prepared in kilogram scale.<sup>11</sup> Its enantiomers have been employed as excellent chiral ligands<sup>12</sup> and auxiliaries<sup>13</sup> in asymmetric syntheses. In our previous work,<sup>14</sup> we found that the condensation of Betti base **8** and aliphatic aldehydes proceeded very efficiently under mild conditions without acidic catalyst. As shown in Scheme 1, when the mixtures of Betti base **8** and 1-butanal in MeOH was stirred at room temperature for 30 minutes, the corresponding *N,O*-acetal **9** was obtained in almost quantitative yield. At the strong encouragement of this result, we tried to explore the condensation between Betti base **8** and  $(\text{MeO})_2\text{CHCHO}$ . To our great surprise, when the mixture of Betti base **8** and aqueous  $(\text{MeO})_2\text{CHCHO}$  (60 wt%) in MeOH was stirred at room temperature for one hour, the desired *N,O*-acetal **10** was obtained in 98% yield even without the use of an acidic catalyst (Scheme 2). The control experiments proved that this success mainly arose from the low solubility of the product **10** in aqueous MeOH. A modest additional rate acceleration was observed by the addition of an extra 10% of water to the reaction.



Scheme 2



Scheme 3

Unfortunately, no alkylated products were obtained when **9** was treated with a variety of Grignard reagents, even under reflux in THF for 1 hour. Since *N,N*-disubstituted Betti base derivatives were alkylated smoothly by Grignard reagents,<sup>13b,c</sup> this problem must be caused by the  $\text{NH}$  group in **9**. This result was in full agreement with that observed in the reaction of *N*-alkylated **5** (with  $\text{NHR}$ ) and Grignard reagents.<sup>9</sup> But in contrast to **9**, the alkylation of **10** by  $\text{MeMgBr}$  (**11a**) was accomplished quickly at room temperature within 30 minutes to give the desired product **12a** in 85% isolated yield. This result strongly implied that the  $\text{C-O}$  bond of *N,O*-acetal group in **10** may be activated by the  $\alpha$ -substituted *O,O*-acetal group. As shown in Table 1, a series of products **12b-o** were obtained by using the corresponding Grignard reagents **11b-o** under the similar conditions. Since the structural assignments of **12a-o** suffered from their ambiguous  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra (they were caused by unusual coalescence phenomenon), they were usually used in the next step without characterization. However, they were purified by simple chromatography to remove the homo-coupling by-products of Grignard reagents, which significantly benefit the product separation in the next step.

It is well known that the hydrogenolyses of the benzylamines substituted by triaryl or diaryl on benzyl carbon are much easier than the regular benzylamine.<sup>15</sup> Thus, the diaryl benzylamine **12a** was *N*-debenzylated quantitatively under mild Pd/C catalytic hydrogenolysis conditions (Scheme 3). Unfortunately, the oily product **3a** was obtained in only 69% isolated yield after it was purified by chromatography to remove the by-product **13**.

Recently, we reported a novel procedure for Pd/C catalytic hydrogenolyses of benzylamines in the presence of  $\text{CH}_2\text{Cl}_2$ <sup>13b</sup> or  $\text{ClCH}_2\text{CHCl}_2$ ,<sup>16</sup> by which the *N*-debenzylation was accelerated significantly and the debenzylated products were directly converted into the corresponding amine hydrochlorides. As shown in Scheme 4, when **12a** was hydrogenolyzed in the presence of  $\text{ClCH}_2\text{CHCl}_2$ , the *N*-debenzylation was accomplished within six hours. After filtration of the catalyst and evaporation of MeOH, the crystalline product **3**-HCl was formed by addition of small amount of  $\text{Et}_2\text{O}$ . Since the by-product **13** had a good solubility in  $\text{Et}_2\text{O}$ , the separation procedure for **3**-HCl was as simple as a filtration.

As shown in Table 2, by using the similar procedure, the desired products **3a-o**-HCl were obtained in excellent yields, which usually were pure enough for most uses without further purification.

**Table 1** Alkylated Products **12a–o** Prepared

<b>11,12</b>	R	Yield of <b>12</b> (%)
<b>a</b>	Me	85
<b>b</b>	Me(CH <sub>2</sub> ) <sub>2</sub>	89
<b>c</b>	Me(CH <sub>2</sub> ) <sub>4</sub>	86
<b>d</b>	3-[(1,3-dioxan-2-yl)-1-propyl]	85
<b>e</b>	cyclopropyl	90
<b>f</b>	cyclopentyl	87
<b>g</b>	Ph	93
<b>h</b>	2-MeC <sub>6</sub> H <sub>4</sub>	93
<b>i</b>	3-MeC <sub>6</sub> H <sub>4</sub>	91
<b>j</b>	4-MeC <sub>6</sub> H <sub>4</sub>	93
<b>k</b>	3,4-Me <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	96
<b>l</b>	2-MeOC <sub>6</sub> H <sub>4</sub>	95
<b>m</b>	3-MeOC <sub>6</sub> H <sub>4</sub>	94
<b>n</b>	4-MeOC <sub>6</sub> H <sub>4</sub>	92
<b>o</b>	3,4-(MeO) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	92

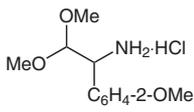
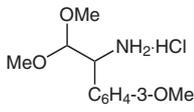
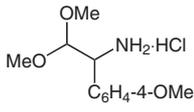
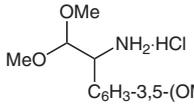
**Scheme 4**

In summary, a novel and general procedure for the preparation of 1-substituted 2,2-dimethoxyethylamine hydrochlorides was developed. The benefits of this method are threefold. First, the commercially available aqueous (MeO)<sub>2</sub>CHCHO was directly used for the condensation with Betti base **8**, by which the important *N,O*-acetal intermediate **10** was obtained efficiently in 98% yield within one hour. Second, by activation of *O,O*-acetal group, the *N,O*-acetal **10** was alkylated smoothly with a variety of Grignard reagents within 30 minutes to give the alkylated products **12a–o** in high yields. Third, in the presence of CICH<sub>2</sub>CHCl<sub>2</sub>, the Pd/C catalyzed hydrogenolyses of **12a–o** directly gave the products as crystalline amine hydrochlorides. The method is extremely convenient and highly efficient with wide substrate scopes.

**Table 2** Final Products **3a–o**·HCl Prepared

Entry	<b>3</b> ·HCl	Yield (%)
<b>a</b>		92
<b>b</b>		94
<b>c</b>		90
<b>d</b>		91
<b>e</b>		91
<b>f</b>		90
<b>g</b>		93
<b>h</b>		98
<b>i</b>		96
<b>j</b>		99
<b>k</b>		96

**Table 2** Final Products **3a–o**·HCl Prepared (continued)

Entry	3·HCl	Yield (%)
<b>l</b>		98
<b>m</b>		94
<b>n</b>		92
<b>o</b>		95

All melting points were determined on a Yanaco melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet FT-IR 5DX spectrometer. The  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on a Jeol JNM-ECA 300 spectrometer in  $\text{D}_2\text{O}$ . The  $J$  values are given in Hz. MS were recorded on a VG-ZAB-MS spectrometer with 70 eV. Elementary analysis data were obtained on a PerkinElmer-241C apparatus. Petroleum ether (PE) used refers to the fraction boiling in the range 60–90 °C.

### 3-(Dimethoxymethyl)-1-phenyl-2,3-dihydro-1*H*-naphtho[1,2-*e*][1,3]oxazine (**10**)

To a stirred solution of Betti base **8** (2.49 g, 10 mmol) in MeOH (30 mL) was added an aqueous solution of 2,2-dimethoxyacetaldehyde (60 wt%, 1.81 g, 12 mmol) at r.t. The resulting mixture was stirred continuously for another 1 h, the white solid **10** (3.28 g, 98%) formed was collected by filtration, and purified by chromatography (silica gel, PE–EtOAc, 5:1). Usually, it was directly used in the next step without purification; mp 147–149 °C ( $\text{CH}_2\text{Cl}_2$ –MeOH).

IR (KBr): 2900, 1620, 1440, 1210, 1230  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = 7.70–7.64 (m, 2 H), 7.28–7.13 (m, 9 H), 5.43 (s, 1 H), 4.74–4.71 (m, 1 H), 4.42–4.41 (m, 1 H), 3.39 (s, 6 H), 2.86–2.83 (m, 1 H).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = 151.6, 142.1, 131.2, 129.0 (2 C), 128.8, 128.5, 128.2, 128.0 (2 C), 127.0, 126.3, 123.0, 122.5, 119.0, 114.3, 103.4, 81.3, 55.6, 55.2, 52.7.

MS (EI):  $m/z$  (%) = 432 ( $\text{M}^+$ , 0.01), 231 (100).

Anal. Calcd for  $\text{C}_{21}\text{H}_{21}\text{NO}_3$ : C, 75.20; H, 6.31; N, 4.18. Found: C, 75.13; H, 6.41; N, 4.12.

### 1-Substituted 2,2-Dimethoxyethylamine Hydrochlorides 3·HCl; General Procedure

To a stirred solution of Grignard reagent **11** (15 mmol) in  $\text{Et}_2\text{O}$  (30 mL) was added a solution of *N,O*-acetal **10** (1.01 g, 3 mmol) in THF (30 mL) at r.t. After stirring the resulting mixture continuously for another 30 min, it was cooled to 0 °C and quenched by the addition of sat. aq  $\text{NH}_4\text{Cl}$  (30 mL). The organic layer was separated and the aqueous layer was extracted with  $\text{Et}_2\text{O}$  (3 × 30 mL). The combined organic layers were washed with  $\text{H}_2\text{O}$  (30 mL) and brine (30 mL),

and dried ( $\text{Na}_2\text{SO}_4$ ). Removal of the solvent gave the crude product, which was purified by chromatography (silica gel, PE–EtOAc, 10:1) to give the pure compound **12** (85–96%). A suspension of product **12** (2 mmol), 10% Pd/C (10 wt%) and  $\text{ClCH}_2\text{CHCl}_2$  (320 mg, 2.4 mmol) in MeOH (30 mL) was hydrogenated at r.t. and atmospheric pressure until the absorption of  $\text{H}_2$  had ceased (2–6 h). After the Pd/C catalyst was filtered off, the solvent was removed on a rotavapor. The residue was diluted with  $\text{Et}_2\text{O}$  (10 mL) and the white crystals of **3**·HCl (90–99%) were collected by filtration. Usually, the product was pure enough for any analytical purposes.

### 1-Methyl-2,2-dimethoxyethylamine Hydrochloride (3a·HCl)

Mp 102–103 °C (MeOH– $\text{Et}_2\text{O}$ ).

IR (KBr): 3422, 2941, 1455, 1395  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 4.42 (d,  $J$  = 4.47 Hz, 1 H), 3.44 (m, 7 H), 1.21 (d,  $J$  = 6.54 Hz, 3 H).

$^{13}\text{C}$  NMR:  $\delta$  = 104.5, 56.9, 55.9, 49.0, 12.9.

MS:  $m/z$  (%) = 119 ( $\text{M}^+$  – HCl, 0.5), 75.05 (100).

Anal. Calcd for  $\text{C}_5\text{H}_{14}\text{ClNO}_2$ : C, 38.59; H, 9.07; N, 9.00. Found: C, 38.60; H, 9.05; N, 9.01.

### 1-Propyl-2,2-dimethoxyethylamine Hydrochloride (3b·HCl)

Mp 133–135 °C (MeOH– $\text{Et}_2\text{O}$ ).

IR (KBr): 3447, 2959, 1453, 1356  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 4.50 (d,  $J$  = 4.47 Hz, 1 H), 3.48 (s, 3 H), 3.47 (s, 3 H), 3.39–3.24 (m, 1 H), 1.65–1.34 (m, 4 H), 0.88 (t,  $J$  = 6.87 Hz, 3 H).

$^{13}\text{C}$  NMR:  $\delta$  = 103.7, 57.0, 55.9, 52.9, 29.9, 17.9, 13.0.

MS:  $m/z$  (%) = 147 ( $\text{M}^+$  – HCl, 13.2), 73 (100).

Anal. Calcd for  $\text{C}_7\text{H}_{18}\text{ClNO}_2$ : C, 45.77; H, 9.88; N, 7.63. Found: C, 45.80; H, 9.91; N, 7.59.

### 1-Pentyl-2,2-dimethoxyethylamine Hydrochloride (3c·HCl)

Mp 109–109.5 °C (MeOH– $\text{Et}_2\text{O}$ ).

IR (KBr): 3423, 2962, 2932, 1506  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 4.50 (d,  $J$  = 4.47 Hz, 1 H), 3.47 (s, 3 H), 3.44 (s, 3 H), 3.34–3.28 (m, 1 H), 1.69–1.25 (m, 8 H), 0.81 (t,  $J$  = 6.85 Hz, 3 H).

$^{13}\text{C}$  NMR:  $\delta$  = 103.7, 57.0, 55.9, 53.2, 30.7, 27.7, 24.1, 21.7, 13.3.

MS:  $m/z$  (%) = 175 ( $\text{M}^+$  – HCl, 1.9), 100 (100).

Anal. Calcd for  $\text{C}_9\text{H}_{22}\text{ClNO}_2$ : C, 51.05; H, 10.47; N, 6.62. Found: C, 51.11; H, 10.51; N, 6.61.

### 1-[3-([1,3]Dioxan-2-yl)-1-propyl]-2,2-dimethoxyethylamine Hydrochloride (3d·HCl)

Mp 112–114 °C (MeOH– $\text{Et}_2\text{O}$ ).

IR (KBr): 3403, 2942, 2902, 1506  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 4.72–4.71 (m, 1 H), 4.54–4.52 (m, 1 H), 4.09–4.06 (m, 2 H), 3.89–3.86 (m, 2 H), 3.50–3.47 (m, 6 H), 3.46–3.49 (m, 1 H), 2.00–1.42 (m, 6 H).

$^{13}\text{C}$  NMR:  $\delta$  = 103.5, 101.4, 67.2(2C), 57.1, 56.0, 52.8, 30.1, 25.2, 22.5.

MS:  $m/z$  (%) = 219 ( $\text{M}^+$  – HCl, 2.0), 117 (100).

Anal. Calcd for  $\text{C}_{10}\text{H}_{22}\text{ClNO}_4$ : C, 46.96; H, 8.67; N, 5.48. Found: C, 46.90; H, 8.71; N, 5.51.

### 1-Cyclopropyl-2,2-dimethoxyethylamine Hydrochloride (3e·HCl)

Mp 141.5–143 °C (MeOH– $\text{Et}_2\text{O}$ ).

IR (KBr): 3352, 3061, 2994, 2932, 1454, 1352  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 4.58 (d,  $J$  = 4.1 Hz, 1 H), 3.53 (s, 3 H), 3.49 (s, 3 H), 2.58–2.54 (dd,  $J$  = 3.8, 10.3 Hz, 1 H), 1.04–0.90 (m, 1 H), 0.68–0.62 (m, 2 H), 0.48–0.33 (m, 2 H).

$^{13}\text{C}$  NMR:  $\delta$  = 104.2, 58.6, 57.2, 56.1, 9.0, 3.4, 2.6.

MS:  $m/z$  (%) = 145 ( $\text{M}^+ - \text{HCl}$ , 0.8), 75 (100).

Anal. Calcd for  $\text{C}_7\text{H}_{16}\text{ClNO}_2$ : C, 46.28; H, 8.88; N, 7.71. Found: C, 46.37; H, 8.92; N, 7.66.

### 1-Cyclopentyl-2,2-dimethoxyethylamine Hydrochloride (3f·HCl)

Mp 137–138.5 °C (MeOH–Et<sub>2</sub>O).

IR (KBr): 3423, 2953, 1450  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 4.59 (d,  $J$  = 2.73 Hz, 1 H), 3.54 (s, 3 H), 3.48 (s, 3 H), 3.25–3.21 (dd,  $J$  = 3.09, 9.63, 1 H), 2.19–2.05 (m, 1 H), 1.86–1.83 (m, 2 H), 1.67–1.57 (m, 4 H), 1.39–1.19 (m, 2 H).

$^{13}\text{C}$  NMR:  $\delta$  = 103.6, 57.9, 57.6, 55.9, 38.9, 29.2, 28.9, 24.5 (2 C).

MS:  $m/z$  (%) = 173 ( $\text{M}^+ - \text{HCl}$ , 1.8), 98 (100).

Anal. Calcd for  $\text{C}_9\text{H}_{20}\text{ClNO}_2$ : C, 51.54; H, 9.61; N, 6.68. Found: C, 51.57; H, 9.62; N, 6.70.

### 1-Phenyl-2,2-dimethoxyethylamine Hydrochloride (3g·HCl)

Mp 129.5–130.5 °C (MeOH–Et<sub>2</sub>O).

IR (KBr): 3423, 2962, 2932, 1623, 1506  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 7.42 (m, 5 H), 4.79 (d,  $J$  = 5.49 Hz, 1 H), 4.41 (d,  $J$  = 5.85 Hz, 1 H), 3.49 (s, 3 H), 3.31 (s, 3 H).

$^{13}\text{C}$  NMR:  $\delta$  = 132.1, 129.8, 129.3 (2 C), 128.0 (2 C), 104.2, 56.7, 56.4, 56.1.

MS:  $m/z$  (%) = 181 ( $\text{M}^+ - \text{HCl}$ , 4.1), 107 (100).

Anal. Calcd for  $\text{C}_{10}\text{H}_{16}\text{ClNO}_2$ : C, 55.17; H, 7.41; N, 6.43. Found: C, 55.24; H, 7.37; N, 6.44.

### 1-(2-Methylphenyl)-2,2-dimethoxyethylamine Hydrochloride (3h·HCl)

Mp 153–155 °C (MeOH–Et<sub>2</sub>O).

IR (KBr): 3437, 3188, 3044, 2934, 1594, 1519, 1377  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 7.34–7.30 (m, 4 H), 4.80 (d,  $J$  = 5.85 Hz, 1 H), 4.7 (d,  $J$  = 5.85 Hz, 1 H, D<sub>2</sub>O exch.), 3.48 (s, 3 H), 3.32 (s, 3 H), 2.35 (s, 3 H).

$^{13}\text{C}$  NMR:  $\delta$  = 137.6, 131.2, 130.7, 129.6, 126.9, 126.4, 104.8, 57.1, 56.8, 52.4, 18.7.

MS:  $m/z$  (%) = 195 ( $\text{M}^+ - \text{HCl}$ , 1.0), 75 (100).

Anal. Calcd for  $\text{C}_{11}\text{H}_{18}\text{ClNO}_2$ : C, 57.02; H, 7.83; N, 6.04. Found: C, 56.98; H, 7.88; N, 5.99.

### 1-(3-Methylphenyl)-2,2-dimethoxyethylamine Hydrochloride (3i·HCl)

Mp 149.5–152.0 °C (MeOH–Et<sub>2</sub>O).

IR (KBr): 3430, 2936, 1615, 1590, 1515, 1397  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 7.35–7.25 (m, 4 H), 4.79 (d,  $J$  = 5.85 Hz, 1 H), 4.39 (d,  $J$  = 5.85 Hz, 1 H), 3.47 (s, 3 H), 3.34 (s, 3 H), 2.32 (s, 3 H).

$^{13}\text{C}$  NMR:  $\delta$  = 139.7, 132.2, 130.4, 129.3, 128.5, 124.9, 104.3, 56.8, 56.4, 56.1, 20.6.

MS:  $m/z$  (%) = 195 ( $\text{M}^+ - \text{HCl}$ , 1.6), 75 (100).

Anal. Calcd for  $\text{C}_{11}\text{H}_{18}\text{ClNO}_2$ : C, 57.02; H, 7.83; N, 6.04. Found: C, 57.05; H, 7.79; N, 6.10.

### 1-(4-Methylphenyl)-2,2-dimethoxyethylamine Hydrochloride (3j·HCl)

Mp 156–158 °C (MeOH–Et<sub>2</sub>O).

IR (KBr): 3425, 3176, 2966, 1590, 1521, 1449, 1359  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 7.33–7.29 (m, 4 H), 4.79 (d,  $J$  = 5.64 Hz, 1 H), 4.39 (d,  $J$  = 5.89 Hz, 1 H), 3.48 (s, 3 H), 3.33 (s, 3 H), 2.30 (s, 3 H).

$^{13}\text{C}$  NMR:  $\delta$  = 140.3, 129.9 (2 C), 129.1, 127.9 (2 C), 104.3, 56.7, 56.2, 56.1, 20.4.

MS:  $m/z$  (%) = 195 ( $\text{M}^+ - \text{HCl}$ , 1.18), 120 (100).

Anal. Calcd for  $\text{C}_{11}\text{H}_{18}\text{ClNO}_2$ : C, 57.02; H, 7.83; N, 6.04. Found: C, 57.05; H, 7.79; N, 6.03.

### 1-(3,5-Dimethyl)-2,2-dimethoxyethylamine Hydrochloride (3k·HCl)

Mp 158.5–160.5 °C (MeOH–Et<sub>2</sub>O).

IR (KBr): 3415, 3223, 2998, 1608, 1510, 1460, 1361, 1210  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 7.11 (s, 1 H), 7.03 (s, 2 H), 4.76 (d,  $J$  = 5.82 Hz, 1 H), 4.33 (d,  $J$  = 5.85 Hz, 1 H), 3.48 (s, 3 H), 3.33 (s, 3 H), 2.26 (s, 6 H).

$^{13}\text{C}$  NMR:  $\delta$  = 139.6 (2 C), 132.3, 131.0, 125.4 (2 C), 104.3, 56.7, 56.4, 56.0, 20.4 (2 C).

MS:  $m/z$  (%) = 209 ( $\text{M}^+ - \text{HCl}$ , 1.4), 134 (100).

Anal. Calcd for  $\text{C}_{12}\text{H}_{20}\text{ClNO}_2$ : C, 58.65; H, 8.20; N, 5.70. Found: C, 58.75; H, 8.18; N, 5.73.

### 1-(2-Methoxyphenyl)-2,2-dimethoxyethylamine Hydrochloride (3l·HCl)

Mp 142–143 °C (MeOH–Et<sub>2</sub>O).

IR (KBr): 3423, 2962, 2932, 1623, 1506  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 7.38–7.33 (m, 1 H), 7.00–6.98 (m, 3 H), 4.75 (d,  $J$  = 5.85 Hz, 1 H), 4.36 (d,  $J$  = 5.82 Hz, 1 H), 3.76 (s, 3 H), 3.43 (s, 3 H), 3.31 (s, 3 H).

$^{13}\text{C}$  NMR:  $\delta$  = 159.3, 133.8, 130.7, 120.5, 115.2, 113.7, 104.2, 56.7, 56.3, 56.1, 55.5.

MS:  $m/z$  (%) = 212 ( $\text{M}^+ - \text{HCl} + \text{H}$ , 34.7), 136 (100).

Anal. Calcd for  $\text{C}_{11}\text{H}_{18}\text{ClNO}_3$ : C, 53.33; H, 7.32; N, 5.65. Found: C, 53.30; H, 7.34; N, 5.61.

### 1-(3-Methoxyphenyl)-2,2-dimethoxyethylamine Hydrochloride (3m·HCl)

Mp 149–151 °C (MeOH–Et<sub>2</sub>O).

IR (KBr): 3418, 2965, 2935, 1608, 1517, 1461, 1306, 1276  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 7.40–7.27 (m, 1 H), 7.27–7.23 (m, 1 H), 7.07–6.98 (m, 2 H), 4.93 (d,  $J$  = 6.87 Hz, 1 H), 4.43 (d,  $J$  = 6.87 Hz, 1 H), 3.81 (s, 3 H), 3.44 (s, 3 H), 3.19 (s, 3 H).

$^{13}\text{C}$  NMR:  $\delta$  = 157.2, 131.5, 130.3, 121.2, 119.6, 111.8, 102.8, 56.2, 55.5 (2 C), 54.3.

MS:  $m/z$  (%) = 211 ( $\text{M}^+ - \text{HCl}$ , 38.2), 136 (100).

Anal. Calcd for  $\text{C}_{11}\text{H}_{18}\text{ClNO}_3$ : C, 53.33; H, 7.32; N, 5.65. Found: C, 53.40; H, 7.37; N, 5.65.

### 1-(4-Methoxyphenyl)-2,2-dimethoxyethylamine Hydrochloride (3n·HCl)

Mp 148.5–149 °C (MeOH–Et<sub>2</sub>O).

IR (KBr): 3407, 2184, 3036, 2966, 1613, 1517, 1460, 1306, 1255  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta$  = 7.38 (d,  $J$  = 8.58 Hz, 2 H), 7.02 (d,  $J$  = 8.58 Hz, 2 H), 4.78 (d,  $J$  = 6.18 Hz, 1 H), 4.38 (d,  $J$  = 5.85 Hz, 1 H), 3.79 (s, 3 H), 3.49 (s, 3 H), 3.34 (s, 3 H).

$^{13}\text{C}$  NMR:  $\delta = 159.8, 129.6$  (2 C), 124.7, 114.8 (2 C), 104.2, 56.7, 56.1, 56.0, 55.5.

MS:  $m/z$  (%) = 212 ( $\text{M}^+ - \text{HCl} + \text{H}$ , 1.7), 136 (100).

Anal. Calcd for  $\text{C}_{11}\text{H}_{18}\text{ClNO}_3$ : C, 53.33; H, 7.32; N, 5.65. Found: C, 53.29; H, 7.30; N, 5.65.

### 1-(3,5-Dimethoxy)-2,2-dimethoxyethylamine Hydrochloride (3o·HCl)

Mp 175–176.5 °C (MeOH–Et<sub>2</sub>O).

IR (KBr): 3432, 3140, 3029, 2938, 1605, 1515, 1469, 1262, 1234  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR:  $\delta = 7.06\text{--}7.02$  (m, 3 H), 4.77 (d,  $J = 7.89$  Hz, 1 H), 4.37 (d,  $J = 5.82$  Hz, 1 H), 3.81 (s, 6 H), 3.46 (s, 3 H), 3.34 (s, 3 H).

$^{13}\text{C}$  NMR:  $\delta = 149.1, 148.5, 125.1, 121.3, 112.1, 111.3, 104.3, 56.8, 56.2, 56.1, 55.9, 55.8$ .

MS:  $m/z$  (%) = 241 ( $\text{M}^+ - \text{HCl}$ , 1.4), 166 (100).

Anal. Calcd for  $\text{C}_{12}\text{H}_{20}\text{ClNO}_4$ : C, 51.89; H, 7.26; N, 5.04. Found: C, 51.82; H, 7.23; N, 5.03.

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