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Received 20 February 2002; revised 15 April 2002

Abstract: A novel Horner–Wadsworth–Emmons (HWE)-type reagent¹ reacted readily with various aldehydes and ketones to produce (E)-vinylimidazoles 2 in good yields. The synthetic utility of 1 was demonstrated by the efficient preparation of four histamine H₃ ligands 3 by simple hydrogenation of 2.

Keywords: Horner–Wadsworth–Emmons reaction, vinylimidazole, hydrogenation, H₃ ligands, immpip

Imidazoles are important as heterocyclic components of many drugs and biologically active molecules.¹² The C-4 substituted imidazole is a common and essential structural feature of the ligands for the histamine H₃ (H₃) receptor.³ Further, it was shown that the current H₃ ligands have affinity for the novel H₄ (H₄) receptor,⁴ which was identified by cloning and pharmacological characterization in 2000. However, only a limited synthetic method for the H₃ ligands has been employed, and many new H₃ ligands have been synthesized using readily available scaffolds like urocainic acid and histamine.⁵ In continuation of our ongoing projects involving synthetic studies on novel H₃ and H₄ ligands,⁵ we required a reliable and effective procedure for C-4 substituted imidazoles.

Griffith et al.⁶ reported an improved synthesis of vinylimidazoles⁷ via Horner–Wadsworth–Emmons (HWE) reaction of N-tritylimidazole-4-carboxaldehyde. However, to our knowledge, an HWE reagent incorporating a functional imidazole group has not been reported to date.⁸ Herein, we report an efficient and convenient synthetic route to vinyl imidazoles 2 using a novel HWE reagent 1 (Scheme 1), which reacts not only with a variety of aldehydes, but also ketones in the presence of KOBu-t to produce (E)-vinylimidazoles 2. To demonstrate the utility of the novel HWE reagent 1, an efficient synthesis of four current H₃ ligands was carried out by subsequent hydrogenation of 2.

Michaelis–Becker reaction⁹ of 4-(chloromethyl)-1-tritylimidazole¹⁰ with lithium diethyl phosphonate, prepared in situ by treatment of diethyl phosphite with LiHMDS, generated diethyl (1-tritylimidazol-4-yl) methylphosphonate (1) in 86% yield, as air-stable needles (Scheme 2). This substitution gave a higher yield than the Arbuzov reaction¹¹ (<10%), which required higher reaction temperature (120 °C) and longer reaction time (12 h) in the case of 4-(chloromethyl)-1-tritylimidazole and triethyl phosphate.

Scheme 1

Scheme 2

When we first attempted the HWE olefination of cyclohexanecarboxaldehyde using deprotonation of 1 with LiHMDS, erthro- (42%) and theo-diastereomers (8%) of β-hydroxyphosphonate 4 could be captured, accompanied with the desired vinylimidazole (E)-2a (34%) (Scheme 3), although direct observation of the intermediate (oxyanion of 4) in the HWE reaction has not been generally possible.⁸ Further, reaction of theo-4 with NaH afforded the (E)-olefin 2a (86%),¹¹ but that of erythro-4 caused only a retro-HWE reaction, with recovery of phosphonate 1. This result was consistent with the observation of Bottin-Strzalko et al.¹² that the erythro intermediate did not give the (Z)-olefin.

After investigation of the reaction under various conditions, phosphonate 1 was found to react readily with aldehydes, in the presence of tBuOK, to produce C-4 vinylimidazoles 2,¹³ which can be easily isolated by column chromatography owing to the readily removable triyl group. The scope of the olefination using 1 was

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ISSN 0039-7881
examined as shown in Table 1. For all substrates, the reactions afforded selectively the $E$-double bond. Thus, phosphonate 1 reacted with aliphatic aldehydes (Table 1, entries 1–5), aromatic and heteroaromatic aldehydes (Table 1, entries 6–8) to give substituted ($E$)-vinylimidazoles in excellent yields. In the case of 2f and 2h, the vinyl and aromatic proton signals were overlapped in $^1$H NMR, but their $E$-geometry was clearly determined by the vinyl proton signals shifted downfield of their deprotected vinylimidazoles, 4-[2-(4-buty1phenyl)]vinyl-1$H$-imidazole hydrochloride ($5f$·HCl) and 4-[2-thiophen-2-yl]vinyl-1$H$-imidazole hydrochloride ($5h$·HCl) obtained by hydrolysis [e.g. $5f$·HCl: $\delta = 7.03$ (d, 1 H, $J = 16.7$ Hz), 7.24 (d, 1 H, $J = 16.7$ Hz)]. Further, cinnamaldehyde afforded a dienyimidazole 2i in good yield (Table 1, entry 9), while cyclohexanone afforded the corresponding 2j in moderate yield (Table 1, entry 10).

**Scheme 3**

(a) (i) LiHMDS (1.0 eq), -70 °C, 1 h; (ii) cyclohexanecarbaldehyde (1.0 equiv), -70 °C to rt, over 1 h; (b) NaH, DMF, 50 °C

**Table 1  Synthesis of 2 Using 1**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1$^a$</td>
<td>CHO</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>72$^b$</td>
</tr>
<tr>
<td>2$^c$</td>
<td>CHO</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>88</td>
</tr>
<tr>
<td>3$^a$</td>
<td>(CH$_2$)$_2$CHO</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>56</td>
</tr>
<tr>
<td>4$^a$</td>
<td>(CH$_2$)$_3$CHO</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>58$^c$</td>
</tr>
<tr>
<td>5$^e$</td>
<td>BN CHO</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>74</td>
</tr>
<tr>
<td>6$^f$</td>
<td>H$_2$C(H$_2$)$_2$CHO</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>99</td>
</tr>
<tr>
<td>7$^g$</td>
<td>CHO</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>87</td>
</tr>
</tbody>
</table>
De Esch et al.\textsuperscript{14} reported a study on the influence of lipophilic moieties attached to a 4-1\textit{H}-imidazole ring on the histamine H\textsubscript{3} receptor activity using H\textsubscript{3} antagonists VUF 5514 (pA\textsubscript{2} = 7.5) and VUF 5515 (pA\textsubscript{2} = 7.8). These compounds have been synthesized by reaction of the oxazoline intermediate with ammonia under heating in a stainless steel bomb. Compounds \textit{2c} and \textit{2d} thus obtained could be easily converted into VUF 5514 and VUF 5515 by their hydrogenation (10\% Pd/C at 3.0 Kg/cm\textsuperscript{2}), respectively (Table 2, entries 1 and 2). Vinylimidazole \textit{2e} similarly afforded a potent and selective H\textsubscript{3} antagonist VUF 4929\textsuperscript{15} (pA\textsubscript{2} = 8.4) in a patent application (Table 2, entry 3). This two-step operation was further applied to an efficient synthesis of immepip (pD\textsubscript{2} = 8.0) which has been extensively used as an H\textsubscript{3} agonist. Immepip was first reported by Vollinga et al.\textsuperscript{16}, the synthesis of which was achieved by starting from 4-pyridine carboxaldehyde in 20\% overall yield, via several steps involving hydrogenation at 50 atmosphere over Pd/C. The present synthetic approach readily provided immepip via \textit{2k} from commercially available 1-benzyl-4-piperidine in nearly quantitative yield (Table 1, entry 11 and Table 2, entry 4).

The preparation of C-4 substituted imidazoles using phosphonate \textit{1} is experimentally straightforward and particularly suitable for the study of novel histamine ligands. Considering the privileged position of imidazole compounds in medicinal chemistry, we believe that the reagent \textit{1} will become a useful tool in the synthesis of bioactive molecules.

\begin{table}[h]
\centering
\caption{Synthesis of \textit{2} Using \textit{1} (continued)}
\label{table:1}
\begin{tabular}{llll}
\hline
Entry & Substrate & Product & Yield (\%) \\
\hline
8\textsuperscript{c} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{CHO}};
\end{tikzpicture} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{N}};
\end{tikzpicture} & 85 \\
9\textsuperscript{c} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{CHO}};
\end{tikzpicture} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{N}};
\end{tikzpicture} & 68 \\
10\textsuperscript{c} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{CHO}};
\end{tikzpicture} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{N}};
\end{tikzpicture} & 58 \\
11\textsuperscript{c} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{CHO}};
\end{tikzpicture} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{N}};
\end{tikzpicture} & 99 \\
\hline
\end{tabular}
\footnotesize{\textsuperscript{a} Reaction conditions: reflux, 3 h.  \\
\textsuperscript{b} The yield was based on \textit{1} (1.0 equiv), aldehyde (1.2 equiv) and \textit{t}-BuOK (1.0 equiv).  \\
\textsuperscript{c} Reaction conditions: reflux, 1 h.  \\
\textsuperscript{d} Reaction conditions: r.t., 14 h.  \\
\textsuperscript{e} Reaction conditions: reflux, 2 h.}
\end{table}

\begin{table}[h]
\centering
\caption{Conversion of \textit{2} into H\textsubscript{3} Ligands}
\label{table:2}
\begin{tabular}{llll}
\hline
Entry & Substrate & Product & Yield (\%) \\
\hline
1 & \textit{2c} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{N}};
\end{tikzpicture} & 90 \\
2 & \textit{2d} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{N}};
\end{tikzpicture} & 92 \\
3 & \textit{2e}\textsuperscript{a} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{N}};
\end{tikzpicture} & \text{quant} \\
4 & \textit{2k}\textsuperscript{a} & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (0,1) -- cycle;
\draw (0,0.5) -- (1,0.5);
\draw (0,1) -- (1,1);
\draw (1,0) -- (1,1);
\node at (1,1) {\text{N}};
\end{tikzpicture} & \text{quant}\textsuperscript{b} \\
\hline
\end{tabular}
\footnotesize{\textsuperscript{a} Hydrochloride of \textit{2} was subjected to hydogenation.  \\
\textsuperscript{b} Isolated as dihydrochloride.}
\end{table}
The melting points were determined on a hot stage apparatus and are uncorrected. 1H and 13C NMR spectra were taken with tetramethylsilane as internal reference. Reactions with air- and moisture-sensitive compounds were carried out under argon. Unless otherwise noted, all extracts were dried over Na2SO4 or MgSO4, and the solvent was removed in a rotary evaporator under reduced pressure. Chromatography was performed on silica gel. THF was distilled from sodium-benzophenone.

**Diethyl (1-Tritylimidazo[4-yl])methylphosphonate (1)**

Lithium hexamethyldisilazide (1 M in THF, 31.2 mL, 31.2 mmol) was added dropwise over 1 h to a solution of diethyl phosphate (4.30 g, 31.2 mmol) in anhyd THF (10 mL) at –70 °C under argon. A solution of 4-(chloromethyl)-1-tritylimidazole 10 (9.30 g, 26.0 mmol) in anhyd THF (80 mL) was then added dropwise to the resulting mixture over 0.5 h. After the reaction mixture was stirred for 15 min at the same temperature, it was allowed to reach r.t. and stirred for 3 h at this temperature. The mixture was diluted with sat. aq NH4Cl (150 mL), and the THF was removed under reduced pressure. The resulting suspension was extracted with EtOAc (4 × 100 mL), and the organic phase was dried and evaporated. The resulting crude solid was dissolved in EtOAc–hexane (1:1, 30 mL), and the resulting crude solid was purified by flash chromatography on silica gel using EtOAc–hexane (1:1) to give I (10.30 g, 86%) as a white powder. This was recrystallized from EtOAc–hexane to give a crude oil. An oil.

**Preparation of threo-4**

NaH (60% dispersion in oil, 0.5 mg, 0.013 mmol) was added in one portion to a stirred solution of threo-4 (7 mg, 0.013 mmol) in anhyd DMF (0.5 mL). The reaction mixture was stirred at 50 °C for 1 h till formation of a white precipitate and diluted with EtOAc (20 mL). The organic layer was washed with H2O (3 × 5 mL), dried, and evaporated to give a crude oil, which was subsequently purified by column chromatography to give threo-4 (2a) (4.4 mg, 86%).

**Vinylimidazoles 2; General Procedure**

BuOK (67 mg, 0.6 mmol) was added to a mixture of phosphonate I (276 mg, 0.6 mmol) and the appropriate aldehyde (0.5 mmol) in THF (5 mL). The mixture was refluxed for 1–3 h under argon (TLC monitoring), and concentrated. After the addition of CHCl3 (20 mL), the organic layer was separated, and the aqueous layer was further extracted with CHCl3 (2 × 20 mL). The combined organic layer was dried (MgSO4) and evaporated. The residue was purified by column chromatography (Table 1).

## 2a

**Yield:** 72%.

## 2b

**Small needles; yield: 88%; mp 211–215 °C (EtOAc–hexane).**

1H NMR (300 MHz, CDCl3): δ = 1.07 (s, 9 H), 6.16 (d, 1 H, J = 16.2 Hz), 6.42 (d, 1 H, J = 16.2 Hz), 6.67 (s, 1 H), 7.10–7.40 (m, 16 H). MS (EL 70 eV): m/z = 392 (M+).

HRMS: m/z calc for C32H28N2O4P (M+): 573.2251; found, 573.2247.

Anal Calcd for C32H28N2O4P: C, 68.43; H, 5.21; N, 6.25. Found: C, 68.42; H, 5.22; N, 6.23.

**2c**

**Viscous oil; yield: 56%.**

1H NMR (300 MHz, CDCl3): δ = 2.48 (q, 2 H, J = 8.4 Hz), 2.77 (t, 2 H, J = 8.4 Hz), 6.26 (d, 1 H, J = 15.6 Hz), 6.27–6.48 (dt, 1 H, J = 15.6, 8.4 Hz), 6.69 (s, 1 H), 7.00–7.60 (m, 15 H). MS (EL 70 eV): m/z = 440 (M+).

HRMS: m/z calc for C34H28N2O4P (M+): 440.2251; found, 440.2254.
2d
Viscous oil; yield: 58%.

1H NMR (300 MHz, CDCl3); δ = 1.77 (quint, 2 H, J = 7.4 Hz), 2.20 (q, 2 H, J = 7.4 Hz), 2.66 (t, 2 H, J = 7.4 Hz), 6.23 (d, 1 H, J = 15.8 Hz), 6.36 (dd, 1 H, J = 15.8, 7.0 Hz), 6.66 (s, 1 H), 7.05–7.45 (m, 21 H).

MS (EI, 70 eV); m/z: 454 (M+).

HRMS: m/z calc'd for C36H26N2 (M+), 454.2407; found, 454.2415.

2e
Viscous oil; yield: 74%.

1H NMR (300 MHz, CDCl3); δ = 1.56 (qd, 2 H, J = 9.0, 4.4 Hz), 1.66–1.78 (dim, 2 H, J = 15.0 Hz), 1.92–2.23 (m, 3 H), 2.88–2.94 (dm, 2 H, J = 15.0 Hz), 3.49 (s, 2 H), 6.19 (d, 1 H, J = 15.5 Hz), 6.32 (dd, 1 H, J = 15.5, 6.7 Hz), 6.66 (s, 1 H), 7.05–7.40 (m, 21 H).

MS (EI, 70 eV); m/z: 509 (M+).

HRMS: m/z calc'd for C36H26N2 (M+), 509.2829; found, 509.2827.

2f
Prisms; yield: 99%; mp 157–159 °C (EtOAc–hexane).

1H NMR (300 MHz, CDCl3); δ = 0.92 (t, 3 H, J = 8.4 Hz), 1.35 (sext, 2 H, J = 8.4 Hz), 1.59 (quint, 2 H, J = 8.4 Hz), 2.58 (t, 2 H, J = 8.4 Hz), 6.85 (s, 1 H), 6.89 (d, 1 H, J = 16.4 Hz), 7.10–7.40 (m, 20 H), 7.45 (s, 1 H).

13C NMR (CD2OD); δ = 13.9, 22.4, 33.5, 35.4, 75.4, 119.3, 119.6, 126.1, 127.1, 128.1, 128.6, 134.8, 135.1, 139.3, 139.5, 141.9, 142.3.

MS (EI, 70 eV); m/z: 468 (M+).

HRMS: m/z calc'd for C29H24N3 (M+), 468.2564; found, 468.2563.

Anal Calcd for C15H17N2: C, 87.21; H, 5.97; N, 6.83. Found: C, 87.28; H, 6.08; N, 6.87.

4-(2-(4-Butylphenyl)vinyl)-1H-imidazole Hydrochloride (5f-HCl)
To determine the (E)-geometry of 2f, it was converted into the unsubstituted imidazole, 5f-HCl as follows. A solution of 2f (194 mg, 0.415 mmol) in aq 2 N HCl (6 mL)–EtOH (4 mL) was refluxed for 1 h and then diluted with H2O (10 mL). After neutralization by addition of NaHCO3, the mixture was extracted with CHCl3 (5 × 10 mL). The extract was dried and evaporated to give a residue, which was subsequently chromatographed using MeOH–CHCl3 (1:9) as eluent to give 5f (74 mg, 80%) as an oil.

1H NMR (500 MHz, CD2OD); δ = 0.95 (t, 3 H, J = 8.4 Hz), 1.38 (sext, 2 H, J = 8.4 Hz), 1.60 (quint, 2 H, J = 8.4 Hz), 2.62 (t, 2 H, J = 8.4 Hz), 7.1 (br s, 4 H), 7.14 (d, 2 H, J = 7.9 Hz), 7.38 (d, 2 H, J = 7.9 Hz).

MS (SIMS); m/z: 227 (M+ + 1).

HRMS: m/z calc'd for C15H19N21 (M+ + 1), 227.1547; found, 227.1546.

5f-HCl
Viscous oil.

1H NMR (500 MHz, CD2OD); δ = 0.91 (t, 3 H, J = 8.4 Hz), 1.37 (sext, 2 H, J = 8.4 Hz), 1.58 (quint, 2 H, J = 8.4 Hz), 2.60 (t, 2 H, J = 8.4 Hz), 7.03 (d, 1 H, J = 16.7 Hz), 7.24 (d, 1 H, J = 16.7 Hz), 7.21 (d, 2 H, J = 7.6 Hz), 7.46 (d, 2 H, J = 7.6 Hz), 7.62 (s, 1 H), 8.92 (s, 1 H).

13C NMR (CD2OD); δ = 14.4, 23.3, 34.7, 36.4, 112.5, 117.0, 127.9, 130.0, 134.2, 134.4, 135.3.
4-(4-Phenylpentyl)-1H-imidazole (VUF5515)\textsuperscript{14}

This compound was synthesized from 2d (132 mg, 0.29 mmol) according to the synthetic procedure for VUF5514 and was obtained as a colorless oil in 92% yield.

\[ ^1H \text{NMR (300 MHz, CD}_2\text{OD): } \delta = 1.30–1.50 (m, 2 H), 1.60–1.80 (m, 4 H), 2.61 (t, 2 H, J = 7.6 Hz), 2.64 (t, 2 H, J = 7.6 Hz), 7.08–7.36 (m, 6 H), 8.45 (s, 1 H). \]

MS (SIMS): m/z: 215 (M⁺ + 1).

HRMS: \textit{m/z}: calced for C\textsubscript{21}H\textsubscript{31}N\textsubscript{2} (M⁺ + 1), 215.1547; found, 215.1551.

Preparation of Immepip [4-(1H-imidazol-4-yl)methylpiperidine] via 2k

Phosphonate 1 (276 mg, 0.6 mmol) and KO\textsubscript{Bu} (67 mg, 0.6 mmol) were added to a solution of 1-benzyl-4-piperidone (95 mg, 0.5 mmol) in THF (6 mL). After the reaction mixture was refluxed for 2 h, sat. aq NH\textsubscript{4}Cl (1 mL) was added and evaporated. The residue was dissolved with saturated aq NH\textsubscript{4}Cl (10 mL) and extracted with CHCl\textsubscript{3} (3 × 20 mL), and the CHCl\textsubscript{3} layer was dried (MgSO\textsubscript{4}) and evaporated. The resulting oily residue was purified by column chromatography (Et\textsubscript{2}O/ac to give 2k (246 mg, 99%) as a colorless viscous oil.

\[ ^1H \text{NMR (300 MHz, CDCl}_3): \delta = 2.30–2.40 (m, 2 H), 2.42–2.60 (m, 4 H), 2.79–2.90 (m, 2 H), 3.52 (s, 2 H), 6.02 (s, 1 H), 6.66 (s, 2 H) 7.08–7.44 (m, 21 H). \]

MS (EL, 70eV): m/z: 495 (M⁺).

HRMS: \textit{m/z}: 495.2681 (calcd for C\textsubscript{35}H\textsubscript{33}N\textsubscript{3}: 495.2673).

Immepip-2HCl

A solution of 2k (162 mg, 0.327 mmol) in aq 1 N HCl (1.5 mL)–EtOH (5 mL) was stirred at r.t. for 10 min, and evaporated to give a residue, which was subsequently dissolved with H\textsubscript{2}O (20 mL) and evaporated to give VUF4929 (68 mg, quant, free amine) according to the synthetic procedure of immepip described above.

\[ ^1H \text{NMR (300 MHz)(CD}_2\text{OD): } \delta = 1.19 (qd, 2 H, J = 13.0, 3.5 Hz), 1.36–1.52 (m, 2 H), 1.60 (t, 2 H, J = 7.2 Hz), 1.70–1.82 (m, 2 H, J = 13.0 Hz), 2.50–2.70 (m, 4 H), 3.00–3.10 (dm, 2 H, J = 13.0 Hz), 6.78 (s, 1 H), 7.59 (s, 1 H). \]

VUF4929-2HCl

The free amine was stirred with aq 1 N HCl–EtOH at r.t. for 15 min and evaporated to give VUF4929-2HCl as a white powder; mp 216–220 °C.

\[ ^1H \text{NMR (500 MHz, CD}_2\text{OD): } \delta = 1.47 (qd, 2 H, J = 13.0, 3.5 Hz), 1.65–1.75 (m, 3 H), 1.97–2.04 (dm, 2 H, J = 13.0 Hz), 2.80 (t, 2 H, J = 7.2 Hz), 3.00 (t, 2 H, J = 13.0 Hz), 3.37–3.43 (dm, 2 H, J = 13.0 Hz), 7.36 (s, 1 H), 8.81 (s, 1 H). \]

\[ ^13C \text{NMR (CD}_2\text{OD): } \delta = 22.4, 29.7, 34.2, 35.6, 45.2, 116.8, 134.7, 135.3. \]

MS (EL, 70eV): m/z: 179 (M⁺).

HRMS: \textit{m/z}: calced for C\textsubscript{18}H\textsubscript{17}N\textsubscript{3}(M⁺), 179.1424; found, 179.1424.

Acknowledgments

We thank Prof. A. Yamatodani, School of Allied Health Science, Faculty of Medicine, Osaka University, for encouraging us in this study. Financial support of this work by the Ministry of Education, Science, and Culture of Japan [Grant No. 11672127] is gratefully acknowledged.

References


(13) All yields are of the pure products after chromatography.