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Simple Preparation of Terminal *N*-Monoprotected Triamines Using Fused Piperazines

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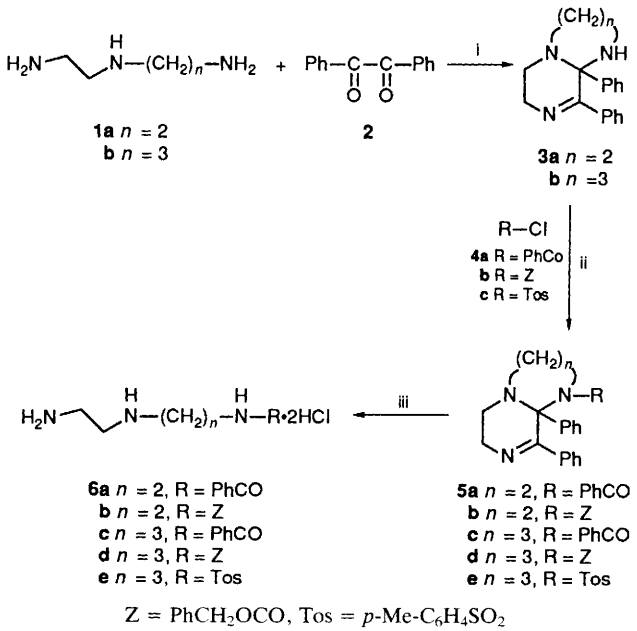
Terminal *N*-monoacylated triamines **6** were easily obtained by hydrolysis of the acylated fused piperazines **5**, which were prepared by the reaction of triamines **1** with benzil **2** followed by acylation.

Triamines are versatile starting compounds and building blocks, which have been applied to syntheses of cryptands and polycyclic amines.[1,2]

Although chemoselective *N*-acylation of triamines has been achieved by various methods,[3–7] these methods resulted in only *N*,*N*′-diacylation of the terminal primary amino group of triamines. In spite of the use of terminal *N*-protected triamines in many fields, effective preparation of selectively *N*-monoacylated triamines has not, to our knowledge, been established.

In connection with our studies on the preparation of fused heterocycles using triamines,[8] we found that fused piperazine derivative **3a** and **b** prepared from triamines **1a** and **b** and benzil **2** were readily acylated to afford **5a–e** followed by hydrolysis with 1 M HCl to give the terminal *N*-monoprotected triamines.

This reaction pathway may be useful for the selective *N*-monoprotection of the terminal primary amino moiety of triamines (Scheme 1).



Scheme 1 *Reagents and conditions*: i, EtOH/AcOH, reflux 3 h; ii, pyridine/EtOH, room temp.; iii, 1 M HCl/EtOH, reflux 0.5 h.

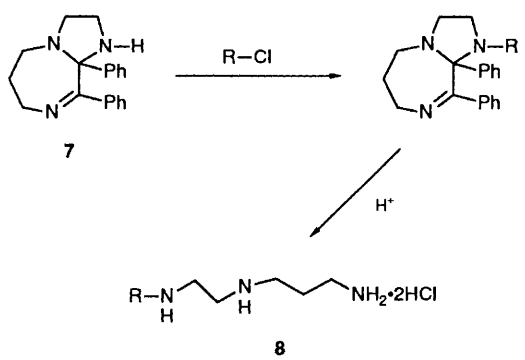
A typical procedure for **6** is as follows: a solution of **5** (10 mmol) in EtOH (10 ml) and 1 M HCl (5 ml) was refluxed for 0.5 h to give **6**. In the case of **6a**, **c** and **e**, the resulting solution was evaporated to dryness and the residue of the dihydrochloride was recrystallized from EtOH. Compounds **6b** and **d** are sensitive to acid at high temperature (above 70 °C). EtOH was removed under reduced pressure below 40 °C, and the aqueous acidic solution was treated with Amberlite IR 45 (OH^- form) and evaporated to dryness. The residue was dissolved in $CHCl_3$, and dry HCl gas was introduced to the solution to yield precipitates of the dihydrochloride, which was recrystallized from EtOH.

The structures of compounds **6a** and **b** were confirmed by IR, ^1H and ^{13}C NMR, and mass spectral data. Concerning the

Table 1 Terminal *N*-monoprotected triamine dihydrochlorides **6a–e**

6	Mp °C	Yield (%)[a]
a	221–222	72
b	118–120	54
c	222–223	76
d	230–231	50
e	237–238	89

[a] Yield from **5**.



Scheme 2

structures of **6c–e**; there are two possible products **3b** and **7** from the reaction of **1b** with **2**. Compound **7** would be subject to acylation followed by hydrolysis affording the monoprotected triamine **8**. To confirm the structures, **8** (R = Tos) was prepared by the reaction of *N*-tosylethylenediamine with acrylonitrile followed by reduction with $LiAlH_4$ and treatment with dry HCl gas. These two compounds, **6e** and **8** (R = Tos), were found to be quite different from comparison of their spectral data. This result confirmed that the product from the reaction of **1b** with **2** was not **7** but **3b**, which was then converted to **6c–e** (Scheme 2).

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