

Yoshinori Tominaga\*, Shigenori Motokawa, Yoshihide Shiroshita,  
and Akira Hosomi\*Faculty of Pharmaceutical Sciences, Nagasaki University, 1-14, Bunkyo-machi,  
Nagasaki 852, Japan

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A new synthesis of imidazo[1,2-*a*]pyridine and imidazo[2,1-*a*]isoquinoline derivatives **4** and **8**, respectively by 1,5-dipolar cyclization reactions of stabilized pyridinium *N*-ylides **3a-e** or isoquinolinium *N*-ylide **7** is described. The starting *N*-ylides **3a-e** and **7** are prepared by the reaction of the corresponding pyridinium salts **1a-e** or isoquinolinium salts **6** with *N*-bis(methylthio)methylene-*p*-toluenesulfonamide (**2**).

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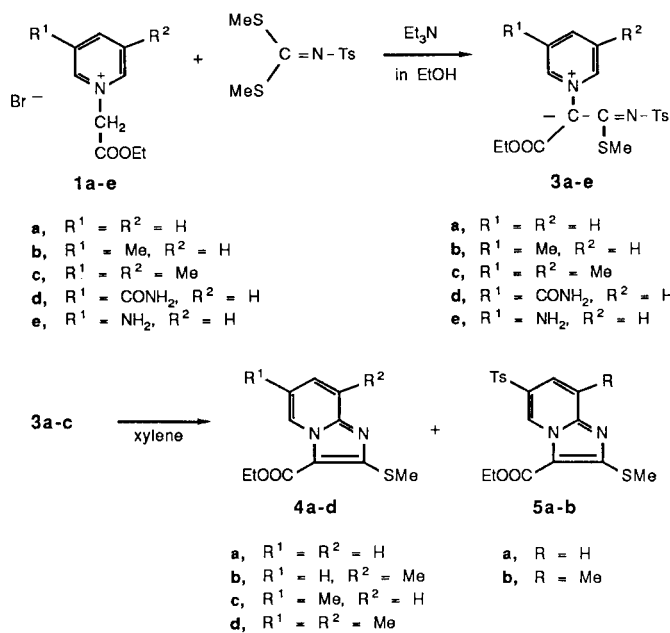
*N*-Bis(methylthio)methyleneamide derivatives are important and versatile reagents which have been extensively utilized in synthesis of biologically active heterocyclic compounds [1-18]. Among those compounds, *N*-bis(methylthio)methylene-*p*-toluenesulfonamide (**2**), is an extremely interesting electrophilic reagent for the introduction of not only an aminomethylene group into amines and active methylene compounds but also a C=N fragment in the synthesis of heterocyclic compounds [1-8]. We now report a new synthesis of imidazo[1,2-*a*]pyridines **4** and imidazo[2,1-*a*]isoquinolines **8** by the 1,5-dipolar cyclization reaction of pyridinium or isoquinolinium *N*-ylides using **2**. Hitherto, in order to investigate their biological activities and physical properties [19-26], the imidazo[1,2-*a*]pyridines and the aza analogs of the indolizine, have been prepared by the condensation of 2-aminopyridines with  $\alpha$ -halocarbonyl compounds [24-25].

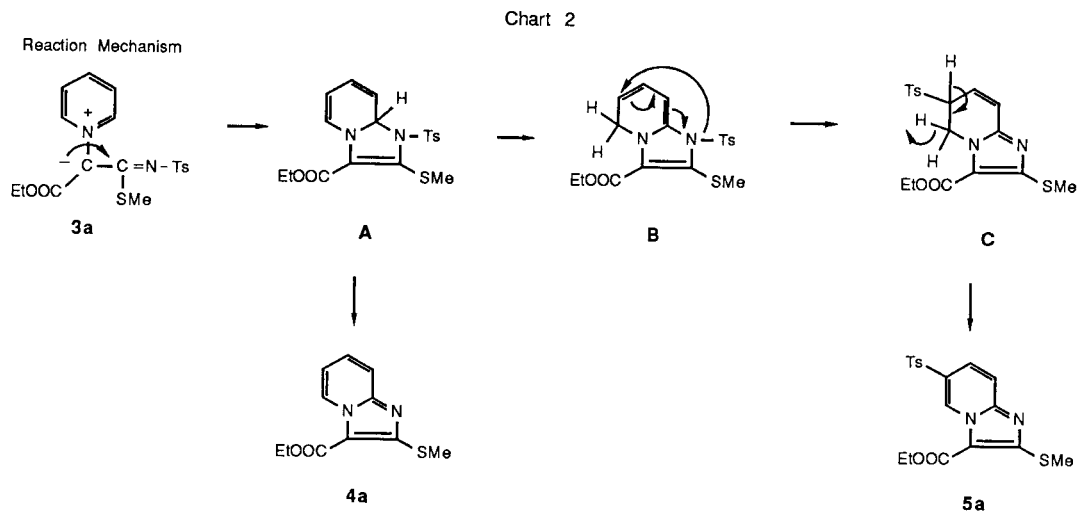
Compound **2** is prepared by the condensation of *p*-toluenesulfonamide with carbon disulfide in dimethylsulfoxide (DMSO) in the presence of sodium hydroxide and by successive treatment of the intermediate with dimethyl sulfate [1,2]. 1-Ethoxycarbonyl-2-methylthio-1-(1-pyridinio)-2-(*N*-*p*-toluenesulfonylimino)ethylides **3a-e**, key intermediates for the synthesis of imidazo[1,2-*a*]pyridines **4**, were readily obtained by the treatment of *N*-ethoxycarbonylmethylpyridinium bromides **1a-e** with **2** [13,14] in boiling ethanol in the presence of triethylamine in good yields except for the case of **3d**.

Pyridinium *N*-ylide **3a** was refluxed in xylene for 30 hours to give two intramolecular cyclization products, ethyl 2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**4a**) and ethyl 2-methylthio-6-*p*-toluenesulfonylimidazo[1,2-*a*]pyridine-3-carboxylate (**5a**), in 7 and 38% yields, respectively (Chart 1). The formation of **4a** may be explained by the 1,5-dipolar cyclization of **3a** followed by the elimination of *p*-toluenesulfonic acid as illustrated in Chart 2. Product **5a** was a stable crystalline solid, the structure of which was strictly confirmed by the elemental and spectro-

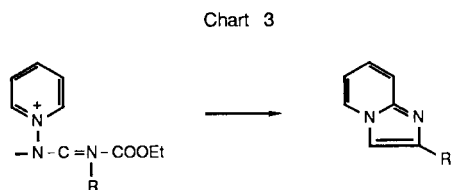
scopic analyses. It seems reasonable that the initially formed intermediate **A** by the 1,5-dipolar cyclization undergoes successively a 1,5-sigmatropic shift of a hydrogen atom, then that of a tosyl group, and finally the elimination of hydrogen to give **5a**. In a similar manner, thermolysis of **3b** gave ethyl 8-methyl- and 6-methyl-2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylates **4b** and **4c**, and the 8-methyl-6-tosyl derivative **5b** in 31, 14 and 12% yields, respectively. The thermal cyclization of **3c** afforded only ethyl 6,8-dimethyl-2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**4d**) in 48% yield. In contrast, **3d** and **3e** were intact under the thermolysis conditions. However, when the reaction was carried out in DMSO instead of xylene, **4a** was obtained in 35% yield. The tosylated product **5b** was not detected in these reactions. Reaction of **3b** in DMSO gave **4b** and **4c** in 31 and 16% yields, respectively.

Chart 1





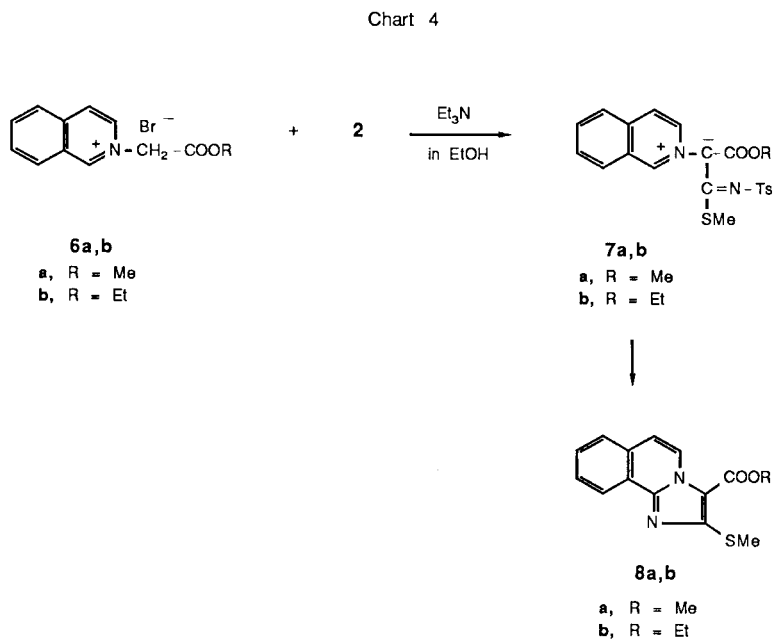
Kakehi and co-workers have reported that the thermolysis of *N*-imidolyiminopyridinium ylides gives 1,2,4-triazolo[1,5-*a*]pyridines by a similar 1,5-cyclization followed by elimination of ethyl formate as illustrated in Chart 3 [27].



Imidazo[2,1-*a*]isoquinolines **8** were prepared according to similar reaction sequences. The required isoquinolinium ylide **7a** was prepared from *N*-methoxycarbonylmethylisoquinolinium bromide (**6a**) and **2**, and was sub-

jected to thermolysis in boiling xylene to give methyl 2-methylthioimidazo[2,1-*a*]isoquinoline-3-carboxylate (**8a**) in 69% yield. In this case, the tosylated product was not obtained. When 1-ethoxycarbonylmethylisoquinolinium bromide (**6b**), in place of the methyl ester **6a**, was allowed to react with **2** in boiling ethanol in the presence of triethylamine, ethyl 2-methylthioimidazo[2,1-*a*]isoquinoline-3-carboxylate (**8b**) was directly formed in 65% yield without isolation of **7b**.

The advantages of the present method are the ready availability of the starting materials and the easy preparation of poly-functionalized imidazo[1,2-*a*]pyridines and imidazo[2,1-*a*]isoquinolines, although yields are not necessarily as good as those with the Tschitschibabin type reaction. Thus, this procedure appears to have considerable



promise as the preparative method of fused imidazole derivatives, and these products can be used as key intermediates for further conversion to 1-azacycl[3.2.2]azine derivatives [28-30].

### EXPERIMENTAL

All melting points were determined in a capillary tube and are uncorrected. Infrared (ir) spectra were recorded using potassium bromide pellets on a JASCO IRA-2 spectrometer, ultraviolet (uv) absorption spectra were determined on a Hitachi EP-S2 spectrometer in 95% ethanol, and the nmr spectra were obtained with JEOL JNM-PS-100 (100 MHz) and JNM-FX-90Q (90 MHz) spectrometers with tetramethylsilane as an internal standard. Mass spectra (ms) were recorded on a JEOL JMS-01SG mass spectrometer.

#### 1-Ethoxycarbonyl-2-methylthio-1-(1-pyridinio)-2-(*N-p*-toluenesulfonylimino)ethylide (**3a**).

A solution of 2.46 g (10 mmoles) of 1-ethoxycarbonylmethylpyridinium bromide (**1a**), 2.75 g (10 mmoles) of **2** [1,2], and 1.01 g (100 mmoles) of triethylamine was refluxed in 100 ml of ethanol for 10 hours, and then ethanol and excess triethylamine were removed. The residue was washed with water and recrystallized from ethanol to give 3.60 g (9.2 mmoles, 92%) of yellow needles, mp 213°; ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  1676 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 228 (4.08), 257 (4.02), 307 (4.30); <sup>1</sup>H-nmr (deuteriochloroform):  $\delta$  1.18 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 2.00 (3H, s, SCH<sub>3</sub>), 2.34 (3H, s, phenyl-CH<sub>3</sub>), 4.15 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 7.13 (2H, d, J = 7.9 Hz, 3', 5'-H), 7.63 (2H, d, J = 7.9 Hz, 2', 6'-H), 7.73-7.89 (2H, m, 3, 5-H), 8.20-8.40 (1H, m, 4-H), 8.64 (2H, dd, J = 1.5, 6.8 Hz, 2, 6-H); ms: m/z 392 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>18</sub>H<sub>20</sub>O<sub>4</sub>N<sub>2</sub>S<sub>2</sub>: C, 55.08; H, 5.14; N, 7.14; S, 16.34. Found: C, 55.04; H, 5.11; N, 7.05; S, 16.54.

#### 1-Ethoxycarbonyl-2-methylthio-1-(3-methyl-1-pyridinio)-2-(*N-p*-toluenesulfonylimino)ethylide (**3b**).

Compound **3b** (3.21 g, 7.9 mmoles) was synthesized in 79% yield from 2.61 g (10 mmoles) of **1b** and 2.75 g (10 mmoles) of **2** in a similar manner to that described for the preparation of **3a**. An analytical sample was recrystallized from ethanol to give yellow needles, mp 218°; ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  1654 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 222 (4.16), 266 (4.07), 307 (4.34); <sup>1</sup>H-nmr (deuteriochloroform):  $\delta$  1.20 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 2.00 (3H, s, SCH<sub>3</sub>), 2.34 (3H, s, phenyl-CH<sub>3</sub>), 2.56 (3H, s, 3-CH<sub>3</sub>), 4.16 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 7.12 (2H, d, J = 7.9 Hz, 3', 5'-H), 7.63 (2H, d, J = 7.9 Hz, 2', 6'-H), 7.68 (1H, dd, J = 1.4, 7.9 Hz, 5-H), 8.07 (1H, bd, J = 9.0 Hz, 4-H), 8.45 (2H, bs, 2, 6-H); ms: m/z 406 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>19</sub>H<sub>22</sub>O<sub>4</sub>N<sub>2</sub>S<sub>2</sub>: C, 56.14; H, 5.45; N, 6.89; S, 15.77. Found: C, 56.06; H, 5.41; N, 6.80; S, 15.88.

#### 1-Ethoxycarbonyl-2-methylthio-1-(3,5-dimethyl-1-pyridinio)-2-(*N-p*-toluenesulfonylimino)ethylide (**3c**).

Compound **3c** (3.37 g, 8.0 mmoles) was synthesized in 80% yield from 2.86 g (10 mmoles) of **1c** and 10 mmoles of **2** in a similar manner to that described for the preparation of **3a**. An analytical sample was recrystallized from ethanol to give yellow needles, mp 192°; ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  (1665 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 220 (4.20), 262 (4.05), 305 (4.30); <sup>1</sup>H-nmr (deuteriochloroform):  $\delta$  1.24 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 2.01 (3H, s, SCH<sub>3</sub>), 2.34 (3H, s, phenyl-CH<sub>3</sub>), 2.50 (6H, s, 3, 5-CH<sub>3</sub>), 4.16 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 7.12 (2H, d, J = 7.9 Hz, 3', 5'-H), 7.62 (2H, d, J = 7.9 Hz, 2', 6'-H), 7.85 (1H, s, 4-H), 8.25 (2H, s, 2, 6-H); ms: m/z 420 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>20</sub>H<sub>24</sub>O<sub>4</sub>N<sub>2</sub>S<sub>2</sub>: C, 57.12; H, 5.75; N, 6.66; S, 15.25. Found: C, 57.01; H, 5.73; N, 6.69; S, 15.39.

#### 1-(3-Carbamoyl-1-pyridinio)-1-ethoxycarbonyl-2-methylthio-2-(*N-p*-toluenesulfonylimino)ethylide (**3d**).

Compound **3d** (0.22 g, 0.5 mmole) was synthesized in 5% yield from 2.90 g (10 mmoles) of **1d** and 10 mmoles of **2** in a similar manner to that described for the preparation of **3a**. An analytical sample was recrystallized from ethanol to give yellow needles, mp 198°; ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  1701 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 220 (4.33), 270 (4.20), 305 (4.33), 388 (3.33); <sup>1</sup>H-nmr (deuteriochloroform):  $\delta$  1.17 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 1.99 (3H, s, SCH<sub>3</sub>), 2.35 (3H, s, phenyl-CH<sub>3</sub>), 4.16 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 5.96 (1H, bs, NH), 7.16 (2H, d, J = 7.9 Hz, 3', 5'-H), 7.62 (2H, d, J = 7.9 Hz, 2', 6'-H), 7.88 (1H, dd, J = 6.8, 7.0 Hz, 5-H), 8.65 (2H, dd, J = 1.5 Hz, 7.0 Hz, 4, 6-H), 9.06 (1H, s, 2-H); ms: m/z 435 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>19</sub>H<sub>21</sub>O<sub>5</sub>N<sub>3</sub>S<sub>2</sub>: C, 52.40; H, 4.80; N, 9.65; S, 14.73. Found: C, 52.29; H, 4.80; N, 9.56; S, 14.75.

#### 1-(3-Amino-1-pyridinio)-1-ethoxycarbonyl-2-methylthio-2-(*N-p*-toluenesulfonylimino)ethylide (**3e**).

Compound **3e** (2.3 g, 4.9 mmoles) was synthesized in 49% yield from 2.63 g (10 mmoles) of **1e** and 10 mmoles of **2** in a similar manner to that described for the preparation of **3a**. An analytical sample was recrystallized from ethanol to give yellow needles, mp 237°; ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  3414 (NH), 1671 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 223 (4.44), 258 (4.23), 308 (4.31); <sup>1</sup>H-nmr (deuteriodimethylsulfoxide + trifluoroacetic acid):  $\delta$  1.19 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 2.02 (3H, s, phenyl-CH<sub>3</sub>), 2.42 (3H, s, SCH<sub>3</sub>), 4.14 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 7.42 (2H, d, J = 8.4 Hz, 3', 5'-H), 7.75 (4H, bd, 2', 6'-H, 4, 5-H), 8.05 (2H, bs, 2, 6-H); ms: m/z 407 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>18</sub>H<sub>21</sub>O<sub>4</sub>N<sub>3</sub>S<sub>2</sub>: C, 53.05; H, 5.19; N, 10.31; S, 15.74. Found: C, 53.16; H, 5.20; N, 10.12; S, 15.75.

#### Ethyl 2-Methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**4a**) and Ethyl 2-Methylthio-6-tosylimidazo[1,2-*a*]pyridine (**5a**).

A solution of 1.96 g (5 mmoles) of **3a** in 10 ml of xylene was refluxed for 30 hours. After evaporation of the xylene, the residue was washed with ethanol and recrystallized from ethanol to give **5a** (0.74 g, 1.9 mmoles) as colorless needles, mp 168°, in 38% yield. The ethanol solution was evaporated. The residue was chromatographed on a neutral alumina column using hexane-benzene (1:1) as the eluent affording **4a** (0.08 g, 0.35 mmole) in 7% yield. Compound **4a** was recrystallized from ethanol to give colorless needles, mp 133° (lit [19] mp 133°).

#### Ethyl 2-Methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**4a**).

This compound had <sup>1</sup>H-nmr (deuteriochloroform):  $\delta$  1.46 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 2.70 (3H, s, SCH<sub>3</sub>), 4.45 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 6.99 (1H, nt, J = 7.0 Hz, 6-H), 7.43 (1H, nt, J = 7.0 Hz, 7-H), 7.66 (1H, bd, J = 7.0 Hz, 8-H), 9.35 (1H, bd, J = 7.0 Hz, 5-H).

#### Ethyl 2-Methylthio-6-tosylimidazo[1,2-*a*]pyridine (**5a**).

This compound had ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  1695 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 242 (4.28), 277 (4.71), 304 (4.11); <sup>1</sup>H-nmr (deuteriochloroform):  $\delta$  1.48 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 2.41 (3H, s, phenyl-CH<sub>3</sub>), 2.67 (3H, s, SCH<sub>3</sub>), 4.48 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 7.32 (2H, d, J = 8.0 Hz, phenyl-H), 7.57 (1H, d, J = 0.9, 9.2 Hz, 8-H), 7.71 (1H, dd, J = 1.8, 9.2 Hz, 7-H), 7.86 (2H, d, J = 8.0 Hz, phenyl-H), 9.90 (1H, dd, J = 0.9, 1.8 Hz, 5-H); ms: m/z 390 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>18</sub>H<sub>19</sub>O<sub>4</sub>N<sub>2</sub>S<sub>2</sub>: C, 55.37; H, 4.65; N, 7.17; S, 16.42. Found: C, 55.62; H, 4.68; N, 7.68; S, 16.40.

#### Cyclization of **3a** in DMSO.

A solution of 1.96 g (5 mmoles) of **3a** in 5 ml of DMSO was heated at 180° for 20 hours. After cooling, 20 ml of water was added to the reaction mixture. The resulting precipitate was collected by filtration to give the corresponding cyclized product **4a** (0.41 g, 1.73 mmoles) in 35% yield. This compound was purified by chromatography on a neutral alumina column using hexane-benzene (1:1) as an eluent and recrystallized from ethanol to give colorless needles, mp 133°.

#### Ethyl 8-Methyl-2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**4b**),

#### Ethyl 6-Methyl-2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**4c**),

and Ethyl 8-Methyl-2-methylthio-6-tosylimidazo[1,2-*a*]pyridine (**5b**).

These cyclized compounds were synthesized from 2.03 g (5 mmoles) of **3b** in a similar manner to the cyclization of **3a** in xylene. The tosylated compound **5b** (0.24 g, 0.59 mmole) was separated from the mixture of the reaction products by recrystallization from ethanol to give colorless needles, mp 166°, in 12% yield. The mother liquor of recrystallization consists of **4b** and **4c**. After the evaporation of ethanol, the residue was chromatographed on a neutral alumina-column using hexane as an eluent to give the 8-methyl derivative **4b** (0.103 g, 0.41 mmole) in 41% yield and hexane-benzene (1:1) as an eluent to give 6-methyl derivative **4c** (0.18 g, 0.72 mmole) in 14% yield. Compounds **4b** and **4c** were recrystallized from ethanol to give colorless needles, mp 88° and mp 113°, respectively.

Ethyl 8-Methylthio-6-tosylimidazo[1,2-*a*]pyridine (**5b**).

This compound had ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  1686 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ), 242 (4.30), 278 (4.76), 300 (4.16);  $^1\text{H-nmr}$  (deuteriochloroform):  $\delta$  1.47 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 2.41 (3H, s, phenyl-CH<sub>3</sub>), 2.69 (3H, s, SCH<sub>3</sub>), 4.42 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 6.98 (1H, bs, 7-H), 8.88 (1H, bs, 5-H); ms: m/z 404 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>19</sub>H<sub>20</sub>O<sub>4</sub>N<sub>2</sub>S<sub>2</sub>: C, 56.42; H, 4.98; N, 6.93; S, 15.85. Found: C, 56.35; H, 4.96; N, 6.97; S, 15.86.

Cyclization of **3b** in DMSO.

This cyclization was conducted in a similar manner to that described for the preparation of **4a** in DMSO. A mixture of **4b** and **4c** was separated by chromatography on an alumina-column using hexane and hexane-benzene (1:1) as the eluent. The yield of **4b** and **4c** were 31% and 16%, respectively.

Ethyl 8-Methyl-2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**4b**).

This compound had mp 88°; ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  1675 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 261 (4.63), 305 (4.05);  $^1\text{H-nmr}$  (deuteriochloroform):  $\delta$  1.46 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 2.61 (3H, s, 8-CH<sub>3</sub>), 2.71 (3H, s, SCH<sub>3</sub>), 4.43 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 6.85 (1H, dd, J = 6.5, 7.0 Hz, 6-H), 7.22 (1H, bd, J = 7.0 Hz, 7-H), 9.09 (1H, bd, J = 6.5 Hz, 5-H); ms: m/z 250 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>12</sub>H<sub>14</sub>O<sub>2</sub>N<sub>2</sub>S: C, 57.58; H, 5.64; N, 11.19; S, 12.81. Found: C, 57.38; H, 5.66; N, 11.01; S, 12.80.

Ethyl 6-Methyl-2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**4c**).

This compound had mp 113°; ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  1676 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 261 (4.65), 304 (4.05);  $^1\text{H-nmr}$  (deuteriochloroform):  $\delta$  1.46 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 2.38 (3H, s, 6-CH<sub>3</sub>), 2.68 (3H, s, SCH<sub>3</sub>), 4.43 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 7.22 (1H, dd, J = 1.8, 8.35 Hz, 7-H), 7.51 (1H, d, J = 8.35 Hz, 8-H), 9.07 (1H, bs, 5-H); ms: m/z 250 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>12</sub>H<sub>14</sub>O<sub>2</sub>N<sub>2</sub>S: C, 57.58; H, 5.64; N, 11.19; S, 12.81. Found: C, 57.52; H, 5.48; N, 11.04; S, 12.95.

6,8-Dimethyl-2-methylthioimidazo[1,2-*a*]pyridine (**4d**).

A solution of 2.10 g (5 mmoles) of **3c** in 10 ml of xylene was refluxed for 30 hours. After evaporation of xylene, the residue was chromatographed on a neutral alumina column using benzene as an eluent to give **4d** (0.64 g, 2.4 mmoles) as colorless needles, mp 105°, in 48% yield. An analytical sample was recrystallized from ethanol; ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  1672 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 263 (4.56), 304 (3.99);  $^1\text{H-nmr}$  (deuteriochloroform):  $\delta$  1.46 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 2.31 (3H, d, J = 0.1 Hz, 6-CH<sub>3</sub>), 2.55 (3H, s, 8-CH<sub>3</sub>), 2.69 (3H, s, SCH<sub>3</sub>), 4.42 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 6.98 (1H, bs, 7-H), 8.88 (1H, bs, 5-H); ms: m/z 264 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>N<sub>2</sub>S: C, 59.07; H, 6.10; N, 10.60; S, 12.13. Found: C, 59.03; H, 6.09; N, 10.55; S, 12.38.

1-Methoxycarbonyl-2-methylthio-1-(1-isoquinolinio)-2-(*N-p*-toluenesulfonylimino)ethylide (**7a**).

Compound **7a** (3.89 g, 9.1 mmoles) was synthesized in 91% yield from 2.82 g (10 mmoles) of **6a** and 10 mmoles of **2** in similar manner to that de-

scribed for the preparation of **3a**. An analytical sample was recrystallized from ethanol to give yellow needles, mp 169°; ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  1667 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 231 (4.70), 270 (4.16), 281 (4.16), 310 (4.32), 344 (shoulder, 3.80), 380 (shoulder, 3.42);  $^1\text{H-nmr}$  (deuteriochloroform):  $\delta$  2.08 (3H, s, SCH<sub>3</sub>), 2.29 (3H, s, phenyl-CH<sub>3</sub>), 3.65 (3H, s, OCH<sub>3</sub>), 7.04 (2H, d, J = 8.0 Hz, phenyl-H), 7.55 (2H, d, J = 8.0 Hz, Phenyl-H), 7.76-8.72 (6H, m, 3, 4, 5, 6, 7, 8-H), 9.38 (1H, s, 1-H); ms: m/z 428 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>21</sub>H<sub>20</sub>O<sub>4</sub>N<sub>2</sub>S<sub>2</sub>: C, 58.86; H, 4.70; N, 6.53; S, 14.96. Found: C, 58.96; H, 4.71; N, 6.49; S, 15.17.

Methyl 2-Methylthioimidazo[2,1-*a*]isoquinoline-3-carboxylate (**8a**).

Compound **8a** (0.93 g, 3.4 mmoles) was synthesized in 69% yield from **7a** (2.14 g, 5 mmoles) in similar manner to that described for the preparation of **4d**. An analytical sample was recrystallized from methanol to give colorless needles, mp 120°; ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  1694 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 210 (4.30), 222 (4.00), 273 (4.76), 318 (4.12);  $^1\text{H-nmr}$  (deuteriochloroform):  $\delta$  2.79 (3H, s, SCH<sub>3</sub>), 4.00 (3H, s, OCH<sub>3</sub>), 7.20 (1H, d, J = 7.5 Hz, 6-H), 7.59-7.83 (3H, m, 7, 8, 9-H), 8.62-8.73 (1H, m, 10-H), 9.01 (1H, d, J = 7.5 Hz, 5-H); ms: m/z 272 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>14</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>S: C, 61.75; H, 4.44; N, 10.29; S, 11.77. Found: C, 61.77; H, 4.46; N, 10.23; S, 11.87.

Ethyl 2-Methylthioimidazo[2,1-*a*]isoquinoline-3-carboxylate (**8b**).

A solution of 2.96 g (10 mmoles) of 1-ethoxycarbonylmethylisoquinolinium bromide (**6b**), 10 mmoles of **2**, and 1.01 g (100 mmoles) of triethylamine in 100 ml of ethanol was refluxed for 30 hours, followed by removal of ethanol and excess triethylamine. The residue was washed with water and recrystallized from ethanol to give 1.86 g (65%) of **8b** as colorless needles, mp 154°; ir (potassium bromide):  $\nu$  max  $\text{cm}^{-1}$  1685 (C=O); uv (ethanol):  $\lambda$  max nm (log  $\epsilon$ ) 271 (4.78), 316 (3.91);  $^1\text{H-nmr}$  (deuteriochloroform):  $\delta$  1.48 (3H, t, J = 7.0 Hz, O-CH<sub>2</sub>-CH<sub>3</sub>), 2.78 (3H, s, SCH<sub>3</sub>), 4.46 (2H, q, J = 7.0 Hz, O-CH<sub>2</sub>), 7.16 (1H, d, J = 7.5 Hz, 6-H), 7.56-7.80 (3H, m, 7, 8, 9-H), 8.60-8.75 (1H, m, 10-H), 8.99 (1H, d, J = 7.5 Hz, 5-H); ms: m/z 274 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>15</sub>H<sub>14</sub>O<sub>2</sub>N<sub>2</sub>S: C, 61.29; H, 5.14; N, 10.21; S, 11.88. Found: C, 61.28; H, 5.15; N, 10.15; S, 11.69.

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- [30] We succeeded in the synthesis of the parent 1-azacycl[3.2.2]azine using 2-methylthioimidazo[1,2-*a*]pyridine as the key intermediate which was prepared by the hydrolysis of **4a** followed by the decarboxylation with polyphosphoric acid. We will publish these results in the forthcoming paper.