Studies on Mesoionic Compounds. IX.\textsuperscript{3} Synthesis of Bicyclic Mesoionic Compounds

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Reaction of the mesoionic 4-amino-1,2,4-triazolium-3-thiolates (I) with cyanogen bromide gave bicyclic mesoionic compounds (III) related to the product (II) obtained on treatment of I with phosgene. Benzoylation, tosylation, and nitrosation at the exocyclic nitrogen of III were also investigated.

Keywords—mesoionic compound; 4-amino-1,2,4-triazolium derivative; cyanogen bromide; bicyclic mesoionic compound; nitrosation

It is known that thioacylhydrazines give mesoionic heterocycles on treatment with phosgene, thiophosgene,\textsuperscript{3} 2,2-dichloroacrylates,\textsuperscript{4} and dichlorides of imidic\textsuperscript{5} and acylimidic acids.\textsuperscript{6} Based on the observation that mesoionic 4-amino-1,5-diphenyl-1,2,4-triazolium-3-thiolate\textsuperscript{7} (Ia) possesses a moiety similar to that of thioacylhydrazine, Lazaris \textit{et al.}\textsuperscript{8} synthesized the novel bicyclic mesoionic compounds, 1,2,4-triazolo[3,4-\textit{b}]-1,3,4-thiadiazolium-2-olate (IIa) and -2-benzoylamidine (Va), by the reaction of Ia with phosgene and benzoylcarbonimidic dichloride, respectively. In connection with our studies on reactions of 4-amino-1,2,4-triazolium-3-thiolates (I),\textsuperscript{1} we synthesized similar bicyclic mesoionic compounds by an alternative procedure.

When the amino compounds (Ia, b)\textsuperscript{1,7,9} were treated with cyanogen bromide, the hydrobromides of the bicyclic mesoionic imino compounds (III) were obtained directly. It was considered that in this reaction the intermediate nitrile formed at the first stage of the reaction was cyclized with the aid of hydrogen bromide. These compounds (III) were characterized by reaction with benzoyl chloride, giving the chlorides of the N-benzoyl derivatives (IV). The salts (IV) readily gave the free mesoionic compounds (V) on treatment with alkali. In the infrared (IR) spectra, absorptions of the carbonyl stretching of the compounds (V) were at lower frequencies than those of the salts (IV). For example, $\nu_{\text{CH}}$ 1560 cm$^{-1}$ for IVa and $\nu_{\text{CO}}$ 1470 cm$^{-1}$ for Va were observed. N-p-Toluenesulfonyl derivatives (VI) were also prepared similarly. Nuclear magnetic resonance (NMR) and mass spectra of the above bicyclic compounds were consistent with theses structures. Furthermore, the compounds (III) afforded N-nitroso derivatives (VII) upon treatment with sodium nitrite

2) Location: \textit{Sugitani, Toyama 930-01, Japan}.
in acetic acid. It is known that pyrolysis of N-nitroso-sydnone imine\(^ {10}\) and N-nitroso-1,2,3,4-oxatiazolium-5-aminide\(^ {11}\) give the corresponding oxo-type mesionic compounds. Thus, in order to obtain II thermolysis of VII in several solvents was attempted. Though II was detected on thin layer chromatography, these reactions resulted in the formation of many complex materials. This may occur because the thiadiazole ring of II easily undergoes ring opening. For example, the oxo-type compounds (II) were changed to the monocyclic mesionic esters (VIII) on heating in ethanol. A similar reaction of mesionic 1,3,4-thiadiazolium-2-olate with aniline giving the semicarbazide derivative has been reported.\(^ {12}\)

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\begin{align*}
\text{R}-\text{N} & \quad \text{BrCN} \\
\text{R} & \quad \text{N} & \quad \text{S}^{-} & \quad \text{NH}_{2} \\
\text{Ia} & \quad \text{c} & \\
\text{COCl}_{2} & \\
\text{R} & \quad \text{N} & \quad \text{S}^{-} & \quad \text{O}^{-} & \quad \text{N} & \quad \text{R} & \quad \text{a}, \text{c} \\
\text{IIa}, \text{c} & \\
\text{C}_{2} & \quad \text{H}_{5} & \quad \text{OH} & \quad \text{R} & \quad \text{N} & \quad \text{S}^{-} & \quad \text{NHCO}_{2} & \quad \text{C}_{6} & \quad \text{H}_{5} & \quad \text{VIIia}, \text{c} \\
\text{Va}, \text{b}, \text{r} & = \text{COC}_{6} & \quad \text{H}_{5} & \quad \text{VIla}, \text{b}, \text{r} & = \text{SO}_{2} & \quad \text{C}_{6} & \quad \text{H}_{5} & \quad \text{CH}_{3} (\rho) & \quad \text{Villa}, \text{b}, \text{r} & = \text{NO} & \quad \text{IVa}, \text{b}, \text{r} & = \text{COC}_{6} & \quad \text{H}_{5} & \\
\text{R} & = \text{R} & = \text{C}_{6} & \quad \text{H}_{5} & \quad \text{b}, \text{r} & = \text{C}_{6} & \quad \text{H}_{5} & \quad \text{CH}_{3} & \quad \text{c}, \text{r} & = \text{C}_{6} & \quad \text{H}_{5} \\
\end{align*}
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Chart 1

Experimental\(^ {13}\)

2-Amino-5,6-diphenyl-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazolium Bromide (IIIa)—A mixture of 4-amino-5,6-diphenyl-1,2,4-triazolo-3-thiolate (Ia)\(^ {3}\) (1.5 g) and BrCN (1.2 g) in CHCl\(_{3}\) (35 ml) was stirred for 2.5 hr with cooling in an ice bath. After concentration, the oily residue was crystallized from ether, and recrystallized from CH\(_{2}\)CN to give 840 mg (40%) of IIIa, colorless fine needles, mp\(_{\text{b}}\)=280°. IR \(\nu_{\text{max}}\) cm\(^{-1}\): 1600. UV \(\lambda_{\text{max}}\) nm (log \(\varepsilon\)): 274 (4.31). MS m/e: 293 (M\(^+\)-HBr). Anal. Calcd. for C\(_{13}\)H\(_{14}\)BrN\(_{5}\)S: C, 48.14; H, 3.23; N, 18.71. Found: C, 48.17; H, 3.00; N, 18.61.

2-Amino-5-methyl-6-phenyl-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazolium Bromide (IIIb)—A solution of BrCN (4 g) in CHCl\(_{3}\) (40 ml) was added to a cooled solution of 5-methyl-1-phenyl-1,2,4-triazolo-3-thiolate (Ib)\(^ {3}\) (1.5 g) in CHCl\(_{3}\) (40 ml) with stirring. The mixture was allowed to stand at room temperature overnight. After evaporation, MeOH was added to the residue and the mixture was filtered. Concentration of the filtrate and recrystallization of the residue from MeOH–isopropyl alcohol gave 922 mg (40%) of IIIb, colorless needles, mp\(_{\text{b}}\)=280°. IR \(\nu_{\text{max}}\) cm\(^{-1}\): 3400–2800. UV \(\lambda_{\text{max}}\) nm (log \(\varepsilon\)): 256 (4.21). NMR (CD\(_{3}\)OD) \(\delta\): 2.8 (3H, s, Me), 7.6 (5H, s, arom.). Anal. Calcd. for C\(_{14}\)H\(_{16}\)BrN\(_{5}\)S: C, 38.53; H, 3.23; N, 18.27. Found: C, 38.72; H, 3.33; N, 22.49.

5,6-Diphenyl-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazolium-2-benzoylamidine (Va)—A mixture of IIIa (100 mg) and benzoyl chloride (3 ml) was heated at 110° for 5 hr. After cooling, the precipitates were collected

13) All melting points are uncorrected. IR spectra were recorded on a JASCO IRA-1 spectrophotometer, and UV spectra were measured with a Hitachi 124 spectrophotometer. NMR spectra were obtained with a JEOL JNM-PXM-60 spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were obtained with a JEOL JMS-01SG instrument.
and washed with ether to give 94 mg of IVa, mp 265—270° (dec.). IR ν max cm⁻¹: 1560. The above salt (IVa) was stirred in saturated aqueous NaHCO₃. Extraction with CHCl₃ and usual work-up of the extract gave 40 mg (37%) of Va, pale yellow cubes, mp 254—259° (CH₃CN—isoamyl alcohol) (lit.⁹ mp 240—240.5°). IR ν max cm⁻¹: 1470. UV λ max nm (log e): 285 (4.13), 320 (4.45). NMR (CDCl₃) δ: 7.1—7.8 (15H, m, arom.), 8.25—8.6 (2H, m, arom.). MS m/e: 397 (M⁺). Anal. Calcd. for C₃₃H₂₉N₅O₆S: C, 66.48; H, 3.80; N, 17.62. Found: C, 66.51; H, 3.52; N, 17.36.

5-Methyl-6-phenyl-1,2,4-triazolo[3,4-b]1,3,4-thiadiazolium-2-benzoylaminide (IVb) — A mixture of IIIb (50 mg) and benzoyl chloride (2 ml) was heated at 150° for 1 hr. After cooling, the precipitates were collected to give 43 mg of IVb. IR ν max cm⁻¹: 1540. The salt (IVb) was treated with NaHCO₃ as described above to afford 25 mg (47%) of Vb, pale yellow prisms, mp 272—275° (EtOH—CHCl₃). IR ν max cm⁻¹: 1450. UV λ max nm (log e): 313 (4.49). NMR (CDCl₃) δ: 2.8 (3H, s, Me); 7.0—7.6 (3H, m, arom.), 7.45 (5H, s, arom.), 8.0—8.2 (2H, m, arom.). MS m/e: 335 (M⁺). Anal. Calcd. for C₃₃H₂₉N₅O₆S: C, 60.88; H, 3.91; N, 20.88. Found: C, 60.96; H, 3.87; N, 20.62.

6,6-Diphenyl-1,2,4-triazolo[3,4-b]1,3,4-thiadiazolium-2-p-toluenesulfonylamidin (VIa) — A solution of KOH (64 mg) in water (0.5 ml) was added to a mixture of IIIa (100 mg) and p-toluenesulfonyl chloride (100 mg) in water (3 ml). The mixture was then heated at 100° for 7 hr. After cooling, extraction with CHCl₃ and usual work-up of the extract gave 32 mg (27%) of VIa, colorless powder, mp > 280° (EtOH). IR ν max cm⁻¹: 1500, 1140, 1085. UV λ max nm (log e): 291 (4.31). MS m/e: 447 (M⁺). Anal. Calcd. for C₃₃H₂₇N₅O₈S₂: C, 59.04; H, 3.89; N, 15.65. Found: C, 59.33; H, 3.85; N, 15.46.

5-Methyl-6-phenyl-1,2,4-triazolo[3,4-b]1,3,4-thiadiazolium-2-p-toluenesulfonylamidin (VIb) — A solution of KOH (40 mg) in water (0.5 ml) was added to a cooled mixture of IIIb (100 mg) and p-toluenesulfonyl chloride (100 mg) in water (3 ml), and the mixture was stirred at room temperature for 6 hr. The precipitates were collected and recrystallized from EtOH to give 56 mg (45.5%) of VIb, colorless powder, mp 260—265°. IR ν max cm⁻¹: 1500, 1130, 1080. UV λ max nm (log e): 282 (4.40). MS m/e: 385 (M⁺). Anal. Calcd. for C₃₃H₂₇N₅O₈S₂: C, 52.97; H, 3.92; N, 18.17. Found: C, 52.86; H, 3.88; N, 18.16.

5,6-Diphenyl-1,2,4-triazolo[3,4-b]1,3,4-thiadiazolium-2-nitrosaminid (VIIa) — A solution of NaN₃ (140 mg) in water (0.5 ml) was added dropwise to a cooled solution of IIIa (432 mg) in AcOH (15 ml) and water (5 ml) at 0—5°. The mixture was stirred for 6 hr, and the resulting precipitates were collected and recrystallized from EtOH—CHCl₃ to give 250 mg (66%) of VIIa, fine yellow needles, mp 156—157° (dec.). IR ν max cm⁻¹: 1510, 1380. UV λ max nm (log e): 319 (4.29). Anal. Calcd. for C₃₃H₂₇N₅O₄S: C, 55.89; H, 3.13; N, 26.07. Found: C, 55.76; H, 3.34; N, 25.97.

5,6-Diphenyl-5-phenyl-1,2,4-triazolo[3,4-b]1,3,4-thiadiazolium-2-olates (IIa and IIc) — Using the reported method,⁹ IIa and IIc were prepared as follows. A solution of COCl₂ (1.8 g) in CHCl₃ (5 ml) was added to a solution of Ia, c₁ (5 mmol) in CHCl₃ (5 ml) at 0—5°. The mixture was refluxed for 1 hr, and the precipitates were filtered off. Concentration of the filtrate and recrystallization of the residue gave IIa, c₁.

IIa: 880 mg (60%), colorless cubes, mp 192—194° (benzene) (lit.⁹ mp 181°). IR ν max cm⁻¹: 1680. UV λ max nm (log e): 280 (4.15). NMR (CDCl₃) δ: 7.0—8.0 (m, arom.). MS m/e: 294 (M⁺). Anal. Calcd. for C₃₃H₂₇N₅O₄S: C, 61.21; H, 3.42; N, 19.04. Found: C, 61.03; H, 3.25; N, 19.82.

IIc: 1.1 g (87%), colorless needles, mp 154—156° (isopropyl alcohol). IR ν max cm⁻¹: 1680. NMR (CDCl₃) δ: 4.1 (3H, s, Me), 7.3—8.0 (5H, m, arom.). Anal. Calcd. for C₃₃H₂₇N₅O₄S: C, 51.71; H, 3.47; N, 24.12. Found: C, 51.48; H, 3.39; N, 24.20.

Alcoholysis of II with Ethanol — a) A suspension of IIa (1 g) in EtOH (5 ml) was refluxed for 1 hr. After cooling, the precipitates were collected and recrystallized from EtOH to give 670 mg (58%) of VIIa, colorless cubes, mp 199—206°. This product was identical with authentic VIIIa (mp 199—201°) by comparison of IR and NMR spectra.

b) A mixture of IIc (100 mg) and EtOH (3 ml) was refluxed for 30 min. Removal of the solvent by evaporation, followed by recrystallization of the residue from isopropyl alcohol gave 98 mg (82%) of VIIc, colorless sticks, mp 94—95°. The IR spectrum of this product was identical with that of authentic VIIc (mp 94—96°).

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