Notes

[Chem. Pharm. Bull. 29(6)1743—1747(1981)]

Studies on Mesoionic Compounds. XII.[1] Synthesis of 1,2,3-Thiadiazolium-4-aminide Derivatives and Their Characterization

Katsutada Masuda,* Jun Adachi, Hikari Morita, and Keiichi Nomura

Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Sugitani, Toyama 930-01, Japan

(Received December 4, 1980)

New mesoionic heterocycles, 1,2,3-thiadiazolium-4-ethoxycarbonylaminides (**9** and **10**), were prepared by alkylation of 1,2,3-thiadiazoles (**5**) followed by treatment with base. Compound (**9**) was hydrolyzed to the hydrochloride of the corresponding 4-imine derivative (**13**), which was converted to the 4-oxo analog (**16**) *via* N-nitrosation.

Keywords——mesoionic compound; alkylation; 1,2,3-thiadiazole; hydrolysis; N-nitrosation

Although preparation and properties of mesoionic heterocycles, as exemplified by sydnone, sydnone imine, *etc.*, have been reported extensively,[2] there are many classes of compounds in this field which have not been synthesized. Mesoionic 3- or 2-substituted-1,2,3-thiadiazole systems possessing a 4-exocyclic hetero atom have not been described with the exception of 3-aryl-1,2,3-thiadiazolium-4-olates.[3] We previously reported that alkylation of 5-acylamino-1,2,3-thiadiazoles gave mesoionic compounds.[1] The present paper describes the synthesis and properties of new mesoionic heterocycles, 3-alkyl-1,2,3-thiadiazolium-4-ethoxycarbonylaminides (**9** and **10**).

According to the reported procedures,[4] 4-ethoxycarbonylamino-1,2,3-thiadiazole (**5a**) was obtained starting from pyruvic acid (**1a**) *via* cyclization of the ethoxycarbonylhydrazone (**2a**) with thionyl chloride and subsequent Curtius reaction of the 1,2,3-thiadiazole-4-carboxylic acid derivative. In a similar manner, the 5-phenyl analog (**5b**) was also prepared. Reaction of **5** with diazomethane did not proceed at all. Methylation of **5** with methyl iodide and base gave the methylamino compounds (**6**). Treatment of **5** with alkyl fluorosulfonate, however, yielded the ring-alkylated products (**7** and **8**). The free bases (**9** and **10**) were obtained by treatment of **7** and **8** with sodium hydrogen carbonate. In the infrared (IR) spectra, the carbonyl stretching absorptions of the free bases appeared at lower frequencies by 110—130 cm^{-1} compared with those of the corresponding salts. A similar phenomenon has been observed in the cases of N-acylsydnone imines and their salts, and was interpreted in terms of carbonyl polarization.[5] In the nuclear magnetic resonance (NMR) spectra of **9** and **10**, it seems that the N-methyl (**9a, b**: δ 4.2) and methylene protons of the N-ethyl group (**10a**: δ 4.9; **10b**: δ 4.6) are deshielded by the nitrogen atoms bearing positive charge, analogously to those of sydnones.[6] On the basis of these results and ultraviolet (UV) and mass spectra (see the experimental section), the formulations of **9** and **10** could be deduced as mesoionic. However, two classes of mesoionic structures obtainable from **5** may be present depending on the position of alkylation (at N-2 or N-3). In order to confirm the position of the alkyl moiety, reductions of **9b** and **10b** were attempted. Reduction with sodium borohydride or aluminum amalgam[7] resulted in recovery of the mesoionic compounds; reduction with lithium aluminum hydride or zinc–acetic acid gave many unidentified products. Hydrogenolysis of these compounds with a platinum catalyst occurred smoothly to yield the aminothiazolinones (**11**), whose identity was confirmed by the spectral features and conversion to the known dioxothiazolidine derivative (**12**).[8] This reaction is considered to involve reductive cleavage of the N–N and

N–S bonds and subsequent intramolecular cyclization of the α-alkylamino-α-thiobenzoylmethylcarbamic acid ester thus formed.

These mesoionic compounds are apparently stable to acid and alkali; *e.g.*, they were unchanged on heating in dilute hydrochloric acid or sodium hydroxide solution. Hydrolysis of **9**, however, could be performed by heating it with concentrated hydrochloric acid in a sealed tube[1] to yield the 4-imine hydrochloride (**13**). Compound (**13**) readily gave the N-acetyl derivative (**14**) on treatment with acetic anhydride and pyridine followed by base. In general, free bases of many imine type mesoionic compounds such as sydnone imine are unstable, while their salts and the free bases of N-acyl derivatives are stable enough to be isolated.[2] However, the free base of **13b** seems to be moderately stable; it could be isolated as a reddish oil, and gave **14b** on acetylation.

On the other hand, interesting examples of conversion of imine-type to oxo-type mesoionic compounds *via* N-nitroso derivatives have been reported.[9] We also investigated the nitrosation of **13** for the preparation of 3-alkyl-1,2,3-thiadiazolium-4-olate, which could not be obtained by the reported method[3] starting from diazonium compounds. The N-nitroso compound (**15a**) was not isolated from the reaction mixture of **13a** with sodium nitrite in acetic acid, but a trace of the desired 4-oxo compound (**16a**) was obtained as a yellow oil. The structure of **16a** was deduced from its spectral data; IR (film): 1600 cm^{-1} (CO); NMR ($CDCl_3$): δ 4.0 (3H, s, NMe), 7.25 (1H, s, 5-H); mass spectrum: *m/e* 116 (M^+), 43 (base peak). Under the same conditions, **13b** or preferably its free base gave **16b** as yellow crystals in 30% yield. The nitroso derivatives (**15**), formed probably at the first stage of these reactions, are considered to be extremely labile in contrast to the 5-nitrosoimine derivatives of the same ring system.[1]

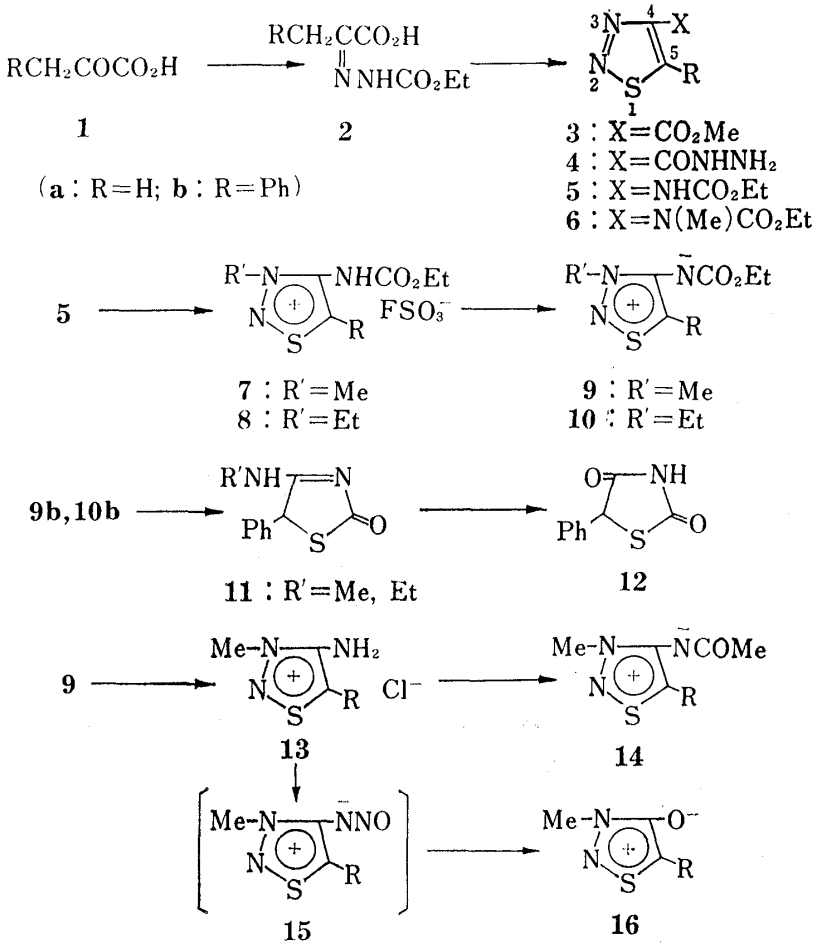

Chart 1

Experimental

All melting points were determined with a Yanagimoto hot-stage apparatus and are uncorrected. IR spectra were taken with a JASCO IRA-1 spectrophotometer, and UV spectra were measured with a Hitachi 124 spectrophotometer. NMR spectra were recorded on a JEOL JNM-PMX-60 spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were obtained with JEOL JMS-01SG-2 and JEOL JMS-D200 instruments.

α-N-Ethoxycarbonylhydrazono-phenylpropionic Acid (2b)——Phenylpyruvic acid[10] (**1b**) (25 g) and ethoxycarbonylhydrazine[11] (15.5 g) in benzene (250 ml) were heated under reflux for 2 hr. The reaction mixture was concentrated to half the initial volume and cooled, then the resulting precipitate was filtered off to give **2b** (35 g, 92%), mp 144—146°. IR ν_{max}^{KBr} cm^{-1}: 3240 (NH), 1730 (CO), 1700 (CO). *Anal.* Calcd for $C_{12}H_{14}N_2O_4$: C, 57.59; H, 5.64; N, 11.20. Found: C, 57.51; H, 5.74; N, 11.08.

Methyl 5-Phenyl-1,2,3-thiadiazole-4-carboxylate (3b)——Ethereal diazomethane [prepared from N-nitrosomethylurea (20 g), 50% KOH (60 ml) and ether (200 ml)] was added to **2b** (3.62 g) in MeOH (50 ml). After 30 min, the mixture was concentrated to yield an oil (3.78 g). The resulting oil (400 mg) and $SOCl_2$ (1 ml) were stirred at room temperature for 16 hr, and then concentrated. Chromatography of the residue on silica gel (3 g, benzene) gave **3b** (180 mg, 54%) as colorless needles, mp 61—62° (iso-PrOH). IR ν_{max}^{KBr} cm^{-1}: 1735 (CO). NMR (CCl_4) δ: 3.95 (3H, s, OMe), 7.45 (5H, s, Ph). *Anal.* Calcd for $C_{10}H_8N_2O_2S$: C, 54.53; H, 3.66; N, 12.72. Found: C, 54.49; H, 3.83; N, 12.65.

5-Phenyl-1,2,3-thiadiazole-4-carboxyhydrazide (4b)——A mixture of **3b** (440 mg), 80% $N_2H_4 \cdot H_2O$ (188 mg) and MeOH (8 ml) was stirred at room temperature for 2 hr. The precipitate was collected and recrystallized from iso-PrOH to yield **4b** (403 mg, 92%) as colorless needles, mp 136—138°. IR ν_{max}^{KBr} cm^{-1}: 3280 (NH_2), 1665 (CO). *Anal.* Calcd for $C_9H_8N_4OS$: C, 49.08; H, 3.66; N, 25.44. Found: C, 49.33; H, 3.37; N, 25.73.

4-Ethoxycarbonylamino-5-phenyl-1,2,3-thiadiazole (5b)——A solution of $NaNO_2$ (81 mg) in water (1 ml) was added to a cooled mixture of **4b** (220 mg), water (2 ml) and conc. HCl (0.1 ml), and the mixture was stirred for 1 hr. The precipitate was collected, washed with water and dried to give colorless crystals (209 mg, 90.5%), mp 90—92°. IR ν_{max}^{KBr} cm^{-1}: 2120 (N_3), 1680 (CO). The resulting azide (3.7 g) and EtOH (25 ml) were heated under reflux for 1 hr. Concentration of the reaction mixture and recrystallization of the residue from benzene afforded **5b** (2.13 g, 61%) as colorless sticks, mp 122—123°. IR ν_{max}^{KBr} cm^{-1}: 3220 (NH), 1700 (CO). UV λ_{max}^{EtOH} nm (log ε): 248 (3.78), 292 (3.82). NMR ($CDCl_3$) δ: 1.15 (3H, t, J=7 Hz, $CH_2\underline{CH_3}$), 4.1 (2H, q, J=7 Hz, $\underline{CH_2}CH_3$), 7.45 (5H, s, Ph). *Anal.* Calcd for $C_{11}H_{11}N_3O_2S$: C, 53.00; H, 4.45; N, 16.86. Found: C, 52.99; H, 4.17; N, 16.67.

4-N-Ethoxycarbonylmethylamino-1,2,3-thiadiazoles (6)——A mixture of **5a**[4b] or **5b** (200 mg), K_2CO_3 (an eq. mole), MeI (1 ml) and EtOH (2 ml) was heated at 40° for 5 hr, and then concentrated. The residue was dissolved in $CHCl_3$, washed with water and dried (Na_2SO_4). Evaporation gave **6** as an oil. **6a**: 167 mg (77%), bp 72° (0.5 mmHg, bath temp.), mp 31—32°. IR ν_{max}^{film} cm^{-1}: 1720 (CO). UV λ_{max}^{EtOH} nm (log ε): 292 (3.24). NMR ($CDCl_3$) δ: 1.35 (3H, t, J=7 Hz, $CH_2\underline{CH_3}$), 3.8 (3H, s, NMe), 4.35 (2H, q, J=7 Hz, $\underline{CH_2}CH_3$), 8.75 (1H, s, 5-H). MS *m/e*: 187 (M^+). *Anal.* Calcd for $C_6H_9N_3O_2S$: C, 38.49; H, 4.85; N, 22.45. Found: C, 38.67; H, 4.91; N, 22.29; **6b**: 207 mg (97%). IR ν_{max}^{film} cm^{-1}: 1720 (CO). NMR ($CDCl_3$) δ: 0.95 (3H, t, J=7 Hz, $CH_2\underline{CH_3}$), 3.4 (3H, s, NMe), 4.0 (2H, q, J=7 Hz, $\underline{CH_2}CH_3$), 7.45 (5H, s, Ph). MS *m/e*: 263 (M^+). *Anal.* Calcd for $C_{12}H_{13}N_3O_2S$: C, 54.73; H, 4.98; N, 15.96. Found: C, 54.95; H, 4.80; N, 15.76.

3-Methyl-1,2,3-thiadiazolium-4-ethoxycarbonylaminides (9)——a) **5a** (500 mg) and FSO_3Me (0.5 ml) were stirred at room temperature for 15 min. Concentration of the mixture gave a crystalline residue, which was washed with ether and dried to afford **7a** (770 mg, 92.5%), mp 84°. IR ν_{max}^{KBr} cm^{-1}: 1740 (CO). NMR (acetone-d_6) δ: 1.3 (3H, t, J=7 Hz, $CH_2\underline{CH_3}$), 4.3 (2H, q, J=7 Hz, $\underline{CH_2}CH_3$), 4.7 (3H, s, NMe), 7.0—7.5 (1H, broad peak, CONH), 9.65 (1H, s, 5-H).

7a (500 mg) was added to a solution of $NaHCO_3$ (291 mg) in water (3 ml) at 0° with stirring. After 10 min, the mixture was diluted with $CHCl_3$ (50 ml), dried (Na_2SO_4) and concentrated. The residue was recrystallized from cyclohexane to give **9a** (270 mg, 72%) as yellow needles, mp 74—75°. IR ν_{max}^{KBr} cm^{-1}: 1610 (CO). UV λ_{max}^{KBr} nm (log ε): 244 (3.64), 299 (3.30), 368 (2.70). NMR ($CDCl_3$) δ: 1.35 (3H, t, J=7 Hz, $CH_2\underline{CH_3}$), 4.2 (2H, q, J=7 Hz, $\underline{CH_2}CH_3$), 4.2 (3H, s, NMe), 9.0 (1H, s, 5-H). MS *m/e*: 187 (M^+). *Anal.* Calcd for $C_6H_9N_3O_2S$: C, 38.49; H, 4.85; N, 22.45. Found: C, 38.27; H, 4.69; N, 22.71.

b) Similarly, **5b** (310 mg) and FSO_3Me (0.5 ml) gave **7b** (425 mg, 93.5%), mp 94°. IR ν_{max}^{KBr} cm^{-1}: 1740 (CO). NMR (acetone-d_6) δ: 1.1 (3H, t, J=7 Hz, $CH_2\underline{CH_3}$), 4.1 (2H, q, J=7 Hz, $\underline{CH_2}CH_3$), 4.7 (3H, s, NMe), 7.3—8.0 (6H, m, CONH+Ph). Treatment of **7b** (423 mg) with $NaHCO_3$ and work-up as above gave an oil, which was purified by chromatography on silica gel (2 g, $CHCl_3$) to afford **9b** (245 mg, 74%) as a yellow oil. IR ν_{max}^{film} cm^{-1}: 1620 (CO). NMR ($CDCl_3$) δ: 1.2 (3H, t, J=7 Hz, $CH_2\underline{CH_3}$), 4.0 (2H, q, J=7 Hz, $\underline{CH_2}CH_3$), 4.2 (3H, s, NMe), 7.1—7.7 (5H, m, Ph). MS *m/e*: 263 (M^+). **9b**·$HClO_4$: colorless plates, mp 115—116° (iso-PrOH). *Anal.* Calcd for $C_{12}H_{14}ClN_3O_6S$: C, 39.62; H, 3.88; N, 11.55. Found: C, 39.42; H, 3.61; N, 11.31.

3-Ethyl-1,2,3-thiadiazolium-4-ethoxycarbonylaminides (10)——A mixture of **5** (4 mmol) and FSO_3Et (3 ml) was stirred at room temperature for 1 hr, and then concentrated. The resulting salt (**8**) was stirred

with a saturated solution of $NaHCO_3$ (340 mg) for 10 min. The mixture was diluted with $CHCl_3$ (100 ml), dried over Na_2SO_4, and then the $CHCl_3$ was evaporated off. The residue was chromatographed on alumina (30 g, benzene) and recrystallized to yield **10**. **10a**: 490 mg (65%), orange plates, mp 106—107° (cyclohexane). IR ν_{max}^{KBr} cm^{-1}: 1605 (CO). NMR ($CDCl_3$) δ: 1.35 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.65 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 4.3 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 4.9 (2H, q, J=7 Hz, $NC\underline{H}_2CH_3$), 9.4 (1H, s, 5-H). MS *m/e*: 201 (M^+). *Anal.* Calcd for $C_7H_{11}N_3O_2S$: C, 41.28; H, 5.51; N, 20.88. Found: C, 41.56; H, 5.70; N, 20.71. **10b**: 682 mg (61%), orange sticks, mp 114—116° (iso-Pr_2O). IR ν_{max}^{KBr} cm^{-1}: 1630 (CO). UV λ_{max}^{EtOH} nm (log ε): 271 (3.83), 380 (3.64). NMR ($CDCl_3$) δ: 1.15 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.6 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 3.95 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 4.6 (2H, q, J=7 Hz, $NC\underline{H}_2CH_3$), 7.3—7.7 (5H, m, Ph). *Anal.* Calcd for $C_{13}H_{15}N_3O_2S$: C, 56.30; H, 5.45; N, 15.15. Found: C, 56.10; H, 5.32; N, 15.09.

4-Alkylamino-5-phenyl-3-thiazolin-2-ones (**11**)——a) A mixture of **9b** (1 g) and $PtO_2 \cdot H_2O$ (200 mg) in MeOH (50 ml) was shaken under a H_2 atmosphere (3 kg/cm^2) at room temperature for 9 hr. Usual work-up of the mixture gave **11** (R'=Me) (188 mg, 24%), colorless sticks, mp 167—170° (benzene). IR ν_{max}^{KBr} cm^{-1}: 1690 (CO). NMR ($CDCl_3$) δ: 2.95 (3H, d, J=5 Hz, $NHC\underline{H}_3$), 5.5 (1H, s, $PhC\underline{H}<$), 6.7—7.2 (1H, m, $N\underline{H}CH_3$), 7.3 (5H, s, Ph). MS *m/e*: 206 (M^+). *Anal.* Calcd for $C_{10}H_{10}N_2OS$: C, 58.23; H, 4.89; N, 13.58. Found: C, 58.16; H, 4.78; N, 13.79.

b) Similarly, **10b** (500 mg) was hydrogenated (3 hr) to give **11** (R'=Et) (141 mg, 64%) as colorless needles, mp 132—133° (benzene–iso-Pr_2O). IR ν_{max}^{KBr} cm^{-1}: 1680 (CO). NMR ($CDCl_3$) δ: 1.15 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 3.45 (2H, d.q, J=5, 7 Hz, $NHC\underline{H}_2CH_3$), 5.5 (1H, s, $PhC\underline{H}<$), 6.2—6.6 (1H, m, NH), 7.3 (5H, s, Ph). MS *m/e*: 220 (M^+). *Anal.* Calcd for $C_{11}H_{12}N_2OS$: C, 59.97; H, 5.49; N, 12.72. Found: C, 59.70; H, 5.64; N, 12.85.

2,4-Dioxo-5-phenylthiazolidine (**12**)——A mixture of **11** (R'=Et) (50 mg) and 10% HCl (0.5 ml) was heated under reflux for 1 hr. Extraction of the mixture and usual work-up of the extract afforded **12** (41 mg, 93.5%) as colorless needles, mp 130—131° (benzene). IR ν_{max}^{KBr} cm^{-1}: 3160 (NH), 1650 (CO). NMR ($CDCl_3$) δ: 5.4 (1H, s, $PhC\underline{H}<$), 7.5 (5H, s, Ph), 8.9—9.5 (1H, broad peak, NH). MS *m/e*: 193 (M^+). *Anal.* Calcd for $C_9H_7NO_2S$: C, 55.94; H, 3.65; N, 7.25. Found: C, 55.87; H, 3.40; N, 7.22. This product was identical with an authentic sample [mp 127—129° (EtOH)] prepared by the reported method[8] (lit. mp 125—126°).

4-Amino-3-methyl-1,2,3-thiadiazolium Chlorides (**13**)——A solution of **9** (1 mmol) in conc. HCl (5 ml) was heated in a sealed tube at 120° for 18 hr. The mixture was evaporated to dryness, and the residue was recrystallized to give **13**. **13a**: 150 mg (quant.), colorless needles, mp 231—234° (dec.) (MeOH–ether). NMR (D_2O) δ: 4.3 (3H, s, NMe), 8.35 (1H, s, 5-H). *Anal.* Calcd for $C_3H_6ClN_3S$: C, 23.76; H, 3.99; N, 27.72. Found: C, 23.82; H, 4.14; N, 27.52. **13b**: 180 mg (79%), pale yellow needles, mp 209—210° (dec.) (iso-Pr_2O–iso-PrOH). UV λ_{max}^{EtOH} nm (log ε): 248 (3.71), 365 (3.77). NMR (D_2O) δ: 4.4 (3H, s, NMe), 7.65 (5H, s, Ph). *Anal.* Calcd for $C_9H_{10}ClN_3S$: C, 47.46; H, 4.43; N, 18.45. Found: C, 47.23; H, 4.44; N, 18.48.

3-Methyl-5-phenyl-1,2,3-thiadiazolium-4-acetylaminide (**14b**)——a) A mixture of **13b** (300 mg), Ac_2O (1 ml) and pyridine (210 mg) was stirred at room temperature for 8 hr. Concentration of the mixture and recrystallization of the residue from iso-Pr_2O gave **14b**·HCl (289 mg, 81%) as pale yellow plates, mp 158—160° (dec.). IR ν_{max}^{KBr} cm^{-1}: 1705 (CO). NMR ($CDCl_3$) δ: 2.3 (3H, s, COMe), 4.6 (3H, s, NMe), 6.7—8.2 (6H, m, CONH+Ph). *Anal.* Calcd for $C_{11}H_{12}ClN_3OS$: C, 48.97; H, 4.48; N, 15.58. Found: C, 48.71; H, 4.73; N, 15.45.

A mixture of the above salt (50 mg) and saturated $NaHCO_3$ solution (2 ml) was stirred for 10 min, and extracted with $CHCl_3$. Usual work-up of the extract afforded **14b** (32 mg, 74%) as yellow plates, mp 139—141° (benzene–iso-Pr_2O). IR ν_{max}^{KBr} cm^{-1}: 1560 (CO). UV λ_{max}^{EtOH} nm (log ε): 253 (3.81), 360 (3.68). NMR ($CDCl_3$) δ: 2.2 (3H, s, COMe), 4.2 (3H, s, NMe), 7.3—7.9 (5H, m, Ph). *Anal.* Calcd for $C_{11}H_{11}N_3OS$: C, 56.63; H, 4.75; N, 18.01. Found: C, 56.39; H, 5.03; N, 17.74.

b) **13b** (300 mg) was added to a cooled solution of 5% KOH (5 ml), and the mixture was stirred for 3 hr. Extraction of the mixture with $CHCl_3$ and usual work-up of the extract gave the free base of **13b** (200 mg, 79%) as a red oil. NMR ($CDCl_3$) δ: 3.9 (3H, s, NMe), 4.7 (1H, s, NH), 7.1—7.7 (5H, m, Ph). MS *m/e*: 191 (M^+). A mixture of this oil (150 mg), Ac_2O (5 ml) and pyridine (3 ml) was stirred at room temperature for 1 hr. After concentration of the mixture, the residue was chromatographed on silica gel (6 g, $CHCl_3$) and recrystallized from benzene–hexane to give **14b** (35 mg, 28%) as yellow plates, mp 138—140°, identical with the product obtained in procedure a).

3-Methyl-5-phenyl-1,2,3-thiadiazolium-4-olate (**16b**)——A solution of $NaNO_2$ (138 mg) in water (0.5 ml) was added to a mixture of the free base (191 mg) of **13b** and AcOH (1 ml) at 0—5° with stirring. After 2 hr, $NaNO_2$ (138 mg) in water (0.5 ml) was again added, and the whole was stirred for 3 hr. The mixture was diluted with water and extracted with $CHCl_3$. The extract was worked up as usual to give an oil. Chromatography on silica gel (1 g, $CHCl_3$) and recrystallization from MeCN afforded **16b** (57 mg, 30%) as yellow cubes, mp 155—156°. IR ν_{max}^{KBr} cm^{-1}: 1600 (CO). NMR ($CDCl_3$) δ: 4.05 (3H, s, NMe), 7.2—8.1 (5H, m, Ph). MS *m/e*: 192 (M^+). *Anal.* Calcd for $C_9H_8N_2OS$: C, 56.22; H, 4.19; N, 14.57. Found: C, 56.38; H, 4.28; N, 14.78.

Acknowledgement We are grateful to Mr. M. Morikoshi and Mr. H. Hori of this University for mass spectral measurements and elemental analyses, respectively.

References and Notes

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[Chem. Pharm. Bull. 29(6)1747—1749(1981)]

A New Route to 4-Unsubstituted β-Lactams through Ureidomethylation of Ketene Silyl Acetals

KIYOSHI IKEDA, YOSHIYASU TERAO, and MINORU SEKIYA*

Shizuoka College of Pharmacy, 2-2-1 Oshika, Shizuoka, 422, Japan

(Received December 17, 1980)

α-Ureidomethylated carboxylates were obtained by the reaction of ketene silyl acetals with benzyl N-(chloromethyl)carbamates in the presence of titanium tetrachloride. Successive hydrogenolysis over palladium-on-charcoal followed by treatment with lithium diisopropylamide gave β-lactams.

Keywords——β-lactam; titanium tetrachloride; ureidomethylation; hexahydro-1,3,5-triazine; benzyloxycarbonyl chloride

Methods for synthesizing monocyclic β-lactams are of particular interest in connection with the synthesis of analogs of the naturally occurring antibiotics such as nocardicin A.[1)]

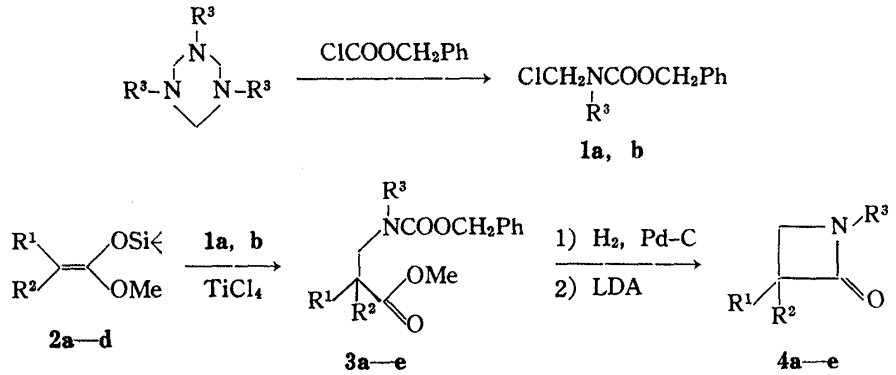

Chart 1