# Synthesis and study of (2*S*,4*S*)-4-arylamino-2-carboxy-5-pyrrolidones

*V. P. Krasnov,* I. A. Nizova, T. A. Sinitsyna, and N. V. Avdyukova*

*Institute of Organic Synthesis, Ural Branch of the Russian Academy of Sciences, 20 ul. S. Kovalevskoi, 620219 Ekaterinburg, Russian Federation. Fax: +7 (343) 244 4133*

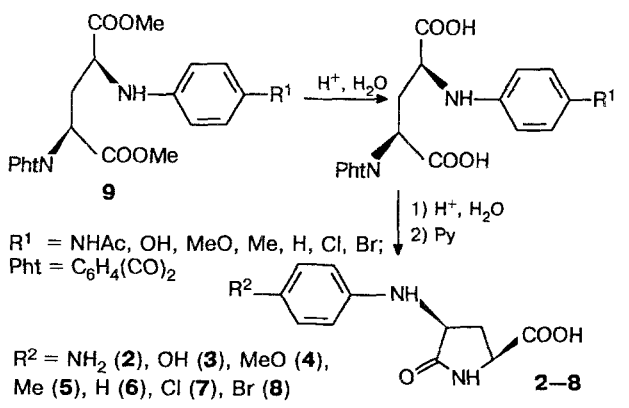
(2*S*,4*S*)-4-Arylamino-2-carboxy-5-pyrrolidones were prepared by hydrolysis of dimethyl (2*S*,4*S*)-4-arylamino-*N*-phthaloylglutamates. The protonation constants of the arylamino group in the synthesized compounds were determined. The pyrrolidone ring is stable in acidic or neutral solutions. The relative stability of the pyrrolidone ring in alkaline solutions was studied by IR spectroscopy.

**Key words:** glutamic acid, acid dissociation constants; 4-arylaminopyroglutamic acid.

It has been shown previously[1] that (2*S*)-2-carboxy-5-pyrrolidone (L-pyroglutamic acid) (**1**) is a convenient synthon for asymmetric synthesis. In recent years, procedures have been elaborated which make it possible to introduce a substituent at position 4 of the pyrrolidone ring without a loss of the optical activity.[2] For example, derivatives of acid **1** having a substituent at the C(4) atom in the *trans* position to the carboxyl group have been synthesized.[3] Using similar methods, *i.e.*, by generation of a carbanion (the derivative of glutamic acid, Glu) with subsequent reactions with electrophiles, the following compounds could be obtained: (2*S*)-4-carboxyglutamic acid,[4] important intermediates for the biosynthesis of aromatic amino acids,[5] proline derivatives,[6] and some others.

We used an alternative procedure for synthesizing the C(4)-derivatives of glutamic and pyroglutamic acids, *viz.*, the introduction of a halogen atom at position 4 of a Glu derivative, its substitution with a suitable nucleophile, and removal of protective groups.[7—9] This method, like that mentioned above, makes it possible to obtain enantiomerically pure products, but is more convenient for synthesizing compounds having a C(4)—heteroatom bond.

**Scheme 1**




In a continuation of these investigations, we obtained a series of hitherto unknown (2*S*,4*S*)-4-arylamino-2-carboxy-5-pyrrolidones (**2—8**) (*cis*-4-arylamino-L-pyroglutamic acids) containing different substituents at the *para* position of the aromatic ring (Scheme 1) and studied their physicochemical properties.

Compounds **2—8** were obtained by acid hydrolysis of the respective dimethyl (2*S*,4*S*)-4-arylamino-*N*-phthaloylglutamates (**9**), which we had prepared previously.[9] The enantiomeric purity of the starting compounds was confirmed by HPLC.

The removal of protective groups requires prolonged heating in a strongly acidic medium. First, hydrolysis of ester groups occurs to give the intermediate (2*S*,4*S*)-4-arylamino-*N*-phthaloylglutamic acids. Sometimes, it is possible to isolate them from the reaction mixture. These compounds are very poorly soluble in 6 *N* HCl normally used to remove the phthaloyl group, which substantially increases the time of hydrolysis, decreases the yield of the target compounds, and increases the probability of racemization. To decrease the reaction time, HCl—AcOH mixtures or HBr were used in some cases.

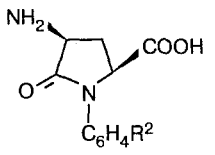
The removal of the phthaloyl group is accompanied by simultaneous closure of the pyrrolidone cycle. The preparation of 4-substituted glutamic acids is frequently accompanied by their partial cyclization to derivatives of acid **1**.[10,11] It should be emphasized that only one cyclization product is formed in this particular case. No (2*S*,4*R*)-4-arylamino-2-carboxy-5-pyrrolidones, which are diastereomeric to the target compounds, were found (TLC), which indicates the absence of noticeable racemization during the removal of the protective groups. Treatment of the reaction mixture with pyridine or silver

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 12, pp. 2087—2090, December, 1993.

1066-5285/93/4212-2001 $12.50 

carbonate resulted in compounds **2—8** as free bases. Their structures were confirmed by data from elemental analysis, UV, IR, and NMR spectroscopy.

The choice between the structures **2—8** and an alternative structure (**10**), in which the pyrrolidone cycle is formed with the involvement of the N atom of the arylamino group, was based on the analysis of the results of potentiometric titration.



**10**

The titration was performed as described earlier;[12] the ionization constants were calculated on a BESM-6 computer using the SCOGS program.[13] Compounds **2—8** have only one amino group capable of protonation ($pK_a$ ~6.9—7.3, Table 1), whereas the $pK_a$ of the α-amino group in amino acids (structure **10**) should be at least 9.5. In the series of compounds **2—8**, the $pK_a$ of the amino group systematically decreases as the Hammett's $\sigma_p$ constants of the $R^2$ substituent increase. However, the differences between these compounds are not as significant as, *e.g.*, in the case of *para*-substituted anilines. Evidently, this is due to the decisive effect of the carboxamide group on the ability of the arylamino group in the compounds under consideration to undergo protonation.

Unlike amino acid **1**, which is readily transformed to Glu in acid or alkaline media, the pyrrolidone cycle in compounds **2—8** is stable in acidic, neutral, and weakly alkaline solutions. The opening of the lactam cycle occurs only in a strongly alkaline medium. Attempts to isolate the respective Glu derivatives as free bases from the alkaline media results in their spontaneous cyclization to the original pyroglutamic amino acids.

In order to reveal the factors affecting the stability of the pyrrolidone cycle in alkaline media, we performed an IR spectroscopic study of the process of hydrolysis by NaOD in $D_2O$ at 80 °C. The ratio of the acyclic and cyclic forms was determined from the ratio of ν(CO) intensities of the lactam and the γ-carboxylic group. Table 1 lists the time required to transform 50 % of the starting amount of compounds **1—8** to the acyclic form. Although the method is not very accurate, the results obtained unambiguously indicate that the rate of opening of the pyrrolidone ring tends to increase as the $\sigma_p$ constant of the $R^2$ substituent increases. This agrees with the known data[15] that the rate of the alkaline hydrolysis of amides increases with a decrease in the electron density at the acyl carbon atom. Compound **3** is an exception. Probably, its relatively high stability is due to the specific features of the effect of the ionized phenolic group on this process. It was found that the pyrrolidone cycle of derivatives **7** and **8** is less stable under the given conditions than in amino acid **1**. The results obtained indicate that the stability of the pyrrolidone cycle in compounds **2—8** in an alkaline medium is to a significant degree determined by electronic factors.

## Experimental

$^1H$ NMR spectra were obtained on Tesla BS-567 A (working frequency 100 MHz) and Bruker WP-200 SY (200 MHz) spectrometers. IR spectra were recorded on a Specord 75 IR spectrophotometer (in vaseline oil). UV spectra of aqueous solutions were recorded on a Specord UV-VIS instrument. Specific rotation was determined on an A1-EPO polarimeter. TLC was performed on Silufol UV-254 plates ($Pr^iOH$—3 % $NH_4OH$, 7 : 3). Potentiometric titration of compounds **2—8** was carried out by 0.1 *N* KOH at 25 ± 0.1 °C in 0.1 *N* $KNO_3$ using an automatic buret and an OP-208/1 pH-meter with glass and calomel electrodes. The initial volume of the solution to be titrated was 50 mL, and the initial concentration of compounds **2—8** was 2.00 mmol $L^{-1}$.

**Synthesis of (2*S*,4*S*)-4-arylamino-2-carboxy-5-pyrrolidones 2—8 (general procedure).** The respective dimethyl *threo*-4-arylamino-*N*-phthaloyl-L-glutamate (10 g) was refluxed in an acid solution (100 mL). After completion of hydrolysis, phthalic acid, which precipitated on cooling, was filtered off. The filtrate was concentrated to dryness *in vacuo*. The residue was dissolved in anh. EtOH and cooled, then pyridine was added

**Table 1.** Properties of compounds **1—8**

| Compound | $\sigma_p$ constant of $R^2$ (Ref. 14) | $pK$ of ionization of the 4-arylamino group | Half-time of conversion/h |
|---|---|---|---|
| **1** | — | — | 0.88 |
| **2** | −0.66 | 7.33[a] | 8.5 |
| **3** | −0.37 | 7.19[b] | 20.0[c] |
| **4** | −0.268 | 7.11 | 5.5 |
| **5** | −0.170 | 7.02 | 0.75 |
| **6** | 0.0 | 7.10 | 1.25 |
| **7** | 0.227 | 6.93 | 0.45 |
| **8** | 0.232 | 6.99 | 0.18 |

[a] $pK$ of ionization of the *para*-arylamino group is 4.21. [b] $pK$ of ionization of the *para*-hydroxyl group is 10.12. [c] The ionized phenolic group has $\sigma_p$ = 0.52 (Ref. 14).

until the product precipitated completely. The mixture was kept in a refrigerator, the precipitate was filtered off, washed with EtOH, and dried *in vacuo*. If necessary, the product was recrystallized from 70 % aqueous EtOH.

**(2*S*,4*S*)-4-(4-Aminophenylamino)-2-carboxy-5-pyrrolidone (2).** The hydrolysis was carried out for 12 h by conc. HBr. The reaction mixture was cooled, phthalic acid was filtered off, and the filtrate was concentrated to dryness *in vacuo*. The residue was triturated with ethanol (100 mL), washed with EtOH, and dried *in vacuo* over KOH to give 6.08 g (80 %) of compound **2** as hydrobromide (crystal hydrate). The product is chromatographically homogeneous; $[\alpha]_D^{20}$ −21.8° (*c* 1, $H_2O$); m.p. 216—221 °C (dec.). Found (%): C, 38.02; H, 4.84; N, 11.93; Br, 23.58. $C_{11}H_{13}N_2O_3 \cdot HBr \cdot 1.5H_2O$. Calculated (%): C, 38.48; H, 4.94; N, 12.24; Br, 23.32.

To obtain the free base, 5 g of the product was dissolved in water (500 mL), $Ag_2CO_3$ (2 g) was added, and the solution was stirred for 2 h. The precipitate was filtered off, and the filtrate was concentrated to dryness. The residue was recrystallized from 70 % aqueous EtOH to give 2.30 g (68 %) of compound **2**, $R_f$ 0.40; $[\alpha]_D^{20}$ −25.9° (*c* 1, $H_2O$); m.p. 233—235 °C (dec.). Found (%): C, 56.47; H, 5.82; N, 17.68. $C_{11}H_{13}N_3O_3$. Calculated (%): C, 56.16; H, 5.53; N, 17.86. IR, $\nu/cm^{-1}$: 3390, 3320, 3230 (NH); 1690 (C=O of lactam). UV, $\lambda_{max}$/nm: 203, 254. $^1H$ NMR ($D_2O$), δ: 7.43 (m, 4 H, $C_6H_4$); 4.73 (m, 1 H, C<u>H</u>—NH); 4.39 (m, 1 H, C<u>H</u>—COOH); 3.09 (m, 1 H, $CH_2$); 2.14 (m, 1 H, $CH_2$).

**(2*S*,4*S*)-4-(4-Hydroxyphenylamino)-2-carboxy-5-pyrrolidone (3).** The hydrolysis was carried out for 12 h by conc. HBr to give 2.10 g (34 %) of compound **3** as a monohydrate, $R_f$ 0.43; $[\alpha]_D^{20}$ −21.7° (*c* 1, $H_2O$); m.p. 228—231 °C. Found (%): C, 52.30; H, 5.97; N, 10.76. $C_{11}H_{14}N_2O_5$. Calculated (%): C, 51.96; H, 5.51; N, 11.02. IR, $\nu/cm^{-1}$: 3370 (NH); 1700 (C=O of lactam ). UV, $\lambda_{max}$/nm: 200, 287. $^1H$ NMR ($D_2O$), δ: 7.17 (m, 4 H, $C_6H_4$); 4.72 (t, 1 H, C<u>H</u>—NH); 4.37 (m, 1 H, C<u>H</u>—COOH); 3.08 (m, 1 H, $CH_2$); 2.17 (m, 1 H, $CH_2$).

**(2*S*,4*S*)-4-(*p*-Anisidino)-2-carboxy-5-pyrrolidone (4).** The hydrolysis was carried out for 16 h by conc. HBr to give 5.46 g (93 %) of compound **4**, $R_f$ 0.69; $[\alpha]_D^{20}$ −26.4° (*c* 1, $H_2O$); m.p. 238—239.5 °C (dec.). Found (%): C, 57.38; H, 5.58; N, 11.40. $C_{12}H_{14}N_2O_4$. Calculated (%): C, 57.60; H, 5.60; N, 11.20. IR, $\nu/cm^{-1}$: 3390 (NH); 1690 (C=O of lactam). UV, $\lambda_{max}$/nm: 200, 247. $^1H$ NMR ($D_2O$), δ: 7.19 (m, 4 H, $C_6H_4$); 4.28 (m, 1 H, C<u>H</u>—COOH); 3.90 (s, 3 H, $CH_3O$); 3.00 (m, 1 H, $CH_2$); 2.12 (m, 2 H, $CH_2$).

**(2*S*,4*S*)-4-(*p*-Toluidino)-2-carboxy-5-pyrrolidone (5).** The hydrolysis was carried out by a mixture of conc. $CH_3COOH$ and conc. HCl (1:1, v/v) for 8 h to give 4.22 g (74 %) of compound **5**, $R_f$ 0.61; $[\alpha]_D^{20}$ −23.3° (*c* 1, $H_2O$); m.p. 239—241 °C (dec.). Found (%): C, 61.54; H, 5.98; N, 11.97. $C_{12}H_{14}N_2O_3$. Calculated (%): C, 61.77; H, 5.76; N, 11.80. IR, $\nu/cm^{-1}$: 3380 (NH); 1690 (C=O of lactam). UV, $\lambda_{max}$/nm: 202, 245. $^1H$ NMR ($D_2O$), δ: 7.31 (m, 4 H, $C_6H_4$); 4.33 (m, 1 H, C<u>H</u>—COOH); 3.05 (m, 1 H, $CH_2$); 2.39 (m, 3 H, $CH_3$); 2.09 (m, 1 H, $CH_2$).

**(2*S*,4*S*)-4-Anilino-2-carboxy-5-pyrrolidone (6).** The hydrolysis was carried out by 20 % HCl for 13 h to give 5.22 g (94 %) of compound **6**. The product was recrystallized from 70 % aqueous EtOH, $R_f$ 0.65; $[\alpha]_D^{20}$ −39.5° (*c* 1, $H_2O$); m.p. 232—234 °C (dec.). Found (%): C, 60.10; H, 5.50; N, 12.53. $C_{11}H_{12}N_2O_3$. Calculated (%): C, 60.01; H, 5.46; N, 12.73. IR, $\nu/cm^{-1}$: 3340 (NH); 1730, 1700 (C=O of lactam). UV, $\lambda_{max}$/nm: 204, 241. $^1H$ NMR ($D_2O$), δ: 7.51 (m, 5 H, $C_6H_5$); 4.43 (m, 1 H, C<u>H</u>—COOH); 3.15 (m, 1 H, $CH_2$); 2.22 (m, 1 H, $CH_2$).

**(2*S*,4*S*)-4-(4-Chlorophenylamino)-2-carboxy-5-pyrrolidone (7).** The hydrolysis was carried out by a mixture of conc. $CH_3COOH$ and conc. HCl (1:1, v/v) for 12 h to give 4.37 g (74 %) of compound **7**, $R_f$ 0.72; $[\alpha]_D^{20}$ −13.0° (*c* 1, $H_2O$); m.p. 236—238 °C (dec.). Found (%): C, 51.80; H, 4.50; N, 10.70; Cl, 13.79. $C_{11}H_{11}ClN_2O_3$. Calculated (%): C, 51.87; H, 4.32; N, 11.00; Cl, 13.95. IR, $\nu/cm^{-1}$: 1690 (C=O of lactam). UV, $\lambda_{max}$/nm: 202, 248. $^1H$ NMR ($D_2O$), δ: 7.46 (m, 4 H, $C_6H_4$); 4.37 (m, 1 H, C<u>H</u>—COOH); 3.03 (m, 1 H, $CH_2$); 2.13 (m, 1 H, $CH_2$).

**(2*S*,4*S*)-4-(4-Bromophenylamino)-2-carboxy-5-pyrrolidone (8).** The hydrolysis was carried out by conc. HBr for 10 h to give 5.35 g (85 %) of compound **8**, $R_f$ 0.59; $[\alpha]_D^{20}$ −7.9° (*c* 1, $H_2O$); m.p. 237—238 °C (dec.). Found (%): C, 44.05; H, 3.58; N, 9.22; Br, 26.92. $C_{11}H_{11}BrN_2O_3$. Calculated (%): C, 44.15; H, 3.68; N, 9.36; Br, 26.76. IR, $\nu/cm^{-1}$: 3380 (NH); 1700 (C=O of lactam ). UV, $\lambda_{max}$/nm: 202, 250. $^1H$ NMR ($D_2O$), δ: 7.46 (m, 4 H, $C_6H_4$); 4.47 (m, 1 H, C<u>H</u>—NH); 4.31 (m, 1 H, C<u>H</u>—COOH); 3.08 (m, 1 H, $CH_2$); 2.16 (m, 1 H, $CH_2$).

**(2*S*,4*S*)-4-(4-Aminophenylamino)-*N*-phthaloylglutamic acid (11).** Dimethyl (2*S*,4*S*)-4-(4-aminophenylamino)-*N*-phthaloylglutamate (3.2 g) was refluxed for 1 h with 20 % HCl. After cooling the reaction mixture to ~20 °C, the colorless crystalline precipitate was filtered off, washed with water, and dried *in vacuo* over KOH. Yield 1.8 g (66 %), m.p. 238—242 °C. Found (%): C, 59.28; H, 4.42; N, 10.88. $C_{19}H_{17}N_3O_6$. Calculated (%): C, 59.53; H, 4.44; N, 10.97. IR, $\nu/cm^{-1}$: 1780 (C=O of the phthaloyl group); 1750, 1720 (COOH). UV, $\lambda_{max}$/nm: 220, 242, 306. $^1H$ NMR ($D_2O$), δ: 7.92 (m, 4 H, $C_6H_4(CO_2)N$); 7.52 (m, 4 H, N—$C_6H_4$—N); 5.19 (m, 2 H, C<u>H</u>—NH, CH—NPht); 2.67 (m, 2 H, $CH_2$).

**(2*S*,4*S*)-4-(*p*-Anisidino)-*N*-phthaloylglutamic acid (12).** Dimethyl (2*S*,4*S*)-4-(*p*-anisidino)-*N*-phthaloylglutamate (5 g) was hydrolyzed for 2 h similarly to the synthesis of compound **11** to give 3.95 g (85 %) of a colorless crystalline precipitate of acid **12**. Found (%): C, 60.51; H, 4.49; N, 7.26. $C_{20}H_{18}N_2O_7$. Calculated (%): C, 60.30; H, 4.52; N, 7.03. IR, $\nu/cm^{-1}$: 1760 (C=O of the phthaloyl group); 1750, 1720 (COOH). UV, $\lambda_{max}$/nm: 208, 220, 306. $^1H$ NMR ($(CD_3)_2SO$), δ: 7.91 (m, 4 H, $C_6H_4(CO_2)N$); 7.37 (d, 2 H, N—$C_6H_4$—N); 6.98 (d, 2 H, N—$C_6H_4$—N); 5.09 (m, 2 H, C<u>H</u>—NH, CH—NPht); 2.67 (m, 2 H, $CH_2$).

**Study of the rate of alkaline hydrolysis of compounds 2—8.** Compound **2—8** (0.5 mmol) was dissolved in a 0.3 *M* solution of NaOD in $D_2O$ (5 mL). The solution was placed in a $CaF_2$ cell (thickness 50 mm) and placed in a thermostat (80 °C). IR spectra of the solutions in the 1800—1400 $cm^{-1}$ region were recorded at regular intervals. The reference channel contained a cell with $D_2O$. The content of the acyclic form was determined from the decrease in the peak optical density for the lactam ν(C=O) at 1660 $cm^{-1}$ calculated by the base line method.

## References


1. G. M. Coppola and H. F. Schuster, in *Asymmetric Synthesis. Construction of Chiral Molecules Using Amino Acids*, Wiley Interscience, New York, 1987, 223.
2. J. E. Baldwin, T. Miranda, M. Moloney, and T. Hokelek, *Tetrahedron*, 1989, **45**, 7459.
3. A. N. Bouler, P. M. Doyle, P. B. Hitchcock, and D. W. Young, *Tetrahedron Lett.*, 1991, **32**, 2679.
4. S. Danischefsky, E. Berman, and L. A. Clizbe, *J. Am. Chem. Soc.*, 1979, **101**, 4385.

5. S. Danischefsky, T. Morris, and L. A. Clizbe, *J. Am. Chem. Soc.*, 1981, **103**, 1602.
6. A. M. P. Koskinen and H. Rapoport, *J. Org. Chem.*, 1989, **54**, 1859.
7. I. M. Bukrina, V. P. Krasnov, V. Kh. Kravtsov, V. N. Biyushkin, and L. V. Alekseeva, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, 2077 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1989, **38**, 1910 (Engl. Transl.)].
8. G. G. Vatulina, T. N. Tuzhilkova, T. V. Matveeva, V. P. Krasnov, N. L. Burde, and L. V. Alekseeva, *Khim.-farm. Zh.* [*Chem.-Pharm. J.*], 1986, **20**, 1078 (in Russian).
9. I. A. Nizova, V. P. Krasnov, O. V. Korotkovskikh, and L. V. Alekseeva, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, 2781 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1989, **38**, 2545 (Engl. Transl.)].
10. Y. Hirose, *J. Chem. Soc. Jpn., Chem. and Ind. Chem.*, 1961, **81**, 794.
11. Yu. N. Belokon', N. I. Chernoglazova, A. S. Batsanov, N. S. Garbalinskaya, V. I. Bakhmutov, Yu. T. Struchkov, and V. M. Belikov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1987, 852 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1987, **36**, 779 (Engl. Transl.)].
12. I. A. Nizova, T. A. Sinitsyna, V. P. Krasnov, L. V. Alekseeva, I. A. Alekseeva, I. V. Podgornaya, and V. P. Zhukov, *Zh. Obshch. Khim.*, 1983, **53**, 2123 [*J. Gen. Chem. USSR*, 1983, **53** (Engl. Transl.)].
13. I. G. Sayce, *Talanta*, 1968, **15**, 1397.
14. A. J. Gordon and R. A. Ford, *The Chemist's Companion*, John Wiley & Sons, New York—London—Sydney—Toronto, 1972.
15. *Comprehensive Organic Chemistry*, vol. 2, Ed. J. O. Sutherland, Pergamon Press, Oxford—New York—Toronto—Sydney—Paris—Frankfurt, 1979.

*Received January 5, 1993*

# Synthesis and transformations of 1,3,5-triazabicyclo[3.1.0]hexanes*

*N. N. Makhova,* A. N. Mikhailyuk, A. E. Bova, T. V. Chabina, and L. I. Khmel'nitskii*

*N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 117913 Moscow, Russian Federation. Fax: +7 (095) 135 5328*

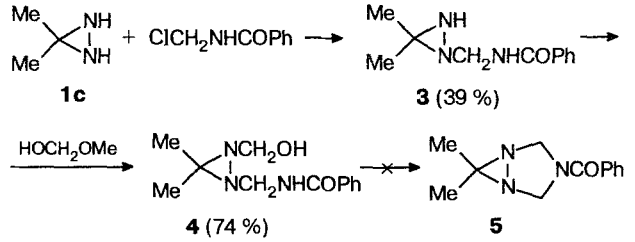
The conditions for the condensation of 1,2-nonsubstituted diaziridines with $CH_2O$ and $NH_3$ (or $AlkNH_2$) to the corresponding 1,3,5-triazabicyclo[3.1.0]hexanes have been found and 3-phenylsulfonyl, 3-trimethylsilyl, 3-nitroso, and 3-nitro derivatives of the latter have been obtained.

**Key words:** diaziridines, condensation; 1,3,5-triazabicyclo[3.1.0]hexanes, α-aminomethylation, nitrosation, denitrosation, silylation, nitration.

It has been shown previously[2—4] that 1,2-nonsubstituted diaziridines (**1**) and 1-alkyldiaziridines (**2**) behave as NH acids in the Mannich reaction and only undergo α-aminomethylation. For example, diaziridines **2** do not react either with each other or with aziridine,[3] and alkoxymethyldiaziridine does not react with compounds having an active H atom, *viz.*, imidazole or $CD_3OD$ in the presence of $CD_3CO_2D$ (*cf.* Ref. 5). The absence of α-aminomethylating ability has been also observed for aziridines[6—8] and oxaziridines.[5] Presumably, this is a general property of three-membered nitrogen-containing heterocycles.[5]

Likewise, we could not overcome this restriction when both the diaziridinoalcohol fragment required for α-diaziridinomethylation and a group with an active H atom (PhCONH) were present in the same molecule: 1-benzamidomethyl-2-hydroxymethyl-3,3-dimethyldiaziridine (**4**), obtained as shown in Scheme 1, did not undergo cyclization into 3-benzoyl-6,6-dimethyl-1,3,5-triazabicyclo[3.1.0]hexane (**5**).

**Scheme 1**




* For the previous communication, see Ref. 1.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 12, pp. 2091—2095, December, 1993.