CROATICA CHEMICA ACTA CCACAA 49 (4) 809—812 (1977)

YU ISSN 0011-1643
CCA-1053 547.789.2
Note

Chemistry of 2,4-Dioxothiazolidine. II. Ammonolysis of 2,4-Dioxothiazolidine and its Derivatives[1]

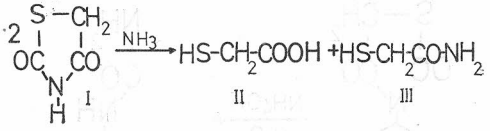
K. Popov-Pergal, M. Pergal, and **D. Jeremić*

*Faculty of Sciences, Institute of Chemistry, 21001 Novi Sad, P.O.B. 187, and **Faculty of Sciences, Department of Chemistry, 11000 Beograd, Yugoslavia*

Received December 12, 1976

It is found that the ammonolysis of 2,4-dioxothiazolidine gives 5-amino-2,3-dithiacaprohydroxamic acid, while 3-phenyl-2,4-dioxothiazolidine is transformed in glycolic acid *N*-(2-amino-1-hydroxyethyl)-anilide. The product of ammonolysis of 3-(3-4-dichlorophenyl)-2,4-dioxothiazolidine proved to be 3,4-dichlorophenylcarbamide.

Many derivatives of 2,4-dioxothiazolidine are known as substances with bacterostatic, bactericide, insecticide, local anesthetic, antispasmatic or anticancer properties. The effect of 2,4-dioxothiazolidine derivatives on Mycobacterium turberculosis is specially investigated[2]. In our complex study of 2,4--dioxothiazolidine chemistry we directed our attention to the behaviour of this type of compounds to ammonia. There is the communication of Erlemann and Knetsch[3], where the reaction between 2,4-dioxothiazolidine (I) and ammonia or amines is treated. The authors reported that they obtained thioglycolic acid (II) and their amide (III) as a result of the reaction between 2,4-dioxothiazolidine and ammonia.



I II III

In our experiments we have found some differences which do not in agreement with the quoted results. Therefore, we studied the reaction in aqueous medium between (*a*) 2,4-dioxothiazolidine (I), (*b*) 3-phenyl-2,4-dioxothiazolidine (IV), and (*c*) 3-(3,4-dichlorophenyl)-2,4-dioxothiazolidine (V).

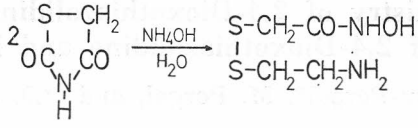
The reaction between ammonia and 2,4-dioxothiazolidine and their mentioned derivatives is carried out by heating the suspended compound in 25% aqueous ammonia under the reflux condenser on the water bath. The compounds are very easily dissolved during heating. In the ammonolyses of 3-substituted derivatives at the end of reaction, crystalline products are spontaneously separated. The reaction product of 2,4-dioxothiazolidine must be isolated by azeotropic distillation.

The infrared spectra of all three products were essentially different. None of isolated compounds was thioglycolic acid or its amide, what is opposite to

* The author for correspondence.

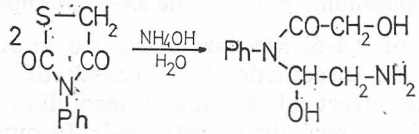
communication of Erlemann and Knetsch[3]. On the basis of IR, MS spectra and other characteristics we found that each examined derivative reacted with ammonia on its own way resulting in different products.

2,4-Dioxothiazolidine (I) in the ammonolysis is transformed in 5-amino-2,3--dithiacaprohydroxamic acid (VI). It could be proposed an opening of heterocyclic ring with fusion of two fragments followed by an oxido-reduction.



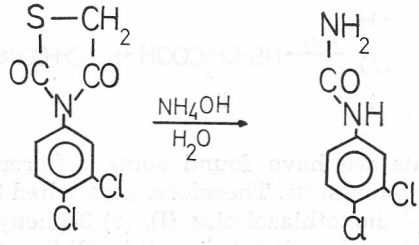
I VI

3-Phenyl-2,4-dioxothiazolidine (IV) in the reaction with ammonia is transformed in glycolic acid *N*-(2-amino-1-hydroxyethyl)-anilide (VII). It could be proposed an opening of the heterocyclic ring in two different ways, followed by extrusion of sulfur, reduction[4] and combination of fragments.



IV VII

3-(3,4-Dichlorophenyl)-2,4-dioxothiazolidine (V) in the ammonolysis gave 3,4-dichlorophenylcarbamide (VIII), which is formed by the degradation of the heterocyclic ring and subsequent reaction between the intermediar fragment and ammonia.



V VIII

The comparison of these three results of the ammonolysis of 2,4-dioxothiazolidine and its derivatives indicates that the flow of the ammonolysis and the type of the final product in the investigated cases depends not only upon the heterocyclic ring but also upon the substitutent in the position »3« (e. g. on the nitrogen), which has a substantional influence on the whole reaction.

EXPERIMENTAL

The structures of all the products were established by elemental analysis, molecular weight determination by mass spectrometry, and by spectral data. The infrared spectra were measured with a Perkin-Elmer spectrophotometer Model 437. The

mass spectra were taken with a Varian MAT CH 5 apparatus. The melting points are uncorrected.

The Ammonolysis of 2,4-Dioxothiazolidine (I)

In a 100 ml flask, fitted with reflux condenser, 350 mg (0.003 mol) of 2,4-dioxothiazolidine (origin Fluka AG) is suspended in 15 ml of aqueous ammonia (25%) and heated 3 h in the water bath. Suspended compound is soon dissolved. After heating the corresponding ammount of ethanol and benzene is added and water is removed by azeotropic distillation. Remaining oil is transferred in a Petri-dish and in short time crystalised 5-amino-2,3-dithiacaprohydroxamic acid (VI). The crystals are carefully washed with absolute ethanol. Yield 100 mg, m. p. 167—8 °C.

Anal. $C_4H_{10}N_2O_2S_2$ (182.2) calc'd.: C 26.36; H 5.53; N 15.37%
found: C 26.11; H 5.46; N 15.42%

Characteristic IR bands: 3220—2800, 1580—1560, 1455, 1430, 1380—1370, 1210 cm^{-1}. MS: 182 (M^+), 164, 137, 119, 109, 79 *m/e*.

The Ammonolysis of 3-Phenyl-2,4-dioxothiazolidine (IV)

In a 50 ml flask, fitted with reflux condenser, 385 mg (0.002 mol) of 3-phenyl-2,4-dioxothiazolidine[1](IV) is suspended in 15 ml of aqueous ammonia (25%) and heated 3 h in the water bath. The suspension is very soon dissolved and only a few minutes after heating crystals started to separate. Complete ammount of crystals is separated after cooling. The crystals of glycolic acid *N*-(2-amino-1-hydroxyethyl)-anilide(VII) are carefully washed with absolute ethanol. Yield 80 mg, m. p. 148 °C.

Anal. $C_{10}H_{14}N_2O_3$ (210.2) calc'd.: C 57.13; H 6.71; N 13.33%
found: C 56.82; H 6.81; N 13.05%

Characteristic IR bands: 3440—3420, 3340—3270, 3220, 3100, 3060, 3040, 2890, 1670—1640, 1615, 1590, 1565—1530, 1500, 1450, 1355, 1305, 1290, 1265—1245, 1150, 1130—1110, 1075, 1035, 905, 860, 775, 750 cm^{-1}. MS: 210 (M^+), 180, 165, 134, 117, 93, 77 *m/e*.

The Ammonolysis of 3-(3,4-Dichlorophenyl)-2,4-dioxothiazolidine (V)

Ammonolysis of 390 mg (0.1115 mol) of 3-(3,4-dichlorophenyl)-2,4-dioxothiazolidine[1](V) was carried out in the same way. The reaction yielded 110 mg of 3,4-dichlorophenylcarbamide(VIII), m. p. 158 °C. The melting point is in agreement with the published data[5].

Anal. $C_7H_6N_2OCl_2$ (204.9) calc'd.: C 41.00; H 2.95; N 13,67%
found: C 39.69; H 2.78; N 13.40%

Characteristic IR bands: 3495, 3430, 3340—3280, 2920, 2850, 1680—1640, 1610, 1580, 1540—1530, 1475, 1395, 1382, 1340, 1125, 1025 cm^{-1}.
MS: 204 (M^+), 186, 161, 145, 133, 125, 75 *m/e*.

REFERENCES

1. First communication: M. Pergal, K. Popov-Pergal, and N. Kobilarov, *Synthesis* (1976) 190.
2. H. Taniyama, Sh. Takemura, B. Yasui, H. Uchida, *J. Pharm. Soc. Jap.* **74** (1954) 113; *Chem. Abstr.* **48** (1954) 6504.
3. G. A. Erlemann and H. Knetsch, *J. Soc. Cosmet. Chem.* **11** (1960) 43; *Chem. Abstr.* **54** (1960) 11358.
4. F. Wöhler, *J. Liebig, Ann.* **26** (1838) 276.
5. D. J. Beaver, D. P Roman, and P. J. Stofell, *J. Amer. Chem. Soc.* **79** (1957) 1236.

SAŽETAK

Kemija 2,4-dioksotiazolidina. II. Amonoliza 2,4-dioksotiazolidina i njegovih derivata

K. Popov-Pergal, M. Pergal i D. Jeremić

Nađeno je da se amonolizom 2,4-dioksotiazolidina dobija 5-amino-2,3-ditiakaprohidroksamska kiselina, dok 3-fenil-2,4-dioksotiazolidin prelazi u *N*-(2-amino-1-oksietil)-anilid glikolne kiseline. Proizvod amonolize 3-(3-4-dihlorfenil)-2,4-dioksotiazolidina je 3,4-dihlorfenilkarbamid.

INSTITUT ZA HEMIJU
V. VLAHOVIČA 2
21001 NOVI SAD
i
PRIRODOSLOVNO-MATEMATIČKI
FAKULTET
ZAVOD ZA HEMIJU
11000 BEOGRAD

Prispjelo 12. prosinca 1976.