ISSN 1070-3632, Russian Journal of General Chemistry, 2013, Vol. 83, No. 7, pp. 1467–1468. © Pleiades Publishing, Ltd., 2013.
Original Russian Text © V.A. Kozlov, K.V. Novikov, T.G. Mokeeva, S.A. Kuz'mina, 2013, published in Zhurnal Obshchei Khimii, 2013, Vol. 83, No. 7, pp. 1221–1222.

LETTERS TO THE EDITOR

Cyclocondensation of Oxoacids with Urea

V. A. Kozlov, K. V. Novikov, T. G. Mokeeva, and S. A. Kuz'mina

Yakovlev Chuvash State Pedagogical University, ul. Marksa 38, Cheboksary, 428000 Russia
e-mail: acetone1987@yahoo.com

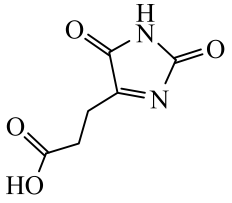
Received February 14, 2013

DOI: 10.1134/S1070363213070323

Azaheterocycles with two nitrogen atoms most frequently used in the organic synthesis are imidazole derivatives. Some of them, i. e., imidazolidine-2,4-diones or hydantoins, have been known for a long time. A widely known method for their synthesis is cyclocondensation of 1,2-bifunctional compounds with urea [1].

The aim of our study was to investigate the possibility of obtaining derivatives of imidazolidine-2,4-dione via cyclocondensation of urea with α-oxoacids and to evaluate the prospects of industrial synthesis of 4(5)-substituted hydantoin derivatives.

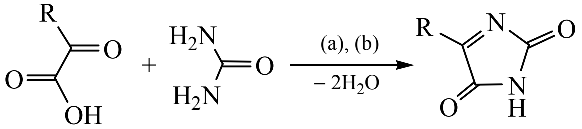
A presumed natural source of hydantoins is para-biochemical reaction in living organisms. It is known that 3-(2,5-dioxo-2,5-dihydroimidazol-4-yl)propionic acid (**I**) is formed from α-ketoglutaric acid and urea in the reaction accompanying the Krebs cycle. Biological necessity of its existence in the living objects can be attributed to the need to urea fixation to reduce the inhibitory effect of its high concentrations on the cell enzymes [2, 3].



I

This process can be reproduced in the laboratory conditions since α-oxoacids can react with urea under mild conditions to form imidazoline-2,4(5*H*)-dione structure. Pyruvic, mesoxalic, glyoxylic acids and their ethyl esters were found to be capable of the cyclocondensation with urea.

The reactions of α-oxoacids **Ia**–**Id** with urea occur at 80–90°C at pH < 4 within 3–3.5 h at a molar ratio of the reagents of 1:1. The solution was of stramineous color, after some time yellow-beige precipitate was formed. After separation of the precipitate the distillation of the filtrate afforded the hydantoin derivatives **IIa–IId.** In a neutral medium, the reaction rate reduces considerably.



Ia–**Id** **IIa**–**IId**

(a) pH 7, 80–90°C, 3 days; (b) pH 1–4, 80–90°C, 3.5 h. R = $(CH_2)_2COOH$ (**a**), $COOC_2H_5$ (**b**), COOH (**c**), CH_3 (**d**).

The structure and composition of the synthesized compounds **IIa**–**IId** were confirmed by gas chromatography, NMR spectra, and elemental analysis. Thus, the ^{1}H NMR spectrum of 3-(2,5-dioxo-2,5-dihydro-4-yl)propionic acid **IIa** contains two multiplets of methylene protons at 1.9 and 2.25 ppm and the singlet of imide proton at 8.1 ppm.

The practical importance of preparing such compounds *in vitro* is that the hydantoin derivatives mostly are the basis for creating unique pharmaceuticals, diagnostics, or antiseptics in cosmetics.

The ^{1}H NMR spectra were recorded on a Bruker DRX-500 instrument operating at 500.13 Hz using DMSO-d_6 as a solvent and HMDS as an internal reference. Identification of compounds obtained in solution was performed using a Shimadzu GCMS-QP2010S gas chromatograph.

REFERENCES

1. *Geterotsiklicheskie soedineniya* (Heterocyclic Compounds), Elderfield, R., Ed., Moscow: Inostrannaya Literatura, 1961, vol. 5, p. 203.
2. Kozlov, V.A., Matkov, K.G., and Lyschikov, A.N., *Eur. J. Natur. Hist*., 2007, no. 6, p. 65.
3. Novikov, K.V., Kozlov, V.A., and Ionova, D.A., *Aktual'nye problemy khimicheskoi nauki, praktiki i obrazovaniya* (Actual Problems of Chemical Sciences, Practics, and Education), Kursk: Kursk. Gos. Tekhn. Univ., 2009, p. 186.