ISSN 1070-3632, Russian Journal of General Chemistry, 2011, Vol. 81, No. 10, pp. 2207–2208. © Pleiades Publishing, Ltd., 2011.
Original Russian Text © L.V. Muzychka, E.V. Verves, I.O. Yaremchuk, O.B. Smolii, 2011, published in Zhurnal Obshchei Khimii, 2011, Vol. 81, No. 10, pp. 1755–1756.

LETTERS TO THE EDITOR

Oxidation of 1,3-Dimethyl-2,4-dioxo-2,3,4,7-tetrahydro-7-(2-propenyl)-1*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylic Acid under the Radziszewski Reaction Conditions

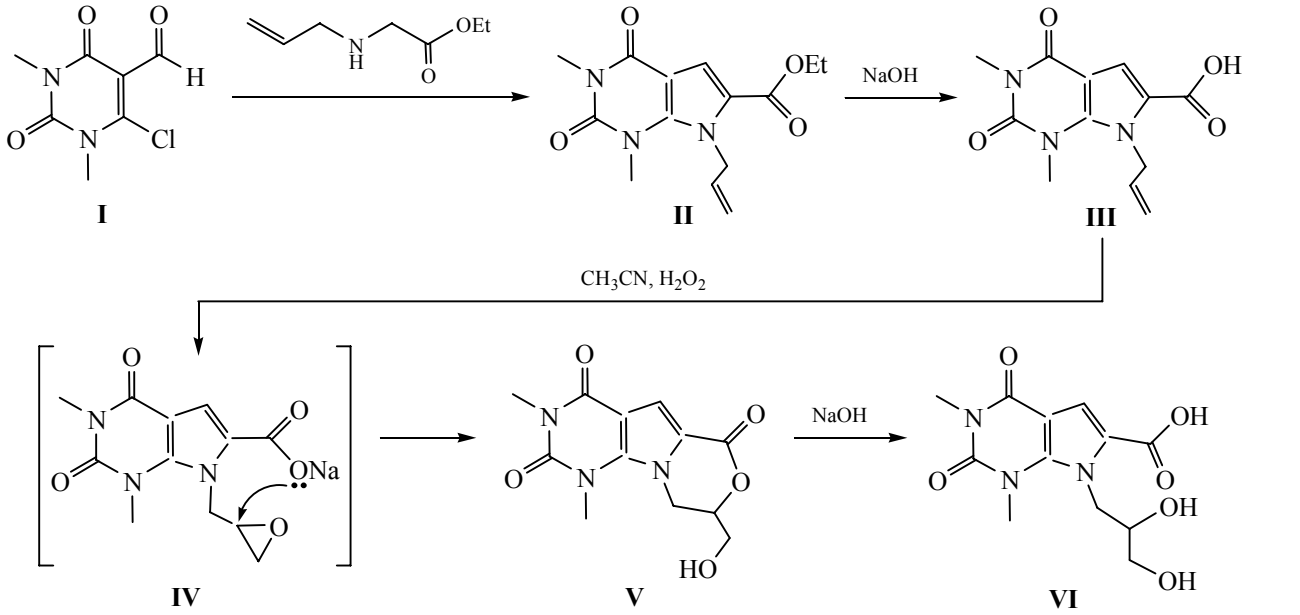
L. V. Muzychka, E. V. Verves, I. O. Yaremchuk, and O. B. Smolii

Institute of Bioorganic Chemistry and Petroleum Chemistry, National Academy of Sciences of Ukraine, ul. Murmanskaya 1, Kiev, 02660 Ukraine
e-mail: smolii@bpci.kiev.ua

Received March 22, 2011

DOI: 10.1134/S1070363211100318

One synthesis approach to the compounds containing oxirane ring is the olefins oxidation under the Radziszewski reaction conditions [1]. We have shown that the available acid **III**, obtained by a known method [2], readily reacts with iminoperacetic acid. Unfortunately, it was impossible to obtain the expected product **IV**, because it undergoes rapidly an intramolecular cyclization to give a tricyclic derivative, pyrimido[5',4':4,5]pyrrolo[2,1-*c*][1,4]oxazine **V**. It is interesting that the oxidation of compounds **II** and **III** with peracetic or 3-chloroperbenzoic acid does not occurs even under prolonged heating.



I **II** **III** **IV** **V** **VI**

When the substrate **V** is heated with sodium hydroxide, lactone ring is opened to form pyrrolo-[2,3-*d*]pyrimidine-6-carboxylic acid **VI** derivative containing 2,3-dihydroxypropyl substituent in position 7 of the heterocycle. The structure of the synthesized compounds was established by the ^{1}H, ^{13}C NMR and IR spectroscopy; the composition was confirmed by the elemental analysis.

Ethyl 1,3-dimethyl-2,4-dioxo-2,3,4,7-tetrahydro-7-(2-propenyl)-1*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylate (II). To a suspension of 2 g of aldehyde **I** in

8 ml of benzene was added dropwise a mixture of 1.85 g of diethyl ether and 1.4 ml of triethylamine in 7.5 ml of benzene while cooling at 0–5°C and a stirring. The reaction mixture was kept for 12 h at 20–25°C. The precipitated triethylamine hydrochloride was filtered off. The filtrate was evaporated. The residue was dissolved in 15 ml of ethanol, and was added dropwise 0.53 g of sodium ethoxide in 4 ml of ethanol. The reaction mixture was heated for 3 h at 20–25°C. The resulting precipitate was filtered off and washed with water. Yield 2.2 g (77%), mp 143–145°C (ethanol). IR spectrum, ν, cm^{-1}: 1554 (C=O), 1659 (C=O), 1691 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.30 t (3H, CH_3, $^3J_{HH}$ 7.0 Hz), 3.24 s (3H, NCH_3), 3.68 s (3H, NCH_3), 4.23 d. d (2H, CH_2, $^3J_{HH}$ 7.0 Hz), 4.73 d (1H, CH, $^3J_{HH}$ 17.5 Hz), 5.19 d (1H, CH, $^3J_{HH}$ 10.5 Hz), 5.36 br.s (2H, CH_2), 6.11 m (1H, CH), 7.28 s (1H, CH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 160.23 (OC=O), 158.22 (2-C=O), 152.09 (4-C=O), 142.46 (C^8), 135.80 ($\underline{C}H=CH_2$), 121.37 (C^6), 115.79 ($CH=\underline{C}H_2$), 114.64 (C^5), 101.21 (C^9), 60.68 (OCH_2), 48.43 (NCH_2), 32.33 (NCH_3), 28.45 (NCH_3), 14.55 (CH_3). Found, %: C 57.62; H 5.80; N 14.46. $C_{14}H_{17}N_3O_4$. Calculated, %: C 57.72; H 5.88; N 14.42.

1,3-Dimethyl-2,4-dioxo-2,3,4,7-tetrahydro-7-(2-propenyl)-1*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylic acid (III). To a suspension of 5 g of ethyl ester **II** in 50 ml of aqueous ethanol (1:1) was added 0.9 g of sodium hydroxide in 5 ml of water. The mixture was heated for 2 h at 60°C, cooled and added 3 ml of glacial acetic acid. The precipitate was filtered off, washed with water and acetone. Yield 3.2 g (71%), mp 202–204°C (ethanol–DMF). IR spectrum, ν, cm^{-1}: 1550 (C=O), 1648 (C=O), 1693 (C=O), 3443 (OH). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.23 s (3H, NCH_3), 3.67 s (3H, NCH_3), 4.68 d (1H, CH, $^3J_{HH}$ 17.2 Hz), 5.16 d (1H, CH, $^3J_{HH}$ 10.8 Hz), 5.41 br.s (2H, CH_2), 6.09 m (1H, CH), 7.21 s (1H, CH), 12.74 br.s (1H, OH). Found, %: C 55.05; H 5.07; N 15.87. $C_{12}H_{13}N_3O_4$. Calculated, %: C 54.75; H 4.98; N 15.96.

8,9-Dihydro-1,3-dimethyl-8-(hydroxymethyl)-2*H*-pyrimido[5',4':4,5]pyrrolo[2,1-*c*][1,4]oxazino-2,4,6-(1*H*,3*H*)-trione (V). To a suspension of 5 g of acid **III** in 20 ml of water was added 0.76 g of sodium hydroxide in 5 ml of water. To this solution were added 5 ml of 50% hydrogen peroxide and 5 ml of acetonitrile. The reaction mixture was kept for 12 h at 20–25°C. The resulting precipitate was filtered off and washed with water. Yield 2.9 g (55%), mp 257–259°C (acetonitrile). IR spectrum, ν, cm^{-1}: 1559 (C=O), 1656 (C=O), 1697 (C=O), 3404 (OH). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.25 s (3H, NCH_3), 3.71 m (5H, NCH_3, CH_2), 4.41 d. d (1H, NCH_2, $^3J_{HH}$ 10.0, $^3J_{HH}$ 13.0 Hz), 4.71 m (1H, CH), 4.83 d. d (1H, NCH_2, $^3J_{HH}$ 13.0, $^3J_{HH}$ 3.0 Hz), 5.29 t (1H, OH, $^3J_{HH}$ 6.0 Hz,), 7.28 s (1H, CH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 158.62 (6-C=O), 158.27 (2-C=O), 151.69 (4-C=O), 139.61(C^{10a}), 117.80 (C^{5a}), 113.15 (C^5), 102.40 (C^{4a}), 77.85 (C^8), 60.89 (C^9), 44.98 (CH_2OH), 32.13 (NCH_3), 28.49 (NCH_3). Found, %: C 51.52; H 4.73; N 15.10. $C_{12}H_{13}N_3O_5$. Calculated, %: C 51.61; H 4.69; N 15.05.

7-(2,3-Dihydroxypropyl-1,3-dimethyl-2,4-dioxo-2,3,4,7-tetrahydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylic acid (VI). To a suspension of 1 g of compound **V** in 10 ml of aqueous ethanol (1:1) was added 0.14 g of sodium hydroxide in 5 ml of water. The mixture was heated for 1 h at 60°C, cooled, and 1 ml glacial acetic acid was added. The precipitate was filtered off and washed with water. Yield 0.65 g (61%), mp 171–173°C (DMF). IR spectrum, ν, cm^{-1}: 1554 (C=O), 1652 (C=O), 1687 (C=O), 3364 (OH). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.22 s (3H, NCH_3), 3.33 m (2H, CH_2), 3.62 br.s (1H, CH), 3.76 s (3H, NCH_3), 4.62 m (1H, NCH_2), 4.75 br.s (1H, OH), 4.87 m (1H, NCH_2), 5.04 br.s (1H, OH), 7.17 s (1H, CH), 12.57 br.s (1H, OH). Found, %: C 48.52; H 5.12; N 14.16. $C_{12}H_{15}N_3O_6$. Found, %: C 48.49; H 5.09; N 14.14.

The ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury-400 (400 MHz) (**III**, **VI**) and Bruker Avance 500 spectrometers (500 and 125 MHz, respectively) (**II**, **V**) in DMSO-d_6 relative to internal TMS. The IR spectra were recorded on a Bruker Vertex 70 FTIR instrument from KBr pellets.

REFERENCES

1. Payne, G.B., *Tetrahedron*, 1962, vol. 18, no. 6, p. 763; *Fieser and Fieser's Reagents for Organic Synthesis*, Moscow: Mir, 1970, p. 74; Yazaki, R., Nitabaru, T., Kumagai, N., and Shibasaki, M., *J. Am. Chem. Soc*., 2008, vol. 130, no. 44, p. 14477.

2. Senda, S. and Hirota, K., *Chem. Pharm. Bull*., 1974, vol. 22, p. 2921; Smolii, O.B., Muzychka, L.V., and Verves, E.V., *Khim. Geterotsikl. Soedin.*, 2009, vol. 45, no. 10, p. 1594.