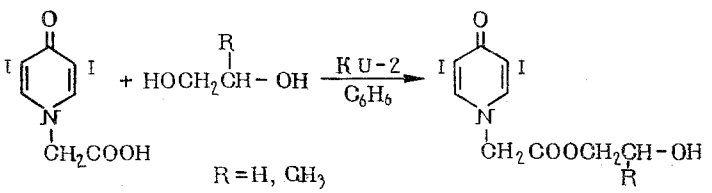
SYNTHESIS OF HYDROXYALKYL ESTERS OF PELVIRONIC ACID

K. S. Shanazarov, M. N. Andreeva,
N. K. Sviridov, I. S. Kas'yanov,
and V. N. Kostin

UDC 615.46:616-073.755.4].012.1

Esters of 3,5-diiodo-4-pyridone-N-acetic or pelvironic acid are of interest as x-ray contrast agents. Thus, n-propyl esters of this acid (propyliodone, Dionosil, Propylix) have found wide application in bronchography [1]. A preparation of Broncho-Abrodil [2] based of the β-hydroxypropyl ester of pelvironic acid has been proposed. It is distinguished by its ability to increase the viscosity with the rise in temperature and by its excellent overall and local tolerances.

Earlier [3, 4] we developed an effective method for the preparation of alkyl-3,5-diiodo-4-pyridone-N-acetates by esterification of pelvironic acid with the corresponding alcohols in the presence of cation-exchange resin KU-2 as catalyst. It appeared promising to use this method for the synthesis of hydroxyalkyl esters. This article deals with the esterification of pelvironic acid by the use of ethylene glycol and 1,2-propylene glycol in the presence of a cation-exchange resin as the catalyst:



It was found that under these conditions the reaction between pelvironic acid and glycols gave a good yield (82-85%) of hydroxy esters of a purity higher than that obtained in the presence of sulfuric acid as the catalyst [5]. It will be noted, however, that the separation of reaction products is in the case of hydroxyalkyl esters more involved than in the case of alkyl esters [4]. The results of the chemo-pharmacological studies will be published at a later date.

EXPERIMENTAL

The starting material 3,5-diiodo-4-pyridone-N-acetic acid was prepared by the reaction between 3,5-diiodo-4-pyridone and monochloroacetic acid according to [6], mp 242-243° (literature data, mp 24° [6], 241-243° [17]). Cation-exchange resin KU-2 had SOE 4.65 mg-eq/g, moisture content 0.5.

β-Hydroxyethyl Ester of 3,5-Diiodo-4-pyridone-N-acetic Acid. A mixture of 30 g of pelvironic acid, 60 ml of ethylene glycol (mp 196-198°, n_D^{20} 1.4312), 150 ml of benzene, and 5 g of cation-exchange resin was refluxed with vigorous stirring for two hours (until the accumulation of water in the water trap ceased). A partial precipitation was observed during the reaction process. After cooling the reaction mixture, 200 ml of acetone was added to dissolve the partially precipitated monoglycol ester. The cation-exchange resin KU-2 was filtered off and, after washing of the filter with acetone (twice, 40 ml each time), it was used in subsequent experiments. The solvent and the major portion of ethylene glycol were removed from the filtrate under reduced pressure in vacuo. Recrystallization of the residue yielded 29.4 g (84.8%) of white crystals of a mp 190.5-191° (literature data [5], mp 186-189°).

β-Hydroxypropyl Ester of 3,5-Diiodo-1-pyridone-N-acetic Acid. A mixture of 50 g of pelvironic acid, 150 g of 1,2-propanediol (bp 95°/20 mm, n_D^{20} 1.4321), 150 ml of benzene, and 7 g of cation-exchange resin KU-2 was stirred at 80-82° for five hours (until the accumulation of water in the water trap ceased). After removing the catalyst, benzene was removed by distillation from the filtrate and 600 ml of cold water was

Moscow Scientific Research X-Ray-Radiological Institute, Ministry of Public Health, Russian Soviet Federated Socialist Republic. Translated from Khimiko-Farmatsevticheskii Zhurnal, No. 4, pp. 21-22, April, 1969. Original article submitted August 5, 1968.

added to the residue. The white crystals were filtered off, washed with water and recrystallized from ethyl alcohol, yielding 48 g (82.4%) of β-hydroxypropyl ester of pelvironic acid, mp 170-172° (literature data [5], mp 169-172°).

LITERATURE CITED

1. H. Bojarska-Dahlig, Przem. Chem., 9, 34 (1953); 10, 266 (1954).
2. A. Distelmajer, C. Dloxhuber, H. Gremmel, et. al., Fortschr. Roentgenstr., 95, 155 (1961).
3. L. S. Rosenshtraukh, V. N. Kostin, K. S. Shanazarov, et. al., Author's Certificate No. 170985, Byull. Izobret, No. 10, 31 (1965).
4. K. S. Shanazarov, L. S. Rosenshtraukh, N. K. Sviridov, et. al., Khim.-Farmats. Zh., No. 4, 40 (1968).
5. English Patent No. 836960 (1960).
6. M. Dohrn and P. Diedrich, Justus Liebigs Ann. Chem. 494, 284 (1932).
7. H. Bojarska-Dahlig, Roczn. Chem., 29, 119 (1955).