SYNTHESIS OF ESTERS OF 5-OXO-3-OXAPENTANECARBOXYLIC ACIDS AND THEIR CYCLIZATION TO GIVE HOMOLOGS OF DIOXANONE AND MORPHOLINONE

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By hydrogenating methyl esters of 4-furyl-3-oxapropanecarboxylic acids on Pt-C we have obtained the corresponding esters of 5-oxo-3-oxapentanecarboxylic acids and have converted these under the conditions of reductive amination into the corresponding homologs of morpholin-3-one and by reduction in an alkaline medium into homologs of 1,4-dioxan-2-one.

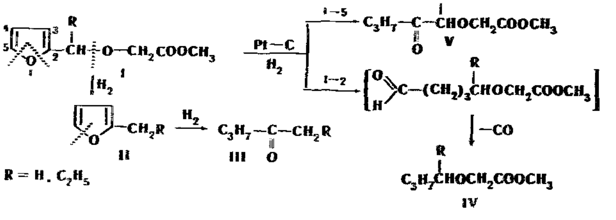
The vapor-phase hydrogenation of furan compounds containing various functional groups (C=O, OH, NH_2, COOH, COOR) in the side chain enables various compounds of the aliphatic, carbocyclic, and heterocyclic series to be obtained, many of which are difficult to prepare by other methods. Thus, for example, the hydrogenation of the monofuryl ethers of 1,2-glycols and their acetates has given homologs of 1,4-dioxene [1] and 3-oxa-1,5-ketoalcohols [2] which are otherwise obtainable only with difficulty.

In the present work we have studied the hydrogenation of methyl esters of 4-furyl-3-oxapropanecarboxylic acids on Pt-C with the aim of obtaining the corresponding esters of 5-oxo-3-oxapentanecarboxylic acids and the synethesis from them of homologs of dioxanone and morpholinone.

We have shown previously that esters of β-furylacrylic and β-furylpropionic acids are readily converted on hydrogenation over Pt-C by the flow method into esters of γ-oxo-enanthic acids from which the corresponding pyrrolidone homologs have been obtained by reductive amination [4].

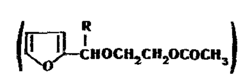
The initial esters of 4-furyl-3-oxapropanecarboxylic acids (I) were obtained by the reaction of alkoxides of furyl carbinols with methyl chloroacetate in yields of 50–60%. The esters synthesized were hydrogenated in a flow system over Pt-C at 180–190° C and normal pressure.

The reactions taking place can be represented by the following scheme:



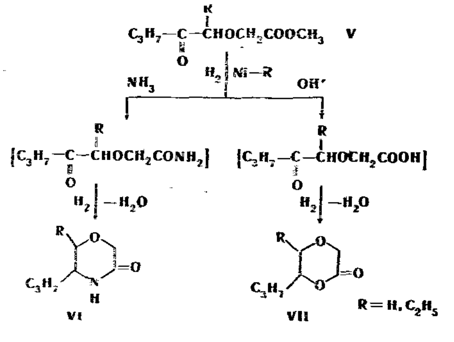
As was to be expected, hydrogenolysis of the furan ring at the 1,5 C—O bond led to the formation of methyl esters of the 5-oxo-3-oxaheptanecarboxylic acids (V, 35–42%) and at the 1,2 C—O bond to the formation of methyl esters of 3-oxahexanecarboxylic acids (IV, 10–11%). A side reaction taking place under these conditions is the cleavage of the ether linkage in the side chain leading to the formation of α-alkylfurans (II, 7–8%) and the products of their hydrogenolysis, the aliphatic ketones (III, 28–36%).

In this case, a marked influence of the alkoxycarbonyl group on the degree of hydrogenolysis of the side-chain ether bond (35%) is observed. The presence of an alkyl radical adjacent to the ether bond in the side chain increases the hydrogenolysis of the latter to 44%. In contrast to this, in the hydrogenation under analogous conditions of the acetates of the furan ether-alcohol [2],



the acetate group and the presence of an alkyl radical have no appreciable influence on the hydrogenolysis of the side-chain ether bond (12–15%). This is obviously connected with the fact that in the esters of the 4-furyl-3-oxa-propanecarboxylic acids the carbonyl group is conjugated with the free electrons of the ether oxygen, while such conjugation cannot exist in the acetates of the furan ether-alcohols.

Under the conditions of reductive amination on Raney Ni, the methyl esters of the 5-oxo-3-oxaheptanecarboxylic acids (V) were converted into the corresponding homologs of morpholin-3-one (VI, 42–50%), and by hydrogenation on a Raney Ni-Al catalyst in an alkaline medium they were converted into the corresponding homologs of 1,4-dioxanone (VII, 65–68%).



EXPERIMENTAL

Methyl 4-furyl-3-oxapropanecarboxylate. With stirring and heating to 100° C, 25 g (1.08 mole) of metallic sodium was gradually added to 250 ml of furfuryl alcohol in 250 ml of absolute toluene. To the alkoxide so obtained was added 120 g (1.1 mole) of methyl chloroacetate in 150 ml of absolute toluene. The reaction mixture was stirred at 50° C for 2 hr, and then 500 ml of aqueous sodium carbonate solution was added and the toluene layer was separated off. The aqueous layer was extracted with ether and the ethereal extracts were combined with the toluene layer. The ether and toluene were driven off and the residue was distilled. Yield 60%. Bp 78°–79° C (2 mm), n_D^{20} 1.4720, d_4^{20} 1.1710. Found, %: C 56.51, 56.57; H 5.86, 5.86, MR_D 40.69. Calculated for $C_8H_{10}O_4$, %: C 56.46; H 5.92; MR_D 40.95.

Methyl 4-ethyl-4-furyl-3-oxapropanecarboxylate was obtained similarly from ethyl furyl carbinol. Yield 48%. Bp 87°–88° C (2 mm), n_D^{20} 1.4670, d_4^{20} 1.0972. Found, %: C 60.37, 60.43; H 6.90, 6.92; MR_D 50.12. Calculated for $C_{10}H_{14}O_4$, %: C 60.59; H 7.11; MR_D 50.18.

The hydrogenation of the methyl esters of the 4-furyl-3-oxapropanecarboxylic acids was carried out in a continuous system on platinized carbon (5% Pt) at 180°–190° C and atmospheric pressure. The starting material was fed into the reaction tube at a space velocity of 0.1 hr^{-1}. The catalyzates were distilled through an efficient column and the substances isolated were identified by determining their physical constants, and by their elementary, spectral, and chromatographic analyses. A UR-10 double-beam spectrograph and LKhM-5 chromatograph with a thermal conductivity detector [column $l = 2$ m, dia. = 6 mm, poly(ethylene glycol succinate) (20%) on Chromosorb W with helium as the carrier gas] were used.

In the hydrogenation of methyl 4-furyl-3-oxapropanecarboxylate, the products were sylvane (7%), 2-pentanone (28%), methyl 3-oxahexanecarboxylate (11%)—bp 44°–47° C (3 mm), n_D^{20} 1.4125 [literature data [5]: bp 180°–180.5° C (766 mm), d_4^{15} 0.9675]—and methyl 5-oxo-3-oxapeptanecarboxylate (42%)—bp 100°–102° C (3 mm), n_D^{20} 1.4425, d_4^{20} 1.0742. Found, %: C 54.90, 54.85; H 8.20, 8.25; MR_D 42.94. Calculated for $C_8H_{14}O_4$, %: C 55.15; H 8.10: MR_D 42.45. The IR spectrum contained a strong absorption band in the 1740 cm^{-1} region (liquid film). **2,4-Dinitrophenylhydrazone**—mp 115°–116° C (from methanol). Found, %: N 15.94, 16.07. Calculated for $C_{14}H_{18}O_7N_4$, %: N 15.81.

Hydrogenation of methyl 4-ethyl-4-furyl-3-oxapropanecarboxylate gave α-propylfuran (8%), 4-heptanone (36%), methyl 4-ethyl-3-oxahexanecarboxylate (10%)—bp 60°–62° C (4 mm), n_D^{20} 1.4270—and methyl 4-ethyl-5-oxo-3-oxaheptanecarboxylate (35%)—bp 92°–93° C (2 mm), n_D^{20} 1.4462, d_4^{20} 1.0370. Found, %: C 59.06, 58.98; H 9.10, 9.12; MR_D 52.02. Calculated for $C_{10}H_{18}O_4$, %: C 59.38; H 8.9; MR_D 51.70. **2,4-Dinitrophenylhydrazone**—mp 84°–85° C (from methanol). Found, %: N 14.98, 15.06. Calculated for $C_{16}H_{22}O_7N_4$, %: N 14.65.

Hydrolysis of the methyl esters of 3-oxahexanecarboxylic acids. A mixture of 10 g of the appropriate ester, 5 g of KOH, and 40 ml of water was boiled for 4 hr. The insoluble matter was separated off and the aqueous layer was made weakly acid with dilute (1:2) hydrochloric acid. The reaction product was extracted with ether and distilled in vacuum.

3-Oxahexanecarboxylic acid —bp 108° C (5 mm), n_D^{20} 1.4270, d_4^{20} 1.0221. MR_D 33.19. Calculated for $C_6H_{12}O_3$: 33.09. Literature data [6]: bp 113°–114° C (9–10 mm), n_D^{20} 1.4263, d_4^{20} 1.0213.

4-Ethyl-3-oxahexanecarboxylic acid—bp 117° C (5 mm), n_D^{20} 1.4360, d_4^{20} 0.9920. MR_D 42.22. Calculated for $C_8H_{16}O_3$: 42.32.

CONVERSION OF THE METHYL ESTERS OF THE 5-OXO-3-OXAHEPTANECARBOXYLIC ACIDS INTO THE CORRESPONDING HOMOLOGS OF MORPHOLIN-3-ONE AND DIOXAN-2-ONE.

1. An autoclave was charged with 0.08 mole of the ester of a 5-oxo-3-oxa-heptanecarboxylic acid, 60 ml of methanol saturated with ammonia at 0° C, and 3 g of Raney Ni-Al catalyst and was heated at 100° C for 10 hr at an initial pressure of hydrogen of 50 atm.

5-Propylmorpholin-3-one—yield 50%, bp 115°–119° C (5 mm), mp 74°–75° C (from petroleum ether). Found, %: N 10.17, 10.28. Calculated for $C_7H_{13}O_2N$, %: N 9.78. The IR spectrum had strong absorption bands in the 1640, 3440, and 3195 cm^{-1} regions (solid state, 0.7 mg/200 mg of KBr).

6-Ethyl-5-propylmorpholin-3-one—yield 42%, bp 126°–130° C (5 mm), mp 59°–60° C (from petroleum ether). Found, %: N 8.70, 8.74. Calculated for $C_9H_{17}O_2N$, %: N 8.18.

2. An autoclave was charged with 0.08 mole of an ester of a 5-oxo-3-oxaheptanecarboxylic acid, 0.15 mole of KOH, 60 ml of water, and 3 g of Raney Ni-Al catalyst and was heated at 100° C for 2 hr at an initial pressure of hydrogen of 50 atm. After the separation of the catalyst, the catalyzate was made weakly acid with dilute hydrochloric acid (1:1) and was extracted with ether. After the ether had been driven off the reaction products were distilled in vacuum.

6-Propyl-1,4-dioxan-2-one—yield 68%. Bp 105°–106° C (5 mm) n_D^{20} 1.4325, d_4^{20} 1.0352. Found, %: C 57.98, 57.90; H 8.22, 8.31; MR_D 36.15. Calculated for $C_7H_{12}O_3$, %: C 58.31; H 8.39; MR_D 35.62. The IR spectrum had a strong absorption band in the 1750 cm^{-1} region (liquid film), which is characteristic for the C=O vibrations of six-membered lactones.

5-Ethyl-6-propyl-1,4-dioxan-2-one—yield 65%, bp 111°–112° C (5 mm), n_D^{20} 1.4490, d_4^{20} 1.0312. Found, %; C 62.46, 62.61; H 9.40, 9.40 MR_D 44.79. Calculated for $C_9H_{16}O_3$, %: C 62.76; H 9.36; MR_D 44.86.

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