SYNTHESIS AND TRANSFORMATIONS OF 4-ACRYLAMIDO-4-METHYLTETRAHYDROPYRAN

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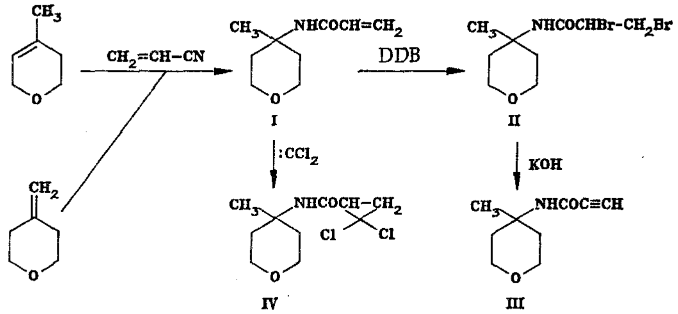
4-Acrylamido-4-methyltetrahydropyran was obtained via the Ritter reaction on the basis of cyclic unsaturated ethers and acrylonitrile. This amide is not hydrolyzed in alkaline media but does add dichlorocarbene and bromine to the double bond. Dehydrobromination of the dibromo derivative leads to the corresponding amide with a triple bond.

For completely understandable reasons, the relative reactivity of the double bond in 5,6-dihydro-2H-pyrans is significantly lower than in the isomeric 2,3-dihydro-4H-pyrans, which are essentially vinyl ethers. The synthetic possibilities of the former are therefore not so diverse. However, the accessibility of 5,6-dihydropyrans constitutes a stimulus for the study of their chemical properties. In a continuation of our previous research [1], we accomplished the synthesis of 4-acrylamido-4-methyltetrahydropyran (I) and studied some of its transformations, which are indicated in the scheme



Compound I was obtained from the industrial-grade pyran fraction, which contains 85% 4-methyl-5,6-dihydro-2H-pyran and 15% 4-methylenetetrahydropyran, and acrylonitrile via the Ritter reaction. It is known [2] that this reaction proceeds via a carbonium ion mechanism; therefore, the same tertiary carbonium cation should be formed from both ethers. As a result, amide I in the form of a single product can be obtained from the mixture of olefins.

The alkaline hydrolysis of amides is a convenient method for the preparation of the corresponding amines. However, in this case, even refluxing of I for 40 h with an eightfold excess of 20% KOH did not lead to the expected 4-amino-4-methyltetrahydropyran, since the starting amide remained virtually unchanged. In all likelihood, the lack of success is explained by steric hindrance. At the very least, a similar phenomenon was previously observed in an attempt to hydrolyze sterically hindered N-substituted amides [3].

On the other hand, the double bond in amide I proved to be completely reactive. We were convinced of this by using a "soft" halogenating agent such as dioxane dibromide (DDB). The dibromo derivative II formed as a result of this reaction, upon refluxing with an alcohol solution of KOH, gives amide III with a triple bond in good yield.

Dichlorocarbene, generated *in situ* from chloroform under the influence of tert-BuOK without special complications, adds to the double bond of I to give the corresponding adduct IV. The structures of the synthesized compounds were proved by the results of elementary analysis and by spectral methods.

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EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Tesla BS-487 C spectrometer (80 MHz) with hexamethyldisiloxane (HMDS) as the standard.

4-Acrylamido-4-methyltetrahydropyran (I). A 98-g (1.0 mole) sample of 95% H_2SO_4 was added with stirring dropwise at 0-3°C to a solution of 49 g (0.5 mole) of the pyran fraction and 53 g (1.0 mole) of acrylonitrile, after which the reaction mixture was stirred at 10-20°C for 3 h and then poured over 200 g of crushed ice. The resulting solution was neutralized with 40% KOH and extracted with $CHCl_3$. The extract was washed with water and dried over $MgSO_4$. The extract was then distilled to remove the solvent, and the residue was recrystallized from hexane to give 54.6 g (65%) of amide I with mp 69-70°C. PMR spectrum ($CDCl_3$): 6.8 (1H, s, NH), 6.05-6.2 (1H, q, $CH=$), 5.4-5.6 (2H, q, $CH_2=$), 3.47-3.75 (4H, m, CH_2-O-CH_2), 1.53-2.25 (4H, m, ring CH_2), and 1.31 ppm (3H, s, CH_3). IR spectrum: 3290 (NH), 1665, 1565 (HNCO), 1635 cm^{-1} (C=C).

4-(2,3-Dibromopropanoyl)amino-4-methyltetrahydropyran (II). A 23-g (0.14 mole) sample of bromine was added with vigorous stirring to 60 g (0.68 mole) of dioxane, which had been distilled over Na, after which 16.9 g (0.1 mole) of amide I was added at 20°C to the resulting suspension of DDB in dioxane, and the reaction mixture was allowed to stand for 24 h. The solvent was removed by distillation, and the residue was dissolved in alcohol and precipitated by means of a large amount of water. Recrystallization from hexane gave 27.6 g (84%) of dibromide II with mp 159-160°C. PMR spectrum ($CDCl_3$): 6.1 (1H, s, NH), 4.3-4.6 (1H, q, CHBr), 3.55-3.88 (4H, m, CH_2Br, $O-CH_2$), 1.6-1.85 (4H, m, ring CH_2), and 1.4 ppm (3H, s, CH_3). Found, %: C 32.8, H 4.6, Br 48.8. $C_9H_{15}BrNO_2$. Calculated, %: C 32.8, H 4.5, Br 48.9.

4-Methyl-4-propiolylamidotetrahydropyran (III). A 3.5-g (0.01 mole) sample of amide I was refluxed in 15 ml of 20% alcoholic KOH solution, after which the alcohol was removed, and the resulting precipitate was washed with ether. The ether extracts were dried over $MgSO_4$, the solvent was removed by distillation, and the residue was recrystallized from hexane to give 1.3 g (77%) of III with mp 74-75°C. PMR spectrum ($CDCl_3$): 6.25 (1H, s, NH), 3.65 (4H, m, CH_2-O-CH_2), 2.5 (1H, s, $CH=$), 1.5-2.1 (4H, m, ring CH_2), and 1.34 ppm (3H, s, CH_3). Found, %: C 70.1, H 7.9, N 8.2. $C_9H_{13}NO_2$. Calculated, %: C 70.2, H 8.0, N 8.1.

4-(2,2-Dichlorocyclopropylcarbonyl)amino-4-methyltetrahydropyran (IV). A 20-ml (0.25-mole) sample of tert-BuOH was placed in a three-neck flask equipped with a reflux condenser with a calcium chloride tube, after which 9 g (0.25 mole) of potassium was added carefully in portions, and the contents of the flask were heated until the metal dissolved completely. An 8.4-g (0.05 mole) sample of amide I was added to the resulting tert-BuOK, and 60 g (0.5 mole) of dry $CHCl_3$ was added dropwise at 10-20°C to this mixture in the course of 3 h. The reaction mixture was then stirred for another hour and allowed to stand at room temperature for 12 h. After this, a twofold volume of H_2O was added, and the organic phase was separated, washed to neutrality, and dried. The $CHCl_3$ was removed by distillation, and the residue was fractionated in vacuo to give 9.8 g (70%) of IV with bp 155°C (4 gPa). PMR spectrum ($CDCl_3$): 6.9 (1H, s, NH), 3.6 (5H, m, CH_2-O-CH_2, $CH-C-CCl_2$), 1.6-2.2 (4H, m, ring CH_2), and 1.15 ppm (2H, m, $C-CH_2-CCl_2$). Found, %: C 47.5, H 5.9, Cl 27.8. $C_{10}H_{15}Cl_2NO_2$. Calculated, %: C 47.6, H 5.9, Cl 27.9.

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