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NITRATION OF 4-METHYL-5,6-DIHYDRO-2H-PYRAN AND SOME ASPECTS OF THE PREPARATION AND ISOMERIZATION OF NITRODIHYDROPYRANS

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UDC 547.812:542.958.1

The reaction of 4-methyl-5,6-dihydro-2H-pyran with acetyl nitrate to give additive and substitutive nitration products has been examined. It is shown that the addition product, 4-acetoxy-4-methyl-3-nitro-tetrahydropyran, is deacylated on treatment with bases to give an α,β-unsaturated nitro-compound which isomerizes under the reaction conditions to a β,γ-unsaturated nitro-compound. 4-Acetoxy-4-nitromethyltetrahydropyran behaves similarly.

It has previously been shown that the addition of acetyl nitrate to 4-methylenetetrahydropyran can be used to obtain nitro-derivatives of dihydro- and tetrahydropyrans, which are of interest as convenient intermediates for the synthesis of functional derivatives of di- and tetrahydropyran [1]. Continuing these studies, we have examined the addition of acetyl nitrate to 4-methyl-5,6-dihydro-2H-pyran and the chemical properties of the reaction products.

The reaction of acetyl nitrate with 4-methyl-5,6-dihydro-2H-pyran proceeds as readily as with 4-methylenetetrahydropyran, to give a mixture of the adduct (I) and the substitution products (II-IV) in a ratio of 7:3. Variations in the temperature of the reaction did not affect this ratio at all, probably in consequence of the independent reaction pathways. In fact, separate experiments showed that the nitroacetate (I) showed no tendency to lose acetic acid under the reaction conditions. Furthermore, it did not undergo deacylation in the presence of sulfuric acid in acetic anhydride, and in the presence of hydrochloric acid only hydrolysis occurred to give 4-hydroxy-3-nitrotetrahydropyran (V). It must therefore be assumed that the unsaturated nitro-compounds (II-IV) are formed in a different way. In all likelihood, nitroacylation leads to the tetrahydropyranilium carbocation as an intermediate, which in addition to reacting with the nucleophile, also undergoes deprotonation.

According to PMR and GC, the major component of the deprotonation products (II-IV) is 4-methyl-3-nitro-3,6-dihydro-2H-pyran (II). In other words, deprotonation of the intermediate tetrahydropyranilium carbocation gives, as would be expected, the nonconjugated

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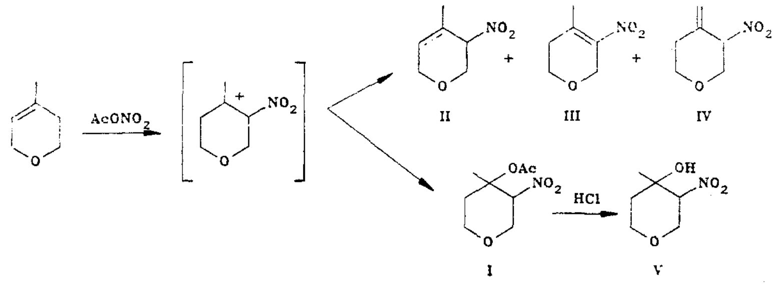
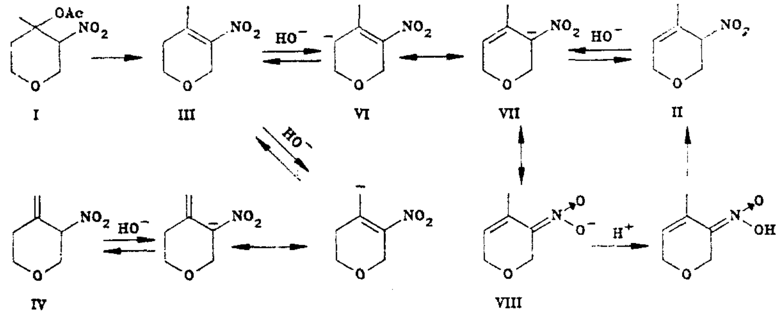


product. In order to obtain the conjugated isomer, 4-methyl-3-nitro-5,6-dihydro-2H-pyran (III), either the mixture of isomers (II-IV) or the nitroacetate (I) was heated with bases. However, on treatment of the mixture (II-IV) with aqueous or alcoholic potassium hydroxide, the amount of the conjugated isomer (III) did not increase. On the contrary, according to GC compounds (III) and (IV) were absent from the reaction product. On the basis of these findings, it may be assumed that they isomerize to (II). It was in fact shown that under the above conditions the nitro-compound (III) is converted into the β,γ-unsaturated isomer (II). It is also noteworthy that according to GC the proportions of the nitro-compounds (II-IV) do not change on treatment with sulfuric acid at 10°C, but at a higher temperature complete resinfication occurs.

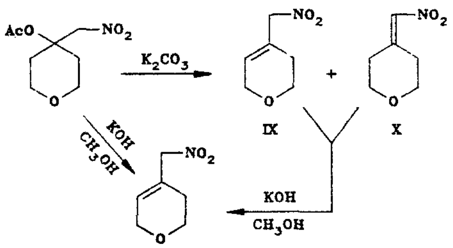
The nitroacetate (I), on heating with potassium carbonate at 90-100°C with simultaneous removal of the reaction products, gives the isomer (III) in 80% yield. On heating the nitroacetate (I) with potassium carbonate without removing organic reaction products or water, a mixture of isomers (II) and (III) is obtained. The elements of acetic acid are also removed on treatment with methanolic potassium hydroxide, to give a single isomer, namely 4-methyl-3-nitro-3,6-dihydro-2H-pyran (II).

These experimental findings show that under the influence of bases the nitroacetate (I) undergoes cleavage with the formation of the α,β-unsaturated nitro-compound (III), which isomerizes under the reaction conditions to the β,γ-unsaturated isomer (II).

These findings may be rationalized as follows. The intermediate allylic carbanion (VII) is for the most part converted into the anion of the unsaturated nitrolic acid (VIII), protonation of which affords the unconjugated nitro-compound (II), as follows:



In order to provide additional support for this hypothesis, we have also examined the behavior of nitro-compounds previously obtained by the addition of acetyl nitrate to 4-methylenetetrahydropyran [1]. It was found that the adduct from this fraction, 4-acetoxy-4-nitromethyltetrahydropyran, on treatment with methanolic potassium hydroxide also gives the β,γ-unsaturated nitro-compound (IX). With potassium carbonate, however, a mixture of (IX) and (X) is obtained. On heating this mixture with alcoholic alkali, (X) is completely isomerized to the nitro-compound (IX).



EXPERIMENTAL

PMR spectra were obtained on a Perkin-Elmer R-12B instrument (60 MHz) in CCl_4, internal standard HMDS. IR spectra were recorded on a UR-20. The purity of the compounds obtained was determined by GC on a Khrom-4 apparatus with a catharometer, on a column of length 2 m with 15% Apiezon L on Chromaton N-AW-HMDS, carrier gas (helium) flow rate 40-60 ml/min; temperature 160-180°C.

Reaction of 4-Methyl-5,6-dihydro-2H-pyran with Acetyl Nitrate. To 102 g (1.0 mole) of acetic anhydride was added dropwise at 20°C 11 g (0.12 mole) of 70% nitric acid. To the resulting acetyl nitrate was added 0°C 9.8 g (0.1 mole) of 4-methyl-5,6-dihydro-2H-pyran, and the mixture stirred without cooling for 1 h. After removal of the acetic anhydride and acetic acid, the residue was distilled in vacuo to give 3.7 g (26%) of a mixture of isomers (II) (81%) and (III), (IV) (19%), bp 80-90°C (3 mm), and 13.4 g (66%) of 4-acetoxy-4-methyl-3-nitrotetrahydropyran (I), bp 92-94°C (3 mm), mp 73°C (from ether). IR spectrum: 1370, 1555 (NO_2), 1740 cm^{-1} (CO). PMR spectrum: 1.7-1.93 (1H, m, OCH_2CH); 1.84 (3H, s, CH_3); 2.13 (3H, s, CH_3); 2.83 and 3.09 (1H, t, OCH_2CH); 3.6-2.82 (2H, m, OCH_3C); 4.03-4.22 (2H, m, OCH_2CNO_2); 4.56 ppm (1H, t, $CHNO_2$). Found, %: C 47.2, H 6.5, N 6.8. $C_8H_{13}NO_5$. Calculated, %: C 47.3, H 6.4, N 6.9.

4-Hydroxy-4-methyl-3-nitrotetrahydropyran (V). A mixture of 6.5 g (0.032 mole) of (I) and 40 ml of 15% HCl was stirred for 4 h at 40°C. The water was distilled off to give 4 g (83%) of (V), mp 76°C (from water). IR spectrum: 1380 and 1550 (NO_2), 3200-3500 cm^{-1} (OH). PMR spectrum (in water): 1.83 (3H, s, CH_3); 1.4-1.6 (2H, t, OCH_2CH_2); 3.3-3.6 (2H, m, OCH_2CH_2); 3.7-3.9 (2H, m, OCH_2CNO_2); 4.2-4.4 ppm (1H, m, $CHNO_2$). Found, %: C 45.0, H 6.9, N 8.5. $C_6H_{11}NO_4$. Calculated, %: C 44.7, H 6.8, N 8.7.

Reaction of the Mixture (II-IV) with Methanolic KOH. To 2.1 g (0.02 mole) of KOH in 30 ml of methanol was added at 20°C 2.9 g (0.02 mole) of a mixture of (II) (81%) with (III) and (IV) (19%), and the mixture stirred for 2 h at 45-50°C. The methanol was distilled off, and the residue acidified with hydrochloric acid and extracted with ether. The extract was dried over $MgSO_4$, the ether removed, and the residue distilled to give 2.3 g (80%) of (II), bp 84-85°C (3 mm); n_D^{20} 1.4940, d_4^{20} 1.1944. IR spectrum: 1355 and 1550 (NO_2), 1660 cm^{-1}, (C=C). PMR spectrum: 1.55-1.7 (3H, m, CH_3); 3.8-4.6 (5H, m, CH_2OCH_2, $CHNO_2$); 5.67-5.85 ppm (1H, m, CH=). Found, %: C 50.2, H 6.2, N 9.9. $C_6H_9NO_3$. Calculated, %: C 50.3, H 6.2, N 9.6.

4-Methyl-3-nitro-5,6-dihydro-2H-pyran (III). A mixture of 2 g (0.01 mole) of (I) and 2.8 g (0.02 mole) of potassium carbonate was heated at 100°C with simultaneous removal by distillation of the products to give 1.1 g (78%) of (III), bp 83-84°C (3 mm), n_D^{20} 1.5015, d_4^{20} 1.2083. IR spectrum: 1350 and 1550 (NO_2), 1640 cm^{-1} (C=C). PMR spectrum: 2.17 (3H, br. s., CH_3); 2.1-2.5 (2H, m, CH_2); 3.83 (2H, t, OCH_2CH_2); 4.23-4.5 ppm (2H, m, OCH_2C=). Found, %: C 50.5, H 6.0, N 9.6. $C_6H_9NO_3$. Calculated, %: C 50.3, H 6.2, N 9.6.

Reaction of 4-Acetyoxy-4-methyl-3-nitrotetrahydropyran (I) with Potassium Carbonate. A mixture of 2 g (0.01 mole) of (I) and 2.8 g (0.02 mole) of K_2CO_3 was heated at 100°C for 30 min, and distilled to give 0.9 g (63%) of a mixture of isomers (II) (90%) and (III) (10%), bp 80-85°C (3 mm), n_D^{20} 1.4910 (CG).

Reaction of 4-Acetoxy-4-methyl-3-nitrotetrahydropyran (I) with Methanolic Potassium Hydroxide. To 1.1 g (0.02 mole) of KOH in 30 ml of methanol was added at 20°C 2 g (0.01 mole) of (I), and the mixture stirred for 3 h at 50°C. The alcohol was distilled off, and the residue acidified with HCl and extracted with ether. The extract was dried over $MgSO_4$, the ether removed, and the residue distilled to give 1.1 g (78%) of (II), bp 85°C (3 mm), n_D^{20} 1.4930.

Isomerization of 4-Methyl-3-nitro-5,6-dihydro-2H-pyran (III). Similarly, from 0.6 g (0.01 mole) of KOH in 30 ml of methanol and 1.4 g (0.01 mole) of (III), there was obtained 1.1 g (80%) of (II), bp 86°C (3 mm), n_D^{20} 1.4940.

4-Nitromethyl-5,6-dihydro-2H-pyran (IX). Similarly, from 1.1 g (0.02 mole) of KOH in 30 ml of methanol and 2 g (0.01 mole) of 4-acetoxy-4-nitromethyltetrahydropyran, there was obtained 1.2 g (83%) of (IX), bp 86-88°C (3 mm), n_D^{20} 1.4910, d_4^{20} 1.1920. IR spectrum: 1350 and 1550 (NO_2), 1660 cm^{-1} (C=C). PMR spectrum: 2.0-2.3 (2H, m, CH_2); 3.7 (2H, t, OCH_2C); 4.0-4.2 (2H, m, OCH_2C); 4.82 (2H, s, CH_2NO_2); 5.85-6.05 ppm (1H, m, CH=). Found, %: C 50.5, H 6.5, N 9.5. $C_6H_9NO_3$. Calculated, %: C 50.3, H 6.2, N 9.6.

Reaction of a Mixture of (IX) and (X) with Methanolic Potassium Hydroxide. Similarly, from 1.1 g (0.02 mole) of KOH in 30 ml of methanol and 2.9 g (0.02 mole) of a mixture of (IX) and (X) (9:1), there was obtained 2.3 g (80%) of (IX), bp 86-87°C (3 mm), n_D^{20} 1.4910.

Reaction of 4-Acetoxy-4-nitromethyltetrahydropyran with Potassium Carbonate. A mixture of 2 g (0.01 mole) of 4-acetoxy-4-nitromethyltetrahydropyran and 2.8 g (0.02 mole) of K_2CO_3 was heated at 100°C with simultaneous removal of the reaction products, to give 1.1 g (78%) of a mixture of (IX) and (X) (9:1), bp 85-88°C (3 mm), n_D^{20} 1.4910. PMR spectrum: 1.9-2.35 (m, CH_2C); 3.6-3.9 (t, CH_2OC); 4.0-4.25 (m, $OCH_2C{=}$); 4.83 (s, CH_2NO_2); 5.85-6.1 (m, $CH{=}$); 6.9-7.0 ppm (${=}CHNO_2$).

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REACTIONS OF HETEROCYCLIC CATIONS WITH N-CONTAINING NUCLEOPHILES.

17.* SYNTHESIS OF PYRYLIUM SALTS WITH THREE-RING AZOLE SUBSTITUENTS†

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543.422

2,6-Diphenylpyrylium perchlorate was hetarylated with imidazo- and pyrrolo-[1,2-*a*]benzimidazoles, and deeply colored 4-azolylpyrylium perchlorates were obtained.

We have described a method for the introduction of monocyclic pyrazole substituents into the pyrylium ring and have found that imidazole, in view of its insufficient local π-surplus character, does not hetarylate pyrylium salts [1]. In the present research we investigated the possibility of the introduction into the pyrylium ring of three-ring azole substituents, viz., imidazo- and pyrrolo[1,2-*a*]benzimidazoles I and II, in which the external imidazole and pyrrole rings are π-surplus rings. The calculated and experimental data provide evidence for high nucleophilicity of the 3 position in imidazo[1,2-*a*]benzimidazoles I [3, 4]. Quantum-mechanical calculations of the electron-density distribution in pyrrolo[1,2-*a*]benzimidazole molecules II indicate the presence in them of two nucleophilic centers, viz., the $C_{(1)}$ and $C_{(3)}$ atoms [4, 5]. It was demonstrated experimentally that in these molecules the 1 position, which is adjacent to the bridge nitrogen atom, initially undergoes electrophilic attack; if the 1 position is occupied, the 3 position then undergoes attack [4, 5].

Refluxing 2,6-diphenylpyrylium perchlorate (III) with I and II in freshly distilled dimethylformamide (DMF) leads to dark-crimson and dark-violet 4-imidazo- and 4-pyrrolo[1,2-*a*]benzimidazolyl-2,6-diphenylpyrylium perchlorates IV and V. The addition of salt III to azoles I and II proceeds via the same mechanism as in the case of methylpyrazoles [1], viz., through a step involving the formation of a 4H-4-hetaryl-2,6-diphenylpyran, which is then converted to pyrylium salt IV or V by the action of starting perchlorate III. However, the liberated perchloric acid does not react with the solvent but rather with azoles I and II, converting them to salts. In these reactions, in contrast to the reactions with pyrrole, indole, methylpyrazoles, and pyrazolones [1], one must therefore introduce equimolar amounts

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*See [1] for communication 16.

†Communication 24 from the series "Research on imidazo[1,2-*a*]benzimidazole derivatives." See [2] for communication 23.

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