THERMAL DECOMPOSITION OF N-NITROSODESTHIOBIOTIN

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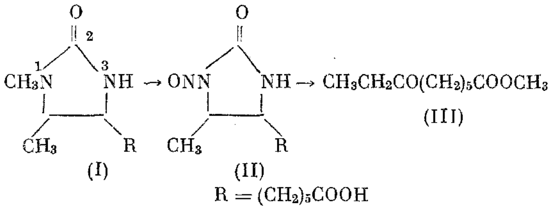
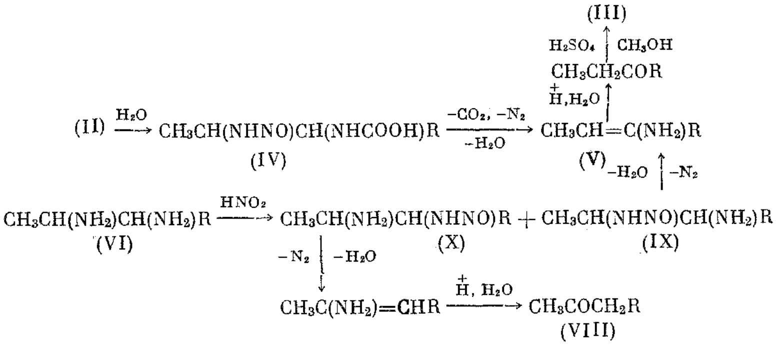
The treatment of desthiobiotin (I) in aqueous solution with excess HNO_2 gave us the mononitroso derivative, which, on the basis of steric hindrance [1] to electrophilic attack at the N^3 nitrogen atom, can be assigned the (II) structure. The obtained N-nitrosodesthiobiotin (II) proved to be an unstable compound even at 10-20°. At 100°, compound (II) undergoes decomposition with the liberation of N_2 and CO_2 and the formation of a tarry mass, the acid hydrolysis and esterification of which gave the 7-ketopelargonic acid ester (III)



The thermal decomposition of (II) probably includes the steps of hydrolytic cleavage of the ureide ring and decomposition of the intermediate nitrosamine (IV) to enamine (V). The acid hydrolysis and esterification of the latter complete the conversion of (II) to (III). The water needed to open the ureide ring can arise as the result of side processes



Evidence in support of the above-indicated scheme for the thermal decomposition of (II) is the conversion of 7,8-diaminopelargonic acid (VI) under the influence of HNO_2 to a mixture of the 7- and 8-ketopelargonic acids (VII) and (VIII), which apparently proceeds via the intermediate nitrosamines (IX) and (X). Compounds (III), (VII), and (VIII) were identified by IR and NMR spectroscopy.

EXPERIMENTAL METHOD

Preparation of N-Nitrosodesthiobiotin (II). A solution of 0.55 g of $NaNO_2$ in 2 ml of water was added in 30 min to a mixture of 0.21 g of (I) [2], 4 ml of water, and 0.8 g of conc. HCl at 0°; the mixture was stirred at 0° for 2.5 h, and the precipitate was filtered and washed with water. We obtained 0.1 g (42%) of (II), mp 75-76° (decomp.), R_f 0.67 (TLC, Silufol R, ethyl acetate, detection of the spots in UV light).

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Ultraviolet spectrum (taken on a Specord UV–VIS instrument in alcohol): λ_{max} 250 nm (ε 6350). Infrared spectrum (taken on a UR-20 instrument with KBr, ν, cm^{-1}): 1705 (COOH), 1740 ($O{=}N{-}\overset{|}{N}{-}\overset{|}{C}{=}O$). Found: C 49.31; H 6.93; N16.96%. $C_{10}H_{17}N_3O_4$. Calculated: C 49.30; H 6.99; N 17.20%.

Thermal Decomposition of (II). Compound (II) (3.5 g) was heated at 100° for 1.5 h and cooled to ~20°; 12 ml of dilute HCl solution (1 : 1) was added, and the mixture was refluxed for 10 h and extracted with ethyl acetate. After removal of the solvent the residue was kept with 0.5 ml of conc. H_2SO_4 in 25 ml of MeOH, after which the mixture was evaporated in vacuo, treated with excess aqueous Na_2CO_3 solution, and extracted with ethyl acetate; the extract was evaporated, and the residue was chromatographed on Al_2O_3 (III activity). Elution with n-heptane gave 0.34 g (18%) of (III), bp 97-98° (1 mm); n_D^{20} 1.4367; R_f 0.69 (Al_2O_3; III activity; 1 : 3 acetone–n-hexane; here and subsequently detection of the spots is by means of I_2 vapors). Infrared spectrum (here and subsequently a liquid film, ν, cm^{-1}): 1710 (C=O), 1735 ($COOCH_3$). NMR spectrum (here and subsequently taken on a DA-60-IL instrument in CCl_4 solution with HMDS, δ, ppm): 0.92 (CH_3CH_2, triplet), 1.40 ($-(CH_2)_3-$, multiplet), 2.25 ($3CH_2CO$, multiplet), 3.50 (CH_3O, singlet).

Nitrosation of (VI) Dihydrochloride. To a stirred solution of 3 g of the (VI) dihydrochloride [2] in 30 ml of water at 0-5°, a solution of 1.6 g of $NaNO_2$ in 10 ml of water was gradually added; the mixture was kept at 0-5° for 2 h, and extraction with ethyl acetate gave 0.28 g of a mixture of (VII) and (VIII), R_f 0.57 (Silufol R, ethyl acetate). Infrared spectrum (ν, cm^{-1}): 1710 (C=O). NMR spectrum (δ, ppm): 0.92 (CH_3CH_2, triplet), 1.35 (nonactivated CH_2 groups, multiplet), 2.00 (CH_3CO, singlet), 2.27 (CH_2CO groups, multiplet), 10.10 (COOH, singlet). Found: C 62.38; H 9.21%. $C_9H_{16}O_3$. Calculated: C 62.79; H 9.30%. The esterification of a mixture of (VII) and (VIII), as described above, gave a mixture of the corresponding methyl esters in 27% yield [when based on (VI)], bp 96-99° (1 mm); n_D^{21} 1.4382; R_f 0.69 (Al_2O_3, III activity, 1 : 3 acetone–n-hexane). Infrared spectrum (ν, cm^{-1}): 1710 (C=O), 1735 ($COOCH_3$). NMR spectrum (δ, ppm): 0.92 (CH_3CH_2, triplet), 1.40 (nonactivated CH_2 groups, multiplet), 2.13 (CH_3CO, singlet), 2.28 (CH_2CO groups, multiplet), 3.50 (CH_3O, singlet).

CONCLUSIONS

1. The thermal decomposition of N-nitrosodesthiobiotin and subsequent acid hydrolysis of the reaction products gives 7-ketopelargonic acid.

2. The reaction of 7,8-diaminopelargonic acid with HNO_2 leads to a mixture of the 7- and 8-ketopelargonic acids.

LITERATURE CITED

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2. R. Duschinsky and L. A. Dolan, J. Amer. Chem. Soc., **67**, 2079 (1945).