INDOLES

XL.* SYNTHESIS OF TRYPTOPHOLS AND HOMOTRYPTOPHOLS FROM CYCLIC SEMIACETALS AND ARYLHYDRAZINES

I. I. Grandberg and T. P. Moskvina

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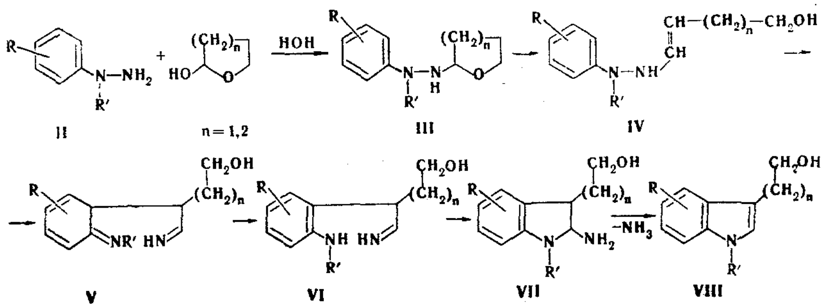
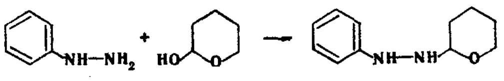
The reaction of arylhydrazines and cyclic semiacetals (α-hydroxytetrahydropyran and α-hydroxytetrahydrofuran) on heating leads, with the evolution of water and ammonia, respectively, to homotryptophols and tryptophols.

In the synthesis of homotryptophols and tryptophols, we have previously investigated cyclic vinyl ethers of the type of Δ^2-dihydropyran and Δ^2-dihydrofuran [2]. The latter, by adding arylhydrazine salts at the activated double bond, undergo opening of the oxygen-containing ring and are converted into hydrazinomethylene derivatives of aliphatic alcohols, which, in the manner of the Fischer reaction, form 3-(hydroxyalkyl)indoles.

We have found that cyclic semiacetals (α-hydroxytetrahydropyran and α-hydroxytetrahydrofuran) on being heated with free arylhydrazines first lose a molecule of water (at 80–100°C) and, at a higher temperature (about 200°C) also split off a molecule of ammonia, giving, respectively, homotryptophols and tryptophols.



In the first stage of the reaction, apparently, the formation of the α-hydrazino ether (III) takes place, and on further heating at a higher temperature, through β elimination, the opening of the tetrahydropyran ring takes place with the formation of the hydrazinomethylene (IV). This hydrazinomethylene, as the result of a sigmatropic (3,3) shift [3], is converted into the 1,5-dienic structure (V), which is stabilized by aromatization into the substituted aniline (VI). The latter undergoes intramolecular addition at the C=N bond, giving the aminoindoline (VII), which aromatizes by the ejection of ammonia to form the tryptophol system (VIII). In confirmation of some stages of the proposed scheme, we have succeeded in isolating an intermediate compound of type (III).



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[*] For Communication XXXIX, see [1].

K. A. Timiryazev Moscow Agricultural Academy. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 90–91, January, 1974. Original article submitted December 30, 1972.

The IR spectrum of substance (III) has no absorption band characteristic for the stretching vibrations of a hydroxy group or for a double C=N bond in the 1620-1640 cm^{-1} region that would be observed in the case of hydrazone. In the UV spectrum the absorption maxima in the 275 nm region and two inflections in the 245 and 300 nm regions likewise do not correspond to a hydrazone structure.

EXPERIMENTAL

Chromatography was performed on Al_2O_3 (activity grade V) in the benzene–isopropanol (9 : 1) system. The UV spectra were taken on a Hitachi EPS-3T instrument in ethanol and the IR spectra on a Jasco IRS instrument with a NaCl prism in chloroform solution or as liquid films.

α-Methyl-β-(tetrahydropyran-2-yl)phenylhydrazine. This was obtained by heating α-methylphenylhydrazine and α-hydroxytetrahydrofuran in benzene with the removal of water by distillation, followed by vacuum distillation. Yield 80%; bp 160-165°C at 1 mm. Found %: C 69.7; H 8.6. $C_{11}H_{16}N_2O$. Calculated %: C 69.9; H 8.7. R_f 0.67. UV spectrum: λ_{max} 245, 275, 300 nm; log ε 3.76, 4.23, 3.00. IR spectrum, cm^{-1}: 3400 (NH), 1590, 1500 (stretching vibrations of the phenyl nucleus).

Homotryptophol. A solution of 5.4 g (0.05 mole) of phenylhydrazine and 5.05 g (0.05 mole) of α-hydroxytetrahydropyran in 50 ml of benzene was boiled on the water bath in a flask with a Dean–Stark trap until the calculated amount of water had been evolved (0.8 ml). The benzene was evaporated off and the residue was slowly heated under a reduced pressure of 130 mm in a current of nitrogen to 230°C for 1 h, and was then distilled at a lower pressure. This gave 6 g of a substance in the form of an oil with bp 197-200°C (2 mm), yield 68%. R_f 0.62. UV spectrum: λ_{max} 224, 280 nm; log ε 4.46, 3.77. IR spectrum, cm^{-1}: 3600, 3480 (OH, NH), 1615, 1600, 1500 (stretching vibrations of the nucleus) [2]. Found %: C 75.2; H 7.5. $C_{11}H_{13}NO$. Calculated %: C 75.4; H 7.5.

7-Methylhomotryptophol. This was obtained similarly from o-tolylhydrazine. Yield 38%, bp 200-203°C (2 mm). Found %: C 76.4; H 7.9. $C_{12}H_{15}NO$. Calculated %: C 76.2; H 8.0. R_f 0.59. UV spectrum: λ_{max} 222, 280, 290 nm; log ε 4.39, 4.10, 4.01. IR spectrum, cm^{-1}: 3580, 3280 (OH, NH); 1620, 1590, 1485 (stretching vibrations of the nucleus) [2].

5-Methylhomotryptophol. This was obtained similarly from p-tolylhydrazine. Yield 48.5%, bp 205-215°C (2 mm), R_f 0.63. UV spectrum: λ_{max} 227, 287, 297 nm; log ε 4.21, 3.63, 3.56. IR spectrum, cm^{-1}: 3480, 3360 (OH, NH), 1590, 1515, 1480 (stretching vibrations of the nucleus) [2]. Found %: C 76.4; H 8.0. $C_{12}H_{15}NO$. Calculated %: C 76.2; H 8.0.

N-Methylhomotryptophol. This was obtained similarly from N-methylphenylhydrazine. Yield 60%, bp 175-178°C (1 mm), R_f 0.65. UV spectrum: λ_{max} 226, 290 nm; log ε 4.46, 3.69. IR spectrum, cm^{-1}: 3620 (OH), 1615, 1550, 1470 (stretching vibrations of the nucleus) [2]. Found %: C 75.7; H 8.1. $C_{12}H_{15}NO$. Calculated %: C 76.2; H 8.0.

Tryptophol. This was obtained from α-hydroxytetrahydrofuran and phenylhydrazine. Yield 37%, bp 170-172°C (1 mm); mp 59°C [from benzene–petroleum ether (1 : 1)]. R_f 0.61. UV spectrum: λ_{max} 224, 264, 280 nm; log ε 3.71, 3.33, 3.24. IR spectrum, cm^{-1}: 3585, 3385 (OH, NH), 1600, 1570, 1510, 1465 (stretching vibrations of the nucleus) [4]. Found %: C 74.9; H 6.9. $C_{10}H_{11}NO$. Calculated %: C 74.6; H 6.8.

LITERATURE CITED

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