INDOLES

XXXII.* METHOD FOR THE SYNTHESIS OF TRYPTOPHOLS

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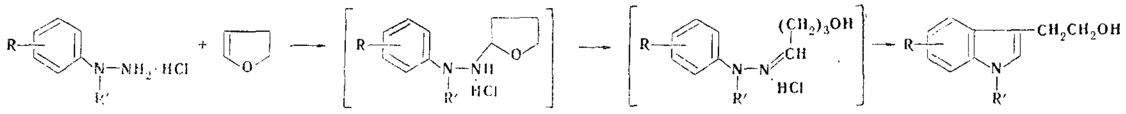
The corresponding tryptophols are obtained when arylhydrazine salts are heated with dihydrofuran in dioxane.

In anhydrous media, vinyl ethers behave like carbonyl compounds in the Fischer reaction with arylhydrazine salts [2]. Homotryptophols are formed when dihydropyran is used as the cyclic vinyl ether [3].

We have studied the reaction of dihydrofuran – a cyclic vinyl ether – with arylhydrazine salts. In this reaction the tryptophols are presumably formed via the following scheme:



The use of aqueous dioxane as the solvent gave the best results. Of the arylhydrazine salts, the hydrochlorides gave the optimum yields. α-Substituted arylhydrazines gave appreciably better yields than hydrazines with a free NH group. The yields decreased somewhat when methyl and methoxy groups were introduced into the phenylhydrazine ring.

EXPERIMENTAL

The chromatography was carried out in a thin layer of activity-V Al_2O_3 with elution with benzene–isopropyl alcohol (9 : 1) and development with iodine (A) and on Silufol UV-254 with elution with methanol–hexane (9 : 1) and development with iodine (B). The IR spectra of CCl_4 solutions or KBr pellets were recorded with a Jasco JR-S spectrometer with a NaCl prism. The UV spectra of ethanol solutions were recorded with a Hitachi EPS-3T spectrometer. The PMR spectra of $CDCl_3$ solutions were recorded with a JNM-4H-60 spectrometer with hexamethyldisiloxane as the internal standard.

General Method for Obtaining Tryptophols. A 0.05-mole sample of arylhydrazine hydrochloride in a mixture of 40 ml of dioxane and 3 ml of water was heated on a boiling-water bath, 0.051 mole of dihydrofuran [4] [bp 54-55°, n_D^{20} 1.4272; the material was 95% pure according to gas–liquid chromatography (GLC)] in 10 ml of dioxane was added with stirring in the course of 15 min, and the mixture was heated on a boiling-water bath for 6 h. The dioxane was removed by vacuum distillation, and 50 ml of hot benzene was added to the residue. The mixture was shaken, the benzene layer was separated, and the other layer was extracted again with 20 ml of benzene. The benzene extracts were combined, the benzene was removed by distillation, and the residue was vacuum-distilled.

Tryptophol. This compound was obtained in 30% yield and had mp 55-56° (from benzene–petroleum ether); R_f 0.60 (A), 0.72 (B). The substance was purified with a column filled with activity-V Al_2O_3 (diameter 2 cm, height 40 cm). The tryptophol was introduced into the column as a benzene solution. The hydrazine was initially removed by elution with benzene, and the product was then eluted with benzene–iso-

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* See [1] for communication XXXI.

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propyl alcohol (9 : 1). IR spectrum: 3585 (OH), 3385 (NH), 1600, 1570, 1510, 1465 cm^{-1} (ring stretching vibrations). UV spectrum: λ_{max} 224, 265, 280 nm; log ε 3.71, 3.32, 3.24. Found: C 74.9; H 6.9%. $C_{10}H_{11}NO$. Calculated: C 74.6; H 6.8%.

5-Methyltryptophol. This compound was obtained in 40% yield and had bp 167° (1 mm) and mp 57° (from pentane); R_f 0.61 (A), 0.74 (B). IR spectrum: 3610 (OH), 3380 (NH), 1610, 1565, 1485 cm^{-1} (ring stretching vibrations). UV spectrum: λ_{max} 219, 260, 288 nm; log ε 4.36, 4.20, 4.16. PMR spectrum,* δ, ppm: 1.9 (s, OH), 2.63 (t, J=6 Hz, 3-α-CH_2), 3.14 (t, J=6 Hz, 3-β-CH_2), 2.35 (s, CH_3), 6.1-7.25 (m, aromatic protons), 8.12 (s, NH). Found: C 75.8; H 7.7%. $C_{11}H_{13}NO$. Calculated: C 75.5; H 7.5%.

7-Methyltryptophol. This compound was obtained in 20% yield and had bp 168° (1 mm); R_f 0.62 (A), 0.71 (B). The product was purified with a column filled with Al_2O_3, as in the case of tryptophol. IR spectrum: 3340 (broad absorption band, OH, NH), 1590, 1505, 1460 cm^{-1} (ring stretching vibrations). UV spectrum: λ_{max} 219, 276, 289 nm; log ε 4.11, 3.95, 3.91. Found: C 75.9; H 7.9%. $C_{11}H_{13}NO$. Calculated: C 75.5; H 7.5%.

7-Methoxytryptophol. This compound was obtained in 25% yield and had bp 170° (1 mm); R_f 0.63 (A), 0.76 (B). The product was purified with a column filled with Al_2O_3, as in the case of tryptophol. IR spectrum: 3590 (OH), 3420 (NH), 1615, 1580, 1505, 1465 cm^{-1} (ring stretching vibrations). UV spectrum: λ_{max} 218, 236, 284 nm; log ε 4.52, 4.23, 3.97. Found: C 64.8; H 6.5%. $C_{11}H_{13}NO_2$. Calculated: C 64.4; H 6.4%.

N-Methyltryptophol. This compound was obtained in 32% yield and had bp 158-160° (1 mm); R_f 0.65 (A), 0.78 (B). IR spectrum: 3600 (OH), 1615, 1600, 1502, 1470 cm^{-1} (ring stretching vibrations). UV spectrum: λ_{max} 225, 285 nm; log ε 3.99, 3.32. Found: C 76.3; H 7.7%. $C_{11}H_{13}NO$. Calculated: C 75.5; H 7.5%.

N-Phenyltryptophol. This compound was obtained in 45% yield and had bp 185° (1 mm); R_f 0.66 (A), 0.81 (B). IR spectrum: 3589 (OH), 1603, 1545, 1505, and 1460 cm^{-1} (ring stretching vibrations). UV spectrum: λ_{max} 219, 260, 288 nm; log ε 4.36, 4.20, 4.16. PMR spectrum, δ, ppm: 1.93 (s, OH), 2.86 (t, J=6 Hz, 3-α-CH_2), 3.66 (t, J=6 Hz, 3-β-CH_2), 6.88-7.23 (m, aromatic protons). Found: C 80.3; H 6.6%. $C_{16}H_{15}NO$. Calculated: C 81.0; H 6.4%.

N-Benzyltryptophol. This compound was obtained in 70% yield and had bp 205-210° (1 mm) and mp 51° (from pentane). Found: C 81.5; H 6.8%. $C_{17}H_{17}NO$. Calculated: C 81.2; H 6.8%. R_f 0.71 (A), 0.82 (B). IR spectrum: 3410 (OH), 1595, 1560, 1493, 1465 cm^{-1} (ring stretching vibration). UV spectrum: λ_{max} 225, 293, 334 nm; log ε 4.36, 3.73, 3.42. PMR spectrum, δ, ppm: 1.97 (s, OH), 2.8 (t, J=6 Hz, 3-α-CH_2), 3.6 (t, J=6 Hz, 3-β-CH_2), 4.97 (s, 1-α-CH_2), 6.8-7.4 (m, aromatic protons).

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*The following abbreviations were used here and elsewhere: s is singlet, t is triplet, and m is multiplet.