## FISCHER REACTION WITH DIHYDROCHALCONE

## PHENYLHYDRAZONES

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2-Phenyl-3-benzylindoles were synthesized by Fischer cyclization of 1,3-diphenyl-1-propanone phenylhydrazones. The structures of the products were confirmed by their IR and PMR spectra.

Our systematic study of a class of chalcones compelled us to use them for the synthesis of 2-phenyl-3-benzylindoles (V-VIII). Only one representative of this series – V, obtained by heating  $\alpha$ -bromodihydrochalcone and aniline in a stream of nitrogen – is described in the literature [1]. This substance is quite difficult to isolate and purify. Benzylindoles having substituents in the benzyl group are unknown. It seemed that the simplest method for the preparation of indoles V-VIII might be the Fischer reaction by cyclization of the phenylhydrazones of the corresponding ketones.

For the realization of the contemplated syntheses, the chalcones were converted by selective hydrogenation of the ethylene bond to dihydrochalcones -1,3-diphenyl-1-propanones (I-IV). The hydrogenation was realized in methanol or ethanol solutions at room temperature in the presence of a Raney nickel catalyst [2]. The next step of the contemplated scheme – the synthesis of the dihydrochalcone phenylhydrazones – was carried out by refluxing I-IV with phenylhydrazine in alcohol solution. The course of the reaction was monitored by means of gas –liquid chromatography (GLC). In the case of ketones I-III, the reaction was complete in 10 h, whereas in the case of ketone IV, the absence of the starting carbonyl compounds in the reaction mixture was observed only after refluxing for 15 h.

The formation of the phenylhydrazones was also confirmed by the IR spectra, in which the absorption at 1680 cm<sup>-1</sup> characteristic for the ketone group of the dihydrochalcones (I-IV) was absent, and absorption at 1600-1610 cm<sup>-1</sup> peculiar to the N=C grouping was observed.



In connection with the fact that the dihydrochalcone phenylhydrazones resinify very rapidly in air, it was more expedient to subject the crude products to subsequent cyclization rather than to isolate them in pure form.

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Ketone phenylhydrazones I-IV were indolized by refluxing in a 10% solution of hydrogen chloride in ethanol. In this case, partial hydrolysis of the azamethine bond with regeneration of starting ketones I-IV occurred along with the formation of the 2,3-disubstituted indoles. Indoles V-VIII were separated from the ketones by repeated crystallization. The IR spectra of the synthesized indole derivatives are characterized by disappearance of the band at 1600-1610 cm<sup>-1</sup>, which is related to the vibrations of the N=C group, by the appearance of an intense band at 3400-3500 cm<sup>-1</sup>, which is characteristic for the NH group of the in-dole ring.

The PMR spectra were recorded for 2-phenyl-3-benzylindole (V) and 2-phenyl-3-(4-dimethylamino-benzyl)indole (VII).

A singlet of the protons of the  $CH_2$  group at 4.44 ppm with an intensity of 2H and the superimposed signals of the singlet of the aromatic protons of the  $CH_2C_6H_5$  group at 7.38 ppm and of the multiplet of the protons of two other phenyl groups at 7.0-8.0 ppm with an overall intensity of 14H are observed in the spectrum of V.

The singlets at 2.95 ppm in the PMR spectrum of indole VII are affiliated with the protons of the  $(CH_3)_2$  group, and the singlet at 4.33 ppm is affiliated with the protons of the  $CH_2$  group (their intensity ratio is 6:2). The signals of the aromatic protons form a complex multiplet at 6.7-8.0 ppm with an overall intensity of 13 H.

## EXPERIMENTAL

The IR spectra were recorded with IKS-22 and UR-10 spectrometers. The PMR spectra of deuteroacetone solutions of the compounds were recorded with a C-60HL spectrometer with an operating frequency of 60 MHz and tetramethylsilane as the standard.

Gas -liquid chromatography was carried out with a Pye-Unicam-104 chromatograph with a flameionization detector and a 2.1 m by 4 mm column filled with 10% SE-30 silicone elastomer on silanized diatomite (100-120 mesh); the nitrogen flow-rate was 29 ml/min and the temperature was 250°.

The retention times of the ketones were as follows: I 5 min, II 8 min, III 13 min, IV 7.5 min, and phenylhydrazone III 45 min.

<u>1,3-Diphenyl-1-propanone (I)</u>. A solution of 10.4 g (0.05 mole) of 1-phenyl-2-benzoylethylene (chalcone) in 100 ml of absolute ethanol was shaken with hydrogen at room temperature in the presence of 1.5 g of Raney nickel A total of one equivalent of hydrogen was absorbed after 1 h. The catalyst was then removed by filtration, and the alcohol was removed by vacuum distillation until crystallization began. Workup gave 10.25 g (98.5%) of colorless crystals with mp 69-70° (from ethanol) (mp 72° [3]).

The remaining 1,3-diphenyl-1-propanones (II-IV) were obtained by hydrogenation of the corresponding chalcones in methanol under conditions similar to those in the preparation of I.

<u>1-Phenyl-3-(4-methoxyphenyl)-1-propane (II)</u>. This compound was obtained in 77.5% yield as color-less crystals with mp  $66-67^{\circ}$  (from isopropyl alcohol) (mp  $67-68^{\circ}$  [4]).

<u>1-Phenyl-3-(4-dimethylaminophenyl)-1-propanone (III)</u>. This compound was obtained in 81% yield as colorless crystals with mp 48-49° (from isopropyl alcohol) (mp 49.5-50.5° [5]).

<u>1-Phenyl-3-(3-chlorophenyl)-1-propanone (IV)</u>. This compound was obtained in 64.1% yield as colorless crystals with mp 74-75° (from methanol). Found: C 73.5; H 5.4; Cl 14.2%. C<sub>15</sub>H<sub>13</sub>ClO. Calculated: C 73.6; H 5.3; Cl 14.5%.

<u>2-Phenyl-3-benzylindole (V)</u>. A solution of 2 g (9.5 mmole) of ketone I and 1.13 g (10.5 mmole) of phenylhydrazine in 20 ml of absolute ethanol was heated on a water bath for 10 h, after which it was vacuum evaporated, and the residual 1,3-diphenyl-1-propanone phenylhydrazone was refluxed for 2 with 20 ml of a 10% alcohol solution of hydrogen chloride. The precipitated ammonium chloride was removed by filtration, the filtrate was evaporated, and the residue was treated with 25% ammonium hydroxide. The reaction products were extracted with benzene, the benzene was removed by distillation, and the residue was vacuum distilled to give a fraction with bp 240-242° (0.5 mm), which slowly crystallized on standing to give 0.95 g (35%) of a product with 115-116° (after successive crystallization from ether and isopropyl alcohol) (mp 119° [1]). Found: C 89.0; H 6.1%. C<sub>21</sub>H<sub>17</sub>N. Calculated: C 89.1; H 6.0%.

2-Phenyl-3-(4-methoxybenzyl)indole (VI). 1-Phenyl-3-(4-methoxyphenyl)-1-propanone (II) was converted to VI by the method used for the synthesis of V. After completion of the Fischer reaction, the mix-

ture was extracted with ether. The ether solution was dried with magnesium sulfate and evaporated, and the residue was crystallized successively from isopropyl alcohol-ether (1:1) and isopropyl alcohol to give a product with mp 150-152° in 26% yield. Found: C 84.4; H 6.2%.  $C_{22}H_{19}NO$ . Calculated: C 84.3; H 6.1%.

<u>2-Phenyl-3-(4-dimethylaminobenzyl)indole (VII).</u> The phenylhydrazone of ketone III, obtained as described above, was heated for 2 h with a 10% alcohol solution of hydrogen chloride, after which the ammonium chloride was separated, the alcohol was removed by distillation, the residue was treated with ammonium hydroxide, and the mixture was diluted with isopropyl alcohol. The precipitate that formed on standing was removed by filtration and recrystallized from 90% methanol to give a product with mp 110-112° in 29% yield. Found: C 84.4; H 6.7; N 8.7%.  $C_{23}H_{22}N_2$ . Calculated: C 84.6; H 6.8; N 8.6%.

<u>2-Phenyl-3-(3-chlorobenzyl)indole (VIII)</u>. This compound was synthesized by the method used to prepare 2-phenyl-3-benzylindole. A fraction with bp 220-225° (0.5 mm) was collected. Successive crystallizations from methanol and isopropyl alcohol gave a product with mp 75-76° in 31% yield. Found: C 79.2; H 5.1%. C<sub>21</sub>H<sub>16</sub>ClN. Calculated: C 79.3; H 5.1%.

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