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SYNTHESIS OF SOME NEW ARYLINDOLES

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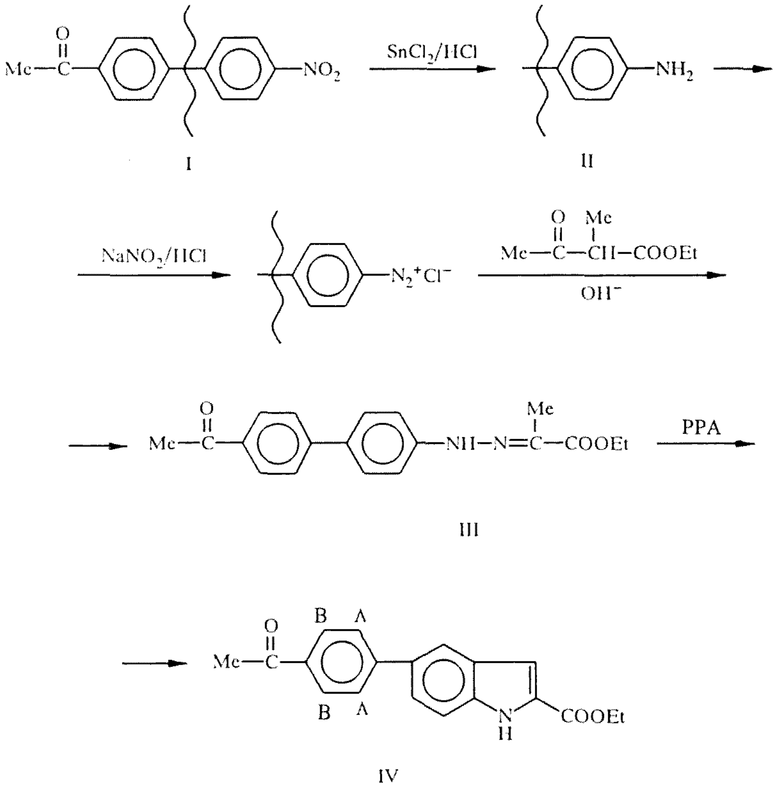
New indole derivatives — 2-ethoxycarbonyl-5-(p-acetylphenyl)indole and para-*substituted 2-diphenylindoles — key compounds for synthesis of new bisindoles, were synthesized from 4-acetyl-4'-nitrodiphenyl.*

Synthesis of some key new indole derivatives — 2-ethyoxycarbonyl-5-(p-acetylphenyl)indole (IV) and 2-(p-aminodiphenyl)indole (VII) from 4-acetyl-4'-nitrodiphenyl (I) is described in the present study. The method of synthesis of indole IV from biphenyl I is shown in the scheme. 4-Acetyl-4'-nitrodiphenyl (I) was reduced with tin(II) chloride while boiling in ethanol.



Pyruvic acid ethyl ester p-acetyldiphenylhydrazone (III) was prepared by diazotization [1] of compound II and subsequent azo coupling with methylacetoacetic acid ethyl ester according to the scheme of the Japp–Klingemann reaction [2].

Indolization of hydrazone III was conducted in polyphosphoric acid at 75-80°C.

2-(p-Aminodiphenyl)indole (VII) was prepared by two paths:

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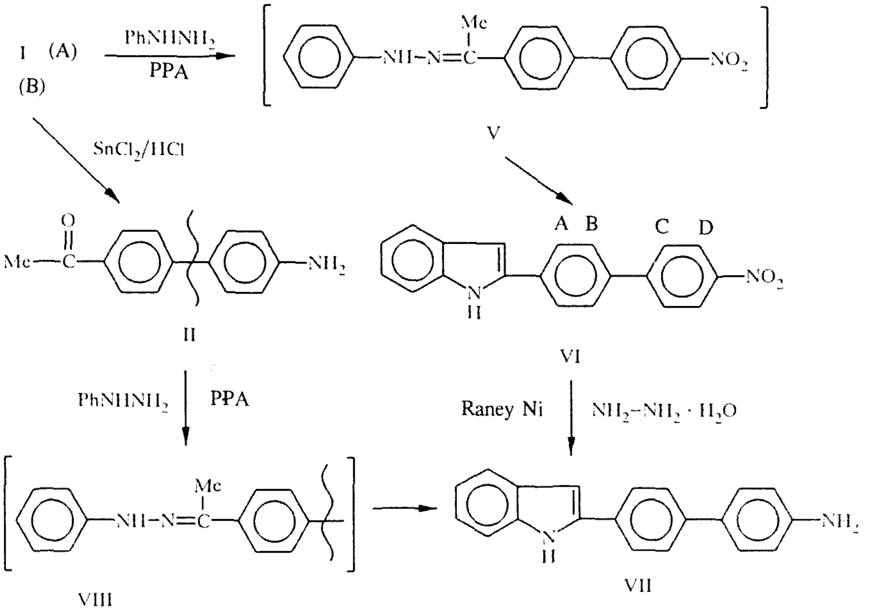

The first path (A) consisted of preliminary preparation of 2-(p-nitrodiphenyl)indole (VI) with subsequent reduction of the nitro group. Indole VI was synthesized by heating a mixture of 4-acetyl-4'-nitrodiphenyl (I) and phenylhydrazine in polyphosphoric acid at 80-85°C without intermediate separation of hydrazone V. The nitro group was reduced with hydrazine hydrate in the presence of Raney Ni.

Counter synthesis of indole VII (path B) from 4-acetyl-4'-aminodiphenyl (II) and phenylhydrazine was conducted similarly — in polyphosphoric acid at 85-90°C.

The data from the IR, UV, PMR, and mass spectra of compounds IV, VI, and VII are reported in Table 1.

The IR spectrum of compound IV contains absorption bands characteristic of the groups: CO acyl, CO ester, and N–H indole at 1670, 1685, and 3310 cm^{-1}, respectively.

There is an absorption band in the 3200 cm^{-1} region of the IR spectrum of compound VII characteristic of a NH_2 group, which is not present in the spectrum of compound VI. There are bands of stretching vibrations in the 3380-3410 cm^{-1} region from a NH indole group in the IR spectra of both compounds VI and VII.

There is no signal from NH_2 group protons, which appears in the spectrum of compound VII at 4.80 ppm in the form of a singlet, in the PMR spectrum of compound VI. The multiplet character and intensity of the signals of the remaining protons in the spectra of compounds VI and VII are identical. In addition, the signals of all protons of compound VII are shifted to the strong field region, which once more indicates the presence of an electron-donor amino group in the molecule of compound VII.

EXPERIMENTAL

The IR spectra were made on a UR-20 in petrolatum, the UV spectra were made on a Specord spectrophotometer in ethanol, and the PMR spectra were made on WP-200SY (200 MHz) and Varian SC-300 (300 MHz) spectrometers in acetone-D_6, TMS internal standard. The mass spectra were recorded on a Ribermag 10-10-B spectrometer; the ionizing electron energy was 70 eV.

The reactions and purity of the compounds were monitored and the R_f were determined on Silufol UV-254 plates, benzene–acetone eluent, 7:1. Silicagel with a particle size of 100-250 μm was used as the sorbent for column chromatography.

The data from elemental analysis for C, H, and N for compounds IV, VI, and VII correspond to the calculated data.

4-Acetyl-4'-aminodiphenyl (II). A previously prepared and cooled solution of 33.9 g (150 mmole) of $SnCl_2 \cdot 2H_2O$ and 52.5 ml of HCl in 75 ml of ethanol was added by drops to a solution of 3.6 g (15 mmole) of 4-acetyl-4'-nitrodiphenyl (I) in 80 ml of ethanol while stirring. It was boiled for 1 h. The solvent was evaporated until crystallization began, 100 ml of water was added, and it was alkalized to pH 8-9. The precipitated yellow sediment was filtered off, washed with water, dried, and recrystallized from 100 ml of benzene. Yield of 2.86 g (90%). Mp = 173-174.5°C.

TABLE 1. Characteristics of Synthesized Compounds IV, VI, and VII

Compound	Empirical formula	mp, °C	R_f	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm log (ε)	PMR^{*2} spectrum, δ, ppm (J, Hz)	Yield, %
IV	$C_{19}H_{17}NO_3$	189...191	0,71	3310 (NH), 1685 (CO w. es.), 1670 (CO)	208 (4,46), 297 (4,59)	12,02 (1H, s, 1-H); 7,21 (1H, s, 3-H); 8,03 (1H, d, J_{46} = 1,6, 4-H); 7,64 (1H, d. d, J_{67} = 8,2; J_{64} = 1,6, 6-H); 7,55 (1H, d, J_{76} = 8,2, 7-H); 3,30 (3H, s, CH_3CO); 4,34 (2H, q, $\underline{CH_2}CH_3$); 1,30 (3H, t, CH_2CH_3); 7,81 (2H, d, A-H); 8,01 (2H, d, B-H); J_{AB}	8
VI	$C_{20}H_{14}N_2O_2$	295 with decomp.	0,32*	3410 (NH), 1320, 1490 (NO_2)	207 (4,50), 241 (4,04) sh, 287 (3,97) sh, 305 (4,00)	10,8 (1H, s, 1-H); 7,04 (1H, m 3-H); 7,60 (1H, d. d, J_{45} = 8,4); 7,04 (1H, m, 5-H); 7,15 (1H, m, 6-H); 7,44 (1H, d. d, 7-H); 8,01 (2H, d, A-H); 7,91 (2H, d, B-H); 7,97 (2H, d, C-H); 8,36 (2H, d, D-H)	74
VII	$C_{20}H_{16}N_2$	300 with decomp.	0,64	3380 (NH), 3200 (NH2)	208 (4,80), 285 (4,09) sh, 339 (4,79)	10,66 (1H, br. s, 1-H); 6,90 (1H, d, J_{37} = 1,1, 3-H); 7,57 (1H, d.d, J_{45} = 8,4, 4-H); 7,01 (1H, m, 5-H); 7,10 (1H, m, 6-H); 7,43 (1H, d. d, 7-H, J_{67} = 8,4); 4,80 (2H, s, NH_2); 7,88 (2H, d, A-H); 7,65 (2H, d, B-H); 7,46 (2H, d, C-H); 6,78 (2H, d, D-H)	49 (A) 25 (B)

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*Benzene—hexane, 3:1.

Pyruvic Acid Ethyl Ester p-Acetyldiphenylhydrazone (III). Here 10 ml (10 mmole) of methylacetoacetic acid ethyl ester and 10 ml of water were added to a solution of 0.56 g (10 mmole) of KOH in 20 ml of ethanol, cooled to −5°C, and a solution prepared by diazotization of 2.1 g (10 mmole) of 4-acetyl-4′-aminodiphenyl (II) was rapidly added, followed by addition of sodium acetate to pH 5-6. It was mixed for 2 h, extracted with ether, dried with anhydrous $CaCl_2$, and the solvent was evaporated. The residue was dissolved in benzene, precipitated with hexane, filtered, and dried. Yield of 2.34 g (72%).

2-Ethoxycarbonyl-5-(p-acetylphenyl)indole (IV). A mixture of 1.9 g (6 mmole) of hydrazone III and 20 ml of PPA was stirred at 70-80°C for 40 min. It was cooled to 30-35°C, and was poured into 200 m of water in a thin jet. The precipitated dark yellow crystals were filtered off, washed with water, and dried. They were purified in a column, benzene eluent. Yield of 0.14 g.

2-(p-Nitrophenyl)indole (VI). A mixture of 12 g (50 mmole) of 4-acetyl-4′-nitrodiphenyl (I), 5 ml (50 mmole) of phenylhydrazine, and 150 g of PPA was stirred at 80-85°C for 1.5 h. It was cooled and poured into 500 ml of cold water in a thin jet. The precipitated crystals were filtered off, washed with water, and dried. They were recrystallized from acetone. Yield of 11.7 g. Found: M$^+$ 314. $C_{20}H_{14}N_2O_2$. Calculated: M 314.

2-(p-Aminodiphenyl)indole (VII). A. Here 2 g of Raney Ni was added to a suspension of 15 g (5 mmole) of 2-(p-nitrodiphenyl)indole (VI) in 15 ml of ethyl alcohol and 400 m of hydrazine hydrate was added by drops at 30-40°C. The reaction mixture was boiled for 1 h while stirring. The hot solution was filtered and cooled. The precipitated crystals were filtered off, dried, and recrystallized from octane. Yield of 0.7 g.

B. A mixture of 0.21 g (1 mmole) of 4-acetyl-4′-aminodiphenyl (II), 0.1 ml (1 mmole) of phenylhydrazine, and 5 ml of PPA was slowly heated to 85-90°C. It was stirred for 1 h, cooled, and poured into 150 ml of water in a thin jet. It was extracted with ether and dried with anhydrous $CaCl_2$. The solvent was evaporated. It was purified in a column, benzene eluent. Yield of 0.07 g.

REFERENCES

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2. I. L. Lutsenko (ed.), Organic Reactions [Russian translation], Inostrannaya Literatura, Moscow (1963), No. 10, p. 148.