

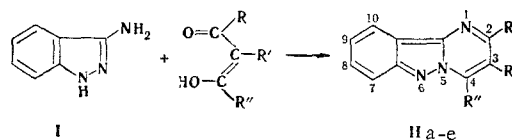
PYRIMIDO [1,2-b]INDAZOLES FROM 3-AMINOINDAZOLES AND β -DIKETONES

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3-Aminoindazole and its hydrochloride react with β -diketones to give pyrimido[1,2-b]indazoles and their hydrochlorides.

3-Aminopyrazoles react with β -diketones with closing of the pyrimidine ring to give pyrazolo[1,5-a]pyrimidines [1]. For 3-aminoindazole (I) the reaction with β -diketones also proceeds quite readily to give pyrimido[1,2-b]indazoles (IIa-e).



The PMR spectra confirm structure II. The signal of the 3-H pyrimidine proton (6.54 ppm) and the signals of two methyl groups at 2.52 and 2.70 ppm (the latter is related to 4-CH₃, inasmuch as it is lower and broader as a consequence of splitting by the pyrimidine proton) are observed in the spectrum of the product of condensation of I with acetylacetone (in carbon tetrachloride). The 3-H proton couples with 4-CH₃ to a greater extent than with 2-CH₃, as a consequence of the fact that the 3-4 bond is primarily a double bond, while the 2-3 bond is primarily a single bond [2]. The doublet at 8.10 ppm with J=9 Hz, related to 10-H, which is deshielded by the electron pair of the nitrogen atom in the 1 position as a consequence of rigid fixing of this atom by the pyrimidine ring, serves as yet another confirmation of the formation of a pyrimidine ring. The corresponding proton (4-H) in the PMR spectrum of the starting 3-aminoindazole absorbs together with the remaining phenylene protons at stronger field.

Three maxima - λ_{\max} , nm (log ϵ): 225-230 (4.11-4.14), 275-280 (4.05-4.12), and 330-335 (3.20-3.25) - are observed in the UV spectra of II. The addition of a drop of concentrated hydrochloric acid to the cuvettes containing alcohol solutions of these compounds does not change the form of the spectra at all; this attests to the low basicity of II.

3-Aminoindazole hydrochloride (III) reacts with β -diketones even more readily than the base. The reaction products are salts IV, which are converted to bases II by the action of ammonia. The 3-H signal in the PMR spectra of salts IV (in trifluoroacetic acid) is shifted sharply paramagnetically (7.30 ppm) as compared with the 3-H signal in the spectrum of II, while the signals of the methyl groups are shifted only slightly (2.62 and 2.75 ppm for IVa).

The PMR spectra serve as a basis for the selection of the structure of the products of condensation of I and III with unsymmetrical β -diketones. Benzoylacetone reacts with III to give one isomer - IVc (one signal of a methyl group at 2.64 ppm is observed in the PMR spectrum of the crude product of condensation). The structure of the condensation product was established on the basis of the character of the phenyl signal, which, together with the signals of the phenylene protons, has the form of a complex band at 7.25-7.75 ppm; the 3-H signal also falls in this region, and its chemical shift is no more than 7.5 ppm. Consequently, the phenyl group is in the 4 position, where its signal is split into two groups of bands, the distance

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TABLE 1. Pyrimido[1,2-b]indazoles (II) and Their Salts (IV)

Compound	R	R'	R''	mp, °C	Empirical formula	Element	Found, %	Calc., %	Yield, %
IIa	CH ₃	H	CH ₃	140	C ₁₂ H ₁₁ N ₃	N	21,3	21,3	94
IIb	C ₆ H ₅	H	C ₆ H ₅	142	C ₂₂ H ₁₅ N ₃	N	13,1	13,1	74
IIc	CH ₃	Cl	CH ₃	170	C ₁₂ H ₁₀ ClN ₃	Cl	15,4	15,3	—*
IId	CH ₃	H	C ₆ H ₅	145	C ₁₇ H ₁₃ N ₃	N	16,0	16,2	—*
Ile	CH ₃	H	C ₃ H ₅ †	102	C ₁₄ H ₁₃ N ₃	N	19,1	18,8	—*
IVa	CH ₃	H	CH ₃	230	C ₁₂ H ₁₁ N ₃ ·HClO ₄	Cl	11,7	11,9	98
IVb	CH ₃	CH ₃	CH ₃	208	C ₁₃ H ₁₃ N ₃ ·HClO ₄	Cl	11,1	11,4	100
IVc	CH ₃	H	C ₆ H ₅	255	C ₁₇ H ₁₃ N ₃ ·HClO ₄	Cl	9,6	9,8	100
IVd	CH ₃	H	C ₃ H ₅ †	195	C ₁₄ H ₁₃ N ₃ ·HClO ₄	Cl	11,0	11,0	96

*Obtained from corresponding salt IV.

†Cyclopropyl.

between the centers of which is no more than 0.4 ppm, which is characteristic for this sort of molecular fragment [3]. The phenyl group in the 4 position, being at a considerable angle relative to the plane of the system, weakly deshields the 3-H proton. The phenyl group in the 2 position is split more strongly and has a stronger effect on 3-H, as attested to by the spectrum of the product of the condensation of I with dibenzoylmethane (IIb in trifluoroacetic acid): despite the superimposition of the signals of the phenylene group and the two phenyl groups, a group of peaks centered at ~7.9 ppm, which corresponds in intensity to two protons, is distinctly isolated in the spectrum, and $\delta_{3-H} = 7.71$ ppm.

On condensation with III, 1-cyclopropylbutane-1,3-dione also gives one isomer (IVd), the structure of which was established on the basis of the fact that the ratio of the heights of the 3-H signals (7.00 ppm) and methyl signals (2.59 ppm) increased markedly as compared with the ratio for IVa. This change in ratios is explained by the fact that the 3-H proton in the product of condensation with cyclopropylbutanedione is not split by the methyl group, which is consequently in the 2 position. In addition, the considerable diamagnetic shift of 3-H in the spectrum of this compound as compared with IVa attests to the fact that the cyclopropyl group is in the 4 position, inasmuch as a cyclopropyl group in the α position relative to the bridge nitrogen atom in the pyrimidine ring in other similar condensed pyrimidinium salts, for example, in 1,3,4-thiadiazolo[3,2-a]pyrimidinium salts [3], markedly shifts the β proton diamagnetically, while a cyclopropyl group in the α position shifts the β proton slightly.

3-Chloroacetylacetone reacts with III like other β -diketones rather than as an α -chloro ketone to give corresponding salt IV, which was converted to base IId.

EXPERIMENTAL

The PMR spectra were recorded with a ZKR-60 spectrometer with hexamethyldisiloxane as the internal standard. The UV spectra of $5 \cdot 10^{-5}$ M ethanol solutions were recorded with an SF-4 spectrophotometer.

3-Aminoindazole hydrochloride was obtained by treatment of 3-aminoindazole [4] with 57% perchloric acid.

Condensation of 3-Aminoindazole (I) and Its Hydrochloride (III) with β -Diketones. A mixture of I or III with a 10-15% excess of the β -diketone was heated on a water bath for 5-10 min (for aliphatic ketones) or for 30-40 min (for benzoylacetone and dibenzoylmethane). The reaction mixture was then cooled and washed repeatedly with ether, and the product was crystallized from ethanol (IV) or aqueous (1:1) ethanol (II). Compound II was also obtained from IV by addition of ammonium hydroxide to an aqueous alcohol suspension of IV. Compound II was obtained as colorless yellowish or yellow (IIb) crystals, while IV was obtained as yellow crystals.

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