2,5-DIMETHYL-4-(p-AMINOBENZYL)PYRIDINE IN THE SYNTHESIS OF SUBSTITUTED QUINOLINES, PYRIDOINDAZOLES, AND ISOQUINOLINOQUINOLINES

N. S. Prostakov, A. P. Krapivko, A. T. Soldatenkov, and N. D. Sergeeva

2,5-Dimethyl-4-pyridyl(6-quinolyl)methane was obtained from 2,5-dimethyl-4-(p-aminobenzyl)pyridine via the Skraup reaction. The product was nitrated to 2,5-dimethyl-4-pyridyl(5-nitro-6-quinolyl)methane, which was reduced to 2,5-dimethyl-4-pyridyl(5-amino-6-quinolyl)methane. It was established that the diazo compound formed from this amino derivative is converted to 1H,3-(2,5-dimethyl-4-pyridyl)-pyrido[2,3-g]indazole as a result of intramolecular cyclization. 9-Methylisoquinolino[7,6-f]quinoline was obtained by catalytic dehydrocyclization of 2,5-dimethyl-4-pyridyl(6-quinolyl)methane. 2,5-Dimethyl-4-pyridyl(5-nitro-6-quinolyl)methane has chemochromic properties.

A previously unknown substituted quinoline, viz., 2,5-dimethyl-4-pyridyl(6-quinolyl)methane (II), was obtained from 2,5-dimethyl-4-(p-aminobenzyl)pyridine (I) via the Skraup reaction. 2,5-Dimethyl-4-pyridyl(6-quinolyl)methane (II), from which amino derivative I was obtained, was used as the oxidizing agent in its synthesis.

We have accomplished the nitration of substituted quinoline II and subsequent transformations at the nitro and amino groups with allowance for the fact that some functionally substituted quinolines have specific physiological properties [2].

As a result of nitration under relatively severe conditions we isolated only one mono-nitro derivative, viz., 2,5-dimethyl-4-pyridyl(5-nitro-6-quinolyl)methane (III). Its PMR spectrum does not contain a signal of the 5-H proton, but the 7-H and 8-H protons of the
quinoline part of the molecule give a spectrum of the AB type, and this constitutes evidence
that the nitro group is attached to the C₅ atom. An ortho orientation of the nitro group
relative to the methylene group is confirmed [3] by the appearance in the mass spectrum of
III of an (M -- OH)⁺ fragment with m/e 276, which has the maximum peak intensity.

Nitro derivative III has chemochromic properties. A colorless solution of III in
methanol turns brick-red when potassium hydroxide or potassium carbonate is added to it.
Nitro form III evidently is converted to nitronic acid salt IIIa in this case.

A significant decrease in the signal of the methylene group (δ 4.08 ppm), the appearance
of two additional (as compared with III) signals of methylene groups, and complication of
the structure of the spectrum in the aromatic region are observed in the PMR spectrum (for
a solution in CD₃OD with tetramethylsilane as the standard) of III recorded after the addi-
tion of a solution of potassium carbonate. We have previously observed a similar conversion
of the nitro form to the aci form in the case of 2,5-dimethyl-4-(p,o-dinitrobenzyl)pyridine
[4]; however, in contrast to the latter, nitroquinolyl(pyridyl)methane III does not display
photochromic properties when its crystals or a methanol solution are illuminated with an
electronic photoflash at +30 to −50°C.

2,5-Dimethyl-4-pyridyl(5-amino-6-quinolyl)methane (IV) was obtained by reduction of
nitro derivative III by means of hydrazine hydrate and Raney nickel. We made an attempt to
replace the amino group in this compound by a hydroxy group by diazotization and subsequent
development of the diazo compound. However, evidently as a consequence of the relative
stability of the resulting diazo compound, as well as the ease of deprotonation of the
methylene group under alkaline conditions, the compound undergoes intramolecular cyclization,
as a result of which 1H,3-(2,5-dimethyl-4-pyridyl)pyrido[2,3-g]indazole (V) — a representa-
tive of a new heterocyclic system — is formed in high yield. The position and the multiplicity
of the signals of the protons of the quinoline and pyridine fragments in the PMR spectrum
of pyridoindazole V are similar to the position and multiplicity of the signals of amino
derivative IV. However, the absence in its spectrum of signals of the protons of the amino
and methylene groups, as well as the appearance of a broad signal at δ 14.3 ppm (1-H), which
is characteristic for indazole [5], confirms the pyridoindazole structure of V.

We obtained 6-(2,5-dimethyl-4-pyridyl)quinoline (VII) from the previously described
2,5-dimethyl-4-(p-aminophenyl)pyridine (VI) [6] via the Skraup reaction. The condensation
was carried out in the presence of 2,5-dimethyl-4-(p-nitrophenyl)pyridine.

Substituted quinoline II was used in the synthesis of a new polynuclear nitrogen-conta-
ining heterocyclic system of the isoquinolino-quinoline type, a representative of which is
9-methylisoquinolino[7,6-f]quinoline (VIII).

The dehydrocyclization of II was carried out on a K-16 dehydrogenating catalyst at
560-580°C. In the course of this reaction hydrogen may be split out from the quinoline
ring at both C₇ (with the formation of a linear condensed system) and C₅ (with the formation
of an angular structure). Only VIII was isolated in the experiment. The localization of
the signal of the 1-H proton at weak field is explained by the angular structure of VIII,
since in the spectra of quinolines the signal of the peri proton is located at stronger
(by ~0.9 ppm) field. The UV spectrum of VIII is also in agreement with its angular struc-
ture [7].

EXPERIMENTAL

The PMR spectra of solutions of the compounds in CDCl₃ were recorded with a Tesla
BS-487C spectrometer (80 MHz) with tetramethylsilane as the internal standard [in the case
of V, the solvent was dimethyl sulfoxide (DMSO), and the standard was hexamethyldisiloxane].
The UV spectra of solutions of the compounds in ethanol were obtained with a Specord UV-vis
spectrophotometer. The mass spectra were obtained using an MKh-1303 mass spectrometer with
a system for direct introduction of the samples into the ion source at an ionizing voltage of
70 V. Intense molecular-ion peaks are present in the mass spectra of all of the synthesized
compounds. Activity II aluminum oxide was used for chromatographic analysis.