SYNTHESIS OF 3-ALKYL-2,4,6-TRIPHENYLPYRIDINES
AND 1,3-DIPHENYL-4- AND -2-AZAFLUORENES

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The previously unknown 3-alkyl-2,4,6-triphenylpyridines were obtained from 1-methyl-3-alkyl-
2,6-diphenyl-4-piperidones. It was established that a mixture of 1,3-diphenyl-4-azafluorene
and 1,3-diphenyl-2-azafluorene is formed in the dehydrocyclization of 3-methyl-2,4,6-triphe-
nylpyridine.

The catalytic dehydrocyclization of 2,5-dimethyl-4-arylpyridines and 2,5-dimethyl-4-arylme-thyl-
pyridines is a convenient method for the synthesis of the difficult-to-obtain and as yet little-investigated

For the study of this reaction it seemed of interest to subject 3-alkyl-2,4,6-triphenylpyridine to de-
hydrocyclization. In this case dehydrocyclization may proceed both at the phenyl group attached to C, and
at the phenyl group attached to C,. In the first case a substituted 4-azafluorene should be formed, whereas
in the second case a similarly substituted 2-azafluorene should be formed. The 3-alkyl-2,4,6-triphenylpy-
ridines were obtained by the method described in [3].

\[
\begin{align*}
&\text{I, IV, VII, X: } R = \text{CH}_3; \quad \text{II, V, VIII, XI: } R = \text{C}_3\text{H}_7-n; \\
&\text{III, VI, IX, XII: } R = \text{CH(CH}_3)_2
\end{align*}
\]

The reaction of phenyllithium with 1,3-dimethyl- (I), 1-methyl-3-propyl- (II), and 1-methyl-3-isopropyl-2,6-diphenyl-4-piperidone (III) gave, respectively, 1,3-dimethyl- (IV), 1-methyl-3-propyl- (V),
and 1-methyl-3-isopropyl-2,4,6-triphenyl-4-piperidol (VI). Each of these piperidones was isolated in the
form of one diastereoisomer. Only one isomer was also detected by thin-layer chromatography (TLC)
of the reaction products.

The magnitude of the spin−spin coupling constants of the protons attached to C₂ and C₃ and C₅ and
C₈ (J₃,3 and J₅,8) in the PMR spectra of piperidones I–III and piperidols IV–VI (Table 1) shows that the
phenyl groups attached to C₃ and C₅ and the alkyl group attached to C₃ are equatorially oriented. The
stereochemistry of addition of organolithium compounds to cyclic ketones containing a substituent in the α
position relative to the keto group [4, 5] makes it possible to assume that the phenyl group attached to
C₄ in the case of piperidols IV–VI is oriented equatorially, whereas the OH group is axially oriented. The
nonequivalence of the methyl groups of the isopropyl group of alcohol VI (the presence in the PMR spec-
trum of two doublets at 0.70 and 0.14 ppm of three proton units each) indicates the hindered character of
rotation of this group.

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TABLE 1. Data from the PMR Spectra of 1-Methyl-3-alkyl-2,6-diphenyl-4-piperidones and 1-Methyl-3-alkyl-2,4,6-triphenyl-4-piperidols

<table>
<thead>
<tr>
<th>Chemical shift, δ, ppm multiplicity</th>
<th>Substituent protons</th>
<th>Spin–spin coupling constant, Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compounds</td>
<td>H-2</td>
<td>H-6</td>
</tr>
<tr>
<td>----------</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>I</td>
<td>2.90</td>
<td>3.33</td>
</tr>
<tr>
<td>II</td>
<td>3.02</td>
<td>3.40</td>
</tr>
<tr>
<td>III</td>
<td>3.23</td>
<td>3.33</td>
</tr>
<tr>
<td>IV</td>
<td>3.23</td>
<td>3.62</td>
</tr>
<tr>
<td>V</td>
<td>3.28</td>
<td>3.63</td>
</tr>
<tr>
<td>VI</td>
<td>3.59</td>
<td>3.60</td>
</tr>
</tbody>
</table>

*It was not possible to determine the spin–spin coupling constants because of overlapping of the signals.

Piperidols IV–VI were dehydrated by means of phosphorus tribromide in refluxing benzene and subsequent treatment of the reaction mixture with ammonium hydroxide. This procedure was used to obtain 1,3-dimethyl-(VII), 1-methyl-3-propyl-(VIII), and 1-methyl-3-isopropyl-2,4,6-triphenylpiperidine (IX). Piperidine VII is formed as a single Δ¹ isomer, as confirmed by the presence in its PMR spectrum of one signal of an N-CH₃ group at δ 1.72 ppm (3-H) and a broad signal of an olefin proton attached to C₅ with δ 5.50 ppm (1H). However, piperidines VIII and IX are mixtures of Δ³ and Δ⁴ isomers. This is proved by the fact that the PMR spectra of VIII and IX contain two singlets of an N-CH₃ group at 1.73 and 1.84 ppm, respectively. The assignment of these signals was confirmed by their splitting on protonation (CF₃COOH) and conversion to a singlet upon subsequent deuterium exchange. The signal of the olefin proton in the spectra of VIII and IX is found at 5.63 ppm. The signal at 1.73 ppm is due to the N-CH₃ group of the Δ⁴ isomer, as follows from the ratio of the integral intensities of this signal and the signal of the olefin proton (3:1). The ratio of the Δ³ and Δ⁴ isomers, determined from the integral intensities of the signals of the N-CH₃ groups, is 1:2 in the case of IX.

The dehydrogenation and N-demethylation of piperidines VII–IX were accomplished with a K-16 catalyst at 350–420°. 3-Methyl (XII) were obtained in 30, 29, and 1% yields, respectively. The dehydrogenation and N-demethylation of piperidines VII–IX give considerably lower yields than the analogous transformations of piperidines that do not contain phenyl substituents attached to the C₂ and C₆ atoms of the piperidine ring. In all cases we established the formation of up to 60% of substances that do not contain a basic nitrogen atom and are apparently products of deamination and hydrogenolysis of the starting piperidines at the C₆–N or C₇–N bonds. It was established experimentally that the nitrogen atom is split out as ammonia during deamination. However, the catalytic hydrogenolysis of benzylamines, which are analogs of the piperidines under investigation, is the usual method of debenzylation. In the case of the catalytic transformations of piperidines VIII and IX, one observes partial cleavage of the alky group and the phenyl group attached to C₂. 2,4,6-Triphenylpyridine (XIII) and 5-isopropyl-2,4-diphenylpyridine (XIV) were isolated from the reaction products. The location of the phenyl groups at C₂ and C₄ in XIV follows unambiguously from the presence in the PMR spectrum of singlets of the α and β protons of the pyridine ring at 9.03 and 7.50 ppm, respectively.

Pyridine base X was subjected to dehydrocyclization on the same K-16 catalyst at 550–560°. In this case we isolated 1,3-diphenyl-4-azafluorene (XV) (with mp 157.5–158° in 27% yield) and 1,3-diphenyl-2-azafluorene (XVI) (with mp 143.5–144.5° in 9.5% yield). In order to confirm structures XV and XVI we carried out the alternative synthesis of XVI. It was obtained by dehydrocyclization of 2,6-diphenyl-4-(o-tolyl)pyridine (XVII) under the same conditions as in the cyclization of X.