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PREPARATION AND PROPERTIES OF 2,3:5,6-BIS[BICYCLO(3.3.1)NONYL]PYRIDINE

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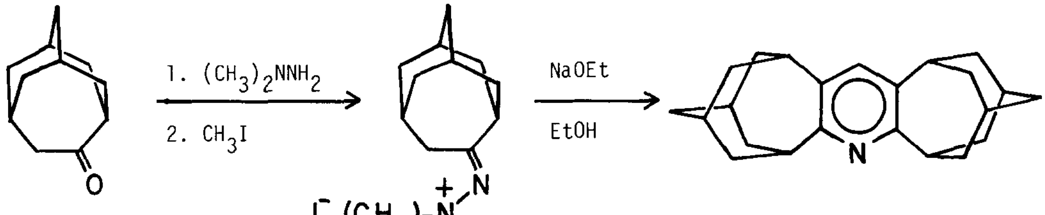
Abstract: A preparation of the title compound is reported and its basicity relative to other bisannelated pyridines is discussed.

We report here the remarkably facile synthesis of a bisannelated pyridine derived from homoadamantanone (1).[1] The trimethylhydrazonium iodide (2)[2] of 1 prepared by methylation of the dimethylhydrazone gives 2,3:5,6-bis[bicyclo(3.3.1)nonyl]pyridine (3) upon refluxing in ethanol with sodium ethoxide. The basicity and ^{13}C NMR characteristics of 3 are discussed in relation to other bisannelated pyridines studied by Thummel and Kohli.[3,4]

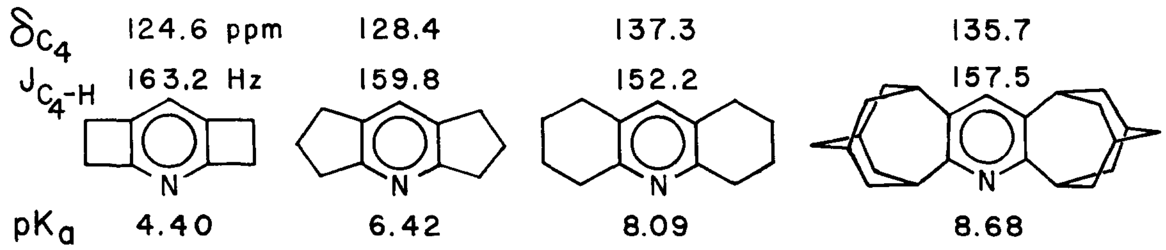


1 2 3

The conversion of 2 to 3 is apparently related to the formation of pyridines from pyrolyses of N,N,N-trimethylhydrazonium fluoborate derivatives of ketones.[5] However, pyrolysis of an iodide, namely acetophenone N,N,N-trimethylhydrazonium iodide gave only very low conversion to 2,6-diphenylpyridine,[5] and treatment with various bases led to non-pyridine products.[6-8] The formation of 3 was an unexpected result of our attempt to utilize the classic Neber rearrangement[9] enroute to an azirine derivative.[10]

In a typical preparation, 4-homoadamantanone was refluxed 5 h with excess 1,1-dimethylhydrazine in absolute EtOH. The dimethylhydrazone was isolated as a clear liquid in 78% yield, bp 120°C: IR 1620 cm^{-1} (C=N); ^1H NMR ($CDCl_3$, 60 MHz) 2.60-2.95 (m, 3H, $CH_2C(=N)CH$), 2.41 (s, 6H), 1.40-2.30 (m, 14H); mass spectrum, m/e 206. Treatment of the hydrazone with excess CH_3I at 25°C for 24 h gave 2 in 85% yield, mp 179-181°C (acetone-ether): ^1H NMR (DMSO, 60 MHz) 3.50 (s, 9H), 3.00-3.05 (m, 3H), 1.4-2.4 (m, 14H). Dry salt 2 (0.015 mole) was added to NaOEt (0.011 mole) in 30 mL absolute EtOH. After refluxing under anhydrous conditions for 4 h the solution was cooled, filtered to remove NaI and concentrated to 10 mL to yield 45% 3, mp 326-328°C: IR (KBr) 1565 cm^{-1}; UV ($CHCl_3$) 277 nm; ^1H NMR ($CDCl_3$, 60 MHz) 6.95 (s, 1H), 3.12 (m, 2H), 2.71 (m, 2H), 1.40-2.30 (m, 24H); ^1H NMR (CF_3COOH, 60 MHz, ext. TMS) 7.50 (s, 1H), 2.50-3.00 (br m, 4H), 1.30-2.10 (m, 24H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ_c 162.9 (C_2), 139.2 (C_3), 135.7 (C_4, J_{CH} 157.5 Hz), 43.1, 38.9, 36.2, 35.3, 34.0, 28.6; mass spectrum, m/e 319 (M^+, 100), 265 (33). Anal. ($C_{23}H_{29}N$). Calcd: C, 86.47; H, 9.15; N, 4.38. Found: C, 86.59; H, 9.06; N, 4.36.

Thummel noted a correlation between the C_4 carbon-hydrogen NMR coupling constant and pK_a values for 2,3,5,6-tetramethylpyridine and bisannelated pyridines containing fused five- and six-membered rings.[3] The quality of the correlation declines when [2,3;5,6]-dicyclobutapyridine is included, but the trends toward lower pK_a and higher J_{CH} values with decreased ring size are preserved.[4] An upfield shift of δ_c at C_4 with smaller ring size was also noted. All these trends were attributed to the effect of rehybridization of the neighboring bridgehead carbons as the ring size changes. Thummel's results for symmetrically bisannelated pyridines are shown below along with our J_{CH}, δ_c and pK_a values for 3. The pK_a for 3 was found by titration with $HClO_4$ in acetic acid with acetic anhydride as solvent, by the recommended procedure.[3]



If 3 is considered to have 7-membered rings (minimum size) fused to pyridine, it is evident that the trend toward increased basicity with increased ring size is still valid, but the NMR variables are not consistent with the previously noted trends. The high basicity of 3 cannot be attributed to increased steric bulk, because that effect would decrease the pK_a value.[11,12] More likely, the J_{CH} and δ_c differ from the expected values perhaps due to some influence of having the flanking alkyl C-H bonds coplanar with the C_4-H bond and pyridine ring rather than out-of-plane as in the methylene groups of the other bisannelated pyridines.

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1. This project was supported by Clarkson College funds and BRSG S07 RR07105-03 from the Biomedical Research Support Grant Program, National Institute of Health.
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