

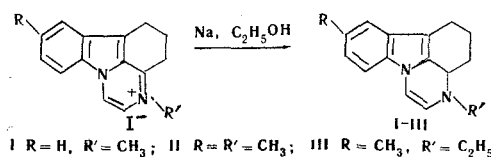
HETEROCYCLIC ENAMINES. DERIVATIVES OF 3a,4,5,6-TETRAHYDRO-3H-PYRAZINO[1,2,3-lm]CARBAZOLE

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Reduction of 5,6-dihydro-4H-pyrazino[1,2,3-lm]carbazole alkylidides with sodium in alcohol affords 3a,4,5,6-tetrahydro-3H-pyrazino[1,2,3-lm]carbazoles, which are heterocyclic enamines. Some reactions of these compounds are examined.

It has been shown previously that reduction of some 5,6-dihydro-4H-pyrazino[1,2,3-lm]carbazoles with sodium in alcohol affords 2,2,3a,4,5,6-hexahydro-1H-pyrazino[1,2,3-lm]carbazoles [1]. In continuation of work aimed at the synthesis of N-alkylhexahydropyrazino[1,2,3-lm]carbazoles, we have reduced 5,6-dihydro-4H-pyrazino[1,2,3-lm]carbazole alkylidides with sodium in alcohol. This reaction is found to proceed anomalously, in that only the C=N bond in the 3,3a position is reduced, giving 3-alkyl-3a,4,5,6-tetrahydro-3H-pyrazino[1,2,3-lm]carbazoles (I-III).



The position of the double bond in these compounds was shown by their PMR spectra (Fig. 1). The double bond protons H₁ and H₂ appear at 5.35 and 6.18 ppm (J = 6 Hz). The value of the constant shows that the hydrogen atoms are in the cis-configuration with respect to each other.

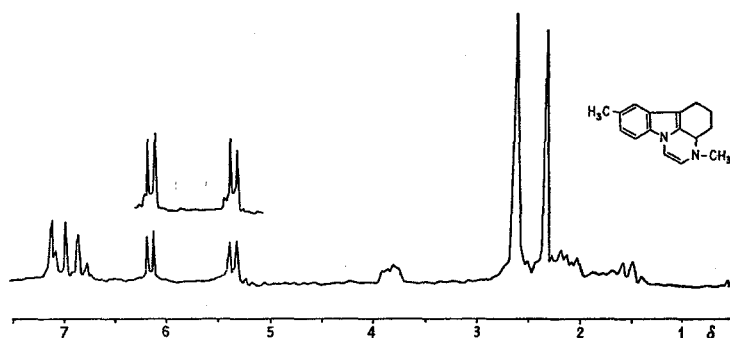


Fig. 1. PMR spectrum of 3,8-dimethyl-3a,4,5,6-tetrahydro-3H-pyrazino-[1,2,3-lm]carbazole (II).

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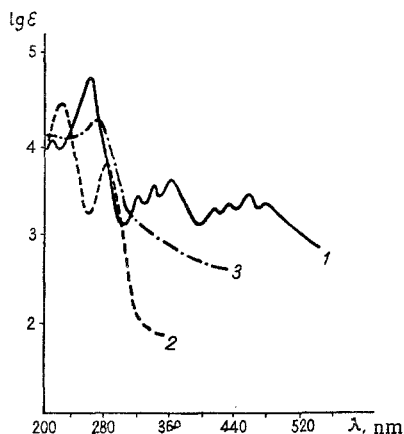
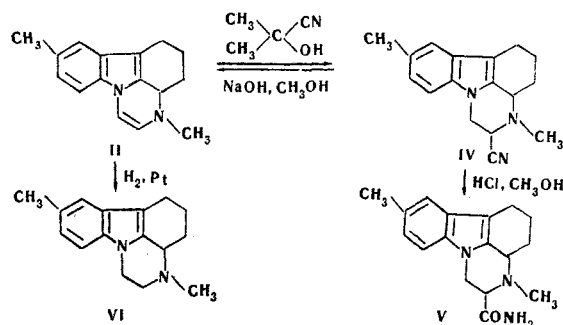


Fig. 2. UV spectra: 1) 5,6-dihydro-4H-pyrazino[1,2,3-lm]carbazole; 2) 2,3,3a,4,5,6-hexahydro-1H-pyrazino[1,2,3-lm]carbazole; 3) 3,8-dimethyl-3a,4,5,6-tetrahydro-3H-pyrazino[1,2,3-lm]carbazole (II).

The enamine structure of these compounds is also confirmed by their IR spectra in vaseline oil. A sharp, intense peak at 1655 cm^{-1} is observed, which is assigned to absorption of the $\text{CH}=\text{CH}$ bond. Similar absorption bands have been noted by a number of authors in the spectra of compounds with the enamine structure [2, 3]. Also, the single IR absorption band at 690 cm^{-1} is characteristic of out-of-plane deformational vibration of hydrogen atoms in cis-disubstituted ethylenes [4], indicating the cis configuration of the hydrogen atoms at the double bond of the pyrazine ring. The sharp band of medium intensity at 2800 cm^{-1} is due to stretching vibrations of the $\text{N}-\text{CH}_3$ group [5].

The UV spectra of 3-alkyl-3a,4,5,6-tetrahydro-3H-pyrazino[3,2,1-jk]-carbazoles differ substantially from those of 5,6-dihydro-4H-pyrazino[3,2,1-jk]carbazoles and 2,3,3a,4,5,6-hexahydro-1H-pyrazino[3,2,1-jk]carbazoles (Fig. 2).

The 3-alkyltetrahydropyrazinocarbazoles I-III are colorless, crystalline solids which are unstable in acid media, and on keeping in the light. The enamine structure of these compounds has been confirmed by a series of chemical conversions.



Treatment of II with acetone cyanohydrin results in addition of hydrogen cyanide to the double bond to form 3,8-dimethyl-2,3,3a,4,5,6-hexahydro-1H-pyrazino[3,2,1-jk]carbazole-2-carbonitrile (IV).

In order to determine the position of the cyano group in IV, the model compound VI was used. The PMR spectrum of VI (Fig. 3) shows strong splitting of the methylene proton signals on the 1-carbon atom. The chemical shifts of protons occupying the equatorial and axial positions at C_1 are 3.98 and 3.68 ppm, respectively, with a geminal spin-spin interaction constant of 12 Hz. The protons at C_1 interact with the methylene protons at C_2 with the constants: $J_{aa} = 12\text{ Hz}$, $J_{ae} = 5\text{ Hz}$, and $J_{ee} = 2\text{ Hz}$. The C_2 protons give signals near 3 ppm, which could not be analyzed as for the first series.

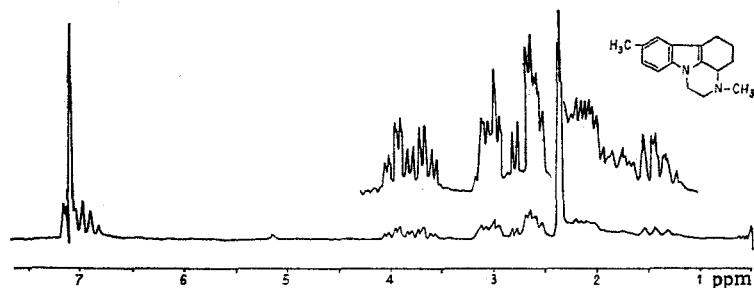


Fig. 3. The PMR spectrum of 3,8-dimethyl-2,3,3a,4,5,6-hexahydro-1H-pyrazino[1,2,3-lm]carbazole (VI).

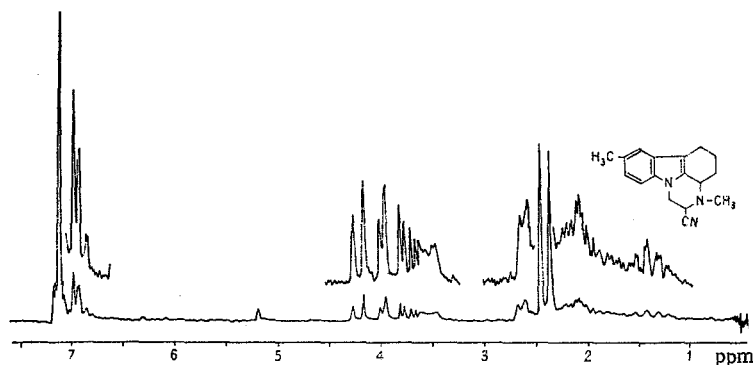


Fig. 4. PMR spectrum of 3,8-dimethyl-2,3,3a,4,5,6-hexahydro-1H-pyrazino[1,2,3-lm]carbazole-2-carbonitrile (IV).

The PMR spectrum of IV (Fig. 4) shows the C₁ methylene protons at 4.25 ppm (equatorial) and 3.78 ppm (axial). The signal from the equatorial proton is a doublet, with $J = 10$ Hz (geminal interaction), the components of which are somewhat split, with $J_1 = 2$ Hz. The signal from the axial proton is also a doublet, the components of which are split to a greater extent ($J_2 = 4$ Hz). The simpler mode of splitting of these protons indicates that one of the C₂ protons has been substituted by the cyano group. The spin-spin interaction constants ($J = 2$ Hz and $J = 4$ Hz) suggest that the proton at C₂ in IV occupies the equatorial position. The correctness of these suggestions is confirmed by the mode of splitting of the C₂ proton signal ($\delta = 4.03$). The signal is a doublet, with $J = 4$ Hz (axial-equatorial interaction), the components of which are split, with $J = 2$ Hz (equatorial-equatorial interaction).

Acid hydrolysis of the nitrile IV gives the amide V, while under alkaline conditions, the cyano group is removed to give the enamine II. The IR spectrum of V shows a carbonyl absorption band at 1680 cm⁻¹, and two bands with maxima at 3190 and 3350 cm⁻¹ which are assigned to amide NH₂ stretching vibrations. The spectrum preserves the band at 2800 cm⁻¹ (N-CH₃) which appears in the spectra of the enamines I-III.

As is also the case in the simplest enamines [6], 3,8-dimethyltetrahydropyrazinocarbazole (II), in contrast to 5,6-dihydro-4H-pyrazino[3,2,1-jk]carbazoles, is readily hydrogenated over a platinum catalyst at room temperature and atmospheric pressure to give 3,8-dimethyl-2,3,3a,4,5,6-hexahydro-1H-pyrazino[3,2,1-jk]carbazole (VI). As would be expected, the IR absorption due to stretching of the ethylene group at 1655 and 690 cm⁻¹ had disappeared in VI. The UV spectrum of VI was completely identical with that of 2,3,3a,4,5,6-hexahydro-1H-pyrazino[3,2,1-jk]carbazole.

EXPERIMENTAL

The PMR spectra were taken on a JEOL-4H-100 (100 MHz) instrument, in deuterochloroform, using tetramethylsilane as internal standard. The IR spectra were taken on a UR-10 instrument, as pastes in vaseline oil. The UV spectra were taken on an EPS-3 instrument, in alcoholic solution.

3-Methyl-3a,4,5,6-tetrahydro-3H-pyrazino[3,2,1-jk]carbazole (I). A suspension of 7 g (0.02 mole) of 5,6-dihydro-4H-pyrazino[3,2,1-jk]carbazole methiodide in 200 ml of absolute alcohol was placed in a three-necked flask fitted with an efficient stirrer and a Dimroth condenser. The mixture was heated to boiling, and 21.2 g (0.92 g-atom) of sodium was added in small portions over 5-10 min. The reaction mixture was boiled with stirring until all the sodium had reacted (15-20 min), then it was diluted with a three-fold volume of water, and the precipitate which separated was filtered off quickly and washed with water until the washings were neutral, to give 90% of I, mp 107-108°. Found: C 80.63, 80.37; H 7.26, 7.50; N 12.25, 12.50%. C₁₅H₁₆N₂. Calculated: C 80.32; H 7.19; N 12.49%.

Similarly were obtained 3,8-dimethyl-3a,4,5,6-tetrahydro-3H-pyrazino[3,2,1-jk]carbazole (II) (yield ~100%, mp 116-117°. Found: C 80.45, 80.33; H 7.43, 7.60; N 11.88, 12.16%. C₁₆H₁₈N₂. Calculated: C 80.63; H 7.61; N 11.75%), and 8-methyl-3-ethyl-3a,4,5,6-tetrahydro-3H-pyrazino[3,2,1-jk]carbazole (III) (yield 82%, mp 113-114°. Found: C 80.91, 80.46; H 7.80, 8.10; N 11.36, 11.34%. C₁₇H₂₀N₂. Calculated: C 80.91; H 7.98; N 11.11%).

3, 8-Dimethyl-2, 3, 3a, 4, 5, 6-hexahydro-1H-pyrazino[3, 2, 1-jk]carbazole-2-carbonitrile (IV). To a solution of 1.19 g (0.005 mole) of II and 0.5 g (0.005 mole) of triethylamine in 5 ml of chloroform was added 4.2 g (0.05 mole) of acetone cyanohydrin, and the mixture was boiled for 2 h. The mixture was cooled, poured into 20 ml of water, and neutralized to Congo with 6 N hydrochloric acid. The chloroform layer was separated, and the solvent was distilled off to give 1.2 g (92%) of IV, mp 183-184° (from methanol). Found: C 77.00, 76.70; H 7.18, 7.04; N 15.68, 15.72%. $C_{17}H_{19}N_3$. Calculated: C 76.95; H 7.21; N 15.83%.

3, 8-Dimethyl-2, 3, 3a, 4, 5, 6-hexahydro-1H-pyrazino[3, 2, 1-jk]carbazole-2-carbamide (V). In a three-necked flask, fitted with a stirrer and a gas inlet tube, was placed 1.4 g (0.005 mole) of the nitrile IV and 100 ml of methanol. Dry hydrogen chloride was passed into the suspension, the solid dissolving as the gas was introduced. The methanol solution was poured into water, neutralized with aqueous ammonia, and the precipitate which separated was filtered off to give 1.4 g (quantitative yield) of V, mp 228-229° (from methanol). Found: C 71.80; H 7.27; N 14.86%. $C_{17}H_{21}N_3O$. Calculated: C 72.05; H 7.47; N 14.82%.

Alkaline Hydrolysis of the Nitrile IV. A mixture of 1.4 g (0.005 mole) of IV, 5 ml of 25% aqueous sodium hydroxide, and 2 ml of ethanol was boiled for 5 h. The solution was poured into water, and the precipitate which separated was filtered off, giving 1.1 g (92%) of II, mp 116-117° (from methanol). The compound gave no depression of mp with the enamine II, obtained by reduction of 5, 6-dihydro-4H-pyrazino[3, 2, 1-jk]carbazole methiodide.

3, 8-Dimethyl-2, 3, 3a, 4, 5, 6-hexahydro-1H-pyrazino[3, 2, 1-jk]carbazole (VI). In a catalytic hydrogenation vessel was placed 4.8 g (0.02 mole) of II, 260 ml of ethanol, and Adams catalyst, obtained from 0.06 g of platinum oxide. Hydrogenation was carried out at room temperature and atmospheric pressure until the theoretical amount of hydrogen had been taken up (4 h). The catalyst was filtered off, and the solvent was removed to give 4.7 g (quantitative yield) of VI, mp 135-136° (from methanol). Found: C 79.65, 79.73; H 8.56, 8.42; N 11.62, 11.50%. $C_{16}H_{20}N_2$. Calculated: C 79.96; H 8.39; N 11.65%.

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