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PHOTODIMERIZATION OF N-BENZYL-1,4-DIHYDRONICOTINAMIDE

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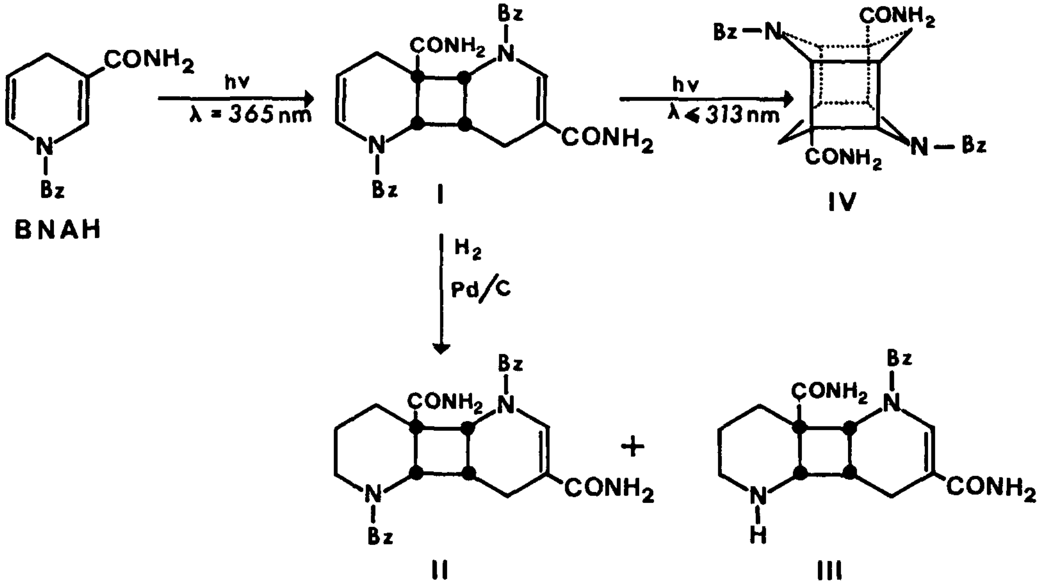
Summary: N-benzyl-1,4-dihydronicotinamide dimerized on irradiation with λ=365nm across 2,3 and 5,6 double bonds to give the product I which closed to centro-symmetric cage dimer IV on further irradiation with $\lambda \leq 313$nm.

The photochemistry of NADH and model compounds has been widely investigated focusing the attention on the reducing properties of these compounds. Besides a number of biological studies, the photoreduction of alkyl halides[1a-b],methylviologen[2], olefins[3], imines[4], phenacyl sulfonium salts[5], by different 1,4-dihydropyridines are reported. However, the knowledge of the behaviour in non-oxidising media could be of interest for a deeper understanding of the photochemistry of these compounds. As,to our knowledge, the 1,4-dihydronicotinamides have not yet been considered from this point of view[6], we undertook the investigation of the photoreactivity of N-benzyl-1,4-dihydronicotinamide (BNAH), a widely studied NADH model.

Irradiation of BNAH in anhydrous methanol (10 mg/ml) was carried out using a medium pressure Hg lamp, filtered with $CuSO_4$ solution in order to cut off wavelengths shorter than 340 nm. Purified N_2 was bubbled through the solution during the irradiation. UV absorption of the solution showed the decrease of the 355 nm peak (BNAH) and the rising of a new peak at 295 nm. The reaction was stopped after the disappearance of the starting material.

Concentration of the irradiated solution afforded a colourless product I which was crystallized from anhydrous methanol (25-30% yield, m.p. 230-235° dec). I slowly decomposed in the solid state, faster in solution. UV spectrum of this compound showed λ_{max}=295 nm (logε =4.31), similar to the absorption spectrum of N-benzyl-1,4,5,6-tetrahydronicotinamide, suggesting a saturation of the 5,6 double bond. Estimated size of the molecule by Gel Permeation Chromatography was



in agreement with a dimeric structure. In the NMR spectrum of I[7] were present signals of two benzylic groups (δ=7.34, δ=7.31 and δ=4.34, δ=4.19) and singlet at δ=7.52 and doublet at δ=6.43 indicating the presence of 2,3 and 5,6 double bonds.

Catalytic hydrogenation of I on Pd/C gave the products II (m.p.211-214°) and III (m.p. 136-138°). The NMR spectra[7] demonstrated for both compounds the presence of 2,3 double bond (δ=7.70 for II and δ=7.55 for III) and the saturation of 5,6 double bond (lack of the doublet near δ=6.4). NMR spectrum of III showed the loss of a benzylic group. Comparison between the chemical shifts of the benzylic protons of III (δ=4.46) with those of II δ=4.53 and δ =3.83) indicated the loss of a benzylic moiety from the saturated ring. III was also obtained by further catalytic hydrogenation of II.

Compound I was irradiated in methanol with unfiltered light of a medium pressure Hg lamp. The irradiated solution gave on concentration a crystalline product IV (40% yield, m.p. 255-258° dec). IV in low yield (15%) was also obtained by direct irradiation of BNAH in methanol with unfiltered light.

Crystals of IV suitable for X-Ray analysis were obtained by slow diffusion of water into a DMSO solution of IV. Diffractometric data[8] demonstrated the centrosymmetric cage structure of IV (fig.1). Consequently the configuration of I is established.

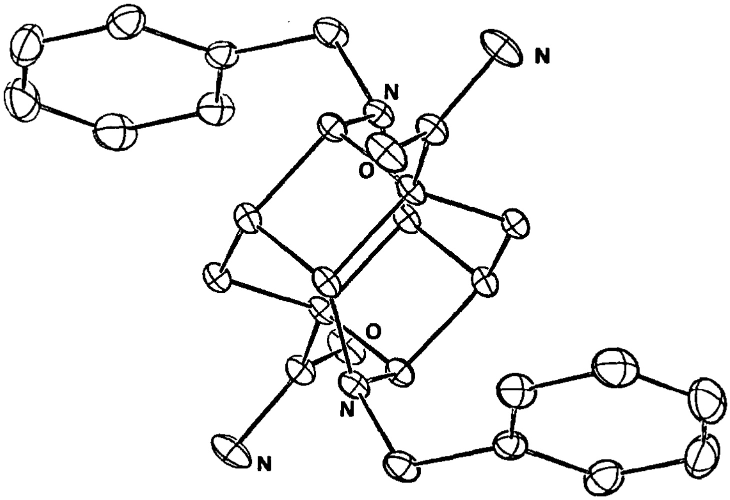


Figure 1 . ORTEP drawing of the dimer IV with 20% probability thermal ellipsoids.

The photodimerization of BNAH showed an high degree of regioselectivity. In fact, quantitative chromatographic analysis (HPLC) of a solution of BNAH after 2 hrs of irradiation, estimated I to constitute about 47% of the reacted material (25%). The chromatograms showed three other main peaks whose nature is under investigation.

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References and Notes

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6) Dissertation of R.H.Reuss (Diss.Abstr.Int. B 1972,33(5), 2002) referred to the irradiation of BNAH. However, no products were isolated.

7) ^{1}H-NMR (60 MHz) (DMSO-d_6) δ ppm (J in Hz) from internal TMS: (I) 1.80-2.50 (br m, 5H), 3.52 (br d, J=6.0, 1H), 3.82 (br d, J=8.0, 1H), 4.19, 4.34 (2s and overlapping m, 5H), 5.60 (exch. br, 1H), 6.28 (exch. br, 2H), 6.43 (d, J=7.8, 1H), 6.90 (exch. br, 1H), 7.31, 7.34 (2s, 10H), 7.52 (s, 1H); (II) 1.75-3.65 (br m, 11H), 3.83 (s, 2H), 4.53 (AB system, J=15.2, 2H), 5.11 (exch. s, 2H), 5.80 (exch. br d, 2H); 7.27, 7.30 (2s, 10H), 7.70 (s, 1H); (III) 1.75-3.70 (br m, 12H), 4.46 (s, 2H); 6.32, 7.09 (exch. 2s, 4H), 7.31 (s, 5H), 7.55 (s, 1H); (IV) 2.21 (m, 2H), 2.82 (m, 1H), 3.37 (d, J=9.1, 2H), 3.92 (s, 2H), 6.80 (exch. br, 2H), 7.24 (s, 5H).

8) Crystal Data: $C_{26}H_{28}N_4O_2$, M=428.52, Asymmetric unit $C_{13}H_{14}N_2O$, orthorhombic space group Pbca, a=17.780(6), b=14.424(5), c=8.213(4) Å, U=2106(3) Å^3, F(000)=114, Z=8, $\bar{\lambda}$=1.5418 Å (Cu-Kα graphite monochromated), $\mu_{\text{Cu-K}\alpha}$ = 7.05 cm^{-1}, 1538 reflections having $I \geq 2.5\ \sigma(I)$ were collected on a Siemens single crystal diffractometer. The structure was solved by direct methods using the SHELX76 program system[9], and refined to a current residual R= 0.054 by full matrix least-squares with anisotropic thermal parameters for non hydrogen atoms. All hydrogen atoms were located from difference Fourier synthesis and refined with a common thermal parameter. Atomic coordinates are available on request from the Directory of the Cambridge Crystallographic Data Centre.

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