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REDUCTION BY A MODEL OF NAD(P)H. XXVI. REDUCTION OF C=C BOND IN 1,3,5-TRINITROBENZENE

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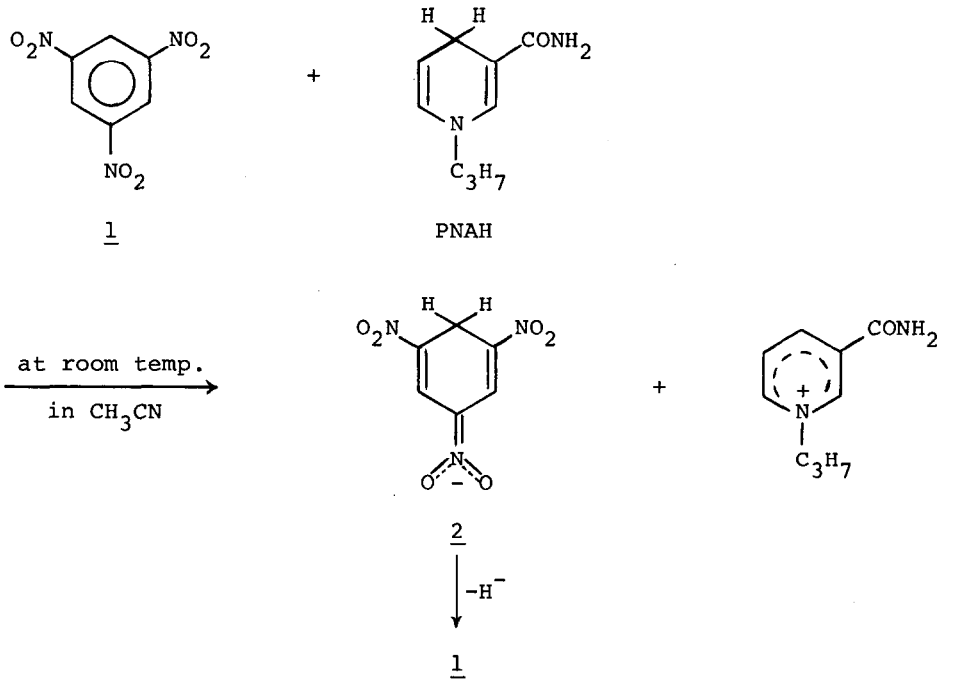
Summary: A model of NAD(P)H reduces the aromatic ring in 1,3,5-trinitrobenzene. Kinetic isotope effects for the reduction and re-oxidation of the product have been studied.

It is known that 1,4-dihydropyridine derivatives, models for NAD(P)H, reduce a variety of functional groups such as carbonyl and thiocarbonyl groups, olefinic double bonds, imines, ammonium and sulfonium salts, inorganic ions, and so on.[1] Oxygenated nitrogen functions have also been subjected to the reduction. Namely, nitrobenzene is reduced to aniline, phenylhydroxylamine, and hydrazobenzene at elevated temperatures.[2]

In this communication, we wish to report a new-type reduction of electron-deficient aromatic compounds by 1-propyl-1,4-dihydronicotinamide (PNAH). When 1,3,5-trinitrobenzene (1) was reacted with an equivalent amount of PNAH in dry acetonitrile at a room temperature under an atmosphere of argon in the dark, the reaction mixture turned red and PNAH was oxidized to 1-propyl-3-carbamoylpyridinium (PNA^+) quantitatively, whereas 1 was recovered quantitatively after the work-up. The UV-visible spectrum of the reaction mixture showed new absorptions with maxima at 482 and 590 nm. The increase in the intensities of the new absorptions corresponded to the decrease in the intensity of original absorption (λ_{max} = 345 nm, PNAH) with an isosbestic point at 390 nm (Figure 1). When the reaction mixture in deuterated acetonitrile was monitored on an NMR spectrometer, the original singlet at δ^{TMS} 9.30 (3H) disappeared completely and new singlets at δ^{TMS} 8.30 (2H) and 3.85 (2H) were recognized. The reduction of 1 was also carried out with PNAH-4-*d* and mass spectral analysis of the recovered 1 confirmed

that 11.4% excess deuterium was incorporated into 1 during the reaction.

The above results clearly indicate that the aromatic ring, instead of a nitro group, in 1 is reduced by PNAH quite easily, but an intermediate anion, 2, is re-oxidized to 1 during the work-up. The reduction was retarded by the presence of magnesium perchlorate.



1 PNAH

2

1

3,5-Dinitro-α,α,α-trifluoroacetophenone behaved similarly, but the reactivity of this compound was much less than that of 1.

Kinetics for the reduction of 1 at 50.0 ± 0.05°C was followed spectrophotometrically by observing the increase in the intensities at 482 and 590 nm. As summarized in Table 1, the reduction was first-order in 1 and in PNAH. From the second-order rate constants, k_2, the kinetic deuterium isotope effect, k_2^H/k_2^D, was calculated to be 7.02 ± 0.02.[3] On the other hand, the kinetic deuterium isotope effect for the oxidation of 2, k_{ox}^H/k_{ox}^D, can be calculated by Eq. 1.

$$\frac{k_{ox}^H}{k_{ox}^D} = \frac{(k_2^H/k_2^D) + 1}{(Y^H/Y^D) - (k_2^H/k_2^D)} \qquad (1)$$

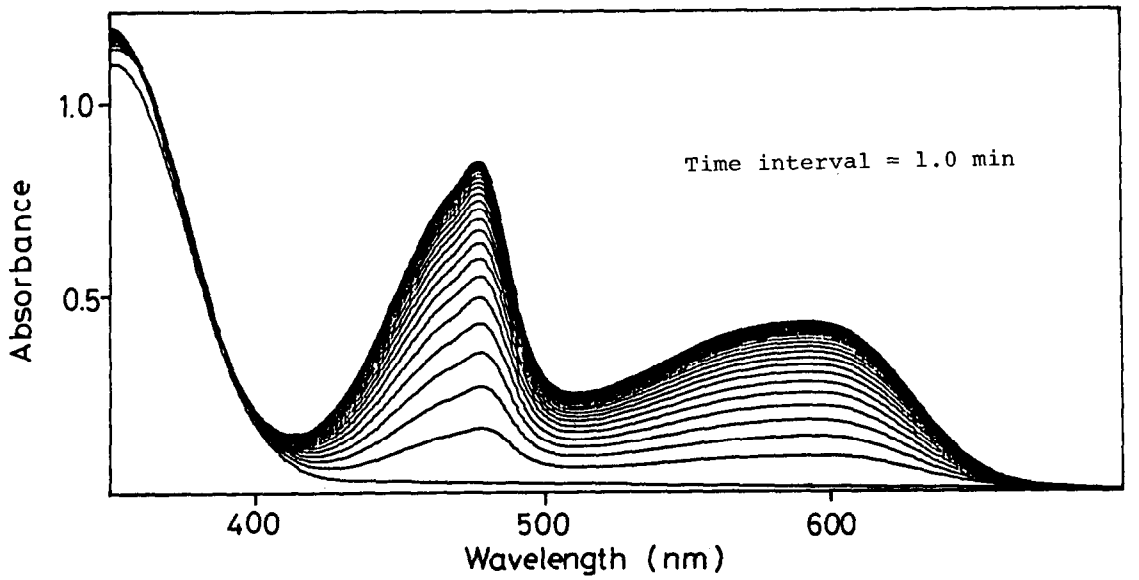
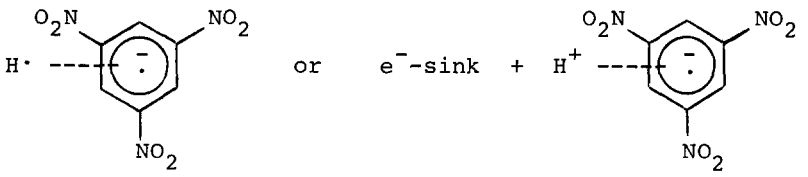


Figure 1. UV-visible spectra of a mixture of PNAH and 1,3,5-trinitrobenzene, 1, in acetonitrile at 50°C; [PNAH] = 3.58 x 10^{-5} *M*, [1] = 8.15 x 10^{-3} *M*

Table 1. Kinetics for the Reduction of 1,3,5-Trinitrobenzene, 1, at 50°C

Model	10^5[Model], *M*	10^2[1], *M*	10^2[Mg^{++}], *M*	$10k_{obsd}$, min^{-1}	k_2, $M^{-1}min^{-1}$	
PNAH	2.51	0.516	0	0.9155	17.89	
PNAH	2.51	0.759	0	1.309	17.24	
PNAH	2.51	1.012	0	1.798	17.77	17.70
PNAH	2.51	1.495	0	2.690	17.99	± 0.310
PNAH	2.51	2.006	0	3.474	17.32	
PNAH	2.55	2.508	0	4.584	18.01	
PNAH	2.55	0.997	1.051	0.1618	1.623	1.624
PNAH	2.55	0.748	1.029	0.1625	1.625	± 0.001
PNAH-4-*d*	2.51	0.759	0	0.7691	10.13	
PNAH-4-*d*	2.51	1.012	0	1.011	9.987	
PNAH-4-*d*	2.51	1.495	0	1.527	10.21	10.11 ± 0.187
PNAH-4-*d*	2.51	2.006	0	1.973	9.385	
PNAH-4-*d*	2.51	2.508	0	2.603	10.38	

, where Y^H/Y^D is the ratio of contents of protiated and deuterated molecules in the recovered 1. Since Y^H/Y^D = 7.8 from the mass spectral data, k^H_{ox}/k^D_{ox} was calculated to be 10. Thus, both the reduction of 1 and oxidation of 2 are associated by extraordinally large kinetic isotope effects.[4,5] This fact seems to suggest that the "hydride" undergoing the migration is relatively free at the transition states. Since free hydride is not expected to be stable, the system of *free* hydride and trinitrobenzene should be stabilized by a charge-transfer type interaction.



In other words, the "hydride" may be better represented by a hydrogen atom or a proton. This conclusion agrees with the previously proposed mechanism for the reduction by an NAD(P)H-model; the oxidation of a 1,4-dihydropyridine ring proceeds through simultaneous electron-proton-electron transfer processes.[6]

Finally, we would like to emphasize that this is the first report on the reduction of an unsubstituted position of a benzene-ring by an NAD(P)H-model.[7]

References and Notes

1. For a recent review, see R. J. Kill and D. A. Widdowson, in "The Redox Chemistry of 1,4-Dihydronicotinic Acid Derivatives," in "Bioorganic Chemistry," Vol. IV, E. E. van Tamelen, Ed., Academic Press, New York, N. Y., 1978, pp 239 - 275.

2. D. C. Dittmer and J. M. Kolyer, *J. Org. Chem.*, 27, 56 (1962).

3. J. J. Steffens and D. M. Chipman, *J. Am. Chem. Soc.*, 93, 6694 (1971).

4. The largest value for k^H_2/k^D_2 so far reported for the reduction by an NAD(P)H model is 5.0 (thiopivalophenone as a substrate); A. Ohno, S. Yasui, K. Nakamura, and S. Oka, *Bull. Chem. Soc. Jpn.*, 51, 290 (1978).

5. The value of 6.67 has been reported for the deprotonation from a protonated aromatic cation; H. Zollinger, *Helv. Chim. Acta*, 38, 1617 (1955).

6. (a) A. Ohno and N. Kito, *Chem. Lett.*, 1972, 369; (b) T. Okamoto, A. Ohno, and S. Oka, *J. Chem. Soc., Chem. Commun.*, 1977, 181; (c) A. Ohno, T. Kimura, H. Yamamoto, S. G. Kim, S. Oka, and Y. Ohnishi, *Bull. Chem. Soc. Jpn.*, 50, 1535 (1977).

7. For *ipso*-substitution, see L. C. Kurz and C. Frieden, *Biochem.*, 16, 5207 (1977) and references cited therein.

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