helpful discussion. We are indebted to Mr. Guênot (Université de Rennes, France) for high-resolution mass spectra.

Registry No. **1a**, 506-32-1; **1b**, 2566-89-4; **2**, 117203-40-4; **3a**, 66-25-1; **3b**, 31823-43-5; **3c**, 13553-09-8; **3d**, 13552-98-2; **4**, 117203-37-9; **5**, 117203-38-0; **6**, 117203-39-1; (carboxybutyl)triphenylphosphonium bromide, 17814-85-6; (*E,Z*)-2,6-dodecadienal, 21662-13-5.

Reduction of Aryl-Nitroso Compounds by 1,4-Dihydronicotinamides

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Nitroso compounds are of considerable current interest since their similarities to aldehydes are well established. The aryl–nitroso group is isosteric and isoelectronic with the aromatic aldehyde group,[1] but much more reactive.[2] In view of using the aryl–nitroso group as an analogue of NADH-dependent reduction of carbonyl compounds in enzymatic and in model systems, we have investigated the mechanism of reduction of aryl–nitroso compounds by NADH and N_1-(2,6-dichlorobenzyl)-1,4-dihydronicotinamide (DBDN-4H_2) in model systems. For this purpose, we have distinguished two types of aryl–nitroso compounds: unsubstituted (representative: nitrosobenzene) and ring substituted inthe ortho or para positions by OH, NH_2, NHR, NR_2, and similar functional groups providing a keto–enol tautomerism (representative: 1-nitroso-2-naphthol).

Nitrosobenzene and 1-nitroso-2-naphthol were readily reduced by NADH and DBDN-4H_2 in the absence of oxygen, in neutral and weakly alkaline aqueous buffers and in dry methanol; the stoichiometry with NADH was

$$\mathrm{ArNO} + \mathrm{NADH} + \mathrm{H^+} \rightarrow \mathrm{ArNHOH} + \mathrm{NAD^+} \quad (1)$$

$$\mathrm{HOArNO} + 2\ \mathrm{NADH} + 2\ \mathrm{H^+} \rightarrow \mathrm{HOArNH_2} + 2\ \mathrm{NAD^+} + \mathrm{H_2O} \quad (2)$$

Under the pseudo-first-order conditions ([nitroso compounds] = (0.5–2) × 10^{-4} M; [NADH] = 2 × 10^{-3} M) in a buffer of pH 7.5, the disappearance of the nitroso group was found to follow the first-order rate law for at least 3 half-times; also, at pH 7.5, reactions 1 and 2 were found to be second order overall.

The product identification of reactions 1 and 2 was performed kinetically and analytically. Both reactions strictly obeyed the stoichiometry kinetically (eq 1, 2). Under the second-order rate conditions ([nitroso compounds] = (0.75–1.5) × 10^{-4} M; [NADH] = 1.5 × 10^{-4} M) at pH 7.5, NAD^+ was identified analytically as the sole product of NADH oxidation, appearing in the product proportionally to the disappearance of nitroso groups according to the stoichiometry (eq 1, 2). In addition, the product of reaction 2, 1-amino-2-naphthol, after acetylation with acetic anhydride was shown to be identical by TLC to an acetylated authentic sample of 1-amino-2-naphthol.

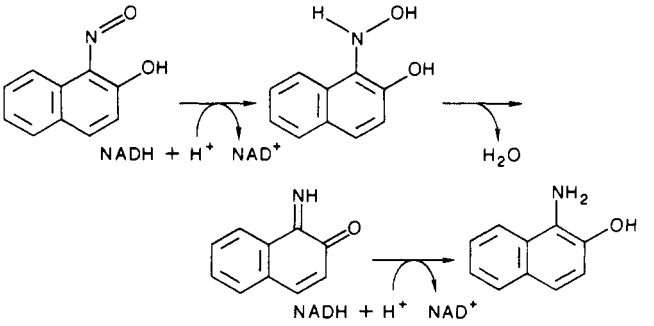
The phenolic group of 1-nitroso-2-naphthol was characterized by a pK of 8.2, which was estimated from the disappearance, in acid, of the alkaline maximum (415 nm) in the absorption spectra (maximum at 380 nm remained pH-unshifted). The change of the alkaline maximum at 415 nm was directly proportional to the pH dependence of the rate constant for the reduction of 1-nitroso-2-naphthol by NADH, with minimal rates in alkali; this indicated that only the phenol form of 1-nitroso-2-naphthol was reduced with NADH and the phenolate form was completely unreactive. Taken together, the above data and the data on the electrochemical reduction of para- and ortho-substituted aryl–nitroso compounds[3,4] supported the following mechanism of reaction 2:

Table I. Second-Order Rate Constants (k_2) for the Reduction of Nitroso Compounds with 1,4-Dihydronicotinamides[a]

	NADH		DBDN-4H_2	
k_2, M^{-1} min^{-1}	buffer[b]	methanol[c]	buffer	methanol
nitrosobenzene	11.350	50	$>10^5$	280
1-nitroso-2-naphthol	95	<1	925	<1

[a] [Nitroso compounds] = (5–8) × 10^{-5} M; [1,4-dihydronicotinamides] = (1–2) × 10^{-4} M; 30 °C, anaerobic conditions. [b] Sodium phosphate buffer, 0.1 M, pH 7.5. [c] Dry methanol.

Scheme I



The above mechanism was supported by the stoichiometry of reaction (NADH:oxidant = 2:1), which was observed for at least 2 half-times ([1-nitroso-2-naphthol] = 7 × 10^{-5} M; [NADH] = 1.6 × 10^{-4} M; pH 7.5 at 30 °C). Since the radical mechanism was excluded (see below), the first redox reaction of Scheme I must be regarded as rate-limiting for the overall process.

The rate constants of reactions 1 and 2 and related reactions were estimated by employing the second-order rate conditions (Table I).

Since both types of nitroso compounds were initially reduced to hydroxylamines, the primary kinetic hydrogen isotope effect of this redox reaction was measured in the temperature range 16.0–45.8 °C (Table II).

The kinetic data of Table II fitted the following Arrhenius equations:

$$\ln k_{HD} = (16.21 \pm 0.01) - (28.05 \pm 0.54\ \mathrm{kJ/mol})/RT \quad (3)$$

$$r = 0.999$$

$$\ln k_{HH} = (16.81 \pm 0.01) - (28.17 \pm 1.04\ \mathrm{kJ/mol})/RT \quad (4)$$

$$r = 0.994$$

From eq 3 and 4, the difference in activation energies ($[E_a]^{HH}_{HD}$) and, after a correction for the isotopic impurity

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0022-3263/88/1953-6123$01.50/0

Table II. Temperature-Dependent Kinetic Isotope Effect (TDKIE) for the Reduction of Nitrosobenzene by DBDN[a]

temp, K	289.0	292.4	297.6	301.5	307.6	313.0	318.1
k_{HD}[b]	93.7	111.0	131.6	148.4	188.7	232.7	275.9
temp, K	289.0	292.4	297.6	302.0	307.8	313.2	318.8
k_{HH}[b]	160.8	184.9	239.8	287.1	347.2	391.5	497.7

[a] [Nitrosobenzene] = 1.24×10^{-3} M; [DBDN-4H_2] and [DBDN-4H,4D] = 1.48×10^{-4} M in dry methanol, anaerobic conditions. [b] Rate constants in M^{-1} min^{-1}.

of DBDN-4H, 4D,[5] the ratio of frequency factors (A_{HH}/A_{DD}) for hydride vs deuterium transfer were calculated:

$$E_a^{HH} - E_a^{HD} = 0.1 \pm 1.6 \text{ kJ/mol}$$

$$A_{HH}/A_{DD} = 9.5 \pm 2.2$$

A large kinetic isotope effect (KIE) indicated that reactions 1 and 2 occurred by a direct hydride transfer from the C4 atom of the dihydronicotinamide ring to the nitroso nitrogen of the substrate[6] and excluded the radical mechanism in Scheme I.

The estimation of ΔE_a and A_{HH}/A_{DD} is sensitive to the secondary KIE and to the isotopic impurity of DBDN-4H,4D;[7-10] the estimation of the primary KIE at different temperatures helps to minimize the random errors but does little to eliminate the systematic errors. Therefore, although the data reflect a substantial primary KIE around room temperature, the sources of inaccuracy in its estimation remain the secondary KIE and the isotopic impurity of DBDN-4H,4D.

Experimental Section

Care has been taken to obtain NADH and NAD^+ of the highest commercial purity. N_1-(2,6-Dichlorobenzyl)nicotinamide bromide was synthesized according to Kröhnke and Ellegast.[11] N_1-(2,6-Dichlorobenzyl)-1,4-dihydronicotinamide was synthesized according to the method of Wallenfels et al.[12] DBDN-4H,4D was synthesized in an analogous manner in D_2O (99.8%); care was taken to recrystallize the product several times to maximize its purity.

Absorption spectra and kinetic measurements were taken in a SPECORD UV-Vis spectrophotometer (Carl Zeiss, Jena, Federal Republic of Germany), in the thermostated cuvettes (±0.1 °C). Anaerobic conditions were obtained essentially as described by Wallenfels and Gerlach.[13] The concentrations of reactants were calculated from their absorption spectra: NADH, ϵ_{340nm} = 6200 cm^2/mol; nitrosobenzene, ϵ_{305nm} = 9570 cm^2/mol; 1-nitroso-2-naphthol, ϵ_{380nm} = 6970 cm^2/mol; all in 0.1 M sodium phosphate buffer, pH 7.5; DBDN-4H_2, ϵ_{357nm} = 7255 cm^2/mol in dry methanol. Concentrations of NAD^+ were estimated analytically as previously described.[14] In measuring the TDKIE (Table II), we took extreme care to bring the reactants to the desired temperature before the reaction and to start the reactions with very small aliquots of nitrosobenzene; reactions were performed anaerobically, as rapidly as possible (10 min), in order to minimize the influence of oxygen[2] and hydrolytic reactions[15] and the photodecomposition of reactants. Repetitive scanning of the absorption spectra (250-800 nm) indicated the photostability of reactants. The secondary KIE was assumed to be equal to unity.[7]

Registry No. NADH, 58-68-4; DBDN-4H_2, 13502-54-0; nitrosobenzene, 586-96-9; 1-nitroso-2-naphthol, 131-91-9; deuterium, 7782-39-0.

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Mild Oxidative Cleavage of Alkynes Using [Bis(trifluoroacetoxy)iodo]pentafluorobenzene

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Hypervalent iodine reagents react with alkynes to give various products depending upon the type of reagent and the reaction conditions, e.g., (i) [hydroxy(tosyloxy)iodo]-benzene reacts with terminal alkynes in chloroform to yield alkynyliodonium tosylates,[1] which are important synthetic intermediates,[2,3] (ii) reaction of [hydroxy(tosyloxy)iodo]-benzene with terminal and internal alkynes in methanol proceeds with oxidative rearrangement resulting in the formation of carboxylic acid esters,[4] (iii) reaction of [(perfluoroalkyl)phenyl]iodonium salts with terminal alkynes yields a mixture of substitution and addition products,[5] (iv) internal alkynes are converted to α-diketones by oxidation with iodosobenzene in the presence of ruthenium(II) catalyst, while terminal alkynes afford carboxylic acids,[6] and (v) [bis(trifluoroacetoxy)iodo]benzene reacts with internal alkynes to give α-diketones;[7] with terminal alkynes, α-hydroxy ketones are obtained.[7,8] Other methods for the oxidation of alkynes to dicarbonyl compounds using metal-based reagents include OsO_4,[9] $KMnO_4$,[10] RuO_4,[11] or $Tl(NO_3)_3$.[12] Ozone also yields di-

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