3 H, OCH_3)), 7.2-8.34 (m, 9 H, Ar H); mass spectra, m/e (M^+) 418.2872, found 418.2862.

Methyl 16-Hydroxyhexadecanoate (14). A solution of dihydroambrettolide (**13**, Columbia, 5.0 g, 19.685 mmol) and *p*-toluenesulfonic acid (PTSA, 1.0 g) in methanol (250 mL) was heated at reflux under N_2 for 18 H. The solution was concentrated to 75 mL, poured into cold H_2O (100 mL), and extracted with ether (3 × 75 mL). The organic layer was washed with 10% aqueous $NaHCO_3$ (2 × 75 mL) and dried ($MgSO_4$). Removal of the solvent left a waxy white solid. Recrystallization (petroleum ether) gave 4.8 g (85.3%) of **14** as a flaky white solid: mp 56-57 °C; IR (melt) 2900-3600 (OH), 1740 cm^{-1} (C=O); ^{13}C NMR ($DCCl_3$) ppm 174.1 (C(1)), 62.8 (C(16)), 52.3 (C(α)), 34.1 (C(2)), 32.8, 29.6, 29.4, 29.2, 29.1, 25.8, 24.9 (C(3)).

Methyl 16-Oxohexadecanoate (3c). Chromium trioxide (6.3 g, 63.0 mmol) wsa added under N_2 to a stirred solution of pyridine (9.9 g, 125.3 mmol) in HC_2Cl_2 (150 mL). After 20 min, a solution of alcohol **14** (3.0 g, 10.489 mmol) in HC_2Cl_2 (20 mL) was added in one portion. After an additional 20 min, the solution was decanted, and the tarry residue was washed with ether (2 × 75 mL). The combined organic solutions were washed successively with 5% aqueous NaOH (4 × 100 mL), 5% aqueous HCl (2 × 100 mL), saturated aqueous $NaHCO_3$ (2 × 100 mL), and saturated aqueous NaCl (150 mL). After drying ($MgSO_4$), the solvent was evaporated to give 2.5 g (83.9%) of crude **3c** as a white solid. This solid was used in subsequent reactions without further purification: mp 67-69 °C; IR (melt) 1720-1740 cm^{-1} (C=O); ^{13}C NMR ($DCCl_3$) ppm 202.4 (C(16)), 173.9 (C(1)), 51.2 (C(α)), 43.7 (C(15)), 34.0 (C(2)), 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 24.8 (C(3)), 22.0 (C(14)).

Methyl 17-(2-Anthryl)-16-heptadecenoate (4c). A solution of the phosphonium salt **2** (2.0 g, 3.753 mmol) in dry Me_2SO (75 mL) was added rapidly under N_2 to a stirred mineral oil dispersion of NaH (50%, 0.2 g, 4.167 mmol). After 10 min, a solution of the crude aldehyde **3c** (1.9 g, 6.69 mmol) in dry ether (50 mL) was added to the blood-red solution. After being stirred for 30 h at room temperature, the mixture was diluted with H_2O (100 mL) and acidified (litmus) with concentrated HCl. The mixture was filtered (vacuum) to give a yellow powder. The filtrate was extracted with $HCCl_3$ (3 × 50 mL). The organic layers were combined and dried (Na_2SO_4). Removal of the solvent left a yellow semisolid. The combined solids were digested in 95% ethanol (40 mL) and air-dried in the dark to give 1.4 g (81.4%) of **4c** as a yellow powder: mp 110 to >250 °C; ^1H NMR ($DCCl_3$) δ 1.1-1.75 (m, 24 H, $(CH_2)12$), 2.17-2.6 (m, 4 H, CH=CHCH_2, C$H_2CO_2CH_3$), 3.65 (s, 3 H, OCH_3), 6.55-6.8 (m, 1 H, ArCH=C*H*, trans), 7.45-8.6 (m, 10 H, Ar H, ArC*H*=CH, trans). A lesser amount of the cis iosomer was present as indicated by the ^1H NMR signals at δ 5.85-6.2 (m, ArCH=C*H*, cis) and 6.8-6.9 (m, ArC*H*=CH, cis). The wide melting point range is probably due to the cis-trans mixture.

Methyl 17-(2-Anthryl)heptadecanoate (1c). A warm solution of **4c** (0.5 g, 1.092 mmol) in ethyl acetate (175 mL) was hydrogenated at atmospheric pressure in the presence of 10% Pd/C (0.1 g) for 4 h. Addition of diatomaceous earth, vacuum filtration, and evaporation of the solvent gave an off-white powder. The solid was recrystallized twice (95% ethanol) and subjected twice to molecular distillation (140 °C (5 × 10^{-4} mm)) to give 0.4 g (80%) of **1c** as a white powder: mp 104.5-105.5 °C; ^1H NMR ($DCCl_3$) δ 1.2-1.85 (m, 28 H, $(CH_2)_{14}$), 2.29 (t, 2 H, C$H_2CO_2CH_3$), 2.79 (t, 2 H, ArCH_2), 3.65 (s, 3 H, OCH_3), 7.2-8.34 (m, 9 H, Ar H); mass spectra m/e (M^+) 460.3341, found, 460.3349.

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Registry No. **1a**, 88229-60-1; **1b**, 88229-61-2; **1c**, 88229-62-3; **2**, 88229-63-4; **3a**, 1931-65-3; **3b**, 1608-77-1; **3c**, 45247-78-7; **4a**, 88229-64-5; **4b**, 88229-65-6; **4c**, 88229-66-7; **6**, 22863-82-7; **7**, 31124-71-7; **9**, 6287-90-7; **10**, 4195-89-5; **11**, 88229-67-8; **12**, 7147-29-7; **13**, 109-29-5; **14**, 36575-67-4; **15a**, 75802-32-3; **15b**, 75802-33-4; **15c**, 75802-34-5; triphenylphosphine, 603-35-0; lithium 11-bromoundecoxide, 88229-68-9; 11-bromoundecanol, 1611-56-9.

Reduction by a Model of NAD(P)H. 45. Mechanism for the Dediazoniation of Arenediazonium Salts Initiated by One-Electron Transfer from an NAD(P)H Model

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Arenediazonium fluoroborates, ArN_2BF_4 (**1a**, Ar = *p*-$CH_3C_6H_4$; **1b**, Ar = *p*-BrC_6H_4; **1c**, Ar = *p*-$NO_2C_6H_4$) react with an NAD(P)H model, *N*-benzyl-1,4-dihydronicotinamide (BNAH), in methanol, giving the corresponding reduction products ArH (**2**). The stoichiometry for the starting materials and reduction products clearly indicates that this reduction involves a radical-chain path initiated by BNAH. The mechanism is supported by the effect of spin-trapping agents on the yields of the products. From the results from experiments with methanol-d_4, we have found that under a nitrogen atmosphere, the radical chain is more favorable in the order **1a** < **1b** < **1c**, which is the same as the order in the thermal dediazoniation of **1** in acidic methanol. The results presented here provide direct evidence for a one-electron transfer mechanism for reduction with an NAD(P)H model.

Within the last three decades, many reports on the mechanism for reduction with an NAD(P)H model have been presented.[1-13] An exciting contradiction concerns the process of net "hydride-ion" transfer from a model to a substrate in the course of the reduction.[6-13] Results based on kinetics[10,11] and product analyses[13] have demonstrated that the reduction proceeds via one-electorn transfer followed by a proton (or a hydrogen atom) transfer. Nevertheless, evidence supporting a one-step hydride-transfer mechanism is not negligible. For example, it has been

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found that the reduction of certain cyclopropane derivatives by an NAD(P)H model occurred without ring-opening, whereas they were reduced by a one-electron donor, affording open-chain products.[14,15] It was claimed that these findings are compatible only with a direct hydride-ion transfer mechanism for reduction with an NAD(P)H model. This claim, however, is not necessarily the case, because the anion radical species generated may be trapped rapidly by a proton (or a hydrogen atom) from the cation radical of the model within a cage of solvent. Thus, decisive evidence in support of either mechanism is lacking.

We believe that the situation is quite similar to that in solvolyses. That is, in solvolytic reactions, there are two extreme mechanisms, unimolecular and bimolecular. Yet most substrates are thought to undergo solvolysis with a mechanism between these two extremes, even though they may be unimolecular- or bimolecular-type substrates.

Focusing on the problem of reduction with an NAD(P)H model, we propose that a reduction whose mechanism appears to be one-step hydride transfer may be considered to have an intrinsic multistep character; that is, the one-step and multistep mechanisms are the opposite poles of a continuous spectrum.[10]

Since results obtained from most reductions by the models are easily interpretable, without certification, in terms of a one-step mechanism, our interest has been focused on evidence to prove the existence of a multistep mechanism. If a certain reduction with an NAD(P)H model is found to involve a free-radical intermediate, it could be direct evidence for a one-electron transfer mechanism. We have already reported the fact that a proton from solvent is incorporated into the product in the reduction of certain thioketones, the first direct evidence for such a multistep mechanism.[13]

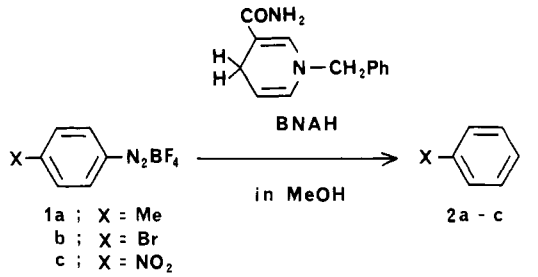
In addition, the intrinsic ability of an NAD(P)H model to initiate a free-radical chain reaction has been suggested in the reduction of bromotrichloromethane to chloroform.[16a] It has also reported that an NAD(P)H model initiated the polymerization of acrylamide.[16b] Although these findings have been employed to support the one-electron transfer mechanism for reduction with an NAD(P)H model, the identity of the chain initiator and/or carrier remains uncertain. In this connection, more definite evidence is necessary to reveal the ability of an NAD(P)H model to be a radical-chain initiator. If found, such evidence would point out the general importance of the one-electron transfer step for reduction with an NAD(P)H model.

Table I. Yields of 2c and Recovered 1c by Varying the Initial Amount of BNAH Based on 1c[a]

[BNAH][b] / [1c]	atmosphere	2c,[c] %	1c,[d] %
0.10	N_2	29	57
0.10	O_2	trace	95
0.50	N_2	65	trace
0.50	O_2	30	45
1.0	N_2	23	trace
1.0	O_2	38	trace

[a] Initial amount of 1c, 6.0×10^{-2} mmol; reaction time, 10 min; in the dark at room temperature. [b] Ratio of the initial amount of BNAH to that of 1c. [c] Yield of 2c. [d] Yield of recovered 1c.

Recently, we found that an NAD(P)H model, BNAH, initiates a free-radical chain reaction in dediazoniation of the arenediazonium salts **1a-c**, forming the corresponding



reduction products **2a-c**.[17] This fact clearly indicates that an NAD(P)H model can act as a free-radical chain initiator, providing direct evidence for a one-electron transfer mechanism in the reduction with an NAD(P)H model.

In this article, we report a detailed mechanism for the dediazoniation of **1a-c** with an NAD(P)H model.

Results

Arenediazonium fluoroborates **1a-c** were allowed to react with *N*-benzyl-1,4-dihydronicotinamide (BNAH) in methanol at room temperature in the dark under a nitrogen or oxygen atmosphere. On the mixing of a solution of BNAH with **1**, it bubbled vigorously in giving up nitrogen molecules. After 10 min, the products were analyzed. The yield of the reduction product **2** was determined on VPC. No other products were detected on VPC. For the reaction with **1c**, the amount of recovered **1c** was determined spectrophotometrically with the aid of a diazo-coupling reaction with 2-naphthol (see Experimental Section). When the amount of BNAH was large, **1c** was not recovered in appreciable amount. In the absence of BNAH, product could not be detected. The yield of **2** (as well as recovered **1c**, in its reaction) was dependent upon the ratio of the initial amount of BNAH to that of **1** but not upon the concentrations of the starting materials in the range used here. Room illumination affected the yield of **2** only in giving slightly scattered data. Results are summarized in Table I and illustrated in Figure 1. Interestingly enough, when the amount of BNAH is small, the amount of **2** produced under a nitrogen atmosphere was larger than the stoichiometric amount for all three substrates. In contrast, under an oxygen atmosphere the amount of **2** was always smaller than the stoichiometric amount. A free-radical chain trapping agent, *N-tert*-butyl-α-phenylnitrone, lowered the yield of **2a** (Figure 1).[18]

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(18) No reaction of BNAH with oxygen or *N-tert*-butyl-α-phenylnitrone took place within the period of the experiments.

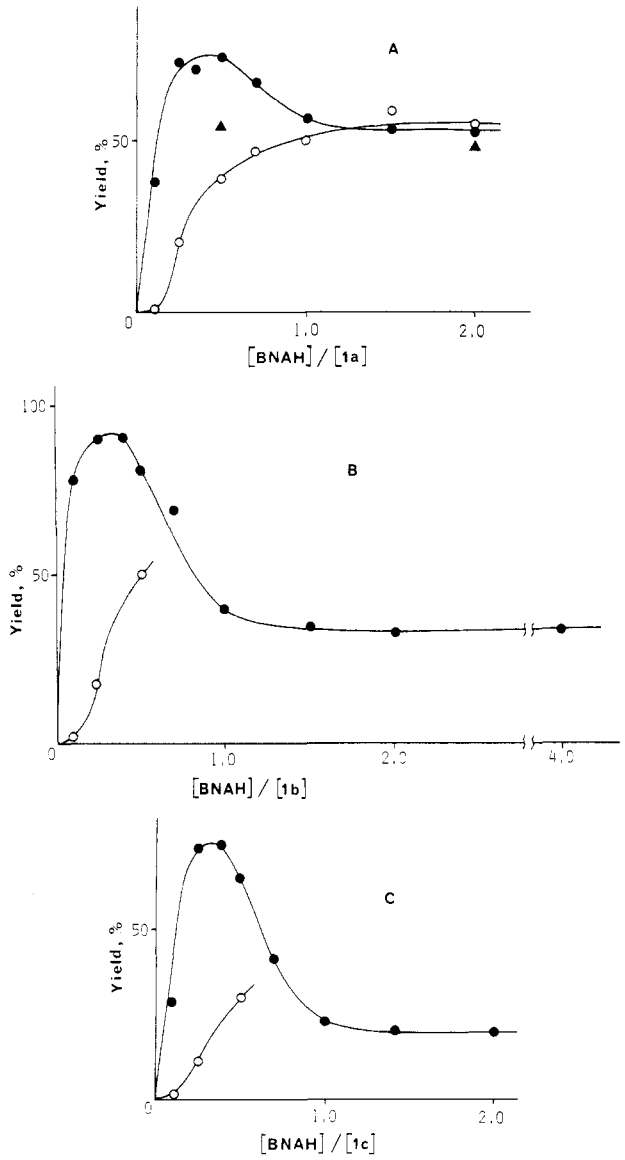

Figure 1. Yields of **2** varying the initial amount of BNAH based on **1**. A, B, and C represent the runs for **1a**, **1b**, and **1c**, respectively. Initial amount of **1**; 6.0×10^{-2} mmol. (● and ○) Yields of **2** under N_2 and O_2 atmosphere, respectively; (▲) yields of **2a** in the presence of 0.85×10^{-2} mmol of *N-tert*-butyl-α-phenylnitrone under N_2 atmosphere.

Product analyses were carefully performed for the reaction in the presence of 2.0 equiv of BNAH under a nitrogen atmosphere, where the yield of **2** was low, and many other unidentified products were found. One product from the reaction of **1a** identified by NMR after its isolation to a trace amount (<2%) was *p,p'*-dimethylbiphenyl. Neither of the starting materials, BNAH or **1**, was recovered under the condition used.

Experiments with methanol-d_4 gave the corresponding deuterated product, whereas such a deuterated product was not formed in appreciable amounts in runs with methanol-*O-d* (Table II). Since BNAH did not incorporate deuterium under our reaction conditions, this fact indicates that a methyl hydrogen in methanol is directly incorporated into the product in the course of the reaction. The yields of nondeuterated (ArH) and deuterated (ArD) products from the experiments with deuterated methanols are summarized in Table II. Under both nitrogen and oxygen atmospheres the yields of ArD decreased after reaching a peak, whereas those of ArH increased steadily with increasing amounts of BNAH. While the yields of ArD were much affected by atmosphere (N_2 or O_2), those of ArH were little affected.

Table II. Yields of Nondeuterated and Deuterated Products Based on **1** in the Reactions in Methanol-d_4 [a]

substrate	[BNAH]/[1] [b]	atmosphere	ArH, [c] %	ArD, [d] %
1a	0.10	N_2	9	29
	0.25	N_2	20	45
	0.25	O_2	15	5
	0.50	N_2	27	48
	0.50	O_2	23	16
	1.0	N_2	37	19
	1.0	O_2	36	14
	2.0	N_2	42	10
	2.0	O_2	45	10
1b	0.10	N_2	9	69
	0.25	N_2	12	78
	0.25	O_2	9	9
	0.50	N_2	18	62
	0.50	O_2	14	36
	1.0	N_2	19	21
	2.0	N_2	25	8
1c	0.10	N_2	3	26
	0.25	N_2	7	67
	0.25	O_2	5	6
	0.50	N_2	8	57
	0.50	O_2	9	21
	1.0	N_2	17	6
	2.0	N_2	17	3
	0.50 [e]	N_2	64	1
	0.50 [e]	O_2	29	1

[a] Initial amount of **1**, 1.5×10^{-2} mmol; in 0.5 mL of CD_3OD; reaction time, 10 min; in the dark at room temperature. [b] Ratio of the initial amount of BNAH to that of **1**. [c] Yield of nondeuterated product ArH. [d] Yield of deuterated product ArD. [e] In methanol-*O-d*.

Discussion

As illustrated in Figure 1, the amount of reduction product **2** produced under a nitrogen atmosphere is larger than the stoichiometric amount of BNAH, when [BNAH]/[1] is small. This leads directly to the conclusion that a free-radical chain path is important in this reaction. This conclusion is also supported by the fact that a free-radical chain inhibitor, either oxygen or *N-tert*-butyl-α-phenylnitrone, lowers the yield of **2**. Since decomposition of these arenediazonium salts **1** does not take place without BNAH, the free-radical chain is most likely initiated by BNAH. Thus, BNAH would donate one electron to **1** in the initiation step of the reaction, which is followed by an immediate delivery of nitrogen from **1**. Incorporation of a hydrogen from the methyl group in methanol into the reduction product indicates that the free-radical chain proceeds by means of taking a methyl hydrogen from the methanol. Consequently, the free-radical chain reaction can be illustrated as in eq 1–3. Equations 2 and 3 are

$$\mathrm{BNAH} + \underset{\mathbf{1}}{\mathrm{ArN_2BF_4}} \xrightarrow[-N_2]{} \mathrm{BNAH^{+}\cdot} + \mathrm{Ar}\cdot + \mathrm{BF_4^-} \quad (1)$$

$$\mathrm{Ar}\cdot + \mathrm{CH_3OH} \rightarrow \mathrm{ArH} + \cdot\mathrm{CH_2OH} \quad (2)$$

$$\cdot\mathrm{CH_2OH} + \mathbf{1} \xrightarrow[-N_2]{} \mathrm{Ar}\cdot + \mathrm{CH_2OH^{+}} + \mathrm{BF_4^-} \quad (3)$$

well-known processes in the thermal dediazoniation of **1** in the presence of an acid[19] or a one-electron donor.[20]

Since deuterium incorporation into the product in experiments with methanol-d_4 was not quantitative (Table II), one may suppose that direct hydride-ion transfer occurs as a competitive process. However, it is difficult to accept

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that BNAH donates simultaneously both an electron and a hydride ion to a substrate. It is more likely that the nondeuterated product, ArH, is formed from the intermediate common to that in the free-radical chain path. Thus, the aryl radical, which is generated through one-electron transfer from BNAH to 1 with a delivery of a nitrogen molecule, would abstract a hydrogen atom (or a proton) from the cation radical of BNAH within the cage of the solvent or would escape from the cage to undergo the well-known free-radical chain reaction abstracting a hydrogen atom from the solvent.[19,20] Then, eq 1 should be rewritten more adequately as eq 1′. Here, "in-cage

$$\text{BNAH} + 1 \xrightarrow[-N_2]{} \underbrace{\overline{\text{BNAH}^+\cdot\text{Ar}\cdot}}_{\text{in-cage radical pair}} + BF_4^- \rightarrow \text{BNAH}^+\cdot + \underbrace{\text{Ar}\cdot}_{\text{free radical}} + BF_4^- \quad (1')$$

radical pair" is proposed as an intermediate that results in both in-cage "hydrogen" transfer and free-radical chain reactions. In reactions with methanol-d_4, nondeuterated and deuterated products are formed via the former and the latter reactions, respectively.

Although the length of the free-radical chain cannot be estimated at this time, it seems reasonable that the larger the ratio of the yield of ArD to that of ArH is, the more favorable the free-radical chain reaction will be. The data listed in Table II show that the free-radical chain for the reaction of 1 is more favorable in this order, **1a** < **1b** < **1c**, which is the same order as that in the thermal dediazoniation of **1** in acidic methanol.[21,22] It is well-known that the course of dediazoniation in acidic methanol is affected by the substituents: **1c** gives **2c**, whereas **1a** gives *p*-methylanisole instead of **2a**; **1b** is dediazoniated to form mainly **2b** under a nitrogen atmosphere and mainly *p*-bromoanisole under an oxygen atmosphere.[21-23] Results from experiments with free-radical initiators and inhibitors have revealed that the reduction product **2** and anisole derivative are formed via a free-radical chain path and an ionic one, respectively.[22]

Moreover, a close survey of Table II affords more useful information concerning mechanistic details. As mentioned before, the yield of the deuterated product ArD, is largely suppressed under an oxygen atmosphere when [BNAH]/[1] is small, which can be easily explained in terms of the role of oxygen as a free-radical chain inhibitor. However, the yield of the nondeuterated product ArH under an oxygen atmosphere remains the same as that under a nitrogen atmosphere within experimental error when other conditions are the same, and the yield of ArH increases gradually with increasing amounts of BNAH under either atmosphere. Thus, we concluded that under either a nitrogen or oxygen atmosphere, the yield of ArH is determined only the amount of the intermediate (the in-cage radical pair) produced, which may concomitantly increase with increasing amounts of BNAH. Further, it is worthwhile to point out that the order **1a** > **1b** > **1c** in the yield of ArH, *i.e.*, the preferential order of in-cage reactions, is opposite that for the free-radical chain ones. This order corresponds to the order of the yields of anisole derivatives formed via an ionic path in the thermal dediazoniation of **1a–c**.[22]

It is of interest that the decrease in the yield of **2** with increases in the amount of BNAH after the maximum is reached is ascribable to the decrease in the yield of ArD. Thus, excess BNAH seems to play an inhibitory role to the free-radical chain reaction. Excess BNAH probably terminates the free-radical chain by trapping the free-radical species generated, whether aryl and/or hydroxymethyl radicals. Failure to detect an appreciable amount of biaryl indicates that the reaction of aryl radical to give biaryl (reaction with 1 or **2**) is not taking place, although such processes leading to biaryl are often important in free-radical chain reactions including aryl radical.[19,20,24] So, aryl radical possibly reacts with BNAH in the present system. The disappearance of starting materials as well as the formation of many unidentified products in the presence of excess BNAH, where the yield of the reduction product is very low, also seems to indicate consumption of generated free radical(s) by excess BNAH, which is undoubtedly followed by complex reactions. Unfortunately, details of such secondary processes are not clear at the present. The more favorable the substrate for free-radical chain reaction, the more sensitive the reaction is to inhibition by BNAH.

As an alternative, there is a possibility of a free-radical chain including BNAH as a hydrogen donor (eq 4 and 5).

$$\text{BNAH} + \text{Ar}\cdot \rightarrow \text{BNA}\cdot + \underset{\mathbf{2}}{\text{ArH}} \quad (4)$$

$$\text{BNA}\cdot + 1 \xrightarrow[-N_2]{} \text{BNA}^+ + \text{Ar}\cdot + BF_4^- \quad (5)$$

Although these processes cannot be ruled out, concentrations of aryl radical (Ar·), BNAH, and 1 are much lower than that of methanol, and such processes seem to contribute little if anything to the reaction. It may be important that eq 4 and 5 cannot explain the decrease in the yield of reduction product with increasing amounts of BNAH.

Our results are summarized as follows: (1) The reaction of **1a–c** with BNAH gives **2a–c** and unidentified products. (2) The yield of **2a–c** is maximized when the molar ratio of [BNAH]/[1] is 0.25–0.5. (3) When the reaction is carried out in methanol-d_4, both deuterated (ArD) and nondeuterated (ArH) products result. However, the yield of ArD drops as the ratio of [BNAH]/[1] is increased above 0.5, while the yield of ArH rises. (4) The presence of inhibitors such as O_2 or *N-tert*-butyl-α-phenylnitrone (or excess BNAH) during the reaction in methanol-d_4 lowers the yield of ArD while having little effect on the yield of ArH.

The dediazoniation of 1 in the presence of BNAH proceeds according to Scheme I. Thus, the reaction is initiated by one-electron transfer from BNAH to 1 and the aryl radical generated undergoes a free-radical chain reaction and in-cage reaction competitively.

From the chemical standpoint, concerning NAD(P)H models, it is particularly important that one-electron transfer from BNAH to 1 does occur in the initial step. We believe that the results of the present study make clear the general importance of one-electron transfer prior to a proton (or a hydrogen atom) transfer in reduction with an NAD(P)H model.

Experimental Section

Materials. Arenediazonium fluoroborates **1a–c** were prepared according to the literature.[25] These materials each gave a single spot on TLC. Preparation of *N*-benzyl-1,4-dihydronicotinamide (BNAH) was described previously.[26] Methanol was purified by

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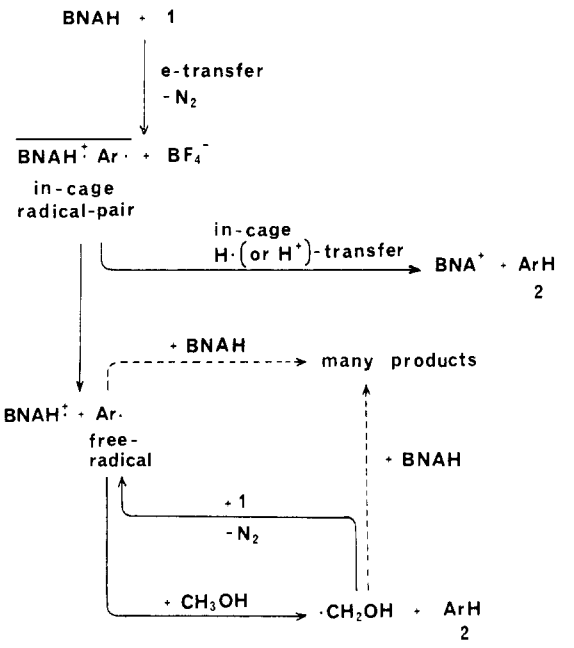
Scheme I



the ordinary method prior to use. Deuterated methanols were commercially available (Commissariat a l'Energy Atomique).

General Procedures. To 6.0×10^{-2} mmol of **1** was added a solution of an appropriate amount of BNAH in 3 mL (for **1a,b**) or 5 mL (for **1c**) of methanol. The reaction mixture was stirred for 10 min in the dark at room temperature under a nitrogen or oxygen atmosphere, and the products were analyzed. The reduction product **2** was analyzed as follows: a 0.25-mL aliquot of the reaction mixture was quenched with 1 mL of water and extracted with 1 mL of ether containing an internal standard for VPC analyses (*p*-xylene, *p*-methylanisole, and *m*-dimethoxybenzene, for **2a-c**, respectively). Then, the organic layer was analyzed on a Yanaco G-180 gas chromatograph (SE-30 column). The deuterium content in **2** from the reaction in deuterated methanols was determined by using a Hewlett Packard 5992B GC/MS spectrometer.

In order to determine the amount of **1c** recovered, a diazo coupling reaction was employed: to 5 mL of water was added 0.5 mL of the reaction mixture, and the aqueous layer was washed twice with 4-mL portions of dichloromethane. A 100-μL aliquot of the aqueous layer was added to a solution with 1.2×10^{-2} mmol of 2-naphthol in 3 mL of ethanol in a UV cell, and the absorbance of the 1-[*p*-(nitrophenyl)azo]-2-naphthol formed was measured on a Hitachi 220 spectrophotometer at 482 nm and compared with that obtained from a reference run (in which BNAH was absent). The spectrum in the reference run was consistent with that of the authentic sample. It was also confirmed that the observed absorbance obeys Beer's law within the range of the concentrations employed.

Moreover, 9.0×10^{-1} mmol of **1a** was allowed to react with 1.8 mmol of BNAH in 45 mL of methanol, with stirring in the dark at room temperature, under a nitrogen atmosphere. After 30 min, the reaction mixture was poured into 50 mL of water and extracted twice with dichloromethane. The organic layer was washed twice with water saturated by sodium chloride, dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue gave many spots on TLC. The mixture was subjected to separation with preparative TLC first with benzene eluenet and second with ethyl acetate eluent. All fractions were analyzed on a JASCO JNM-FX 100 FT NMR spectrometer, but only one (<4 mg, <2%) was identified, as *p,p'*-dimethylbiphenyl. One of the products gave an NMR spectrum ascribable to the structure of *N*-benzyl-6-(4'-methylphenyl)-1,4,5,6-tetrahydronicotinamide. However, a small amount of contaminat(s) prevented us from identifying it. The other products could not be identified at all.

Registry No. **1a**, 459-44-9; **1b**, 673-40-5; **1c**, 456-27-9; BNAH, 952-92-1; NADH, 58-68-4.

Structural Determination and Synthesis of a Chemical Signal of the Male State and a Potential Multipurpose Pheromone of the Mouse *Mus musculus*

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exo-7-Ethyl-5-methyl-6,8-dioxabicyclo[3.2.1.]oct-3-ene (1) has been isolated from urine of the male mouse of the species *Mus musculus*. It is one of a small number of volatile constituents that signal the adult male state and induce intermale aggression. It may also be regarded as a potential multipurpose male mouse pheromone. Its structure elucidation and synthesis are described.

Chemical constituents in the urine of adult male mice have long been known to produce diverse behavioral and endocrine responses in both female and male mice.[1-3] During a detailed investigation[4,5] of volatile urinary constituents by high-resolution, gas-phase analytical techniques (capillary gas chromatography, combined with both low- and high-resolution mass spectrometry and Fourier-transform infrared spectroscopy), we have focused attention especially on those compounds that were clearly associated with the masculinity of this animal species. While the mouse urine samples contain well over 100 volatile components,[4,5] only a small number of these (less than five) show clear dependency on the male hormone, testosterone. These may be suspected to be potential male pheromones.

One compound in particular stood out as an indicator of the adult male state: it was practically absent in both females and castrated males, but its normal urinary concentration was readily renewed through treatment with testosterone.[6] We have now identified the structure of

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