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Nickel(I) Octaethylisobacteriochlorin Anion. An Exceptional Nucleophile. Reduction and Coupling of Alkyl Halides by Anionic and Radical Processes. A Model for Factor F-430

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Abstract: Nickel(I)octaethylisobacteriochlorin anion ($\mathrm{Ni^IOEiBC^-}$) reacts extremely rapidly with aliphatic halides and methyl tosylate in homogeneous DMF solution. The reactivity sequence, CH_3 > primary > secondary ≳ tertiary, and the rate law accord with an S_N2-like process for the carbon–halogen bond scission. However, the main products of the reactions derive from free radicals. The rate for methyl chloride is 2000 times faster than the corresponding reaction with the super nucleophile $\mathrm{Co^IB_{12s}^-}$ and the rate constant for isopropyl bromide is 350 times greater than that observed with $\mathrm{CpFe(CO)_2^-}$. The results indicate $\mathrm{NiOEiBC^-}$ is the fastest nucleophile on record. Studies of the influence of solvent and reactant deuteration and the influence of anion and radical scavengers upon the product distribution suggest the intermediacy of at least one and possibly two nickel alkyls of fleeting lifetime. A novel explanation for the unusual speed of these reactions is put forward. It entails the participation of three metal electrons in the initial and rate-limiting bond-breaking process. The reactions observed are consistent with the activity of methanogenic bacteria to dehalogenate a broad range of substrates via the participation of factor F-430.

Introduction

Factor F-430, a nickel corphin[1] obtained from methanogenic bacteria,[2] is believed to play a key role in the biochemical hydrogenolysis of methyl–sulfur bonds[3] in the final step in the biogenesis of methane.[2,4] Apparently, the strong reducing capacity of this cofactor is also manifest in the ability of methanogens to cleave carbon–halogen bonds.[5] As a part of our study of the molecular nature of biodehalogenation processes[6] we use, in this work, the sodium salt of the anion nickel(I) octaethylisobacteriochlorin ($\mathrm{Ni^IOEiBC^-}$) as a model for reduced F-430. The two macrocycles are depicted in Figure 1. An electrochemical generation of this anion[7] in the presence of alkyl halides[8] indicates that $\mathrm{Ni^IOEiBC^-}$ is a strong nucleophile. In this work we have generated the anion via a sodium amalgam reduction in dimethylformamide. A study of the homogeneous kinetics, scope, and mechanism of these reactions demonstrates that the reactions are much faster than expected and points up the unusual nucleophilicity of $\mathrm{Ni^IOEiBC^-}$. Moreover, free radicals are generated as part of, or immediately following, the initial scission of the carbon–halogen bond.

Experimental Section

Octaethylisobacteriochlorin was prepared by minor modification of reported procedures.[9] The sodium isoamyl alcohol reduction was followed by chromatography on a MgO column. A hexane–benzene gradient was employed to separate the chlorin from the isomeric isobacteriochlorins and bacteriochlorin. The beautiful blue-violet nickel(II) complex was prepared under argon by refluxing the ligand with $\mathrm{Ni(OAc)_2{\cdot}4H_2O}$ in absolute ethanol[9b] for 15 min. A mixture of benzene and aqueous carbonate–bicarbonate buffer was added. The mix was shaken and the benzene phase was washed again with buffer and twice with water, dried over NaCl, and concentrated to dryness in vacuo. The Nickel(II) complex could be recrystallized by layering an ether solution on to MeOH. Crystals were washed with MeOH and vacuum dried. Protection of the complex from air by rapid manipulation and the use of argon-purged solvents was advantageous in preventing oxidation to the chlorin.

Reactions and Product Analysis

Depending upon desired conditions, the Ni(I) complexes were obtained by shaking homogeneous solutions of the Ni(II) adduct in DMF with a 0.7% sodium amalgam under argon. The argon (99.998%) was first passed through an oxy-trap column (Alltech) for this purpose. Small reaction vessels were made from sealed off stopcock tubes. The tube above the stopcock was serum capped. The volume of the reaction chamber was approximately 200 μL and the volume above the stopcock was 100 μL. The exact volume of each vessel was calibrated. For a reaction, typically 40 μL of a homogeneous red-magenta $\mathrm{Na^+Ni^IOEiBC^-}$ solution was transferred to a reaction vessel and 0.5 μL of alkyl halide was added under argon. In some instances, e.g., the MeX data in Table I, a 20-μL solution of the halide was employed. For the data in Figure 4, methyl iodide was diluted to half the final volume before addition of the $\mathrm{Ni^I}$ solution. For the CD_3CD_2I runs (Table V) dry DMF solutions of $\mathrm{Ni^I}$ were added to the requisite amount of water and mixed, and reaction was initiated by addition of the halide. Reactions were conducted in the absence of amalgam. Products were qualitatively analyzed by a combination of GC and GC-MS procedures and by ^{13}C NMR. Quantitation was accomplished by GC. External authentic standards were employed. Several columns were used: 6 ft × $^1/_8$ in. Porapak Q at 60 °C (methane, ethane, methyl halide, ethylene, methylene chloride); a 30 M capillary GS-Q at 80 °C (propylene, propane), 120 °C (butene-1, butane), 50–120 °C ramp (ethylene, ethane, butane, ethyl iodide, butenes, 1,1-dichloropropane), 130 °C (fluorodichloromethane, fluorotrichloromethane); a Superox 30 M capillary at 30 °C (2,3-dimethylbutane, isopropyl halides), 30–160 °C ramp (benzene, biphenyl, iodobenzene); a 30 M DB-17 at 25 °C (*n*-butyl chloride, octane) and at 40 °C (*n*-butyl bromide, *n*-butyl iodide, octane). GC-MS analysis was conducted with a Hewlett Packard 5989A mass spectrometer fitted with a 5980 chromatograph and data station.

Yields of all reactions were an average of at least three separate runs. The reproducibility was typically ±10% of the reported values. All yields were calculated as 200 (moles of product/moles of $\mathrm{Ni^I}$ consumed). The $\mathrm{Ni^I}$ consumed was determined spectrophotometrically. When halide was in excess, this was equal to the initial charge.

The data in Table IV contain a blank in that water (0–1.8 M) has no effect. In addition, blank runs with acetic acid demonstrated this acid did slowly oxidize $\mathrm{Ni^I}$. The reaction was $\sim 10^8$ shower than reaction with methyl iodide.

The reaction set in Table V was repeated twice. All yields were determined by GC as indicated above. The ratio of C_2D_5H/C_2D_6 was determined by GC-MS for the ethane peak. P + 1 ions were not ob-

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(1) (a) Pfaltz, A.; Juan, B.; Fässler, A.; Eschenmöser, A.; Jänchen, R.; Giles, H. H.; Diebert, G.; Thauer, R. K. *Helv. Chem. Acta* **1982**, *65*, 828–865. (b) Juan, B.; Pfaltz, A. *J. Chem. Soc., Chem. Commun.* **1986**, 1327–1329.

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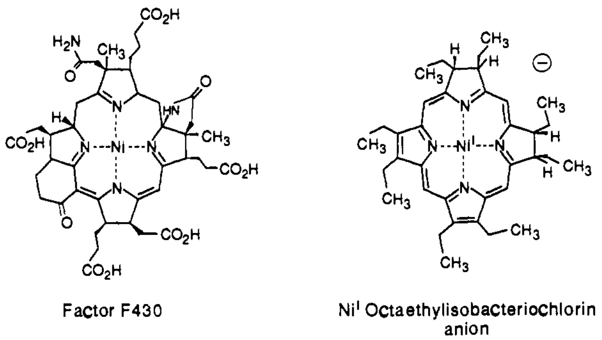


Figure 1. Factor F-430 and the *all-trans* isomer of Ni^{I}OEiBC$^-$.

Table I. Products of the Reactions of Na$^+$Ni^{I}OEIBC$^-$ with RX in DMF at 23 °C

substrate	product[a]	yield[b]
methyl chloride	methane	50
	ethane	50
methylene chloride[c]	methyl chloride	0.2
	methane	7
	ethylene	20
carbon tetrachloride[d]	chloroform	53
	methylene chloride	47
fluorotrichloromethane[c]	fluorodichloromethene	57
1,2-dichloroethane	ethylene	88
1,1-dichloroethane[c]	ethylene	1
	ethane	0.5
	cis-butene	8
	trans-butene	22
1,1,2-trichloroethane	vinyl chloride	100
benzyl chloride[c,d]	toluene	78
	bibenzyl	22
acetyl chloride[d]	acetaldehyde	40
n-butyl chloride	*n*-butane	74
	n-octane	26
isopropyl chloride	propane	70
	2,3-dimethylbutane	30
	propylene	5
methyl bromide	methane	27
	ethane	73
n-butyl bromide	*n*-butane	50
	n-octane	50
isopropyl bromide	propane	68
	2,3-dimethylbutane	32
tert-butyl bromide	isobutane	*e*
cyclopropylcarbinyl bromide	butene-1	95
methyl iodide	methane	24
	ethane	76
n-butyl iodide	*n*-butane	42
	n-octane	58
isopropyl iodide	propane	70
	2,3-dimethylbutane	30
iodobenzene	benzene	99
	biphenyl	1

[a] All determined by GC and confirmed GC-MS except where indicated. [b] The yields (200 mol of product/mol of Ni^1 consumed) represent an average of three separate runs and were reproducible to ±10. [c] Material balance in these runs was not good. [d] Determined by ^{13}C NMR. [e] No other product was detected, but the reaction was not quantitated.

served. The ratio of parent ions from a 1:1 mixture of C_2D_6:C_2D_5 was 0.9 ± 10%. Authentic gases were prepared by reduction of C_2D_5I with $LiAlH_4$ and $LiAlD_4$ in THF and by hydrolysis of the corresponding Grignards (D_2O/H_2O). Thus, in line 3 the overall yield of ethane was 20% and the ratio of C_2D_6/C_2D_5H was 1 ± 0.1.

All organic halides were commercial research grade and pure as judged by GC and NMR analysis. The trihalide 1,1,2-trichloroethane was redistilled before use.

Reactions with ^{13}C-labeled substrates were conducted in sealed NMR tubes. A General Electric QE-300 instrument was employed for analysis.

Carbon tetrachloride-^{13}C (MSD isotopes), benzyl chloride-α-^{13}C, and acetyl chloride-1-^{13}C (Aldrich) were employed directly. Ethylene dichloride-*1,2*-$^{13}C_2$ was obtained from the sulfuryl chloride chlorination of ethylene-*1,2*-$^{13}C_2$ as previously described[6] for the ^{14}C compound.

Table II. The Ratio of Hydrogenolysis to Coupling as a Function of Alkyl Moiety and Halide

	RH/RR			
alkyl moiety	OTs	Cl	Br	I
methyl[a]	2.8	1.0	0.35	0.31
n-butyl[b]		2.8	1.0	0.73
isopropyl[c]		2.4	2.2	2.9

[a] Initial concentrations were $[Ni^I]_0 = 2.9 \times 10^{-3}$ and $[RX]_0 = 0.13\text{–}0.18$ M. [b] $[Ni^I]_0 = 4.5 \times 10^{-3}$, $[RX]_0 = 0.11\text{–}0.12$. [c] $[Ni^I]_0 = 6.5 \times 10^{-3}$, $[RX]_0 = 0.12\text{–}0.14$.

DMF-d_7, D_2O, and ethyl iodide-d_5 were commercial samples from Aldrich and contained a minimum of 99% mole atom D.

Kinetics. Reactions were monitored by following the disappearance of Ni^I spectrophotometrically at 572 or 501 nm (cf. Figure 1). In general, Ni^{I-} solutions were prepared over sodium amalgam by adding stock concentrated Ni^{II}OEiBC to argon purged DMF. The 1-cm cuvettes were shaken until the spectrum of the cherry red Ni^I complex persisted. This process scavenged traces of oxidant (presumably oxygen) in the DMF solution. Reactions were initiated by the addition of a small amount (~3 μL) of a concentrated alkyl halide solution in DMF. For slower reactions ($k_2 \leq \sim 1$ L mol^{-1} s^{-1}) higher concentrations of reactants and 0.1 cm path length cells were employed. Very fast reactions were examined in dilute solution with 5.0 cm length cells. Note, iodobenzene was the single halide that reacted faster with the amalgam than it did with the Ni^I anion. These runs were conducted in the absence of amalgam. The reaction of amalgam with Ni^{II}OEiBC at the interface was slow on the time scale of these experiments.

The reaction of methyl iodide with Ni^{I}OEiBC$^-$ was also examined at −116 °C by UV-vis. For this purpose, a cuvette was immersed in a clear quartz dewar filled with liquid N_2–ethyl ether. The reaction was monitored in a Cary-118 C spectrophotometer. Diethyl ether was used as solvent.

Results

Stoichiometry. The products and yields of the reactions of a wide range of organic halides with Ni^{I}OEiBC$^-$ in DMF are given in Table I. The overall reaction is that given in eq 1, but three

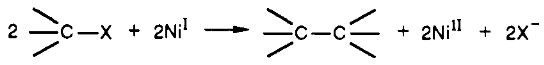
$$RX + 2Ni^I \rightarrow RH + R_2 + 2Ni^{II} \qquad (1)$$

general reactions were observed with monohalides:

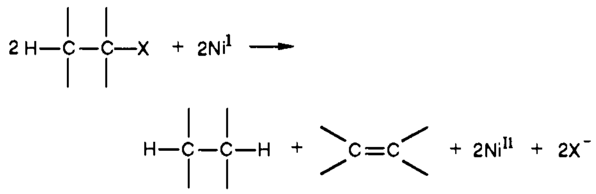
(a) hydrogenolysis


(2)

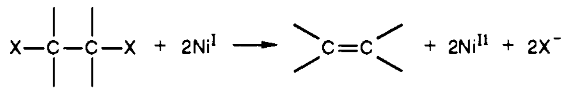
(b) coupling


(3)

(c) elimination


(4)

With vicinal dihalides generation of the olefin occurred readily:


(5)

With polyhalomethanes, a sequential reductive hydrogenolysis ensues:

$$CCl_4 \rightarrow CHCl_3 \rightarrow CH_2Cl_2 \qquad (6)$$

From the data in Table I, the relative yields of hydrogenolysis to coupling can be obtained as a function of halide for the methyl, n-butyl and iso-propyl series. These product ratios are compared in Table II.

These data were collected under the standard set of conditions indicated in the table. It will be noted that for the methyl and

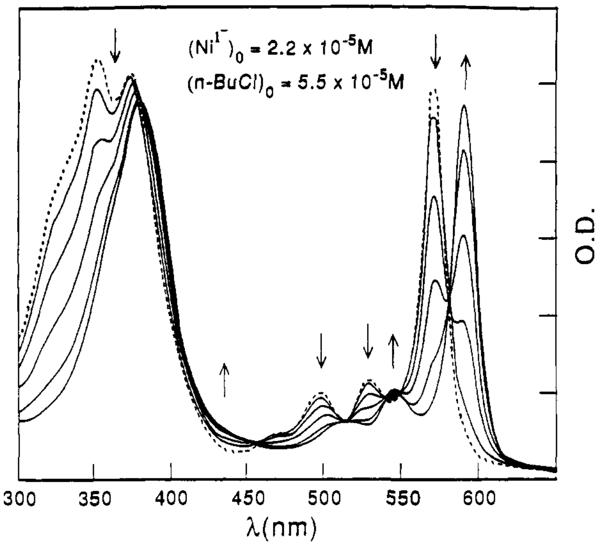


Figure 2. Visible spectrum of the reaction of *n*-butyl chloride with Ni^{I}OEiBC$^-$ at times 0 (---), 0.5, 5.5, 15.5, 45.5, and 10 min after addition of *n*-BuCl to 3.6 × 10^{-3} M.

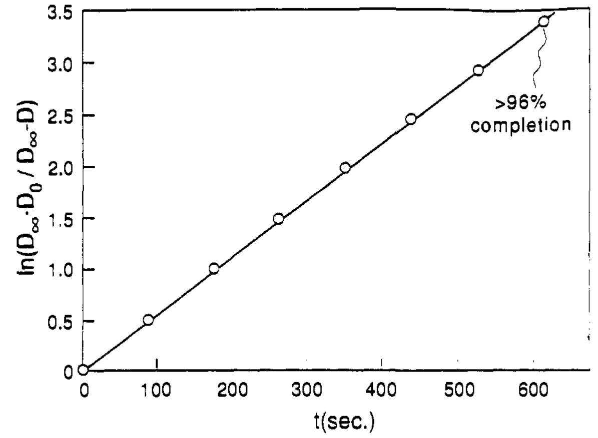


Figure 3. Rate plot for the reaction of Ni^{I}OEiBC$^-$ with 1,2-dichloroethane in DMF at -4 °C.

n-butyl series, the amount of coupling relative to hydrogenolysis increases as a function of halogen, but only mildly, in the order Cl < Br < I. The isopropyl halides all show nearly the same distribution of products within experimental error. Hydrogenolysis occurs to about twice the extent of coupling in this case, and reaction in DMF-d_7 yielded only propane-H.

Spectra of the Nickel Macrocycle. The visible spectrum of the reaction of *n*-butyl chloride with Na$^+$Ni^{I}OEiBC$^-$ in DMF at 25 °C is shown in Figure 2 as a function of time. The spectra depicted for this reaction are typical. Good isosbestic points were observed for the Ni^I to Ni^{II} conversion. No other entity was detected by UV–vis for any of these reactions at room temperature. Attempts to detect intermediates from the methyl iodide reaction at lower temperature by UV-vis (−116 °C) and NMR (−60 °C) failed. The ^{1}H NMR of the Ni^{II}OEiBC complexes matched that reported.[10] A reaction with ^{13}CH$_3$I revealed resonances for the starting halide and ethane (7.0 δ). No evidence for a NiCH$_3$ bond was observed.

Ligation of Ni. Attempts to ligate Ni^I and Ni^{II}OEiBC with a variety of reagents known to strongly complex iron porphyrins failed. Potential reactions were monitored by UV–vis. In all cases, the spectrum of the nickel complex shown in Figure 1 remained unchanged. The ligands examined were CO, NO, thiophenol, *N*-methylimidazole, diphenylphosphine, hydroxide, di-*n*-butyl sulfide, cyanide, and piperidine.

Table III. Rate Constants for the Reaction of Na$^+$Ni^{I}OEiBC$^-$ with RX in DMF at 23.5 °C

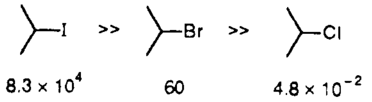
substrate	k (L/mol^{-1} s^{-1})^a
CH_3I, CH_3Br, CCl_4, $HCCl_3$ $FCCl_3$, CH_3CCl_3, $CH_3O_2CCH_2Cl$	$\geq 10^5$
i-PrI	8.3×10^4
$PhCH_2Cl$	2.0×10^4
n-BuBr	1.7×10^4
CH_3Cl	1.1×10^4
CH_3OTs	1.3×10^3
CH_2Cl_2	1.3×10^2
i-PrBr	60
$(CH_3)_2C\ Cl_2$	59
t-BuBr	59
$ClCH_2CH_2Cl$	45
CH_3CHCl_2	30
n-BuCl	11
$CH_2{=}CCl_2$	4.0
$ClCH_2CHCl_2$	2.2
PhI	2.0
1-adamantyl-Br	6.2×10^{-2}
i-PrCl	4.8×10^{-2}
t-BuCl	2.0×10^{-2}
PhBr	1.9×10^{-2}
$CH_2{=}CHCl$, PhCl, $PhCF_3$, $PhCH_2F$	$\leq 10^{-5}$ NR

^{a} Average of three independent runs; reproducibility ±15%.

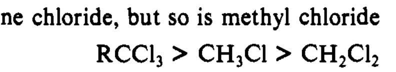
Kinetics. Reactions were monitored by UV–visible spectroscopy at 572 nm. A typical plot for ethylene dichloride at −4 °C is shown in Figure 3. For this halide, the activation parameters are $\Delta H^\ddagger$ = 12.2 kcal/mol and $\Delta S^\ddagger$ = −11 eu. For all cases, the rate law

$$d[Ni^{II}]/dt = k_2(Ni^IOEiBC^-)[RX]$$

was valid. The second-order rate constants are listed in Table III. The alkyl halide substrates are listed in a decreasing order of reactivity. Generally alkyl iodides react much more rapidly than the corresponding bromides. The latter are much more reactive than the chlorides. A good example is



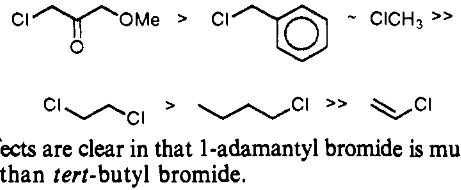
Iodides react ~10^3 faster than bromides and the latter are ~10^3 faster than chlorides. While primary halides react much more rapidly than secondary halides, the latter react only somewhat faster or about at the same rate as tertiary compounds. For example



All tri- and tetrahalomethanes are much faster reactants than methylene chloride, but so is methyl chloride

$$RCCl_3 > CH_3Cl > CH_2Cl_2$$

(R = CH$_3$, H, Cl, F). For primary chlorides, the following sequence obtains:



Steric effects are clear in that 1-adamantyl bromide is much slower to react than *tert*-butyl bromide.

The Influence of Reactant Concentrations upon Product Distribution. Coupling vs Hydrogenolysis. Though an extremely fast reaction, the simplicity and directness of the GC analysis for methane and ethane prompted an examination of the methyl iodide reaction in some detail.

The ratio of coupling to hydrogenolysis in this reaction was effected by the initial concentration of reactants. Generally, coupling was increased with increases in both [Ni^I]$_0$ and [RX]$_0$

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[10] Johansen, J. E.; Angst, C.; Kraty, C.; Eschenmöser, A. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 141-143.

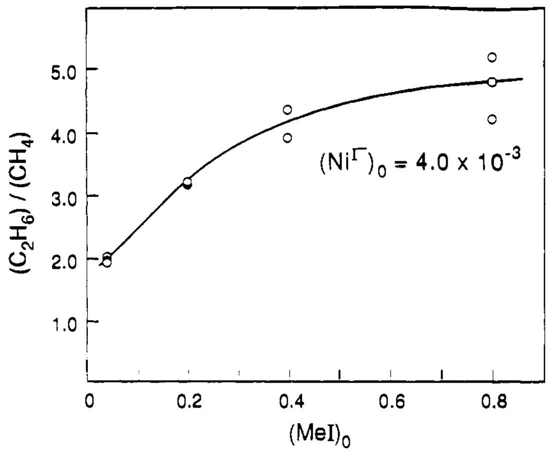


Figure 4. Ethane/methane ratios as a function of initial MeI concentration; $[Ni^IOEiBC]_0 = 4.0 \times 10^{-3}$ M.

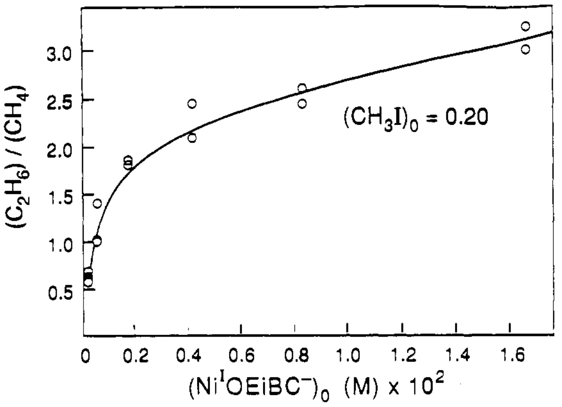


Figure 5. Ethane/methane ratios as a function of initial Ni^IOEiBC^- concentration, $[MeI]_0 = 0.20$ M.

Table IV. Influence of Protic Anion and Radical Scavengers upon the Ethane/Methane Ratio from the Reaction of Ni^IOEiBC^- with CH_3I

	concentration (mol/L)			
scavenger	$[Scavenger]_0$	$[Ni^I]_0$	$[CH_3I]_0$	C_2H_6/CH_4
water	0–1.8	0.011	0.13	2.2
acetic acid	0.4	0.008	0.19	0.1
toluene	4.7	0.004	0.18	2.0
diphenylmethane	1.2	0.013	0.32	2.1
diphenylphosphine	0.27	0.0037	0.19	0.12
	0.07	0.0037	0.19	0.66
thiophenol	0.9	0.008	0.18	0.001
	0.2	0.008	0.72	0.1
benzaldehyde	0.47	0.0036	0.19	1.9

Table V. Influence of Solvent Deuteration upon the Reaction of CD_3CD_2I with Ni^IOEiBC^a

		ethane			
H_2O	DMF	C_2D_5H	C_2D_6	ethene	butane
H	H	33	7	4	57
D	H	25	8	7	62
H[b]	D	10	10	5	77
D	D	3	11	9	77

[a] $[Ni^I]_0 = 7.2 \times 10^{-3}$ M, $[CD_3CD_2I]_0 = 0.057$ M, $[water]_0 = 3.8$ M. [b] For this set $[CD_3CD_2I]_0 = 0.14$ M, $[Ni^I]_0 = 8.0 \times 10^{-3}$ M.

with this halide though these effects were small (Figures 4 and 5). At fixed $[CH_3I]_0$ increasing $[Ni^I]_0$ from 0.0002 to 0.016 M increased the amount of coupling relative to hydrogenolysis by about 5. At a fixed initial concentration of Ni^I, changing the CH_3I initial concentration from 0.05 to 0.8 M increased the coupling only 2-fold.

The Influence of Protic and Hydrogen Atom Donors. In efforts to determine the source of the hydrogen atom in RH, a variety of proton and hydrogen atom donors were added to the reaction medium of the methyl iodide reaction. Their influence is given in Table IV.

No effect was observed with water, toluene, benzaldehyde, or diphenylmethane. All of these showed an ethane/methane ratio of 2.0 ± 0.2. On the other hand, thiophenol, diphenylphosphine, and acetic acid all greatly enhanced the yield of methane. The ionization constants for these latter are $\sim 10^{-5}$, $\sim 10^{-23}$, and 10^{-5}.

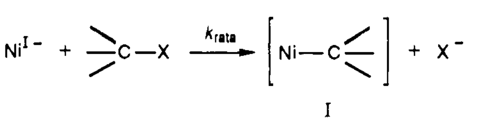
In addition, a variety of experiments were conducted with ^{13}C-labeled substrates in DMF-d_7 in the presence of H_2O. The substrates included benzyl chloride-*1*-^{13}C, acetyl chloride-*1*-^{13}C, and carbon-^{13}C tetrachloride. In all cases only the corresponding C–H compound was produced as indicated from ^1H NMR and ^{13}C NMR spectra. The products show no ^{13}C–D coupling.

A potential competing reaction in our system was a base-catalyzed elimination caused by reaction of amalgam with trace quantities of water in the DMF. Thus, in order to assess the significance of radical disproportionation and more directly monitor the influence of solvent deuteration, a series of experiments were conducted with CD_3CD_2I as substrate. These results are presented in Table V. For this series, the ethane fraction of the product was analyzed by GC-MS for the relative distribution of C_2D_6 and C_2D_5H. It will be noted that the overall product distribution does change with solvent deuteration, but not markedly. The amount of butane relative to ethane increases most upon deuteration of DMF. However, the C_2D_5H/C_2D_6 ratio does diminish considerably in the all-D system and there is an overall decrease in ethane production going down the table. The largest change occurs in the amount of C_2D_5H produced. A qualitatively similar result was obtained with bromobenzene. Reaction of this halide in 4 M D_2O in DMF-H_7 produced a mixture of phenyl-*D* (37%) and phenyl-*H* (63%). Corresponding reactions of the isopropyl halides in DMF-d_7 produced ≥97% propane-*H*. In the presence of 3.6 M D_2O 34% of the propane was the 2-deuterio product.

Discussion

The speed of these reactions and the influence of halocarbon structure upon it establish a reaction pathway that entails a fast nucleophilic substitution in the initial rate-limiting step. However, a complex series of reactions must ensue following the carbon–halogen bond scission. The deuterium-labeling studies along with the effect of reactant concentration and anion and radical scavengers upon the product distribution imply the presence of at least one and perhaps two distinct but fleeting nickel–alkyl intermediates. Moreover, free radicals are generated.

The First Step: Attack by an Exceptional Nucleophile upon the C–X Bond. All of the structural and kinetic data presented above accord with a direct nucleophilic attack by the nickel(I) anion at carbon



(7)

I

to generate a fleetingly stable formally nickel(III) alkyl (I) and halide ion. This formulation is in keeping with quite recent structural and spectroscopic studies of nickel(I) hydroporphyrins[7,8,11,12] and Factor F-430.[13a] These data[11,12] clearly

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(11) Renner, M. W.; Furenlid, L. R.; Barkigia, K. M.; Forman, A.; Shim, H. K.; Simpson, D. J.; Smith, K. M.; Fajer, J. *J. Am. Chem. Soc.* **1991**, *113*, 6891–6898.

(12) Stolzenberg, A. M.; Stershic, M. T. *J. Am. Chem. Soc.* **1988**, *110*, 6391.

(13) (a) Zimmer, M.; Crabtree, R. H. *J. Am. Chem. Soc.* **1990**, *112*, 1062–1066. (b) Direct analysis for the d^7Ni(III) system is not available. The rapid dissociation (see below) of I to radicals and Ni(II) that our results implies suggests the bonding for Ni^{III} is not favorable. (c) Rates of the same order of magnitude, or slightly faster, have been reported for electrochemically generated Ph_2Bi^- and Ph_2Sb^- with isopropyl bromide: Dessey, R. E.; Pohl, R. L.; King, R. B. *J. Am. Chem. Soc.* **1966**, *88*, 5121–5124.

Table VI. Rate Constants for Reaction of Transition Metal Anions with Alkyl Halides and Methyl Tosylate

	k_2 (M^{-1} s^{-1})		
RX	$Co^IB_{12s}^{-\,a}$	$CpFe(CO)_2^{-\,b}$	Ni^IOEiBC^-
MeI	3.4×10^4	2.8×10^6	($\sim 10^8$)^c
i-PrI	2.3×10^2		8.3×10^4
MeCl	5.0		1.1×10^4
i-PrBr	1.8	$1.7 \times 10^{-1\,d}$	60
n-BuCl	2.8×10^{-2}		11
MeOTs		2.4×10^2	1.3×10^3

^{a}Data taken from ref 14, solvent MeOH. ^{b}From ref 15, THF solvent. ^{c}An estimate based upon competition of radical scavenging by Ni^{I-}. Trends in the kinetic data (RI ≫ RCl) would set the rate for MeI at $\sim 10^{10}$. ^{d}Data from Dessey et al. cf. ref 13c; solvent glyme.

show that the negative charge in nickel(I) isobacteriochlorins resides on the metal and that the macrocycle is flexible enough to allow an oxidation of the metal to Ni^{II} to occur.[13b] The rates we observe here in homogeneous solution rank Ni^IOEiBC^- as the *fastest* transition metal nucleophile on record and one of the fastest of all types.[13c] A comparison of the rates of selected reactions with the cobalt(I) complex B_{12s}[14] and the iron anion $CpFe(CO)_2^-$[15] is given in Table VI. These latter are extremely rapid nucleophiles or "super nucleophiles". As pointed out by Pearson and Figdore,[15] it is difficult to reckon the fastest nucleophile since solvent effects may dominate. In this work the polar DMF solvent favors separated ions, but it does not favor the charge dispersion present in the classic S_N2 transition state. On the basis of the lack of coordination of Ni^I by a variety of potentially strong ligands (see Results) we infer the anion exists in DMF and DMF–H_2O as the unsolvated species and that a prior association of the halide with the metal does not occur. Thus, the nucleophilic attack depicted in (7) reflects the reaction of the bare metal centered anion radical at carbon and this in part accounts for the rapidity of reactions observed here. Our results in homogeneous solution support the high degree of nucleophilicity attributed to Ni^IOEiBC^- by Stolzenberg and Stershic[8] based principally upon electrochemical rates of the NiOEiBC catalyzed reduction of methyl iodide. We find the homogeneous rate for methyl chloride approximates that estimated for methyl iodide from the electrochemical data. Moreover, *i*-PrI reacts 10^6 times faster than *i*-PrCl. Thus, both the actual rate constants and the differences between them are much larger than previously estimated.[8] The MeI reaction was too fast to measure in our hands, but the initial increase in coupling with initial concentrations of both MeI and Ni^{I-} (Figures 4 and 5) suggest the halide displacement and generation of radicals (see below) competes with their scavenging by Ni^I. Radical scavenging rates by related paramagnetic ions[16a] and Ni(II) cyclam complexes[16b] are of the order of 10^8–10^9 L mol^{-1} s^{-1}. Thus, reaction 7 with MeI must proceed very rapidly.

The relatively small differences in rate (Table III) observed for the isopropyl and *tert*-butyl series might be taken as a switch in mechanism to a one-electron bond cleavage process for the tertiary halides. However, the more sterically encumbered adamantyl bromide reacts about 1000 times slower than *tert*-butyl bromide. The adamantyl radical has been deduced to be more stable than the *tert*-butyl radical from studies of the decarbonylation of the corresponding acyl radicals.[17a]

The Fate of NiR (I). The first presumed neutral nickel alkyl resulting from the initial substitution is clearly unstable. There are three reasonable transformations I may undergo. Our data suggests two of them may occur.

(i) Hydrolysis to Alkane. In our view this pathway does not

$$NiR + H^+ \rightarrow Ni^{III} + RH \qquad (8)$$

occur readily in competition with others although alkanes are major products of these reactions. Thus, the reaction of ethyl iodide-d_5 with Ni^I clearly results in the incorporation of water protons (deuterons) into the generated ethane (Table V). However, the degree of proton incorporation from water into methane from the corresponding reaction with methyl iodide (Table IV) does not vary with initial water concentration. Methane and ethane are the only products of this reaction, and the amount of water present in the reaction medium does not alter their relative yields. On the other hand, acetic acid greatly increases the yield of methane (Table IV). We conclude a more basic entity than I is responsible for the proton transfer from water, but we cannot eliminate a protonation of I by acetic acid.[17b]

(ii) Reduction by Ni^IOEiBC^-. Both Ni^I and N^{III} are paramagnetic species and a fast reaction between them might be

$$NiR + Ni^{I-} \rightarrow \underset{\mathrm{II}}{NiR^-} + Ni^{II} \qquad (9)$$

expected. However, Ni^I–Ni^{II} exchange rates have been estimated to be slow.[18] The self-exchange rates for Ni^+ and Ni^{2+} cyclam derivatives in water were calculated from the Marcus relationship by Meyerstein and colleagues.[18] The rates are surprisingly slow ($\sim 10^{-3}$ L mol^{-1} s^{-1}). In our system, both thermodynamics and the electrostatics would favor a more rapid reaction for (9). Whether it is competitive with other radical processes and whether I has a long enough lifetime for it to occur are unknown. The steric bulk of the macrocycle would seem to preclude a rapid rate for (9).

(iii) A Rapid Dissociation to Radicals. We believe this is the

$$NiR \rightarrow Ni^{II} + R^\bullet \qquad (10)$$

dominant fate of I. Indeed, the reaction characteristics are much more in keeping with I as a radical complex of Ni^{II}. The evidence for radicals in these reactions rests with their scavenging by thiophenol and diphenylphosphine, the generation of C_2D_6 from ethyl iodide-d_5 in all protic milieu, the rearrangement of the cyclopropylcarbinyl to the 1-butenyl skeleton upon reaction with cyclopropylcarbinyl bromide, and the fact that coupling products are significant.

(a) Radical Scavengers (Table IV). The results with diphenylphosphine are clear cut in that the pK_a for this substance is $\sim$23.[19] Hence, the increased yield of methane must result from H atom abstraction. The thiophenol data, while impressive, are nonetheless ambiguous. This thioalcohol is acidic enough (pK_a $\sim$ 5) such that it may (like acetic acid) function as a proton donor as well.

(b) Radical Disproportionation. Some of the best evidence for radicals results from the deuteration studies presented in Table V. There are two key points in the table. One is that C_2D_6 is produced from the reaction of CD_3CD_2I in all protic milieu. We interpret this to indicate that the generated perdeuterioethyl radicals disproportionate (reaction 11).[20] The second result of

$$2CD_3\dot{C}D_2 \rightarrow D_2C{=}CD_2 + CD_3CD_3 \qquad (11)$$

note is that a small (3%) but detectable yield of CD_3CD_2H is obtained in all deuterated milieu. These results suggest that ethyl radicals may, to a small extent, abstract hydrogen atoms from the periphery of the macrocycle. A most likely site would be the β pyrole reduced ring positions (reaction 12). A ligand radical

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(14) Schrauzer, G. N.; Deutsch, E. *J. Am. Chem. Soc.* **1969**, *91*, 3341.

(15) Pearson, R. G.; Figdore, P. E. *J. Am. Chem. Soc.* **1980**, *102*, 1541–1547.

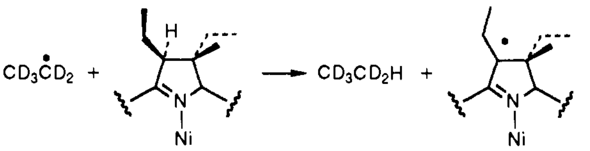
(16) (a) Kochi, J. K. In *Frontiers of Free Radical Chemistry*; Pryor, W. A., Ed.; Academic Press: New York, 1980; pp 297–353 and references therein. (b) Kelley, D. C.; Marchaj, A.; Bakac, A. J.; Espenson, H. *J. Am. Chem. Soc.* **1991**, *113*, 7583–7587.

(17) (a) Isaacs, M. S. *Reactive Intermediates in Organic Chemistry*; John Wiley and Sons: New York, 1974; pp 324–325. (b) The existence of I is not necessary to explain these observations.

(18) Jubran, N.; Ginzburg, G.; Cohen, H.; Karesh, Y.; Meyerstein, D. *Inorg. Chem.* **1985**, *24*, 251. Jacobi, M.; Meyerstein, D.; Lilie, J. *Inorg. Chem.* **1979**, *18*, 439.

(19) Terekhova, M. I.; et al. *J. Gen. Chem. USSR* **1982**, *52*, 452–455.

(20) A potential, but unlikely anionic process for C_2D_6 generation is eliminated by virtue of the high concentration of water (3.8 m). A similar radical process, D abstraction from CD_3CD_2I by $C_2D_5^\bullet$, could well occur. H abstraction from the isopropyl halides in DMF-d_7 is the dominant process leading to propane in that system.



(12)

of this kind could undergo further H abstraction to yield a chlorin. It may disproportionate to chlorin and isobacteriochlorin, and it may simply isomerize by reduction with Ni^I (internally or externally) back to the isobacteriochlorin. We have at this time no additional evidence for this process.

(c) Rearrangement of the Cyclopropylcarbinyl Skeleton. The radical rearrangement (reaction 13) proceeds[21] at 10^8 s^{-1}. The

(13)

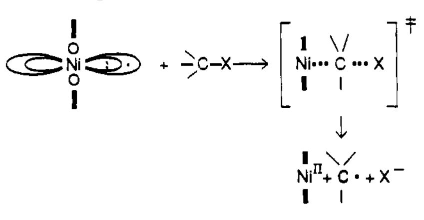
near quantitative yield of butene-1 obtained from the reaction of cyclopropylcarbinyl bromide again supports the intermedicacy of radicals in these reactions.

(d) Radical Coupling. Another route to coupling can be envisioned for this system

$$\underset{\text{II}}{\text{NiR}^-} + \text{RX} \rightarrow \text{Ni}^{\text{II}} + \text{R}_2 + \text{X}^- \qquad (14)$$

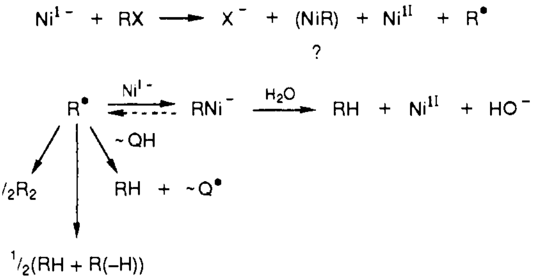
This reaction could proceed in some analogy with the first step of the reaction. It would represent a nucleophilic attack by a negatively charged Ni^{II} alkyl upon starting halide. We note that there is no dramatic increase in coupling as the halide is varied from Cl to Br to I (Table II). Given the unusually wide disparity in rates between alkyl iodides, bromides, and chlorides that results from the reaction with Ni^{I-} (Table III), a much enhanced rate of coupling product might be expected with iodides, say if (14) were to occur. The isopropyl halides exhibit almost no change at all in the amount of coupling relative to hydrogenolysis. In the methyl series the best leaving group from a nucleophilic displacement, tosylate, exhibits the smallest amount of coupling. Thus we believe (14) is not a significant part of the overall reaction pathway. Rather radicals, their rate of generation, and steady state concentration determine product distribution.

Does I Have Any Lifetime at All? The very rapid C–X bond scission and generation of radicals can be explained by an intriguing alternative to the processes outlined above. In this formulation I has no lifetime. A radical is generated concomitantly with halide ion as a result of the initial attack at carbon by Ni^{I-}. The unusual speed of the reaction, or the extreme nucleophilicity of Ni^{I-}, is imparted to the anion by the extra electron in the complex. That is, the initial scission is the result of a three-electron attack. The extra electron for this purpose resides in the ground state, in an antibonding $d^*_{x^2-y^2}$ orbital.[11] Thus an attack by the nickel-centered anion, using electrons in a combination of nonbonding and antibonding metal orbitals that are favorably disposed, could yield a radical and X^- directly. The process drawn below is but a crude conceptualization



The reactivity would parallel that of an S_N2 like process, but with *no bond formed* (NBF). In this formulation the incipient carbocation receives an electron from the metal. The radical, Ni^{II}, and halide ion result from collapse of the transition state. We theorize that the nonbonding electrons in the metal d_{z^2} orbital function as the nucleophilic pair and that the electron is transferred from the HOMO $d^*_{x^2-y^2}$ orbital as part of the bond-breaking process.[22a] The S_N2-NBF formulation nicely explains the vast

Scheme I



differences in reactivity between $Co^IB_{12s}{}^-$ and Ni^IOEiBC^-. The Co^I system is isoelectronic with Ni^{II}, but it contains the same charge as Ni^I. An extra participating electron on Ni^I rather than solvation or steric effects would seem to explain the ~2000-fold (!) difference in rates with which these anions react with methyl chloride.[22b] Certainly, in the case of Ni^IOEiBC, some release of steric strain and ligand distortion may additionally contribute to the speed of these reactions in that a more favorable bonding geometry for Ni^{II} is generated. However, this factor alone or along with the existence of an apparently bare charge on Ni would seem inadequate to explain these astonishing rates. If I has no lifetime, however, then the lack of response of the product distribution to increased water concentration (Table IV) would indicate a prior dissociation of II to R^- and Ni^{II}. In this case acetic acid may protonate II (rather than I) directly. This interpretation would imply a reversibility for reaction 15.

The Generation and Fate of II. As noted above a NiR^- species (II) could result from an electron transfer reaction of $NiOEiBC^-$ with I (eq 9) though this is not likely. On the other hand, radical scavenging by paramagnetic metal ions[16] and Ni^I complexes[18] is quite rapid. In this system II should be rapidly formed following the dissociation of I to radicals and in competition with radical–radical and hydrogen abstraction processes (reaction 15).

$$\text{R}^\bullet + \text{Ni}^- \rightarrow \underset{\text{II}}{\text{RNi}^-} \qquad (15)$$

Once formed the most reasonable path for the disappearance of II is hydrolysis

$$\text{RNi}^- + \text{H}_2\text{O} \rightarrow \text{RH} + \text{Ni}^{\text{II}} + \text{HO}^- \qquad (16)$$

We attribute the base line hydrolysis in the presence of water (Table IV) to this process. It may entail a dissociation to carbanion and Ni^{II} (see above).

The Disposition of Radicals. From the data in Table V the relative disposition of perdeuterioethyl radicals can be ascertained. From line 1, it may be deduced that 33% of the product (C_2D_5H) results from hydrogen atom abstraction and scavenging of radicals by Ni^I and hydrolysis of NiR^-, processes 15 and 16. From line 2, the amount of H-atom abstraction from DMF (and possibly the porphyrin) is 25%. In all protic milieu then, the amount of scavenging by Ni^I is 33–25 or about 8%. Approximately the same number is obtained from line 3 directly (10%) or by applying a

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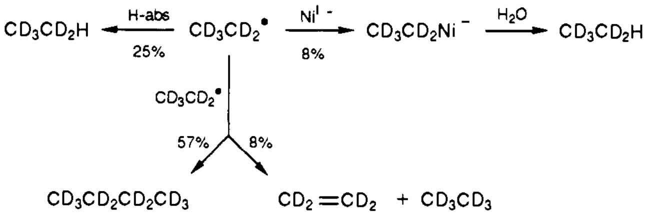
[21] Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317–328.

[22] (a) Given that it is impossible to state with certainty the exact distribution of electrons in the nickel complex as it approaches carbon, one possible formulation for the overall reaction is described. Assume reaction commences via attack of the pair of nonbonding $d_z{}^2$ electrons of the metal upon the antibonding σ^* orbital on carbon corresponding to the sp^3–p MO of the carbon–halogen bond. In the transition state, the system approaches a planar sp^2 bonding for carbon and what is usually formulated as an extended p orbital perpendicular to this plane and into which (in this case) Ni^- is attacking and halide ion is leaving. At this point, the antibonding $d_{x^2-y^2}$ σ^* has the right geometry and symmetry to overlap (with at least one lobe) with the antibonding sp^2 MO's on carbon and the electron is transferred. The macrocycle falls away as Ni^{II}. The carbon radical is formed (via redistribution to the p orbital on carbon) and the halide ion leaves. More simply, this process can be thought of as an initial polarization of the C–X bond that facilitates the electron transfer and C–X bond rupture. (b) The S_N2-NBF process also accords with the vastly accelerated rate of $CO–CH_3$ homolysis (10^{15}) attendant upon reduction of methylcobalamin to the anion radical. In this case, the $CO–CH_3$ bond is weakened from 37 to 12 kcal mol^{-1}, cf.; Martin, B. D.; Finke, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 585–592.

small correction for the C_2D_5H obtained in all deuterated milieu $(10 - 3 = 7\%)$.

Thus, in all protic milieu



The yield of ethene measured at 4% is in fair agreement with the 7% calculated from the mass spectral intensity of the C_2D_6 parent.

A general reaction path that accommodates all of our findings is shown in Scheme I. Only dominant processes are portrayed.

The Relationship of This Work to Other Ni^{I} Reactions, Factor F-430, and Other Bioreductants. The reactions of a series of reactions of Ni^{I} macrocycles with alkyl halides in aqueous milieu, primarily saturated cyclam derivatives, have been examined in detail by Espenson and colleagues.[23-26] The rates of these reactions show an opposite response to halide structure (tertiary > secondary > primary) than that observed here, and these workers have established that radicals are produced by an innersphere bond cleavage process. Most compellingly, a highly hindered macrocycle slowed the rates considerably. These reactions with positively charged Ni^{I} adducts resemble in character those observed with neutral high-spin iron(II) prophyrins and hemeproteins.[27,28] On the other hand, work with a variety of cobalt(I) complexes including B_{12s} by Schrauzer and colleagues[29] has established the extreme nucleophilicity of the B_{12s} system. The character of the reaction studied herein is similar to that reported for the Co^{I-} nucleophile. The major difference between Ni^{I}OEiBC^{-} and B_{12s} reactions lies in their rates and the stability of the initially formed metal alkyls. The hypothetical NiR resulting from attack by Ni^{I-} upon the halide is but a fleeting intermediate, if it exists at all. The corresponding cobalt derivatives are stable.

Major differences in physical properties do not seem to accompany the attachment of a conjugated exocyclic cyclohexanone moiety (like that present in F-430) to the isobacteriochlorin skeleton.[11] Moreover, reaction of F-430 methyl ester with MeI in DMF–D_2O results in methane-*D*. This result is similar to the general observations observed herein. Thus, to the extent that octaethylisobacteriochlorin is a model for F-430, it may well be that nature's most rapid nucleophile resides in F-430 rather than B_{12s}.

The results of this study accord with the capacity of ***Methanosarcina barkeri***[5] and ***Methanobacterium thermoautotrophicum***[30] to reductively dehalogenate a broad range of alkyl halides. Both bacteria are known to contain factor F-430. However, our findings do not address the mechanism of cleavage of thioether linkages or the biogeneration of methane. Recent studies with cell free suspensions of ***Ms. barkeri*** indicate some stereochemical integrity (a partial net inversion) for the hydrogenolysis of an appropriately labeled ethyl coenzyme M derivative.[31] In addition, processes involving cleavage of a methylthiyl radical[32] by Ni^{I} and a Ni^{II}–Ni^{III} redox cycle[33] have been proposed as mechanistic models for F-430 linked methanogenesis.

Acknowledgment. This work was supported in part by the National Science Foundation (BCS-88-20924). We are grateful for this support. We are indebted to Professors G. N. Schrauzer and M. F. Rettig for valuable discussions.

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(29) For summarizing review cf.: Schrauzer, G. N. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 417–426.

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