Alkyl Exchange Reactions of Organocobalt Porphyrins. A Bimolecular Homolytic Substitution Reaction

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Abstract: Reaction of organocobalt(III) porphyrins with a cobalt(II) complex of a distinguishable porphyrin or tetrapyrrole resulted in the reversible exchange of the organic axial ligand. The exchange reaction was facile in such solvents as benzene, toluene, dichloromethane, chloroform, and pyridine; was unaffected by total exclusion of light; was faster than would be expected for a homolytic process given known Co−C bond dissociation energies; and was of broad scope with respect to the organic ligand. Methyl, benzyl, primary alkyl, secondary alkyl, and acyl groups exchanged, but phenyl groups did not. The position of the exchange equilibrium was independent of the direction of approach and was nonstatistical. The relaxation to equilibrium appeared to be consistent with that of a second-order process. The rate of the reaction varied with the identity of the R group in the order Bzl ≥ Me > Et ≈ *n*-Pr > *i*-Pr > *i*-Bu > acetyl ≈ neopentyl ≈ 2-adamantyl. However, the total variation in reaction rates was remarkably small. Attempts to find evidence of free-radical intermediates by trapping with TEMPO or CO or by alkyl group interchange with an excess of an alkyl halide of a distinct alkyl group were unsuccessful over a time scale comparable to multiple half-lives of the exchange reaction. In addition, no rearrangement products were detected in exchange reactions of the 5-hexenyl group. Use of cobalt porphyrin reactants that were sterically encumbered on both faces with groups large enough to prevent formation of a bridged, Co−C−Co structure resulted in a 5 or more order of magnitude decrease in the rate of methyl exchange, if not its outright cessation, when run with total exclusion of light. The decrease in the rate of the thermal exchange process revealed the existence a slow photochemical exchange process that was driven by room lights. All evidence was consistent with a bimolecular S_H2 mechanism for the thermal exchange mechanism.

Introduction

Reactions in which an alkyl group is transferred between a metal and either a second metal or a metalloid or heteroatom are of considerable importance in both biochemistry and synthetic chemistry. Methyl group transfers to or from the cobalt atoms of corrinoid cofactors and the nickel atoms of F430 and CO dehydrogenase/acetyl-CoA synthase are central steps in the metabolic processes of acetogenic and methanogenic archaebacteria.[1−5] Methyl transfer reactions of methylcobalamin are also important in the synthesis of methionine from homocysteine[6] and the biomethylation of toxic heavy elements including mercury, arsenic, lead, and tin.[7,8] Transmetalation reactions[9] are essential to many useful organometallic synthetic procedures. Examples include the preparation of higher order mixed cyanocuprate reagents[10] and transfers of alkyl groups to palladium from a variety of organometallic reagents in such procedures as the Suzuki or Stille coupling reactions.[9,11]

Although alkyl transfer reactions are of quite broad scope, most mechanistic studies were conducted with alkylcobalt(III) complexes. This reflects both the relevance of these reactions to B_{12} chemistry and the ready availability and relative stability of alkylcobalt(III) complexes. The types of alkylcobalt(III) complexes investigated include cobalamins, cobamides, cobaloximes, and various tetradentate chelates with nitrogen or nitrogen and oxygen donor ligands. The studies have demonstrated alkyl transfer from cobalt complexes to chromium,[12−16] cobalt,[17−32] gold,[33] mercury,[23,33−41] nickel,[42] palladium,[43]

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platinum,[33,44−47] rhodium,[17] thallium,[33,37] and tin[48,49] compounds. Other studies have shown alkyl transfer from chromium to chromium,[50] chromium to cobalt,[14,15] iron to iron,[51] nickel to chromium,[52] and rhodium to rhodium.[53]

The mechanisms of alkyl transfer that were observed are diverse, which is not unexpected given the broad range of reaction partners that were examined. Metal−carbon bond cleavage can occur in three different manners: homolytically or heterolytically with two opposite polarizations. Thus, the alkyl group can transfer as a carbanion, eq 1 ; a radical, eq 2; or a

$$[\mathrm{R{-}M^{\mathit{x}}L_n}]^{q} + [\mathrm{{*}M^{\mathit{y}}L_p}]^{r} \rightarrow [\mathrm{M^{\mathit{x}}L_n}]^{(q+1)} + [\mathrm{R{-}{*}M^{\mathit{y}}L_p}]^{(r-1)} \tag{1}$$

carbocation, eq 3; where M and *M represent the different

$$[\mathrm{R{-}}M^{x}\mathrm{L_n}]^{q} + [\mathrm{{*}M^{\mathit{y}}L_p}]^{r} \rightarrow [\mathrm{M^{(\mathit{x}-1)}L_n}]^{q} + [\mathrm{R{-}{*}M^{(\mathit{y}+1)}L_p}]^{r} \tag{2}$$

$$[\mathrm{R{-}M^{\mathit{x}}L_n}]^{q} + [\mathrm{{*}M^{\mathit{y}}L_p}]^{r} \rightarrow [\mathrm{M^{(\mathit{x}-2)}L_n}]^{(q-1)} + [\mathrm{R{-}{*}M^{(\mathit{y}+2)}L_p}]^{(r+1)} \tag{3}$$

metals, x and y are their respective initial oxidation numbers, L_n and L_p represent their associated ligand sets, and q and r are the initial charges of the complexes. The transfers in eqs 2 and 3 involve changes in the formal oxidation states of the metals. Mechanistically, the electron transfer and alkyl group transfer processes can occur concurrently or sequentially. The electron transfer process can be outer sphere or inner sphere. The alkyl group transfer process can involve a freely diffusing alkyl intermediate or occur in a bimolecular intermediate. Several specific examples illustrate the range of mechanisms. Transfers of primary alkyl groups from Co(III) complexes to Hg(II) are examples of a simple bimolecular, S_E2 mechanism.[23,35,36,38] Consistent with this mechanism, alkyl transfer from *erythro*-3,3-dimethylbutyl-*1,2-d*$_2$-pyridinatobis(dimethylglyoximato)-cobalt(III) to mercuric ion occurs with inversion of configuration at the α-carbon.[23] Methyl transfer from $\mathrm{MeCo^{III}(dmgBF_2)py}$ to $\mathrm{Ni^{I}(tmc)^+}$ has a more complicated mechanism. It occurs by initial outer sphere electron transfer from Ni(I) to Co(III), Co−C bond homolysis of the resulting anionic methylcobalt(II) complex, and coligation of the methyl free radical by a second $\mathrm{Ni^{I}(tmc)^+}$ molecule.[42] An even more complicated mechanism was observed for alkyl transfer to platinum. The reaction requires both Pt(II) and Pt(IV) complexes and involves a termolecular intermediate.[46]

Of particular interest are alkyl exchange reactions, reactions in which M and *M are identical and their ligand sets are similar. Exchange reactions are nearly thermoneutral because there is essentially no redox driving force ($E° \approx 0$) or net change in metal−carbon bond energies. Consequently, exchange reactions tend to be reversible and can be studied in both forward and reverse directions. In addition, exchange reactions tend to be less rapid than transfer reactions for which M ≠ *M and a large $\Delta G°$ provides a significant driving force that dominates and lowers the activation energy (i.e. early transition state). Thus, exchange reactions are often well suited for study of the effects of steric and electronic factors on the "intrinsic" barriers to reaction. Several examples of exchange reactions are among those whose mechanism have been investigated. Alkyl transfer from alkylrhodium(III) macrocycles to rhodium(I) macrocycles[53] and alkylcobaloxime(III) complexes to cobaloxime(I) complexes[17,23,25] proceed by an S_N2-like mechanism. Equivalently, the mechanism can be viewed as a carbon-bridged inner-sphere two-electron-transfer process. Evidence for the mechanism includes a second-order kinetic rate law, the effects of the steric size of the alkyl group on rate constants, and the observation of inversion of configuration at the α-carbon of the transferred alkyl group. Alkyl transfer from alkyliron(III) porphyrin to iron(II) porphyrin is reported to proceed by homolytic dissociation of the Fe−C bond and subsequent capture of the alkyl free radical by iron(II).[51] Finally, alkyl transfers from alkylcobalt(III) macrocycles and cobaloximes to cobalt(II) macrocycles and cobaloximes are reported to proceed by an S_H2 mechanism,[22,24,25,27] the one-electron homolytic analogue of the S_N2 mechanism.[54−56] Equivalently, the mechanism can be described

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as a carbon-bridged inner-sphere one-electron-transfer process.[27] The evidence supporting the S_H2 mechanism is of similar type to that in the S_N2 case.

Alkyl exchange between alkylcobaloxime(III) complexes and cobaloxime(II) complexes is regarded as one of the best documented examples of an S_H2 reaction at a saturated carbon atom, which is relatively rare.[55,56] Unfortunately, alkyl exchange between alkylcobaloxime(III) complexes and cobaloxime(I) or cobaloxime(II) complexes containing differently substituted oxime ligands is complicated by the concurrent exchange of the equatorial oxime ligands.[25] The evidence suggests that the equatorial exchange of the oxime ligands follows alkyl exchange rather than provides a mechanism for an apparent alkyl exchange. Nonetheless, additional evidence from a system without complicating side reactions would help confirm the S_H2 mechanism.

Recently, we discovered that alkyl exchange occurs between methyl- and ethylcobalt(III) porphyrin and cobalt(II) hydroporphyrin complexes, eq 4 .[57] The Co−C bond dissociation energies

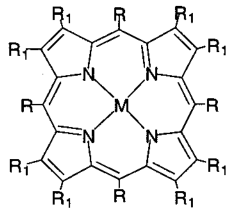
$$\mathrm{R{-}Co^{III}(P) + Co^{II}(P^*) = Co^{II}(P) + R{-}Co^{III}(P^*)} \quad (4)$$

of these five-coordinate, primary alkyl complexes are expected to be significantly greater than the 30 kcal/mol BDEs of six-coordinate $Co(OEP)(CH_2Ph)(PR_3)$ complexes.[58] The benzyl complexes undergo homolysis at appreciable rates only at elevated temperatures. In light of this, the facility of the alkyl exchange reactions at room temperature was remarkable. We therefore decided to investigate the mechanism of the alkyl exchange reactions of cobalt tetrapyrroles. For sake of convenience, the investigation was conducted with a series of porphyrins that had different peripheral substitution. Hydroporphyrins are not as readily available as porphyrins and can be converted to porphyrins through oxidative dehydrogenation[59] under certain conditions. This paper reports the results of our investigation, which provide unequivocal evidence for the S_H2 mechanism.

Results

^{1}H NMR of $Co^{II}(P)$ Complexes. Abbreviations for the porphyrins used in this investigation are defined in Scheme 1. Table 1 lists ^{1}H NMR data for the paramagnetic, low-spin d^7 cobalt(II) complexes of these porphyrins. Data are generally those at 25 °C in C_6D_6, the conditions employed in most experiments. Exceptions include Co(TpFPP) and $Co(TpNO_2PP)$, whose limited solubility in C_6D_6 required use of $CDCl_3$ and elevated temperature to observe complete spectra.[60] All peaks are broad in comparison to the line widths typical of diamagnetic complexes. The data also illustrate that the chemical shifts are both temperature and solvent dependent. Consistent with dipolar coupling, line widths and the magnitude of the paramagnetic shift of individual peaks decrease with the distance of the corresponding protons from the cobalt center.[61]

Scheme 1



Porphyrin	R_1	R
OEP	Et	H
TPP	H	Ph
TTP	H	4-methylPh
TpFPP	H	4-fluoroPh
$TpNO_2PP$	H	4-nitroPh
T2,6MeOPP	H	2,6-dimethoxyPh
T3,5tBuPP	H	3,5-di-*t*-butylPh
T2,6FBzOPP	H	2,6-bis($C_6F_5CH_2O$)Ph

Table 1. ^{1}H NMR Data for $Co^{II}(P)$ Complexes[a]

P	meso	CH_2	CH_3
OEP	29.98	8.77	6.06
OEP[b]	27.66	8.50	5.60

P	β-H[c]	*o*-H[c]	*m*-H[c]	*p*-H[d]
TPP	16.12	13.06	9.65	9.43
TPP[b]	15.21	12.66	9.48	9.30
TTP	16.35	13.10	9.87	—[e]
TTP[b]	15.36	12.66	9.35	—[f]
TTP[g]	15.80	13.00	9.71	—[h]
TpFPP[g,i]	15.24	12.74	9.49	—
$TpNO_2PP$[g]	15.62	13.14	10.74	—
T2,6MeOPP	15.81	—[j]	8.53	9.12
T3,5tBuPP	16.88	14.10	—[k]	10.21
T2,6FBzOPP	15.17	—[l]	8.70	9.05

[a] ppm relative to TMS at 25 °C in C_6D_6 solution, unless otherwise noted. [b] At 75 °C. [c] br s, 8H. [d] br s, 4H. [e] CH_3 group, 3.87 ppm (s, 12H). [f] CH_3 group, 3.76 ppm. [g] $CDCl_3$ solution. [h] CH_3 group, 4.14 ppm. [i] At 60 °C (sealed tube), due to poor solubility. [j] CH_3O group, 3.11 ppm (s, 24H). [k] *t*-Bu group, 2.75 ppm (s, 72H). [l] $ArCH_2O$ group, 4.72 ppm (s, 16H).

Preparation and ^{1}H NMR Characteristics of $R{-}Co^{III}(P)$ Complexes. Five-coordinate $R{-}Co^{III}(P)$ complexes were prepared by reaction of $Co^I(P)^-$ with excess R−I or R−Br, eq 5.[62−65] Reduction of $Co^{II}(P)$ by $NaBH_4$ in pyridine/ethanol

$$\mathrm{Na[Co^{I}(P)] + R{-}X \rightarrow R{-}Co^{III}(P) + NaX} \quad (5)$$

afforded the $Co^I(P)^-$ anion for P = TPP and TpFPP. For P = TTP, OEP, and other porphyrins complete reduction to $Co^I(P)^-$ required sodium amalgam in THF. Owing to the reactivity of nitro groups with reducing agents, $R{-}Co^{III}(P)$ complexes were prepared only by alkyl exchange for P = $TpNO_2PP$. Use of excess alkyl halide increased conversion to products and limited the possibility that alkyl exchange between the initially formed $R{-}Co^{III}(P)$ and unreacted $Co^I(P)^-$, eq 6, might occur and result in rearrangement of certain R groups.

$$\mathrm{R{-}Co^{III}(P) + Co^{I}(P^*)^- \rightarrow R{-}Co^{III}(P^*) + Co^{I}(P)^-} \quad (6)$$

Equation 5 is synthetically useful for a wide range of R groups including alkyl, acyl, benzyl, aryl, cycloalkylmethyl, ω-halo,

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Table 2. ^{1}H NMR Data for Axial Alkyl Groups of Co(OEP)R Complexes[a]

R	α-CH	*β*-CH	*γ*-CH	*δ*-CH	*ϵ*-CH
Me	−4.47 (s, 3H)				
Et	−3.58 (b, 2H)	−5.13 (t, 3H)			
n-Pr	−3.68 (b, 2H)	−4.60 (m, 2H)	−1.94 (t, 3H)		
i-Pr	−3.40 (b, 1H)	−5.13 (d, 6H)			
n-Bu	−3.65 (b, 2H)	−4.76 (qn,[b] 2H)	−1.62 (m, 2H)	−0.97 (t, 3H)	
i-Bu	−3.78 (d, b, 2H)	−5.39 (m, 1H)	−2.19 (d, 6H)		
$CH_2C(CH_3)_3$	−3.93 (s, 2H)		−2.40 (s, 9H)		
$(CH_2)_2CHCH_2$	−3.73 (t, b, 2H)	−3.94 (m, 2H)	3.29 (dd, 1H)	2.94 (m, 2H)	
$(CH_2)_3CHCH_2$	−3.69 (t, b, 2H)	−4.67 (qn, 2H)	−0.98 (m, 2H)	3.37 (m, 1H)	−[c]
$(CH_2)_4CHCH_2$	−3.70 (t, b, 2H)	−4.78 (qn, 2H)	−1.63 (qn, 2H)	0.06 (q, 2H)	4.40 (m, 1H) 4.30 (m, 2H)[d]
$(CH_2)_4CH_2Br$	−3.84 (b, 2H)	−4.94 (qn, 2H)	−1.86 (qn, 2H)	−0.43 (qn, 2H)	1.61 (t, 2H)
CH_2(*c*-C_3H_5)	−3.75 (d, 2H)	−4.66 (m, 1H)	−3.17 (b, 2H) −2.02 (m, 2H)		
CH_2(*c*-C_5H_9)	−3.63 (d, 2H)	−4.62 (m, 1H)	−2.35 (m, 2H) −1.43 (m, 2H)	−0.12 (m, 4H)	
Ph		0.35 (d, 2H)[e]	4.50 (t, 2H)[f]	4.91 (t, 1H)[g]	
Bzl	−2.60 (s, 2H)		3.24 (d, 2H)[e]	5.63 (t, 2H)[f]	6.49 (t, 1H)[g]
COMe		−2.59 (s, 3H)			
CO(*n*-Pr)		−2.58 (t, 2H)	−1.46 (m, 2H)	−1.35(t, 3H)	
CO(*i*-Pr)		−3.05 (m, 1H)	−2.13 (d, 6H)		
2-adamantyl	−3.26 (s, 1H)	−4.87 (s, 2H)	−3.12 (d, 2H)[h] −0.84 (d, 2H)[i] −0.64 (m, 4H)[j]	−0.15 (s, 1H)	0.30 (s, 2H)

[a] ppm relative to TMS at 25 °C in C_6D_6 solution. [b] Quintet. [c] Peak for the alkenyl CH_2 group appears to be under the OEP ethyl group CH_2 multiplet at 3.93 ppm. [d] Peak for the *ω*-CH alkenyl CH_2 group. [e] *o*-H. [f] *m*-H. [g] *p*-H. [h] Syn axial. [i] Syn equatorial. [j] Anti.

and *ω*-alkenyl. In certain cases the reaction afforded a mixture of products that could not be separated. Cyclopropylmethyl bromide reacted with $Co^I(OEP)^-$ to afford mixtures of (cyclopropylmethyl)Co(OEP) and (3-butenyl)Co(OEP). The steric hindrance of the reactive site in neopentyl bromide slowed its rate of reaction with $Co^I(P)^-$ relative to the rates of reaction of alkyl halide impurities contained in this substrate. Given the use of excess alkyl halide in the reaction, the neopentylcobalt porphyrin complexes obtained contained roughly 20% isobutylcobalt porphyrin and other trace impurities. Steric hindrance and/or a tertiary center also led to complications in the reaction of $Co^I(OEP)^-$ with 1-bromoadamantane. Although a sharp singlet was observed at an upfield chemical shift that would be appropriate for the six equivalent *β*-protons of (1-adamantyl)-Co(OEP) (−5.46 ppm), other upfield resonances were too numerous and had shifts inconsistent with those expected for the remaining protons of a 1-adamantyl group. The OEP meso proton resonances established that multiple compounds were present. Hence, the 1-adamantyl complex was not pursued further. In contrast, (2-adamantyl)cobalt porphyrin complexes were readily obtained from reaction of 2-bromoadamantane with $Co^I(OEP)^-$.

The $R-Co^{III}(P)$ complexes typically were purified by recrystallization. Chromatography was useful in separating $R-Co^{III}$-(P) complexes from $Co^{II}(P)$ that might be present in the reaction mixture or grow in upon prolonged storage, but generally was not able to separate $R-Co^{III}(P)$ complexes with different R groups. Moreover, some isomerization of alkyl groups occurred in contact with chromatographic supports. Chromatography of pure, recrystallized (1-propyl)Co(OEP) on alumina with 1:5 CH_2Cl_2/hexane led to varying but significant amounts of (2-propyl)Co(OEP) in the eluate.

Table 3. ^{1}H NMR Data for Co(P)CH_3 Complexes[a]

P	*δ* of CH_3 group
OEP	−4.47
TPP	−3.99
TTP	−3.92
TpFPP	−4.06
TpNO_2PP	−4.25[b]
T2,6MeOPP	−3.64
T3,5tBuPP	−3.77
T2,6FBzOPP	−4.44

[a] ppm relative to TMS at 25 °C in C_6D_6 solution, unless noted otherwise. [b] In C_5D_5N solution.

$R-Co^{III}(P)$ complexes were generally quite stable in solution and as solids in the absence of O_2. Exceptions included the cyclopropylmethyl complex, which converted to the 3-butenyl complex. The speed of the conversion in solution varied with the sample, but generally took over 24 h. When stored as a solid, conversion was complete in 3 months. Secondary alkyls such as isopropyl slowly decompose in solution to $Co^{II}(P)$ and undetected organic products, presumably propene and hydrogen. Exposure of $R-Co^{III}(P)$ complexes to O_2 led to formation of the peroxo complexes $ROO-Co^{III}(P)$. The later were readily detected by the characteristic chemical shift of their meso protons (P = OEP) and by the significant downfield shifts (≥2 ppm) of the proton resonances for the axial alkylperoxo groups relative to those of the corresponding $R-Co^{III}(P)$ complexes.[64,66]

The ^{1}H NMR data for the axial R groups of the $R-Co^{III}$-(OEP) and $Co^{III}(P)CH_3$ complexes are collected in Tables 2 and 3, respectively. The chemical shifts of the porphyrin protons are relatively invariant and thus are not tabulated individually. The ring current of the porphyrin strongly shields the protons of the axial R group. The resulting upfield shifts are greater for OEP than for tetraaryl porphyrins, Table 3. The shielding decreases rapidly with the distance above the porphyrin plane. However, as is evident from the data in Table 2, the chemical shifts do not increase monotonically with position along the R group. Although the complexes are virtually diamagnetic, paramagnetic shifts arise from temperature-independent paramagnetism and result in inversion of the chemical shifts of the α- and *β*-protons. In addition, coupling of the α-protons to the quadrupolar Co nucleus results in anomalously large line

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widths.[67] The magnitudes of the paramagnetic shifts and quadrupolar coupling depend on the temperature, solvent, and ligation state of cobalt so the observed chemical shifts and line widths are variable. The dispersion of proton shifts is sufficiently great, though, that the order of shifts from most negative (upfield) to most positive (downfield) does not vary from β-H $<$ α-H $<$ γ-H $<$ δ-H $<$ ϵ-H and assignment of individual protons is generally straightforward. Exceptions to this are the olefinic protons of the 5-hexenyl, 4-pentenyl, and 3-butenyl groups, whose low-intensity multiplets can be difficult to observe or obscured by other peaks.

The ability of the porphyrin ring current to differentiate the chemical shifts of the inequivalent γ-geminal protons of cycloalkyl complexes is noteworthy. For Co(OEP) complexes, shift differences of 1.15 and 0.92 ppm respectively are observed for these protons in axial cyclopropylmethyl and cyclopentylmethyl groups. Moreover, the γ-syn-axial protons of the 2-adamantyl group, whose C−H bonds point toward the porphryin plane, are 2.28 ppm upfield of the γ-syn-equatorial protons. This is even more remarkable given that the γ-syn-axial protons are typically 0.5 to 0.7 ppm downfield of the γ-syn-equatorial protons in 2-substituted adamantanes.[68,69] In contrast, the porphyrin ring current does not markedly differentiate the chemical shifts of geminal cycloalkane protons that are farther removed from the cobalt atom.

The synthesis of Co(T2,6FBzOPP)CH_3 presented special difficulties. We attempted to prepare the complex by the Grignard route[63,70,71] rather than by reductive alkylation because the benzylic ether groups present in the porphyrin can be cleaved by the reducing agents required to produce $Co^I(P)^-$. Aerobic oxidation of Co(T2,6FBzOPP) in methanolic HBr afforded pure Co(T2,6FBzOPP)Br in near quantitative yield. Reaction of the latter with a 35-fold excess of methylmagnesium iodide afforded a mixture of Co(T2,6FBzOPP)CH_3, Co(T2,6FBzOPP)Br, and Co(T2,6FBzOPP) in which the desired alkyl complex constituted less than 50% of the material. The upfield singlet at −4.44 ppm for the axial methyl group of Co(T2,6FBzOPP)CH_3 establishes that the ring currents of the four perfluorobenzyloxy groups surrounding the methyl group contribute a further 0.45 ppm of shielding relative to that in TPP. Attempts to separate the mixture by chromatography failed. Apparently, the perfluorobenzyloxy groups on the exterior of the complexes effectively hide the cobalt and its ligand from the support and lead to near identical interactions with the chromatographic support. The reductive alkylation route was attempted with a smaller than normal excess of sodium amalgam. As soon as the color change suggested reduction to $Co^I(P)^-$ was complete, the solution was separated from the amalgam and reacted with excess methyl iodide. The ^{1}H NMR spectrum showed that the product was predominantly Co(T2,6FBzOPP)CH_3 but also contained small amounts of products that had lost one or more perfluorobenzyloxy ether groups. The singlet at −4.44 ppm had a shoulder and a broad, low-intensity peak on its low-field side. In addition, several small broad peaks were just observable above the baseline noise between −1 and −3 ppm. Consistent with the presence of additional compounds, small shoulders also were observed on the porphyrin pyrrole β-proton peak at 8.78 ppm.

Alkyl Exchange Reactions. Reaction of a solution of five-coordinate R−Co^{III}(P) with a solution of four-coordinate Co^{II}(P*) results in facile transfer of the alkyl group between the two cobalt porphyrins, eq 4. Because the total numbers of cobalt(II) porphyrin and alkylcobalt(III) porphyrin molecules in the population are preserved, to a first approximation the reaction has $\Delta G° = 0$ and is an exchange reaction.[72] The reaction is readily followed by ^{1}H NMR spectroscopy. Its rate is sufficiently slow on the NMR time scale that individual resonances are neither shifted nor noticeably broadened compared to their appearance in the spectrum of the pure compound. Thus, every resonance in the spectra of reaction mixtures, which consist of four compounds, can be definitively identified by comparison to spectra of authentic samples prepared by direct synthesis.

Solutions used in our investigations of the exchange reaction were typically 1−3 mM in porphyrin complex. Lesser concentrations led to difficulties in observing NMR signals of interest. The upper part of the range was dictated by the maximum solubility of some complexes. We used C_6D_6 as the solvent in most experiments. Exchange reactions are also facile in C_7D_8, $CDCl_3$, CD_2Cl_2, and C_5D_5N solutions. The predominant species in the latter solvent are six-coordinate R−Co^{III}(P)(C_5D_5N) and five-coordinate Co^{II}(P*)(C_5D_5N).

The scope of the alkyl exchange reaction is quite broad. In addition to methyl groups, all primary and secondary alkyl groups investigated were observed to exchange. This included isobutyl and neopentyl, primary alkyls that are sterically hindered by an adjacent branched carbon, and the highly branched 2-adamantyl. Acyl and benzyl groups exchanged, too. Phenyl was the only group for which no trace of transfer could be detected, even at times as long as 4 days after mixing the Co^{III}(P)(C_6H_5) and Co^{II}(P*) reactants.

R−Co^{III}(P) complexes are susceptible to photochemical homolysis of the Co−C bond. Control experiments with R = CH_3 established that there was no discernible difference in rate or outcome of the alkyl exchange reaction between otherwise identical solutions that were prepared and reacted with complete exclusion of light or with exposure to regular intensity room lights. Nonetheless, all experiments were prepared and conducted under subdued room lights.

The rate of the alkyl exchange reaction for R = CH_3 was too rapid to permit a detailed study of the kinetics, given certain limitations of our NMR equipment. The initial spectrum could not be obtained in much less than 10 min after the sample was mixed. At this point in time, the room temperature exchange already had completed roughly 2 half-lives of reaction. It was not possible to initiate the reaction at a controlled low temperature in the spectrometer cavity by thawing a sample that had been rapidly frozen upon mixing because the NMR control software does not permit temperature control until the NMR is shimmed and locked on the sample.

The reaction quotient Q is defined by the expression in eq 7 and is identical with the equilibrium constant K when the system is at equilibrium. Q was determined at a particular time by

$$Q = \frac{[\mathrm{Co^{II}(P)}][\mathrm{R{-}Co^{III}(P^*)}]}{[\mathrm{R{-}Co^{III}(P)}][\mathrm{Co^{II}(P^*)}]} \tag{7}$$

substituting the concentration of each of the four compounds in eq 7 with the value of the integration of a well-resolved peak

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Table 4. Equilibrium Constants for Alkyl Transfer from $Co^{III}(OEP)R$ to $Co^{II}(P^*)$[a]

P*	R	K
$TpNO_2PP$[b]	Me	0.63
TpFPP	Me	0.66
TPP	Me	0.86
TTP	Me	1.20
TTP	Et	1.13
TTP	*i*-Pr	1.10
TTP	Bzl	1.15

[a] At 25 °C in C_6D_6 solution unless noted otherwise. [b] In C_5D_5N solution.

characteristic of that compound divided by the number of equivalent protons responsible for that peak. The presence of paramagnetic $Co^{II}(P)$ compounds speeds proton relaxation sufficiently that adequate delay times for accurate integration were not an issue.

The Q values of different alkyl exchange reactions were examined as a function of time. Initially, the value of Q changed but then became constant for a considerable period of time. The time required to achieve constant Q was small compared to the time required for decomposition of the individual alkyl complexes involved in the reaction. In the worst case, exchange of the isopropyl group achieved constant Q in 2−3 h while decomposition typically required 8 h. For a given alkyl group and pair of porphyrins, the constant value of Q was independent of the direction of alkyl transfer. Thus, the alkyl exchange reactions achieve true equilibria, and the constant value of Q is the equilibrium constant K. Values of K are presented in Table 4. Equilibrium constants could not be determined for alkyl exchange between Co(TPP) and Co(TTP) complexes. The chemical shift differences between the alkyl resonances of these complexes were too small for adequate resolution and integration.

Despite the lack of quantitative kinetic data, some information about reaction kinetics was apparent from general observations. First and most importantly, the differing times to achieve equilibrium, all other factors held constant, established that the rate of reaction depends on the identity of the R group. The rate order was Bzl $\geq$ Me $>$ Et $\approx$ *n*-Pr $>$ *i*-Pr $>$ *i*-Bu $>$ acetyl $\approx$ neopentyl $\approx$ 2-adamantyl. Second, variation of reaction rate with alkyl group was striking for its small range. Under typical conditions, exchange of methyl groups achieved equilibrium in about 20 min. Exchange of the bulkier *i*-Pr group reached equilibrium in roughly 2 to 3 h. Even acetyl, neopentyl, and 2-adamantyl exchange achieved equilibrium within 12 to 24 h. (The exchange of these last three groups was not examined at sufficient intervals to determine the typical time to achieve equilibrium more precisely.) Third, within the limited range of concentrations investigated, equilibrium appeared to be achieved faster for more concentrated rather than more dilute solutions. Although by no means conclusive, this would appear to be more consistent with the relaxation to equilibrium of a second-order process rather than a first-order process.[72] Finally, the identity of the solvent did not appear to have a noticeable effect on the time to achieve equilibrium.

Mechanistic Probes. (i) Radical Traps. Several reagents that can trap or intercept radicals were investigated as probes of the involvement of free radicals in alkyl exchange reactions. The stable nitroxide free radical TEMPO (2,2,6,6-tetramethylpiperidinyl-1-oxy) has been used in the kinetic measurement of Co−C bond dissociation energies. Experiments with several classes of alkylcobalt(III) complexes have shown that TEMPO concentrations of 10^{-2} M are sufficient for completely efficient trapping of alkyl free radicals (i.e. the homolysis rate is limiting and independent of TEMPO concentration) when the complex concentration is 10^{-5} M.[58,73,74] Toluene solutions that were 2×10^{-5} M in $Co(OEP)CH_3$ and 2×10^{-2} M in TEMPO monitored by UV/vis spectroscopy were completely unchanged after 20 h of reaction in the dark at 25 °C.[75] In contrast, UV irradiation of the solution for 1 min resulted in complete conversion of the alkyl complex to Co(OEP).

The radical traps bromotrichloromethane and organotin hydrides proved unsatisfactory for use in the alkyl exchange reaction. Control experiments established that when present in the large molar excesses required to efficiently trap alkyl radicals, bromotrichloromethane, tributyltin hydride, and triphenyltin hydride each reacted directly with cobalt(II) porphyrins to affect partial conversion to either trichloromethyl- or triorganotin−cobalt(III) porphyrin complexes. The same complexes also result from reaction of the trapping reagents with alkylcobalt(III) porphyrin complexes. Both series of reactions occur by free-radical mechanisms.[76] However, the rates of these processes are substantially slower than alkyl exchange, even when a 100-fold excess of trapping reagent is present.

Alkyl group interchange between radicals of one alkyl and an excess of the alkyl halide of a second alkyl, eq 8, was demonstrated for alkyliron(III) porphyrin complexes .[77] Because

$$R^\bullet + R'{-}X \rightarrow R'^\bullet + R{-}X \tag{8}$$

alkyl halides do not react with cobalt(II) porphyrins at any significant rate, we investigated the course of the alkyl exchange reaction in the presence of an alkyl halide that had a distinguishable alkyl group. One equivalent each of $Co(OEP)CH_3$ and Co(TTP) were reacted in C_6D_6 in the presence of 100 equiv of C_2H_5I, *i*-C_3H_7I, or *n*-C_4H_9Br. The exchange of the methyl group achieved equilibrium in the normal time period. Upfield peaks corresponding to the alkyl groups of Co(P)Et, Co(P)(*i*-Pr), or Co(P)Bu were not detected after 12 h of reaction, a time that corresponds to more than 100 half-lives of exchange. Exchange reactions of $Co(OEP)CH_3$ and Co(TTP) conducted in CD_2Cl_2 or $CDCl_3$ solution also provided no evidence of alkyl group interchange between methyl radicals and solvent after 1 day.

Alkyl radicals can be captured by CO to afford acyl radicals, eq 9. The reaction is exothermic and has a sufficiently rapid forward rate constant for $R = CH_3$ that it can compete with radical capture by cobalt(II) tetraazamacrocycle complexes.[78]

$$R^\bullet + CO \rightarrow RC^\bullet O \tag{9}$$

The equilbrium constants for eq 9 are favorable in most cases. Rate constants for decarbonylation of acyl radicals, the reverse of eq 9, are small except for benzylic radicals.[79] CO does not bind to or react with cobalt(II) porphyrins. The applicability of using CO as a probe for the presence of alkyl radicals was demonstrated by the rapid thermal conversion of alkyliron(III) porphyrin complexes to acyliron(III) porphyrin complexes when

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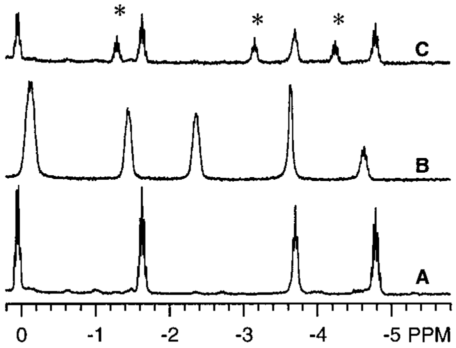

Figure 1. Upfield regions of ^{1}H NMR spectra in C_6D_6: (A) (5-hexenyl)Co^{III}(OEP), (B) (cyclopentylmethyl)Co^{III}(OEP), (C) 1:1 mixture of (5-hexenyl)Co^{III}(OEP) and Co^{II}(TTP) after 5 h of exchange. The asterisk denotes peaks due to (5-hexenyl)Co(TTP). The δ-CH$_2$ peak of (5-hexenyl)Co(TTP) is not shown because it was obscured by a silicone grease impurity peak.

exposed to 1 atm of CO.[80] In addition, acetyl-cobalamin was produced by photochemical reaction of CO and methylcobalamin.[81]

Alkyl exchange between Co(OEP)CH$_3$ and Co(TTP) was not affected when the reaction was run under 1 atm of CO. The upfield singlet of the acetyl group of Co(P)(COCH$_3$) was not detected after 12 h of reaction, a time that corresponds to over 100 half-lives of exchange. In separate experiments, solutions of Co(OEP)CH$_3$ or Co(OEP)(i-C$_3$H$_7$) were placed under 1 atm of CO and stored in the dark between acquisition of spectra. After 2 days, CO had inserted into the Co−C bond to afford the acyl complexes Co(OEP)(COCH$_3$) or Co(OEP)(COCH(CH$_3$)$_2$) in less than 2% yield. The acyl complexes were not present at detectable levels during the first 12 to 24 h of reaction.

(ii) Cyclizable Probes. The existence of free radical intermediates frequently is examined by use of cyclizable probes, substrates whose free radicals undergo rapid intramolecular radical rearrangments that result in rearranged products.[82,83] These substrates are called free-radical clocks when they are used to provide quantitative rate data for radical processes.[82] Two commonly used cyclizable probe substrates are 1-bromo-5-hexene and cyclopropylmethyl bromide. The 5-hexenyl radical cyclizes to the cyclopentylmethyl radical with a rate constant of 2.2×10^5 s^{-1} at 25 °C.[84] Rearrangement of the cyclopropylcarbinyl radical is substantially faster. It opens to the 3-butenyl radical with a rate constant of 1.0×10^8 to 1.2×10^8 s^{-1} at 25 °C.[85,86]

Authentic samples of (5-hexenyl)Co(OEP) and (cyclopentylmethyl)Co(OEP) were prepared by reaction of Co^I(OEP)$^-$ with 6-bromo-1-hexene and cyclopentylmethyl iodide, respectively. The upfield region of the ^{1}H NMR spectra of the two complexes are compared in traces A and B of Figure 1. The complexes are readily distinguished by the number, relative intensities, and multiplet patterns of their resonances. The spectra also show that the (5-hexenyl)cobalt porphyrin produced by reaction of 6-bromo-1-hexene with Co^I(P)$^-$ does not contain detectable quantities of the rearrangement product (cyclopentylmethyl)cobalt porphyrin. The small baseline features in the spectrum of (5-hexenyl)Co(OEP) result from the reaction of Co^I(P)$^-$ with the alkyl halide impurities present in the 95% pure 6-bromo-1-hexene reagent.

Trace C of Figure 1 shows the spectrum of a mixture of 1 equiv each of (5-hexenyl)Co(OEP) and Co^{II}(TTP) after more than 5 h of reaction. Neither (cyclopentylmethyl)Co(OEP) nor (cyclopentylmethyl)Co(TTP) are present in detectable quantities. Thus, transfer of the 5-hexenyl group from one cobalt porphyrin to the second must occur with negligible rearrangement if none of the rearranged products can be observed after roughly 20 half-lives of exchange.

We were unable to obtain (cyclopropylmethyl)Co(OEP) as a pure compound. Reaction of cyclopropylmethyl bromide with Co^I(OEP)$^-$ gave a mixture of (cyclopropylmethyl)Co(OEP) and (3-butenyl)Co(OEP) whose composition varied somewhat in different preparations. Chromatography was ineffective for separation of the two complexes. Because a 2:3 mixture was the best we obtained, it was used to investigate alkyl exchange. A sample of the mixture was dissolved in C_6D_6 and split into two equal portions. One portion was combined with about 1 equiv of Co(TTP), based on total contained Co(OEP) in the portion, and monitored by NMR to follow the exchange reaction. The second portion of the mixture was monitored to follow its conversion to (3-butenyl)Co(OEP). In the initial phase of the exchange reaction, peaks due to (3-butenyl)Co(TTP) appeared and grew in intensity and those due to (3-butenyl)Co(OEP) decreased in intensity. The equilibrium between these two compounds was achieved in about 2 h time. The peaks corresponding to (cyclopropylmethyl)Co(OEP) disappeared completely in 12 to 24 h. Peaks attributable to (cyclopropylmethyl)Co(TTP) were present at most at barely detectable levels a few hours into the reaction. Conversion of the second portion of the mixture to (3-butenyl)Co(OEP) was not complete in 24 h. In separate experiments, the exchange reactions of (3-butenyl)Co(OEP) and (isobutyl)Co(OEP) with Co(TTP) were examined. Exchange of the 3-butenyl group achieved equilibrium in roughly 2 h, consistent with observations during the initial phase of the exchange reaction for the mixture. Exchange of the isobutyl group, which should have a steric size similar to or slightly larger than the cyclopropylmethyl group, occurred over a time scale of 3 to 6 h. Thus, transfer of the cyclopropylmethyl group appears to occur predominantly, if not completely, with concurrent rearrangement to a 3-butenyl group.

(iii) Effects of Sterically Encumbered Porphyrins. We investigated the effect of increasing the minimum distance of separation between the cobalt atoms of the porphyrin complex reaction partners in alkyl exchange by examining the effect of increasing the steric bulk of the porphyrin. The exchange reaction can occur at either face of the cobalt(II) porphyrin. Hence, steric bulk must be present on both faces of the porphyrin.

Initially, we investigated alkyl exchange reactions with porphyrins derived from disubstituted benzaldehyde precursors that were readily available. Substitution of TPP with *tert*-butyl groups at all eight meta positions slowed, but did not stop methyl exchange. Under comparable conditions, the exchange reaction between Co(OEP)CH$_3$ and Co(T3,5tBuPP) reached equilibrium in about 1 h as compared to about 20 min for exchange between Co(OEP)CH$_3$ and Co(TTP). Substituents in ortho positions produced a greater effect. Exchange between Co(OEP)CH$_3$ and Co(T2,6MeOPP) required about 2 h to achieve equilbrium.

The the ortho perfluorobenzyloxy groups of Co(T2,6FBzOPP) had a substantial effect on the exchange reaction. Solutions of

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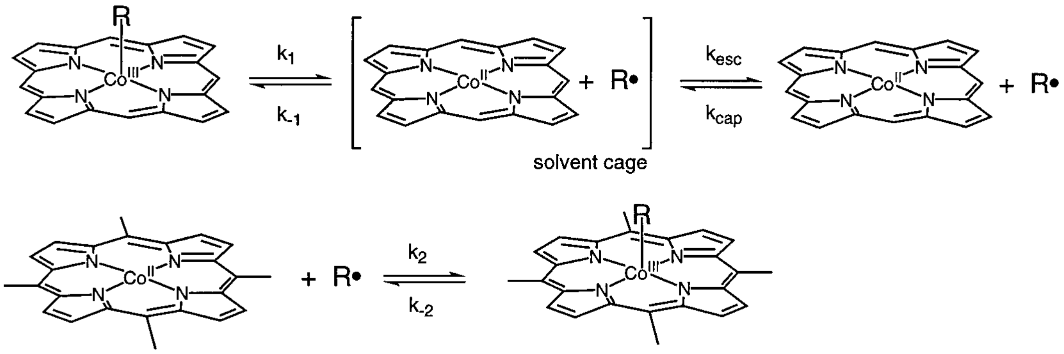
Scheme 2



Co(TTP)CH_3 and Co(T2,6FBzOPP) were prepared and mixed in foil-wrapped glassware under subdued light to prevent exposure to light. Half of the solution was sealed in an NMR tube and allowed to stand continuously under normal room lights. After 1.5 h of reaction under room light, the singlet due to Co(T2,6FBzOPP)CH_3 was just detectable over the spectral noise. With time, the singlet grew in intensity and the Co(TTP)CH_3 singlet decreased in intensity. Alkyl exchange between these porphyrins appeared to achieve equilibrium in roughly 24 h. The second half of the solution was sealed in an NMR tube that was wrapped in aluminum foil and stored in a light-tight container at all times that it was not in the NMR spectrometer probe. The reaction was monitored for 19.5 days. At no point during that time was any new upfield peak observed. Consequently, the slow exchange observed in the reaction conducted under room lights must be photochemically activated.

Exchange reactions between nearly pure Co(T2,6FBzOPP)CH_3 and Co(TTP) were prepared and run as described above for the exchange in the opposite direction. As above, alkyl exchange under room lights achieved equilibrium in roughly 24 h. In contrast, only a small amount of Co(TTP)CH_3 was present after 13 days of exchange when the reaction was run with total exclusion of light. The Co(TTP)CH_3 present appeared to have resulted from exchange of Co(TTP) with the portion of the Co(T2,6FBzOPP)CH_3 sample whose perfluorobenzyloxy groups had been partially cleaved. The small upfield impurity peaks decreased in intensity relative to the singlet at −4.44 ppm during the experiment.

Discussion

Alkyl Exchange Equilibria. Our results establish that alkyl group exchange equilibria are not merely statistical. The experimental values of K reported in Table 4 are distinguishable from 1.00. However, the energy differences from statistical exchange represented by these K are small. Marginally, the data suggest that porphyrins that are more electron rich are more effective competitors for methyl groups. In addition, bulkier R groups favor octaalkylporphyrins over tetraarylporphyrins, which have more bulk close to the axial R group. These trends are consistent with but somewhat smaller than those seen for alkyl exchange between cobalt porphyrins and hydroporphyrins.[57]

Relatively few reports of equilibrium constants for alkyl exchange exist in the literature. Examples include exchange between alkylcobalt(III) and cobalt(II) macrocyclic complexes,[22,27,57] methylcob(III)alamin and cob(II)inamides or cob(I)inamides,[29−31] and methylcob(III)inamide and nonalkyl cobinamides. [32] The latter reaction leads to equilibration of the α- and β-diastereomers of methylcob(III)inamide. Because of the facile exchange of oxime ligands,[25] equilibrium data for cobaloxime complexes are not available unless forward and reverse rate constants can be measured independently.[27] In general, equilibrium constants for Co(III) to Co(II) transfer are relatively small unless the macrocycles are significantly different. The preference for the less crowded β-methylcobinamide diastereomer showed that the exchange equilibrium is affected by steric factors.

Mechanism of Alkyl Exchange Reaction. Several different mechanisms can be envisioned for the transfer of an alkyl group from an alkylcobalt(III) complex to a cobalt(II) complex, eq 4. In some mechanisms alkyl group transfer and electron transfer occur concurrently. In others, redox processes are independent steps. The mechanistic possibilities are enumerated and evaluated in light of the evidence in the following discussion.

A homolytic, free-radical process for exchange, Scheme 2, must be considered as a strong possibility in light of the role of coenzyme B_{12} as a “reversible free-radical carrier”.[87] Homolysis of the Co−C bond could occur either photochemically or thermally. Scheme 2 explicitly shows a caged radical pair, which can play important roles in the chemistry of radical species.[74,88] Under conditions in which cage escape is efficient (i.e. $F_C = k_{-1}/[k_{-1} + k_{esc}]$ is small) and the concentration of $Co^{II}(P^*)$ is large compared to that of $Co^{II}(P)$, the rate of exchange will be first order in $R{-}Co^{II}(P)$. The activation energy for the homolysis step is closely related to the bond dissociation energy,[89] which is related to the stability of the alkyl radical. It should be noted that the persistent radical effect would be important in the presence of intentionally added 10^{-3} M $Co^{II}(P^*)$, a stable metalloradical.[90,91] The effect would suppress the equilibrium concentration of alkyl free radicals and alkyl radical self-recombination products will not form to any significant extent.

The S_H2 mechanism, Scheme 3, requires a bridged intermediate. Consequently, the reaction kinetics will be mixed second order. Because the 3-electron, 3-centered bridged intermediate involves both partial breaking of the original Co−C bond and partial making of the new Co−C bond, the activation energy will not be directly related to the bond dissociation energy.

Several mechanisms involving outer-sphere electron transfer are possible. Two mechanisms that involve Co−C bond homolysis to afford an alkyl radical are outlined in eqs 10

$$R{-}Co^{III}(P) + Co^{II}(P) \rightarrow R{-}Co^{IV}(P)^+ + Co^{I}(P^*)^- \qquad (10)$$

$$R{-}Co^{IV}(P)^+ \rightarrow Co^{III}(P)^+ + R^\bullet \qquad (11)$$

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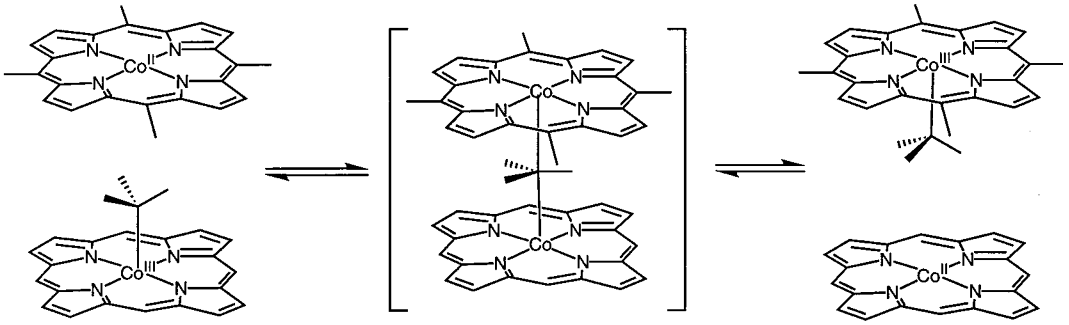
Scheme 3



$$R^{\bullet} + Co^{I}(P^*)^- \rightarrow R{-}Co^{II}(P^*)^- \quad (12)$$

$$Co^{III}(P)^+ + R{-}Co^{II}(P^*)^- \rightarrow Co^{II}(P) + R{-}Co^{III}(P^*) \quad (13)$$

$$R{-}Co^{III}(P) + Co^{II}(P^*) \rightarrow R{-}Co^{II}(P)^- + Co^{III}(P^*)^+ \quad (14)$$

$$R{-}Co^{II}(P)^- \rightarrow Co^{I}(P)^- + R^{\bullet} \quad (15)$$

$$R^{\bullet} + Co^{III}(P^*)^+ \rightarrow R{-}Co^{IV}(P^*)^+ \quad (16)$$

$$Co^{I}(P)^- + R{-}Co^{IV}(P^*)^+ \rightarrow Co^{II}(P) + R{-}Co^{III}(P^*) \quad (17)$$

through 13 and eqs 14 through 17. Both one electron oxidation[92−95] and one electron reduction[96,97] of cobalt in alkylcobalt(III) complexes are known to decrease the Co−C bond dissociation energy and increase the rate of bond homolysis, eqs 11 and 15, as well as other modes of cleavage.[98] Although there would appear to be two distinct initial electron-transfer processes possible, eqs 10 and 14, the necessity to readjust oxidation states after alkyl radical capture by the second cobalt porphyrin links the two. Exchange along eqs 10 through 13 is seen to be the microscopic reverse of exchange along eqs 14 through 17, when the distinction between the two different porphyrins is ignored. Thus, the following discussion will be simplified by including the alternate pathways that follow eq 10 but not the related ones following eq 14. The alkyl radical also can be captured by a second Co^{II}(P*), eq 18, in which case another electron transfer follows to convert the intermediate Co^{III}(P)$^+$ to product Co^{II}(P), eq 19 . Nonhomolytic, bimolecular

$$R^{\bullet} + Co^{II}(P^*) \rightarrow R{-}Co^{III}(P^*) \quad (18)$$

$$Co^{III}(P)^+ + Co^{I}(P^*)^- \rightarrow Co^{II}(P) + Co^{II}(P^*) \quad (19)$$

processes are also possible following electron transfer, eq 10. S$_N$2 displacement of a carbocation from R−Co^{IV}(P)$^+$ by Co^{I}(P*)$^-$ affords an excited state of Co^{II}(P), eq 20 , that has

$$R{-}Co^{IV}(P)^+ + Co^{I}(P^*)^- \rightarrow Co^{II}(P)_{exctd} + R{-}Co^{III}(P^*) \quad (20)$$

two electrons in the d$_{z^2}$ orbital and one electron in a t$_{2g}$-derived d orbital. On the other hand, S$_N$2 displacement of a carbocation from a second R−Co^{III}(P) by Co^{I}(P*)$^-$, eq 21, requires a subsequent electron transfer to convert the intermediate Co^{I}(P)$^-$ to product Co^{II}(P), eq 22. Exchange products may also be obtained by an S$_E$2 reaction, eq 23, following the electron transfer in eq 24.

$$R{-}Co^{III}(P) + Co^{I}(P^*)^- \rightarrow Co^{I}(P)^- + R{-}Co^{III}(P^*) \quad (21)$$

$$R{-}Co^{IV}(P)^+ + Co^{I}(P)^- \rightarrow R{-}Co^{III}(P) + Co^{II}(P) \quad (22)$$

$$R{-}Co^{II}(P)^- + Co^{III}(P^*)^+ \rightarrow Co^{II}(P) + R{-}Co^{III}(P^*) \quad (23)$$

Several reasons lead us to consider the mechanisms involving electron transfer to be quite unlikely. Electron transfer creates a charge separation. Singly oxidized organocobalt(III) porphyrin complexes have electronic structures that vary between organocobalt(IV) porphyrin and organocobalt(III) porphyrin π-cation radical and whose nature is affected by the identity of the R group, the solvent, and the presence of axial bases.[95] Given these, the rate of alkyl exchange would be expected to be quite sensitive to the identity, polarity, and coordinating ability of the solvent. This was not observed. Co^{I}(P)$^-$ intermediates should be rapidly consumed by reaction with CDCl$_3$ or CD$_2$Cl$_2$, solvents in which exchange proceeded smoothly. Organocobalt(IV) porphyrin complexes undergo rapid intramolecular rearrangement to afford *N*-alkyl Co(II) porphyrin complexes.[65,95] Such species were not produced during alkyl exchange reactions. Finally, it can be estimated that electron-transfer processes in eqs 10 and 14 are disfavored by more than 1.61 and 1.55 V, respectively.[64] Thus, the concentrations of reactive species will be extremely small.

Although quantitative rate data for alkyl exchange are not available, the qualitative data are more consistent with a displacement reaction occurring at the α-carbon of the alkyl group than with a homolytic reaction. Control experiments conducted in the dark established that alkyl exchange is a thermal rather than photochemical process. The exchange reactions are much faster at room temperature than would be expected for thermal homolysis of the Co−C bond given known dissociation energies in organocobalt(III) porphyrins.[58] The exchange rate decreases as the degree of substitution and steric bulk at the α-carbon of the alkyl group increases. The trend is the reverse of that which would be expected for a homolytic process where increasing substitution would stabilize the alkyl radical and lower the activation energy for homolysis. Finally, the apparent reactant concentration dependence of the relaxation of alkyl exchange to equilibrium also is inconsistent with the homolytic mechanism of Scheme 2.

The variation in rate with alkyl group observed for cobalt porphyrins is qualitatively similar to that observed for alkyl exchange reactions of cobaloxime compounds[25] and organoco-

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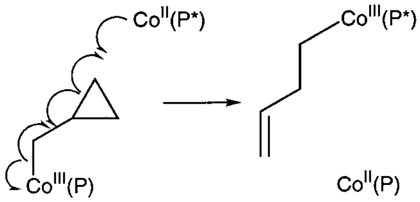
balt Schiff-base compounds.[22] Moreover, at similar reactant concentrations the half-times to achieve equilibrium for methyl exchange appear to be comparable (within roughly an order of magnitude) for cobaloxime,[25] cobinamide,[32] and cobalt porphyrin complexes. The complete failure of phenyl groups to transfer and the sluggishness of acyl group transfer in both porphyrin and Schiff-base systems is noteworthy. The quantitative variation in rate with alkyl group appears to be considerably smaller for cobalt porphyrin compounds than for cobaloxime compounds. For cobalt porphyrins the ratio of rates of exchange for methyl and isobutyl groups is about 20 and for methyl and neopentyl groups is approximately 10^2 (although see caveat, below). In contrast, exchange of a methyl group is roughly 10^6 times faster than exchange of an isobutyl group for cobaloxime complexes.[25] Alkyl exchange in cobinamides appears to have an even larger variation of rate with alkyl group. Groups larger than methyl do not exchange thermally and thus must have rate constants at least several orders of magnitude smaller.[32] The variation in rate for alkyl exchange of alkylcobalt porphyrins also appears smaller than that for typical S_N2 reactions where the ratio of methyl to isobutyl exchange rates is 10^3 and of methyl to neopentyl is 3×10^6.[99] These observations may suggest that steric interactions are less significant in the transition state for alkyl exchange of cobalt porphyrins than in that of either cobaloximes or S_N2 reactions.

The existence of free-radical intermediates in alkyl exchange reactions was investigated by use of several different radical traps. Attempts to transfer the radical chain by flooding the exchange reaction with an alkyl halide of a distinct alkyl group, eq 8, were unsuccessful. In addition, CO did not trap alkyl radicals by conversion to acyl radicals, eq 9. Acetylcobalt(III) porphyrin complexes appeared in the reaction mixture at a rate that was between 3 and 4 orders of magnitude slower than alkyl exchange. In this context, it is noteworthy that exchange of acyl groups between cobalt porphyrins occurs under an N_2 atmosphere without detectable decarbonylation of the acyl complexes to afford the corresponding alkyl complexes. Thus, if alkyl and acyl radicals are intermediates in the exchange reactions, the failure of CO to trap alkyl radicals cannot reflect the instability and lability of the acyl radical.

One might argue that the failure to trap alkyl radicals in the presence of added $Co^{II}(P^*)$ is a consequence of the persistent radical effect. In other words, the traps fail to compete with $Co^{II}(P^*)$ in capture of radicals. However, the failure after 20 h of 10^{-2} M TEMPO in the absence of added $Co^{II}(P^*)$ to trap any methyl radicals that should form by homolysis of 10^{-5} M $Co(OEP)CH_3$ eliminates this possibility. If the mechanism in Scheme 2 occurs, the half-life for homolysis of the dilute $Co(OEP)CH_3$ solution should be less than or equal to the half-life for alkyl exchange under typical conditions, given that Co−C bond homolysis is a first-order process. Thus, the TEMPO trapping experiment, whose duration was more than 100 times the half-life of alkyl exchange, provides strong evidence against a significant role for free radicals in alkyl exchange.

Experiments with cyclizable probe substrates appeared to give contradictory results. Alkylation of $Co^I(OEP)^-$ with 6-bromo-1-hexene afforded (5-hexenyl)Co(OEP) cleanly, a result that establishes alkylation of cobalt(I) porphyrin by primary alkyl bromides proceeds via an S_N2 reaction rather than an electron transfer, free-radical mechanism. No rearranged cyclopentylmethyl products were detected during alkyl exchange reactions of the 5-hexenyl group, Figure 1C, even at times sufficient for multiple complete alkyl exchanges to have occurred. In contrast, alkylation of $Co^I(OEP)^-$ with cyclopropylmethyl bromide afforded a mixture of (cyclopropylmethyl)Co(OEP) and (3-butenyl)Co(OEP). Exchange experiments with the mixture show that transfer of the cyclopropylmethyl group occurs predominantly, if not completely, with rearrangement to a 3-butenyl group.

Scheme 4



The apparent contradiction in results between the hexenyl and cyclopropylmethyl cyclizable probes can be rationalized in one of two different ways. If the mechanism in Scheme 2 applies and radicals are involved in the reaction, the results would require that the lifetime of the radicals prior to capture be too short for 5-hexenyl to cyclize to cyclopentylmethyl but long enough for cyclopropylmethyl to open to 3-butenyl. There is about a 5×10^2 difference in the first-order rate constants for rearrangement of the radicals, so this might be possible. Further reflection suggests, though, that the lifetime cannot be that of a free radical but rather must be that for diffusion of a radical from one porphyrin to a second within a solvent cage. Given that colligation rate constants for the second-order capture of $CH_3^{\bullet}$ by cobalt(II) macrocycles are $(1-4) \times 10^8$ M^{-1} s^{-1} and are relatively insensitive to steric effects of the alkyl radical,[100,101] the roughly $(1-3) \times 10^{-3}$ M concentration of cobalt(II) porphyrins in solution would lead one to expect an observed first-order rate constant for capture of free radicals of $k_2[Co^{II}(P^*)] \approx (1-12) \times 10^5$ s^{-1}. The 2.2×10^5 s^{-1} first-order rate constant for rearrangement of 5-hexenyl radicals, an irreversible process, is comparable in size. Thus, significant levels of rearrangement should be observed if the reaction time is extended to multiple half-lives for exchange. This was not the case. The second rationalization is that the 3-butenylcobalt(III) porphyrin is a product of a bimolecular attack of a cobalt(II) porphyrin on a cyclopropylmethylcobalt(III) porphyrin at one of the carbons γ to the cobalt, resulting in opening of the cyclopropyl ring and displacement of the originally attached cobalt porphyrin, Scheme 4. The reaction is analogous to the S_H2' reaction in which an organic radical attacks at the γ-carbon of a 3-substituted allylcobaloxime(III) and displaces a cobaloxime(II) to afford a 3-substituted 1-butene.[55,102] Radical attack on cyclopropyl rings is known to cause homolytic opening of the ring.[103−105] A reversible reaction like that in Scheme 4 was proposed as the mechanism for the equilibration of 1-methylbut-3-enylcobaloxime and 2-methylbut-3-enylcobaloxime[106] and is consistent with observations made during the isomerizations of cyclopropylmethylcobalamin[107] and cy-

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clopropylmethylcobaloxime[108] to their respective 3-butenyl complexes. A nucleophilic attack of a cobalt(I) porphyrin anion on initially formed cyclopropylmethylcobalt(III) porphyrin analogous to the homolytic attack in Scheme 4 could explain why the alkylation reaction using cyclopropylmethyl bromide invariably produces a mixture that contains (3-butenyl)cobalt(III) porphyrin.

It should be possible to differentiate between the two mechanistic possibilities suggested above. The S_H2 mechanism absolutely requires a bridged transition state that has a Co−C−Co linkage. Radical transfer in a solvent cage only requires that both cobalt porphyrin complexes be in the cage. Thus, use of a porphyrin that is sufficiently sterically encumbered to prevent formation of the bridged transition state must stop alkyl exchange if it occurs by an S_H2 mechanism. A sterically encumbered porphyrin would only slow a radical exchange process in a solvent cage by increasing the distance that the radical must diffuse.

Two major challenges had to be overcome to realize an experimental implementation of this strategy. First, the sterically encumbered porphyrin employed in the experiments must have steric bulk on both faces of the porphyrin because the exchange reaction can occur at either face of the cobalt(II) porphyrin. Although numerous porphyrins have been prepared that have a steric superstructure on one face of a porphyrin,[109,110] relatively few porphyrins have been synthesized that have steric superstructures on both faces.[111] We chose to utilize tetraarylporphyrins with ortho-disubstituted or meta-disubstituted *meso*-aryl groups because precedents exist that make planning a successful synthesis of these compounds relatively straightforward.[111−116] The second challenge is to select a steric superstructure that is sufficiently large to prevent formation of the bridged transition state, but not so large as to prevent synthesis of the sterically encumbered porphyrin or its alkylcobalt(III) complex. We first examined “off-the-shelf” porphryins of this type that had simple substituents and were either commercially available (T3,5tBuPP) or could be prepared from a disubstituted benzaldehyde precursor that was readily available (T2,6MeOPP). If necessary, larger structures would be prepared and attached to the *meso*-aryl groups by an aryloxy ether linkage, a synthetic strategy that is well precedented.[111−116]

Simple substituents at all ortho or meta positions slowed the alkyl exchange reaction but did not prevent it. The exchange reaction between Co(OEP)CH_3 and Co(T3,5tBuPP) required roughly 3 times longer to reach equilibrium than exchange between Co(OEP)CH_3 and Co(TPP). The *o*-methoxy groups of Co(T2,6MeOPP) slowed exchange with Co(OEP)CH_3 by a factor of 6 relative to Co(TPP). Thus, these substituents are either insufficienly large to block formation of a bridged intermediate or cage transfer occurs.

Literature evidence supports the first contention. The *o*-methoxy groups of $Fe^{II}[T(2,4,6\text{-}MeO)_3PP]$ prevent formation of μ-peroxo and μ-oxo complexes upon reaction with O_2, but the *m*-methoxy groups of $Fe^{II}[T(3,4,5\text{-}MeO)_3PP]$ do not.[117] X-ray data for μ-oxo compounds $[Fe(TPP)]_2O$ and $[Fe(TPC)]_2O$ show that the 24-atom mean porphyrin plane to bridging oxygen distance should be roughly 2.3 Å (typical plane to Fe distances of 0.54 Å plus Fe−O distances of 1.76 Å).[118] Thus, *o*-methoxy groups on two adjacent porphyrins are sufficiently large to prevent an approach as close as 4.6 Å, plane-to-plane. The mean plane to C distances in alkylcobalt(III) porphyrin complexes are roughly 2.08 Å (plane to Co distances of 0.10 Å plus Co−C distances of 1.98 Å).[67,119] Structural data for several trigonal-bipyramidal methyl groups that linearly bridge two Al or Zr metal centers establish that the M−C distances in these 3-center 2-electron systems are roughly 0.2 Å longer than terminal M−C distances.[120−123] Thus, the Co−C distance in the 3-center 3-electron Co−CH_3−Co bridged transition state is expected to be 2.3 Å or longer. If ortho substituents are present on only one of the two porphyrin partners in the exchange reaction, it may be reasonable that a group larger than methoxy is required to prevent formation of a bridged transition state.

Next, we investigated alkyl exchange reactions with porphyrins that had significantly larger steric superstructures. No evidence of exchange between Co(TTP)CH_3 and Co(T2,6FBzOPP) could be detected after 19.5 days of reaction in complete darkness. If one conservatively assumes that the lower limit of detection of exchange is 5% conversion to Co(T2,6FBzOPP)CH_3, this observation corresponds to a decrease in the rate of methyl exchange by more than 7×10^4. Exchange reactions of these complexes conducted under room lights led to observation of a new singlet at −4.44 ppm. This was tentatively assigned as the methyl peak of Co(T2,6FBzOPP)CH_3, which had not been independently prepared at the time of this experiment. However, the larger upfield chemical shift of this singlet compared to the methyl resonances of other methylcobalt(III) tetraarylporphyrin complexes was of concern.

The kinetic analysis above implicitly assumes that the thermodynamics of the exchange reaction are favorable. The analysis would be incorrect if Co(T2,6FBzOPP)CH_3 was either so unstable as to be inaccessible or sufficiently unstable relative to Co(TTP)CH_3 that detectable levels of Co(T2,6FBzOPP)CH_3 would not be present at equilibrium. Thus, Co(T2,6FBzOPP)CH_3 was synthesized directly to confirm the NMR assignment and to demonstrate that its exchange with Co(TTP) was slow and did not go to completion to form exclusively Co(TTP)CH_3. The presence of the *o*-perfluorobenzyloxy ether groups caused difficulties that prevented us from obtaining pure samples of Co(T2,6FBzOPP)CH_3. Side products were present that had lost one or more ether groups by reductive cleavage while in contact with the sodium amalgam during reduction to cobalt(I). Nonetheless, our results demonstrated that Co(T2,6FBzOPP)CH_3 is accessible and has reasonable stability in solution.

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Exchange reactions between Co(T2,6FBzOPP)CH_3 and Co(TTP) run in complete darkness were extremely slow. Small amounts of Co(TTP)CH_3 were detected after 13 days of exchange. However, this appeared to result from reaction of Co(TTP) with the portion of the sample that had suffered partial cleavage of perfluorobenzyloxy groups rather than from reaction with intact Co(T2,6FBzOPP)CH_3. Thus, the apparent slow exchange is truly a kinetic phenomenon rather than a thermodynamic one.

The enormous slowing, if not outright cessation, of the thermal exchange reaction caused by blocking the porphyrin faces revealed the existence of a slower photochemical exchange reaction. At the intensity of normal room lights, the photochemical exchange reaction required roughly 24 h to achieve equilibrium. Clearly, the photochemical exchange is much too slow to contribute to the exchange reactions of benzyl, methyl, primary, and secondary alkyl groups. However, given that the time required to achieve equilibrium for the slow exchange reactions of acetyl, 2-adamantyl, and neopentyl groups was not precisely defined and the reactions were not carried out with total exclusion of light, it is not clear whether these exchanges proceed by a thermal mechanism, a photochemical mechanism, or a combination of both.

In summary, the evidence presented in this paper is completely consistent with an S_H2 mechanism for the thermal alkyl exchange reaction. The facility of the reaction is greater than would be expected if the Co−C bond dissociation energy was the major contribution to the activation energy. The dependence of reaction rate on alkyl group structure is that which corresponds to steric effects on a displacement reaction rather than stability effects on radicals in a homolysis reaction. The apparent concentration dependence of the time required to relax to equilibrium suggests the exchange reaction has second-order kinetics. The facility and similarity of rates of exchange in several different solvents is inconsistent with mechanisms that lead to significant polarization or charge separation in transition states or intermediates. All attempts to trap or find evidence of radical intermediates were unsuccessful. Use of a porphyrin with steric encumberance sufficient to prevent formation of a Co−C−Co bridged transition state decreased the rate of the reaction by approximately 5 orders of magnitude, if not more. The existence of the photochemical pathway, which presumably involves homolysis to alkyl radicals, shows that the steric superstructure of this porphyrin does not prevent radical diffusion, in or out of a solvent cage.

Implications of This Work. We established here that alkyl exchange reactions of cobalt porphyrins and tetrapyrroles proceed by a bimolecular, S_H2 mechanism, Scheme 3. As such, the exchange reactions can be viewed as group transfer reactions or equivalently as alkyl-bridged, inner-sphere electron-transfer reactions. Carbon is now numbered among the other elements for which atom transfer reactions involving metalloporphyrins have been demonstrated. These elements include halogens,[124,125] nitrogen,[126−129] oxygen,[130−132] sulfur,[132,133] and selenium.[132,133]

A comparison of the alkyl exchange reactions of iron porphyrins[51] and with those of cobalt porphyrins is informative. The Fe−C bond dissociation energies of organoiron(III) porphyrins are 10−15 kcal/mol weaker than the corresponding Co−C bonds of organocobalt(III) porphyrins.[134] The S_H2 mechanism is not available to iron(II) because it does not have the correct orbital population. The d_{z^2} orbital, which is used in forming the metal−carbon bond, is vacant. The alkyl exchange reactions of alkyliron(III) porphyrins with iron(II) porphyrins were reported to proceed by a homolytic mechanism. This conclusion was based upon the similarity of the time scales of alkyl exchange and such radical-based reactions as CO "insertion",[80] alkyl group interchange with iodoalkanes,[77] and metathesis with tributyltin hydride.[135] Despite the different reaction mechanisms, the time scales of the alkyl exchange reactions of iron and cobalt porphyrins appear to be quite similar. Thus, the binding of the second cobalt porphyrin to the alkyl group in the Co−C−Co bridged transition state and the earlier placement of the transition state along the Co−C bond homolysis pathway combine to compensate for the unfavorable activation entropy of assembling the S_H2 transition state and stabilize it by about 10−15 kcal/mol relative to homolysis.

The wide variations in the sensitivity of S_H2 reactions of different cobalt macrocycles to the steric bulk at the α and β positions of the alkyl group is remarkable and important. Groups larger than methyl do not transfer by an S_H2 mechanism for corrinoids.[32] A wider range of groups transfer for cobaloximes, but the sensitivity to the alkyl structure is greater than that of the typical S_N2 nucleophilic displacement reaction.[25] In contrast, our results show that alkyl exchange reactions of cobalt porphyrins have a rather limited sensitivity to the alkyl structure. The variation in sensitivity could reflect the extent to which the substituents on the outsides of the pair of cobalt macrocycles reach into the region between them to contact the substituents on the bridging carbon in the S_H2 transition state. Corrinoids and cobaloximes both are flexible and have groups that could project into this region. Porphyrins, on the other hand, are more rigid flat molecules whose substituents are also further removed from cobalt and from the bridging region of the transition state. Only the methyl groups of the ethyl substituents can project up from the macrocycle plane in OEP complexes. The greater steric bulk of corrinoids in the Co−C region compared to porphyrins is supported by results of an investigation of the reaction of their cobalt(I) complexes with secondary alkyl halides. The reaction mechanism was reported to shift from S_N2 for porphyrins to electron-transfer, free radical for corrinoids because of the latters' steric bulk.[136]

Espenson and co-workers discounted an S_H2 mechanism for the carbon−carbon bond forming reaction that occurs when aliphatic free radicals react with alkylcobaloximes.[137] They concluded from the literature that an S_H2 mechanism must exhibit marked sensitivity to the bulk of the alkyl group on cobalt. Our results show that this need not be true. Thus, the S_H2 mechanism should be reconsidered for the above reaction.

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Cobalt(I) complexes have been termed supernucleophiles because of their excellence as nucleophiles in S_N2 reactions.[138] This is attributed to the high polarizability and charge density of an electron pair in the $3d_{z^2}$ orbital, which also has a greater spatial extent than the sp^n hybrid HOMOs of many typical nucleophiles. Cobalt(I) complexes are also reasonably good leaving groups. Methyl-coenzyme M[139] and methionine[6] are both formed biosynthetically by nucleophilic attack of the related thiolate on methylcobalamin, which results in cob(I)alamin displacement. Nucleophiles also displace cobalt(I) complexes from alkylcobaloximes and alkylcorrinoids in vitro.[25,30,140] The facility of the S_H2 alkyl exchange reactions studied herein suggests that cobalt(II) complexes are both excellent radical ($1e^-$) nucleophiles and radical leaving groups. It is likely that this stems from the similarity of the electronic configurations and properties of cobalt(II) and cobalt(I), which differ in having a half-filled $3d_{z^2}$ orbital rather than a completely filled one.

The low activation energy for S_H2 alkyl exchange of organocobalt(III) tetrapyrroles and tetraazamacrocycles with their respective cobalt(II) complexes and the ability of the cobalt(II) complexes to function as good leaving groups suggest that S_H2 displacement of the organo group by other radical species also should be facile. Indeed, the steric contacts in the bridged transition state should be much reduced if a typical radical species replaced one of the pair of cobalt macrocycles in the alkyl exchange reaction. Precendents for radical displacements at organocobaloximes already exist,[137,141−143] provided the reconsideration of mechanism that we suggested above is correct.

The known biosynthetic methylation reactions of methylcobalamin proceed by heterolytic cleavage of the methyl−Co bond in nucleophilic substitutions. Our results suggest that homolytic biosynthetic methylation involving radical species and methylcobalamin must be considered as a viable mechanism, too. Alkylations with groups larger than methyl may also be possible. Such groups could be transiently bound to corrinoids prior to displacement by other radicals.

Experimental Section

Materials. Reactions, recrystallizations, and sample manipulations were carried out on a vacuum line, under a nitrogen atmosphere with standard Schlenk techniques, or in a Vacuum/Atmospheres drybox. Organocobalt(III) complexes were handled under subdued lights. Reagents and solvents were of reagent grade or better. Alkyl halides were examined for purity and distilled if necessary. Cyclopentylmethyl iodide was obtained by reaction of cyclopentanemethanol with iodine, imidazole, and triphenylphosphine.[144] Solvents were dried by appropriate methods and thoroughly degassed prior to use. NMR solvents were treated to remove traces of water and acid immediately before use by passage down a dry column of grade I basic alumina. The initial runnings were discarded.

The *meso*-tetraarylporphyrins H_2(TPP), H_2(TTP), H_2(TpFPP), and H_2(TpNO$_2$PP) were prepared from pyrrole and the appropriate substituted benzaldehyde by the Adler-Longo method.[145] H_2(T2,6MeOPP) was prepared from pyrrole and 2,6-dimethoxybenzaldehyde by the Lindsey method.[114] H_2(OEP) was prepared by literature methods.[146] H_2(T3,5tBuPP) was purchased from Strem. The cobalt(II) complexes of the above porphyrins were prepared by literature methods.[147] Organocobalt(III) porphyrin complexes were prepared by reaction of the anionic cobalt(I) complex of the porphyrin with an alkyl, aryl, benzyl, or acyl halide. Procedures and purification methods were described previously.[57,67]

Exchange Reactions. Exchange reactions were run in NMR tube scale reactions in deuterated solvents. Solutions of individual complexes in exchange reactions were prepared at specific concentrations in the solvent of choice in the drybox. Concentrations typically ranged between 1×10^{-3} and 3×10^{-3} M. Measured volumes of a solution of an alkylcobalt(III) porphyrin and of a solution of a cobalt(II) porphyrin were transferred to an NMR tube. The tube was capped and the contents were quickly and thoroughly mixed. The tube was immediately removed from the drybox and loaded in the spectrometer without delay. If the reaction was intended to be monitored over an extended time, either the NMR tube used was sealed off under vacuum or an NMR tube blown onto a J Young rotary valve was used for the reaction. Some reactions were run with total exclusion of light. Glassware used for these reactions was wrapped with aluminum foil and solution preparation and transfer in the drybox was performed under minimal lights. NMR tubes for these reactions were kept wrapped in foil and stored in a light-tight container at all times that they were not in the NMR spectrometer probe. Tubes were loaded into the spectrometer and NMR data acquired with the room lights off.

^{1}H NMR spectra (270.17 MHz) were recorded on a JEOL Eclipse 270 spectrometer. The control software did not permit temperature control until the instrument was shimmed and locked on the sample. A frozen sample would thaw and come close to room temperature during this process. Thus, it was not possible to study the initial part of the exchange reaction by rapidly freezing a reaction mixture upon mixing and thawing in the probe. The initial spectrum could not be obtained in much less than 10 min after mixing.

The exchange reactions were examined at selected time intervals. Equilibrium constants were calculated from the ratios of the integrations of selected ^{1}H resonances of the two diamagnetic alkylcobalt(III) complexes and the two paramagnetic cobalt(II) complexes. Assignment of the resonances in the spectra of the mixtures was straightforward, given that the four individual complexes had been independently prepared and spectroscopically characterized.

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