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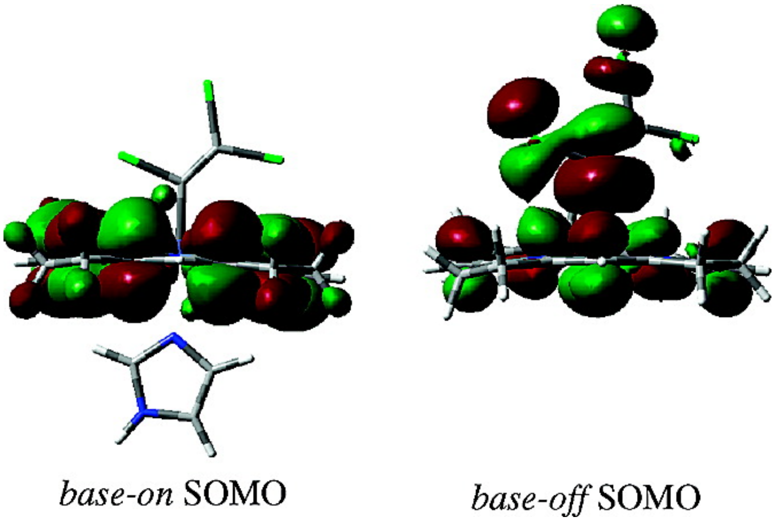

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Theoretical Investigations into the Intermediacy of Chlorinated Vinylcobalamins in the Reductive Dehalogenation of Chlorinated Ethylenes

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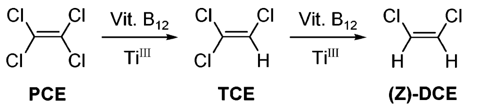
Abstract: The reductive dehalogenation of perchloroethylene and trichloroethylene by vitamin B_{12} produces ~95% (*Z*)-dichloroethylene (DCE) and small amounts of (*E*)-DCE and 1,1-DCE, which are further reduced to ethylene and ethane. Chloroacetylene and acetylene have been detected as intermediates, but not dichloroacetylene. Organocobalamins (RCbls) have been proposed to be intermediates in this process. Density functional theory based approaches were employed to investigate the properties of chlorinated vinylcobalamins and chlorinated vinyl radicals. They reveal that all vinyl radicals studied have reduction potentials more positive ($E^\circ \geq -0.49$) than that of the Co^{II}/Co^{I} couple of B_{12} ($E^\circ = -0.61$ V), indicating that any (chlorinated) vinyl radicals formed in the reductive dehalogenation process should be reduced to the corresponding anions by cob(I)alamin in competition with their combination with Co(II) to yield the corresponding vinylcobalamins. The computed Co−C homolytic bond dissociation enthalpies (BDEs) of the latter complexes range from 33.4 to 45.8 kcal/mol. The substituent effects on the BDEs are affected by the stabilities of the vinyl radicals as well as steric interactions between (*Z*)-chloro substituents and the corrin ring. The calculated E° values of the cobalamin models were within ~200 mV of one another since electron attachment is to a corrin ring π^*-orbital, whose energy is relatively unaffected by chloride substitution of the vinyl ligand, and all were >500 mV more negative than that of the Co^{II}/Co^{I} couple of B_{12}. Reduction of the base-off forms of vinyl- and chlorovinylcobalamin models also involves the corrin π^* orbital, but reduction of the base-off dichlorovinyl- and trichlorovinylcobalamin models occurs with electron attachment to the σ_{Co-C}^* orbital, yielding calculated E° values more positive than that of the calculated Co^{II}/Co^{I} couple of B_{12}. Thus, cob(I)alamin is expected to reduce these base-off vinyl-Cbls. Heterolytic cleavage of the Co−C bonds is much more favorable than homolysis (>21 kcal/mol) and is significantly more exergonic when coupled to chloride elimination.

Introduction

Vitamin B_{12} (cyanocobalamin) catalyzes the reductive dehalogenation of chlorinated alkenes including the ubiquitous pollutants perchloroethylene (PCE) and trichloroethylene (TCE, eq 1).[1] In addition to this nonenzymatic catalyst system, a B_{12} analogue is present in several dehalogenases that catalyze reductive dehalogenation of PCE and TCE.[2]



(1)

Mechanistic studies on the abiotic process with titanium(III) citrate as the stoichiometric electron donor have shown that the transformation of PCE to TCE involves electron transfer from the Co^{I} form of the catalyst (cob(I)alamin) to the electron-deficient alkene to produce chloride anion and a vinyl radical.[3,4] What is not clear is why the cob(II)alamin formed does not combine with the trichlorovinyl radical to produce trichlorovinylcobalamin (**1**) given the diffusion-controlled rate of reaction of cob(II)alamin with organic radicals[5] (Scheme 1). We have previously suggested that **1** might have a reduction potential less negative than the Co^{II}/Co^{I} potential of B_{12}, and that it would therefore be reduced under the reaction conditions, preventing its detection.[6] Unfortunately, it has not been possible to test this hypothesis because we have not been able to synthesize

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(1) (a) Gantzer, C. J.; Wackett, L. P. *Environ. Sci. Technol.* **1991**, *25*, 715−722. (b) Habeck, B. D.; Sublette, K. L. *Appl. Biochem. Biotechnol.* **1995**, *51/52*, 747−759. (c) Lesage, S.; Brown, S.; Millar, K. *Ground Water Monit. Rem.* **1996**, *16*, 76−85. (d) Glod, G.; Angst, W.; Holliger, C.; Schwarzenbach, R. P. *Environ. Sci. Technol.* **1997**, *31*, 253−260. (e) Burris, D. R.; Delcomyn, C. A.; Smith, M. H.; Roberts, A. L. *Environ. Sci. Technol.* **1996**, *30*, 3047−3052. (f) Burris, D. R.; Delcomyn, C. A.; Deng, B. L.; Buck, L. E.; Hatfield, K. *Environ. Toxicol. Chem.* **1998**, *17*, 1681−1688. (g) Semadeni, M.; Chiu, P. C.; Reinhard, M. *Environ. Sci. Technol.* **1998**, *32*, 12071213.

(2) (a) Holliger, C.; Wohlfarth, G.; Diekert, G. *FEMS Microbiol. Rev.* **1998**, *22*, 383−398 (b) Kräutler, B.; Fieber, W.; Ostermann, S.; Fasching, M.; Ongania, K.-H.; Gruber, K.; Kratky, C.; Mikl, C.; Siebert, A.; Diekert, G. *Helv. Chim. Acta* **2003**, *86*, 3698−3716.

(3) Glod, G.; Angst, W.; Holliger, C.; Schwarzenbach, R. P. *Environ. Sci. Technol.* **1997**, *31*, 3154−3160.

(4) Shey, J.; van der Donk, W. A. *J. Am. Chem. Soc.* **2000**, *122*, 12403−12404.

(5) (a) Endicott, J. F.; Ferraudi, G. *J. Am. Chem. Soc.* **1977**, *99*, 243−245. (b) Endicott, J. F.; Netzel, T. L. *J. Am. Chem. Soc.* **1979**, *101*, 4000−4002. (c) Lott, W. B.; Chagovetz, A. M.; Grissom, C. B. *J. Am. Chem. Soc.* **1995**, *117*, 12194−12201. (d) Daikh, B. E.; Finke, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 2938−2943.

10.1021/ja047915o CCC: $30.25

Scheme 1

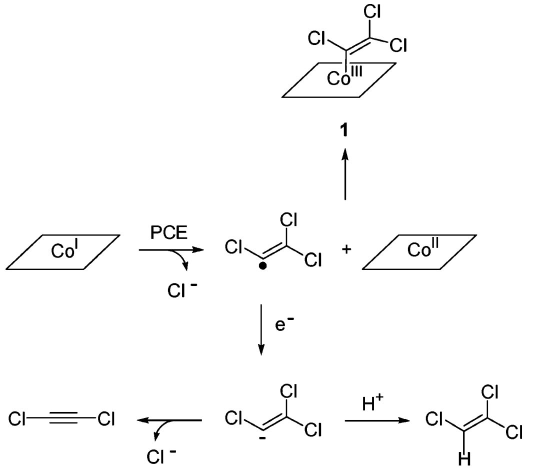
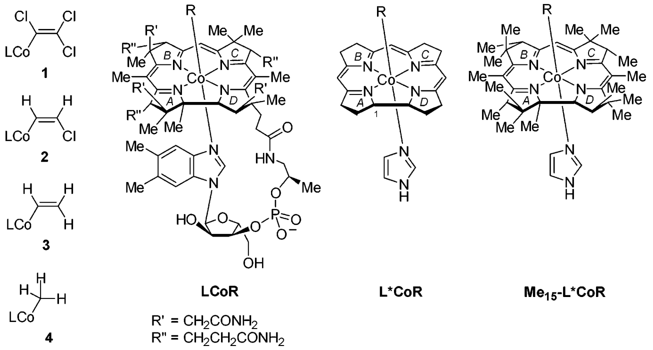


Chart 1



the authentic complex. Another reason that might preclude the formation of **1** involves rapid reduction of the trichlorovinyl radical to the corresponding anion[7] by either Ti^{III} or cob(I)alamin (Scheme 1). At present, the redox potentials of chlorinated vinyl radicals are not available. In this paper, we present the results of computational efforts to investigate the properties of **1** and the redox properties of chlorinated vinyl radicals.

Although **1** has not been detected, chlorinated vinylcobalamins and cobalamin analogues are observed during the reductive dechlorination of TCE and dichloroethylenes (DCEs).[8,9] We have prepared and crystallographically characterized both (*Z*)-chlorovinylcobalamin (**2**) and vinylcobalamin (**3**) (Chart 1).[6] These complexes were unique in that they represented the first two structures of organocobalamins with the metal bound to an sp^2-hybridized carbon. The crystal structures revealed some unexpected features such as the lengthening of the Co−N bond in **3** compared to **2** whereas the Co−C bond is shorter in **3** than in **2**, which is opposite the so-called inverse or anomalous trans effect[10] that is typically observed in organocobalamins.[11−13] A number of other properties of these vinylcobalamins are of interest. Complex **2** is reduced with remarkable ease, producing cob(I)alamin and acetylene.[12] The exact mechanism of this transformation is unclear at present and may involve either homolytic or heterolytic Co−C bond cleavage.

Historically, the Co−C bond strength in organocobalamins has been of great interest to chemists and biochemists because coenzyme B_{12} (adenosylcobalamin) dependent enzymes catalyze its homolytic cleavage.[14] At present Co−C bond dissociation enthalpies (BDEs) are not available for vinylcobalamins. Unfortunately, the increased bond strength imparted by the sp^2 character of the hybrid orbital on the vinyl carbon has so far prevented an experimental determination of the BDE of **2** and **3**.[6,12] In addition to the aforementioned theoretical studies on trichlorovinylcobalamin, we also present here the computational determination of the BDE of a series of models for chlorinated vinylcobalamins and compare their computed structures with those determined experimentally by X-ray crystallography. Investigation into the mode of reductive Co−C bond cleavage suggests this would occur in heterolytic fashion following one-electron reduction.

Results and Discussion

Structures and Co−C Bond Dissociation Enthalpies of Chlorinated Vinylcobalamin Models. The structures of models of methylcobalamin, vinylcobalamin, and its seven chlorinated congeners were optimized using gradient-corrected density functional theory (DFT) with the (U)B3LYP functional[15] and a 6-31G(d) basis set[16] for the main elements (C, N, H, Cl) and TZV basis set[17] for Co.[18] At this level of theory,[19] treatment of the complete ligand system present in cobalamins (L, Chart 1) leads to extremely long computation times even with supercomputer access. Hence, to bring the system to manageable proportions, the equatorial corrin ring of these structures was simplified by omitting the side chains at both the α- and β-faces and replacing the axial dimethylbenzimidazole ligand with imidazole (L*, Chart 1). As discussed below, the influence of omitting the substituents on the corrin ring system was addressed

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(6) McCauley, K. M.; Wilson, S. R.; van der Donk, W. A. *J. Am. Chem. Soc.* **2003**, *125*, 4410−4411.

(7) Reduction of the organic radical would alleviate the so-called persistent radical effect that serves as an extremely effective radical trap. See: (a) Daikh, B. E.; Finke, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 2938−2943. (b) Fischer, H. *J. Am. Chem. Soc.* **1986**, *108*, 3925−3927. An alternative circumvention of the persistent radical effect involves reduction of cob(II)alamin to cob(I)alamin. For an example, see: (c) Shey, J.; McGinley, C. M.; McCauley, K. M.; Dearth, A.; Young, B.; van der Donk, W. A. *J. Org. Chem.* **2002**, *67*, 837−846.

(8) Lesage, S.; Brown, S.; Millar, K. *Environ. Sci. Technol.* **1998**, *32*, 2264−2272.

(9) (a) McCauley, K. M.; Wilson, S. R.; van der Donk, W. A. *Inorg. Chem.* **2002**, *41*, 393−404. (b) Rich, A. E.; DeGreeff, A. D.; McNeill, K. *Chem. Commun.* **2002**, 234−235.

(10) De Ridder, D. J. A.; Zangrando, E.; Buergi, H.-B. *J. Mol. Struct.* **1996**, *374*, 63−83.

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(12) McCauley, K. M.; Pratt, D. A.; Shey, J.; Wilson, S. R.; Burkey, T. J.; van der Donk, W. A. *J. Am. Chem. Soc.*, in press.

(13) Although correlations of the Co−C and Co−N bond lengths in X-ray structures of organocobalamins show this inverse trans effect, calculations on the effect of stretching/shortening the Co−C bond on the Co−N bond length in individual alkylcobalamins show a normal effect. That is, upon lengthening the Co−C bond, the Co−N bond shortens. See refs 21d and 28b.

(14) Banerjee, R., Ed. *The Chemistry and Biochemistry of B12*; Wiley: New York, 1999.

(15) (a) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098−3100. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652. (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785−789.

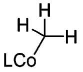
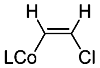
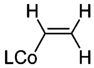
(16) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257−2261.

(17) Schäfer, A.; Huber, C.; Ahlrichs, R. *J. Chem. Phys.* **1994**, *100*, 5829−5835.

(18) This basis set is not balanced; i.e., cobalt is described with a triple-ζ basis, whereas all other atoms are described by split-valence (double-ζ) basis sets supplemented by a single set of polarization functions on the heavy atoms. This approach has been shown to better describe the Co−C bond in the methylcobalamin model (L*CoMe) and contains fewer basis functions than employing a fully balanced (TZV) basis set for all atoms; see ref 34.

(19) DFT has been widely applied to study transition-metal systems in biochemistry. See: Siegbahn, P. E. M.; Blomberg, M. R. A. *Chem. Rev.* **2000**, *100*, 421−437.

Table 1. Comparison of the Co−C and Co−N_{Base} Bond Lengths (Å) in Methyl-, (*Z*)-Chlorovinyl-, and Vinylcobalamins by X-ray Crystallography and Their Models in the Gas Phase by B3LYP/6-31G(d) with the TZV Basis for Co

	Expt.	Calc.[a]	Calc.[b]	Expt.	Calc.[a]	Calc.[b]
	r(Co-C)	r(Co-C)	r(Co-C)	r(Co-N_{dBzm})	r(Co-N_{Im})	r(Co-N_{Im})
	1.99[c] 1.97[d]	1.960	1.957	2.19[c] 2.09[d]	2.241	2.268
	1.954	1.932	1.928	2.128	2.191	2.211
	1.914	1.923	1.919	2.156	2.236	2.251

[a] L*CoR. [b] Me_{15}-L*CoR. [c] Methylcobalamin, ref 71. [d] Coα-(1*H*-imidazolyl)-Co*β*-methylcobamide, ref 20a.

by examining the pentadecamethylated analogue (Me_{15}-L*, Chart 1) for some representative family members.

The effect of replacing the dimethylbenzimidazole (dBzm) ligand with imidazole (Im) has been addressed previously, both experimentally[20] and computationally.[21] The higher basicity of Im (pK_a(conjugate acid) = 7.0)[22] as compared to dBzm (pK_a-(conjugate acid) = 6.0)[23] results in a stronger predicted interaction of the metal with the former.[24] Indeed, the X-ray crystallographic structure of an analogue of methylcobalamin in which the dBzm ligand is replaced with Im displays a shorter Co−N bond by 0.1 Å.[20a] Moreover, *N*-methylimidazole has shown unusually large enthalpies of binding to alkylcobinamides (B_{12} analogues lacking the intramolecular dBzm ligand), which is not observed with other bases.[20d,25,26] Importantly, for the present work, both experimental and computational studies have shown that the substitution of dBzm with Im introduces virtually no differences in the Co−C bond length,[20b−d,21a,b,d] and the Co−C bond strength.[21c,27] Accordingly, although the replacement of dBzm with Im in this study clearly introduces differences that must be kept in mind when evaluating the computational results (vide infra), with respect to investigating the trends in the structure and Co−C BDEs in the otherwise poorly understood series of chlorinated vinylcobalamins, the substitution of the base is not expected to introduce any major changes.

Representative computed bond lengths for the model systems are compared with experimental values in Table 1. The calculations reproduce the crystallographic bond lengths reasonably well, including the expected shortening of the Co−C bond upon going from an sp^3-hybridized carbon ligand (methyl) to the sp^2-hybridized ligands. As has been observed in previous DFT calculations on alkylcobalamin models,[21a,b,d] the Co−N_{base} bond lengths are not captured as well as the Co−C bond lengths (i.e., $\Delta r_{Co-N} \approx 0.05-0.08$ Å vs $\Delta r_{Co-C} \approx 0.01-0.03$ Å), a feature that has been attributed to a relatively shallow potential energy surface with respect to the Co−N stretch.[21a,28b] It is noteworthy that the DFT results reinforce the conclusion drawn from crystallographic studies[12] that the vinylcobalamins do not follow the trend of the inverse trans effect[10,11] of decreasing Co−N_{base} bond lengths with contracting Co−C bond lengths observed for other organocobalamins. That is, while r_{Co-C} increases along the series vinyl → (*Z*)-chlorovinyl → methyl, the trend in r_{Co-N} is different: (*Z*)-chlorovinyl → vinyl → methyl.

In comparison to the structure of cobalamins, our L*CoR model and similar models used in previous DFT studies on organocobalamins[21a−d] have major differences with respect to the corrin substituents. In the B_{12} literature, steric compression of the interaction of the corrin ring with the axial alkyl substituents has often been invoked as a means by which adenosylcobalamin-dependent enzymes may achieve their remarkable acceleration of the cleavage of the Co−C bond. Recent spectroscopic work, however, shows no change in the Co−C bond upon binding of the cofactor to several enzymes.[28] In the current study, the introduction of 15 methyl groups at positions of the corrin ring that are occupied by methyl, acetamido, and propionamido groups in organocobalamins (Me_{15}-L*CoR) leads to only minor changes in the Co−C and Co−N_{Im} bond lengths of the three organocobalamin models (Table 1). A similar observation was reported when just one methyl group was introduced on the α-face of L* at C1 (Chart 1).[21d] Furthermore,

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(20) (a) Fasching, M.; Schmidt, W.; Kräutler, B.; Stupperich, E.; Schmidt, A.; Kratky, C. *Helv. Chim. Acta* **2000**, *83*, 2295−2316. (b) Puckett, J. M.; Mitchell, M. B.; Hirota, S.; Marzilli, L. G. *Inorg. Chem.* **1996**, *35*, 4656−4662. (c) Scheuring, E.; Padmakumar, R.; Banerjee, R.; Chance, M. R. *J. Am. Chem. Soc.* **1997**, *119*, 12192−12200. (d) Sirovatka, J. M.; Finke, R. G. *J. Am. Chem. Soc.* **1997**, *119*, 3057−3067.

(21) (a) Andruniow, T.; Zgierski, M. Z.; Kozlowski, P. M. *J. Phys. Chem. B* **2000**, *104*, 10921−10927. (b) Jensen, K. P.; Sauer, S. P. A.; Liljefors, T.; Norrby, P.-O. *Organometallics* **2001**, *20*, 550−556. (c) Andruniow, T.; Zgierski, M. Z.; Kozlowski, P. M. *J. Am. Chem. Soc.* **2001**, *123*, 2679−2680. (d) Dölker, N.; Maseras, F.; Lledós, A. *J. Phys. Chem. B* **2001**, *105*, 7564−7571. Recent calculations of the electronic spectra of B_{12} derivatives indicate that the complete ligand system is essential to explain the experimental spectra. See: (e) Stich, T. A.; Brooks, A. J.; Buan, N. R.; Brunold, T. C. *J. Am. Chem. Soc.* **2003**, *125*, 5897−5914. (f) Ouyang, L.; Randaccio, L.; Rulis, P.; Kurmaev, E. Z.; Moewes, A.; Ching, W. Y. *THEOCHEM* **2003**, *622*, 221−227.

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(24) A similar difference in pK_a values has been reported for protonated 5,6-dimethyl-1-(α-D-ribofuranosyl)-1*H*-benzimidazole (5.56) and 1-(α-D-ribofuranosyl)-1*H*-imidazole (~7.0), i.e., the complete structures of the axial ligands that are covalently attached to the corrin ring in organocobalamins. See: Brown, K. L.; Hakimi, J. M.; Nuss, D. M.; Montejano, Y. D.; Jacobsen, D. W. *Inorg. Chem.* **1984**, *23*, 1463−1471. See also ref 20a.

(25) Sirovatka, J. M.; Finke, R. G. *Inorg. Chem.* **1999**, *38*, 1697−1707.

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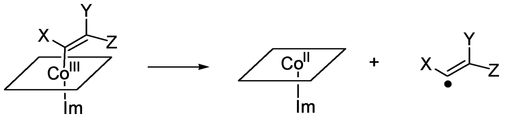
(27) Brown, K. L.; Zou, X.; Banka, R. R.; Perry, C. B.; Marques, H. M. *Inorg. Chem.* **2004**, *43*, 8130−8142.

(28) (a) Sension, R. J.; Cole, A. G.; Harris, A. D.; Fox, C. C.; Woodbury, N. W.; Lin, S.; Marsh, E. N. G. *J. Am. Chem. Soc.* **2004**, *126*, 1598−1599. (b) Brooks, A. J.; Vlasie, M.; Banerjee, R.; Brunold, T. C. *J. Am. Chem. Soc.* **2004**, *126*, 8167−8180 (c) Huhta, M. S.; Chen, H.-P.; Hemann, C.; Hille, C. R.; Marsh, E. N. G. *Biochem. J.* **2001**, *355*, 131−137. (d) Dong, S. L.; Padmakumar, R.; Maiti, N.; Banerjee, R.; Spiro, T. G. *J. Am. Chem. Soc.* **1998**, *120*, 9947−9948.

semiempirical studies of cobalamin and corrin models found the nucleotide loop and the amide side chains to have little influence on the Co−C and Co−N bond lengths.[29] In the current work, the Co−C bond lengths actually decrease slightly in Me_{15}-L*CoR, whereas the $Co-N_{Im}$ bonds lengthen by a small amount. The overall trends do not change, however, with the Co−C bond length decreasing in the order Me > (*Z*)-chlorovinyl > vinyl, and the Co−N bond lengths decreasing according to Me > vinyl > (*Z*)-chlorovinyl.

Given the accurate reflection of trends in bond lengths between experiment and theory, the gas-phase Co−C BDEs were calculated for the models of methylcobalamin and vinylcobalamin and its seven chlorinated congeners. The values were obtained by calculating the enthalpies of the organocobalamin models and subtracting the enthalpies of the axial organo radical and cob(II)alamin model according to eq 2.



(2)

Similar to previous studies,[21c,d] the absolute value calculated for the Co−C BDE of the methylcobalamin model (22.8 kcal/mol) is substantially lower than the experimental value (37 ± 3 kcal/mol)[30] when using the B3LYP functional.[31] One of us noted in a previous study that the B3P86 exchange-correlation functional[15b,32] is significantly more accurate for the calculation of BDEs of bonds between two heavy atoms.[33] Indeed, the computed Co−C BDE of the methylcobalamin model is 5.5 kcal/mol closer to the experimental value when single-point energies are calculated with this functional (28.3 kcal/mol). Recently, Jensen and Ryde[34] have identified that a main source of the problem of calculating accurate Co−C BDEs of cobalamins and related compounds with DFT is the inclusion of exact Hartree−Fock exchange in hybrid exchange functionals, such as Becke's three-parameter hybrid "B3". When single-point energies were calculated with the combination of the simpler "B" gradient-corrected exchange functional and the P86 correlation functional, the calculated Co−C BDE in the methylcobalamin model increased to 35.9 kcal/mol, a result that is now within the margin of error of the experimental result (Table 2).[35]

With each of the density functionals tested, the predicted Co−C BDEs decrease with increased chlorine substitution. Interestingly, the value obtained for the trichlorovinylcobalamin model is in fact smaller than that of the methylcobalamin model, a somewhat unexpected result given the different hybridizations at carbon in the two Co−C bonds. A linear correlation similar to that observed between calculated Co−C bond lengths and BDEs for alkylcobalamin models using the B3LYP functional[21c] is also observed when using the B3LYP, B3P86 (not shown), or BP86 functional to calculate the Co−C BDEs in the vinylcobalamin models (Figure 1).[36] A larger slope by 46 (kcal/mol) $Å^{-1}$ for the alkylcobalamin models is indicative of a greater sensitivity of their Co−C BDE to changes in bond length.

In an attempt to interrogate the factors determining the calculated BDEs for the vinylcobalamin models, the C−H BDEs were computed for the corresponding ethylenes (see the Supporting Information). Interestingly, the C−H bond strengths vary much less (ΔBDE = ∼5 kcal/mol) than the corresponding Co−C bond strengths in **6**−**13** (ΔBDE = ∼12 kcal/mol). This is most strikingly illustrated in Figure 2, where the relationship of Co−C and C−H BDEs is plotted. The data fall into two groups in which the vinyl ligand on the cobalamin models does or does not contain a chlorine substituent *Z* to the cobalt atom. The steeper slope observed for the former correlation provides a measure of the additional steric destabilization of the Co−C bond in complexes **7**, **10**, **12**, and **13** due to the *Z* geometry of chlorine and cobalt.

This steric destabilization of the Co−C bond in complexes **7**, **10**, **12**, and **13** is also reflected in the Co−C═C bond angles, which vary from 140.8° to 134.9° (Table 3), roughly 10° larger than for those complexes that do not have a chlorine and cobalt in a *Z* disposition (**6**, **8**, **9**, and **11**). The calculated angles for **6** and **7** are in excellent agreement with the experimental data.[12] Also included in Table 4 are the calculated fold angles[37] along with the experimental data for **2**, **3**, and MeCbl. Although the fold angles of the models follow the trend in flattening of the corrin ring system on going from methyl to vinyl to (*Z*)-chlorovinyl, they are much smaller than those observed in the X-ray crystallographic structures. Examination of the fold angles in the three Me_{15}-L*CoR structures reveals that this is partly the result of the omission of the methyl, acetamido, and propionamido groups of the corrin ring in the L*CoR models, as the fold angles increase significantly upon inclusion of 15 methyl groups in place of these substituents (Table 3). An additional calculation for L*CoMe where the axial imidazole ligand was replaced with dimethylbenzimidazole revealed an increased fold angle of 9.6°. Hence, both the corrin substituents and the dimethylbenzimidazole contribute significantly to the fold angle, and their omission in simple models that have been typically used in theoretical studies leads to an underestimation of the upward fold.

Reduction Potentials of Chlorinated Vinyl Radicals. Since trichlorovinylcobalamin has not been observed as an intermedi-

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[29] Jensen, K. P.; Mikkelsen, K. V. *Inorg. Chim. Acta* **2001**, *323*, 5−15.

[30] Martin, B. D.; Finke, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 585−592.

[31] Calculated differences in electronic energies for bond homolysis in the Me_{15}-L*CoR models for R = methyl, vinyl, and (*Z*)-chlorovinyl were not significantly different (<0.6 kcal/mol) from the values obtained for the L*CoR models.

[32] Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 8822−8824.

[33] DiLabio, G. A.; Pratt, D. A. *J. Phys. Chem. A* **2000**, *104*, 1938−1943.

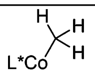
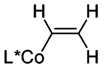
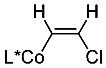
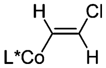
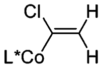
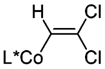
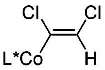
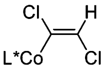
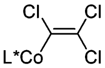
[34] Jensen, K. P.; Ryde, U. *J. Phys. Chem. A* **2003**, *107*, 7539−7545.

[35] Since we are concerned largely with substituent effects in these studies, we have omitted the contributions of relativistic effects (increases the BDE) and basis set superposition error (decreases the BDE) in our calculations since we would expect them to be roughly identical throughout the series. In ref 34, Jensen and Ryde find these contributions to be negligible for the Co−C BDE in a model of methylcobalamin when calculated with B3LYP and a basis set similar in size to that used in this work.

[36] The equation of the (lower) B3LYP line in Figure 1, BDE(Co−C) = [−122.2 (kcal/mol) $Å^{-1}$][*r*(Co−C)] + 267.50 kcal/mol, can be compared with the correlation documented by Andruniow et al.[21c] for a series of alkylcobalamin models: BDE(Co−C) = [−168.3 (kcal/mol) $Å^{-1}$][*r*(Co−C)] + 355.88 kcal/mol. The fact that the data for the vinylcobalamin (shown) and alkylcobalamin (not shown)[21c] models lie on different lines is likely due to the difference in hybridization at the carbon bound to cobalt. The calculations of Andruniow et al. in ref 21c were performed with the same combination of B3LYP and 6-31G(d)/TZV basis sets, but the Co−C BDE reported for methylcobalamin is without zero-point energy and thermochemical corrections, and is therefore greater than our value by ca. 5 kcal/mol. Thus, to compare the results in ref 21c with those reported here, it is necessary to adjust the previous *y*-intercept by ca. 5 kcal/mol given that all of the Co−C BDEs in the previous work omit these corrections. The inclusion of these corrections would not be expected to significantly change the slope of the line.

[37] The fold angle is defined as the dihedral angle between the best planes through rings A + B and C + D (Chart 1). Glusker, J. P. In *B12*; Dolphin, D., Ed.; John Wiley: New York, 1982; Vol. 1, pp 23−106.

Table 2. Calculated Gas-Phase Co−C and Co−N$_{Im}$ Bond Lengths and Co−C BDEs in Methylcobalamin, Vinylcobalamin, and Chlorinated Vinylcobalamin Models at 298 K

		r(Co-C) (Å)	r(Co-N$_{Im}$) (Å)	BDE(B3LYP)[a] (kcal/mol)	BDE(B3P86)[b] (kcal/mol)	BDE(BP86)[c] (kcal/mol)
5		1.960	2.241	22.8[d]	28.3[d]	35.9[d]
6		1.923	2.236	31.5	37.5	45.0
7		1.932	2.191	31.2	37.2	44.2
8		1.927	2.195	32.6	36.6	45.8
9		1.950	2.197	29.1	32.9	42.3
10		1.942	2.175	30.1	33.9	42.9
11		1.963	2.173	29.4	34.3	42.2
12		1.979	2.173	25.3	31.7	38.0
13		2.015	2.171	20.8	26.2	33.4

[a] Calculated by (U)B3LYP/6-31G(d) with the TZV basis set for Co. [b] Calculated by (U)B3P86/6-31G(d)//(U)B3LYP/6-31G(d) with the TZV basis set for Co. [c] Calculated by (U)BP86/6-31G(d)//(U)B3LYP/6-31G(d) with the TZV basis set for Co. [d] The experimental BDE is 37 ± 3 kcal/mol (ref 30).

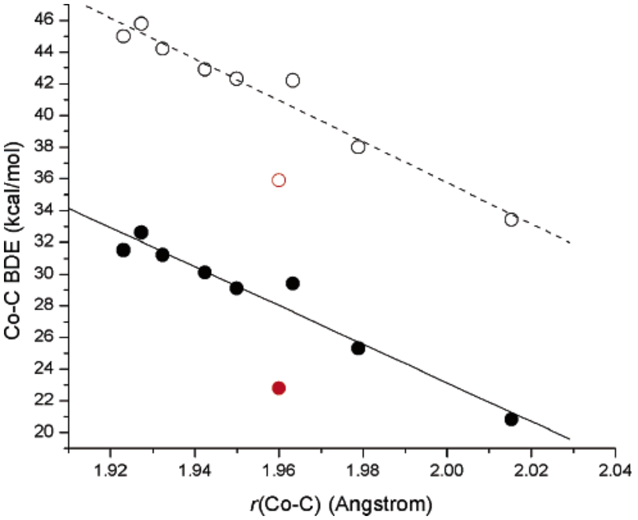


Figure 1. Co−C BDEs of vinylcobalamin models as a function of Co−C bond length (data from Table 2): filled circles/solid line, (U)B3LYP/6-31G(d) data; empty circles/dashed line, (U)BP86/6-31G(d)//(U)B3LYP/6-31G(d) data; red circles, methylcobalamin model.

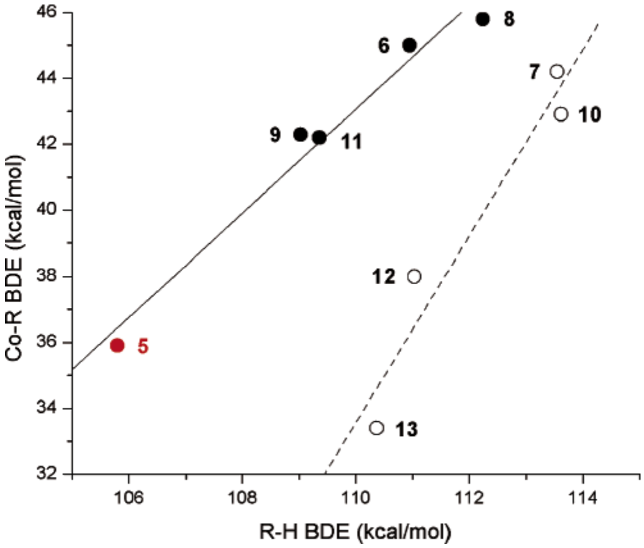
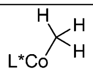
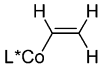
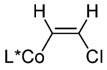
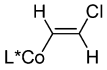
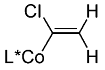
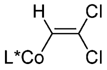
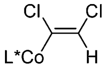
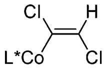
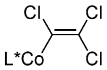


Figure 2. Co−R BDEs as a function of C−H BDEs in R−H (data from Tables 2 (BP86) and 3 (B3LYP)): filled circles/solid line, complexes containing a (*Z*)-*β*-chloro substituent; empty circles/dashed line, complexes without a (*Z*)-*β*-chloro substituent.

ate in the reductive dechlorination of PCE, reduction of the trichlorovinyl radical by cob(I)alamin (or titanium(III) citrate) to yield the trichlorovinyl anion (Scheme 1) may compete with the diffusion-controlled combination of the trichlorovinyl radical and cob(II)alamin to yield **1**. Unfortunately, the reduction potentials of vinyl radicals are not known. Therefore, we set out to investigate them using theoretical approaches.

The first column in Table 4 lists the B3LYP/6-311+G(2d,-2p)-calculated vertical electron attachment energies (EA_{vert}) for

Table 3. Calculated Co−C═C and Fold Angles in Chlorinated Vinylcobalamin Models[a,b]

		∠(Co-C=C)	Expt.	Fold Angle[37]	Expt.
5		--	--	4.1 (7.0)[c]	14.6,[e] 12.5[f]
6		129.8 (129.0)[c]	128.4[d]	3.4 (6.9)[c]	12.5[d]
7		140.8 (139.1)[c]	140.5[d]	3.1 (3.9)[c]	5.8[d]
8		128.2		3.4	
9		127.8		3.3	
10		139.7		3.2	
11		124.4		3.3	
12		137.6		7.7	
13		134.9		9.4	

[a] B3LYP/6-31G(d) with the TZV basis set for Co. [b] All values in degrees. [c] $Me_{15}L^*CoR$. [d] Reference 12. [e] Methylcobalamin; see ref 71. [f] Coα-(1*H*-imidazolyl)-Coβ-methylcobamide; see ref 20a.

the vinyl radical and its seven chlorinated congeners. Since DFT has, on occasion, been shown to generate spurious EA data,[38] the results were compared to those calculated with coupled-cluster theory (CCSD(T)/aug-cc-pVTZ) at the DFT-optimized geometries. The results fit an intuitive picture of larger EA_{vert} values with increasing chlorine substitution of the vinyl radical. Relaxation of the geometry for the vinyl anion yields an adiabatic electron attachment energy (EA_{adia}) of 15.1 kcal/mol by B3LYP/6-311+G(2d,2p) and 14.8 kcal/mol by CCSD(T)/aug-cc-pVTZ. Corresponding electron affinities, following enthalpic corrections to 298 K, are 15.7 and 15.5 kcal/mol, respectively, both in excellent agreement with the NIST-reviewed "best" experimental value of 15.4 ± 0.6 kcal/mol.[39] Interestingly, all chlorovinyl anions that do not possess a chlorine atom on the α-carbon (entries B, C, and E) were found to be unbound at this level of theory and eliminated chloride with concomitant formation of the corresponding acetylene during the geometry optimizations. In these cases, the EA_{adia} values were calculated for infinitely separated chloride and acetylene products.

For the bound ions, the calculated gas-phase free energy changes for reduction were combined with calculated $\Delta\Delta G_{\text{hyd}}^*$(vinyl anion − vinyl radical)[40] obtained using the SM5.42R continuum solvation model[41] to derive standard reduction potentials ($E°$) versus the normal hydrogen electrode (NHE). Recently, Patterson et al. performed similar calculations while investigating the mechanism of reductive dechlorination of hexachloroethane.[42]

The calculated $E°$ values for vinyl, 1-chlorovinyl, (*Z*)-dichlorovinyl, (*E*)-dichlorovinyl, and trichlorovinyl radicals are −0.43, 0.09, 0.35, 0.33, and 0.49 V, respectively. Although an aqueous-phase standard reduction potential of the vinyl radical has not been reported for comparison, it can be estimated from existing literature thermodynamic data. The gas-phase acidity of ethylene (or proton affinity of the vinyl anion) has been determined at 298 K to be $\Delta G_{\text{acid,g}}° = 401.0 \pm 0.5$ kcal/mol,[39] and the solution pK_a (referenced to water) of ethylene is commonly cited as 44,[43] corresponding to $\Delta G_{\text{acid,aq}}° = 60.1$ kcal/mol. The difference between the experimental gas-phase and

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(38) For a nice review of problems (and misconceptions of problems) with DFT and electron affinities see: Rienstra-Kiracofe, J. C.; Tschumper, G. S.; Schaefer, H. F.; Nandi, S.; Ellison, G. B. *Chem. Rev.* **2002**, *102*, 231−282.

(39) Ervin, K. M.; Gronert, S.; Barlow, S. E.; Gilles, M. K.; Harrison, A. G.; Bierbaum, V. M.; DePuy, C. H.; Lin, W. C. *J. Am. Chem. Soc.* **1990**, *112*, 5750−5759.

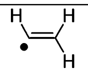
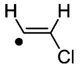
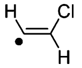
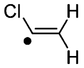
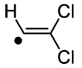
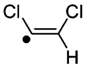
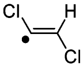
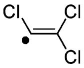
(40) For a definition of $\Delta\Delta G_{\text{hyd}}^*$, see ref 42.

(41) Li, J.; Zhu, T.; Hawkins, G. D.; Winget, P.; Liotard, D. A.; Cramer, C. J.; Truhlar, D. G. *Theor. Chem. Acc.* **1999**, *103*, 9−63. Implemented in AMSOL Version 6.9: Hawkins, G. D.; Giesen, D. J.; Lynch, G. C.; Chambers, C. C.; Rossi, I.; Storer, J. W.; Li, J.; Zhu, T.; Thompson, J. D.; Winget, P.; Rinaldi, D.; Liotard, D. A.; Cramer, C. J.; Truhlar, D. G., Regents of the University of Minnesota, Minneapolis, MN, 2003.

(42) Patterson, E. V.; Cramer, C. J.; Truhlar, D. G. *J. Am. Chem. Soc.* **2001**, *123*, 2025−2031. Two relatively subtle differences are noted: we use B3LYP/6-311+G(2d,2p) geometries and triple-ζ basis sets (aug-cc-pVTZ) for our calculations at the CCSD(T) level of theory, whereas those described by Patterson et al. are for BPW91/aug-cc-PVDZ geometries and CCSD(T)/aug-cc-PVDZ energies.

(43) Maskornick, M. J.; Streitwieser, A. *Tetrahedron Lett.* **1972**, *17*, 1625−1628.

Table 4. Gas-Phase Vertical and Adiabatic Electron Attachment Energies for Chlorinated Vinyl Radicals at 0 K and Aqueous-Phase Standard Reduction Potentials versus the Normal Hydrogen Electrode at 298 K

Entry		B3LYP[a]			CCSD(T)[b]		
		EA_{vert}[c] (kcal/mol)	EA_{adia}[d] (kcal/mol)	$E°$ (V)	EA_{vert}[c] (kcal/mol)	EA_{adia}[d] (kcal/mol)	$E°$ (V)
A		3.4	15.1	-0.43	1.9	14.8	-0.45
B		25.4	(68.8)	--	23.3	(64.8)	--
C		29.4	(67.3)	--	27.3	(63.4)	--
D		20.0	40.5	0.09	19.0	39.4	0.05
E		37.8	(66.3)	--	36.0	(61.0)	--
F		37.6	53.5	0.35	36.3	51.7	0.27
G		35.1	53.5	0.33	33.7	52.9	0.30
H		45.2	60.6	0.49	44.0	60.4	0.48

[a] (U)B3LYP/6-311+G(2d,2p). [b] (U)CCSD(T)/aug-cc-pVTZ//(U)B3LYP/6-311+G(2d,2p). [c] Vertical electron attachment energy. [d] Adiabatic electron attachment energy. Values in parentheses correspond to cases where the anion is unbound; the energy given corresponds to the dissociated (chlorinated) acetylene and chloride products.

aqueous-phase acidities implies that $\Delta\Delta G_{hyd}° = -340.9$ kcal/mol. Given that experimental $\Delta G_{hyd}°$ values are known for ethylene (1.3 kcal/mol[44]) and the proton (−263.6 kcal/mol[45]), we can derive a value of $\Delta G_{hyd}°$ for the vinyl anion of −76.0 kcal/mol in excellent agreement with the calculated value of $\Delta G_{hyd}^* = -76.4$ kcal/mol. This value allows the derivation of a reduction potential for the vinyl radical making the assumptions that $\Delta G_{red,g}° \approx \Delta H_{red,g}° = -15.4$ kcal/mol[39] and $\Delta G_{hyd}°$(vinyl radical) $\approx$ $\Delta G_{hyd}°$(ethylene) = 1.3 kcal/mol.[44] This affords an "experimental" $E°$ of −0.47 V versus NHE in very good agreement with our calculated values of −0.43 V (DFT) and −0.45 V (CCSD(T)). The important conclusion from the values for $E°$ in Table 4 is that in aqueous solutions *all of the vinyl radicals studied here can be reduced by cob(I)alamin ($E° = -0.61$ V)[46] or titanium(III) citrate ($E° \approx -0.6$ V).[8,47]*

Competing with the protonation of the putative intermediate chlorinated vinyl anions (see calculated free energies and associated derived pK_a values in the Supporting Information) is elimination of chloride with the concomitant formation of an acetylene (Scheme 1). The DFT- and CCSD(T)-calculated barriers for elimination of chloride from the bound (*Z*)-dichlorovinyl, (*E*)-dichlorovinyl, and trichlorovinyl anions are given in Table 5 along with the overall reaction free energy change in aqueous solution ($\Delta G_{r,aq}°$). The barriers (ΔE_e) were calculated by DFT to be 0.96 and 10.5 kcal/mol for the (*Z*)- and (*E*)-dichlorovinyl anions, respectively, whereas that for the trichlorovinyl anion was 6.3 kcal/mol. The CCSD(T)-calculated barriers were somewhat higher. Zero-point vibrational and thermochemical corrections to obtain $\Delta G^{\ddagger}{}_{g}°$ did not have a substantial effect on the barrier, and $\Delta\Delta G_{hyd}^*$ was close to zero for each of the anions.

The unimolecular rate constant for the elimination of chloride from the trichlorovinyl anion can be estimated by transition-state theory using the DFT- and CCSD(T)-calculated barrier heights in Table 5 to be 5.0×10^8 and 1.2×10^7 s^{-1}, respectively. Both of these values are significantly lower than the pseudo-first-order diffusion-controlled rate constant expected for protonation of the vinyl anion in aqueous solution ($\sim 10^{11}$ s^{-1}).[48] Thus, despite the substantial driving force for formation of dichloroacetylene and chloride from the trichlorovinyl anion (22.7−27.5 kcal/mol), protonation is likely to occur faster than elimination in aqueous solution. This accounts for the lack of observation of dichloroacetylene in reductive dechlorinations of PCE. In the case of the (*Z*)-dichlorovinyl anion, the very low barrier suggests that elimination may be competitive with protonation. Indeed, the estimated unimolecular rate constants for elimination are 2.3×10^{12} and 7.0×10^{11} s^{-1} by DFT and CCSD(T), respectively, now on the same order as that of a diffusion-controlled protonation in aqueous solution. This would

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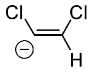
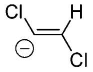
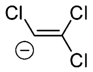
(44) Ben-Naim, A.; Marcus, Y. *J. Chem. Phys.* **1984**, *81*, 2016−2027.
(45) Trasatti, S. *Pure Appl. Chem.* **1986**, *58*, 955−966.
(46) Lexa, D.; Savéant, J.-M. *Acc. Chem. Res.* **1983**, *16*, 235−243.
(47) Zehnder, A. J. B. Ph.D. Thesis, ETH, Zürich, Switzerland, 1976; No. 5716.
(48) Kresge, A. J. *Acc. Chem. Res.* **1975**, *8*, 354−360.

Table 5. Barriers for Elimination of Chloride from the (*Z*)-Dichlorovinyl, (*E*)-Dichlorovinyl, and Trichlorovinyl Anions (kcal/mol)

	Method	ΔE_e	$\Delta G^{\ddagger}{}_{g}{}^{\circ}$	$\Delta G^{\ddagger}{}_{aq}{}^{\circ}$	$\Delta G_{r,aq}{}^{\circ}$
	B3LYP[a]	0.96	0.59	0.55	-32.5
	CCSD(T)[b]	1.7	1.3	1.3	-30.7
	B3LYP[a]	10.5	9.8	9.4	-34.9
	CCSD(T)[b]	14.8	14.1	13.7	-32.3
	B3LYP[a]	6.3	5.6	5.6	-27.5
	CCSD(T)[b]	8.4	7.8	7.8	-22.7

[a] B3LYP/6-311+G(2d,2p). [b] CCSD(T)/aug-cc-pVTZ//B3LYP/6-311+G(2d,2p).

yield both (*Z*)-DCE and chloroacetylene, which have both been observed in reductive dechlorinations of PCE and TCE.[1,49]

Redox Behavior of Chlorinated Vinylcobalamins. The results presented in the previous section suggest that trichlorovinyl radicals will be rapidly reduced under the conditions of the reductive dehalogenations, and this accounts for the lack of observation of **1** (Scheme 1). Alternatively, **1** might have a reduction potential less negative than the Co^{II}/Co^{I} potential, and would therefore be reduced under the reaction conditions, preventing its detection. As such, we set out to investigate the redox potentials of **1** and the other chlorinated vinylcobalamins using theoretical approaches.

Reductive cleavage of the Co−C bond in alkylcobalamins has been described in terms of two unoccupied low-energy orbitals involving the corrin (π_8*, usually the LUMO) and the antibonding combination of the Co $3d_{z^2}$ and sp^3 orbitals on the metal and alkyl ligand, respectively (usually LUMO + 1 or LUMO + 2).[50,51] On the basis of electrochemical evidence, Scheffold and co-workers[51] suggested that reduction of organocobalamins proceeds by a fast electron transfer to the empty corrin-based orbital prior to a rate-limiting electronic transition to the σ* orbital associated with the Co−C bond. Indeed, in our calculations, the methylcobalamin and vinylcobalamin models have LUMOs centered on the corrin ring (π_8*) with no contribution from either the Co $3d_{z^2}$ or the two axial ligands. Attachment of an electron to each of these species yields vertical electron attachment energies ranging from 78.4 to 85.6 kcal/mol (Table 6). The substituent effects are relatively small since the chlorine atoms do not directly interact with π_8*.

Relaxation of the cobalamin model geometries gives way to structures with slightly shorter Co−C and $Co-N_{Im}$ bonds (generally $\Delta r \approx 0.1$ Å) with a small increase in the positive charge on the cobalt atom ($\Delta C \approx 0.01$e) and a large change in the negative charge on the corrin ring ($\Delta C \approx 0.9$e). The adiabatic electron attachment energies track the vertical energies very well (not shown), and after thermochemical corrections to the free energy at 298 K and calculated differences in the solvation free energies of the Co^{III} and Co^{II} complexes, their standard reduction potentials were computed versus the NHE. These results are presented in Table 6 alongside experimental cathodic peak potentials obtained by cyclic voltammetry in DMF.[6,52,53] The calculated and experimental data for the Co^{II}/Co^{I} couple are also presented for comparison.[6,46]

It should be pointed out that the solution-phase free energies and the standard reduction potentials derived therefrom were calculated using solvation free energy differences obtained with the polarizable conductor model COSMO[54] as it is implemented in the Gaussian-03 suite of programs. The AMSOL SM5.42R methodology of Cramer and Truhlar[41] that was used to calculate aqueous-phase free energies for the determination of $E°$ of the (chlorinated) vinyl radicals is not parametrized for cobalt complexes. Although it is possible to calculate solvation free energies with the COSMO model, they neglect contributions from the cobalt atom to the (nonelectrostatic) dispersion and repulsion terms of the solvation free energy. Furthermore, the computed *aqueous standard* reduction potentials in this work are compared with experimental *peak* potentials determined in *DMF*. Thus, the absolute calculated data should be considered with caution,[55] and we will focus on the effects of the chlorine substituents on the calculated free energy changes (and reduction potentials derived therefrom) within the series.

The calculated effects of adding two and three chlorine atoms to the vinyl ligand are not substantial. In fact, all of the calculated $E°$ values for the chlorinated vinylcobalamin models are within a very narrow range (-1.84 ± 0.05 V). These reduction potentials are far too negative for efficient reduction by the Co^{I} form of B_{12}, suggesting that trichlorovinyl- and dichlorovinylcobalamins are not viable intermediates in the reductive dehalogenation pathway as they would be essentially inert and should have been detected under the reaction conditions. However, another possibility exists.

Scheffold and co-workers found that the electrochemistry of [(methoxycarbonyl)methyl]cobalamin ($LCoCH_2COOCH_3$, **14**) showed two irreversible cathodic waves corresponding to the reduction of the base-off and base-on forms of the cobalamin

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(49) If the (*E*)-dichlorovinyl anion is formed (as theory and experiments suggest, albeit in much smaller amounts relative to the (*Z*)-isomer), the barrier to elimination is large owing to the *Z* orientation of the departing chloride relative to the negative charge. In this case we would then expect only (*E*)-DCE and none of the elimination product chloroacetylene.

(50) Salem, L.; Eisenstein, O.; Anh, N. T.; Burgi, H. B.; Devaquet, A.; Segal, G.; Veillard, A. *Nouv. J. Chim.* **1977**, *1*, 335−348.

(51) Zhou, D.-L.; Tinembart, O.; Scheffold, R.; Walder, L. *Helv. Chim. Acta* **1990**, *73*, 2225−2241.

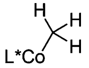
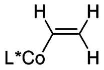
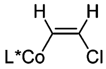
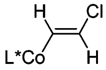
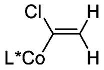
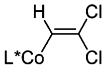
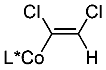
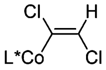
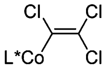
(52) McCauley, K. M.; van der Donk, W. A. Unpublished results.

(53) Lexa, D.; Savéant, J.-M. *J. Am. Chem. Soc.* **1978**, *100*, 3220−3222.

(54) Barone, V.; Cossi, M. *J. Phys. Chem. A* **1998**, *102*, 1995−2001.

(55) This comparison is further confounded by the problem that a very fast follow-up reaction occurs in the electrochemical experiments, causing the peak to shift to a less negative value. We have previously estimated the contribution of this follow-up reaction to the peak potential to be ≤120 mV.[6]

Table 6. Gas-Phase Vertical Electron Attachment Energies at 0 K (EA_{vert}) (kcal/mol) and Derived Aqueous-Phase Standard Reduction Potentials ($E°$) (V) of Methylcobalamin and Vinylcobalamin Models[a]

	Base-on		Base-off		Expt.
L*Co-R	EA_{vert}	$E°$	EA_{vert}	$E°$	$E°$ or E_{pc}
5 	78.4	-2.02	86.9	-1.85	-1.72[c] (-1.36[d])
6 	79.4	-2.03	87.8	-1.82	-1.61[e]
7 	80.5	-1.87	89.7	-1.74	-1.23[e]
8 	83.4	-1.88	91.9	-1.73	--
9 	82.1	-1.89	90.5	-1.75	--
10 	84.1	-1.87	94.7	-1.13	--
11 	85.2	-1.79	97.4	-1.08	--
12 	83.3	-1.89	98.5	-1.02	--
13 	85.6	-1.87	105.9	-0.72	--
Co^{II}/Co^{I} couple[b]		-1.20			-0.83[f] (-0.61[g])

[a] Calculated from (U)B3LYP/6-31G(d)/TZV energies and thermochemical corrections and COSMO solvation energies obtained at the same level of theory (see the Theoretical Methods). Experimental redox potentials of the corresponding cobalamins determined versus NHE are presented for comparison. [b] Corresponds to base-on cob(II)alamin being reduced to base-off cob(I)alamin. [c] E_{pc} in DMF, ref 52. [d] $E°$ in DMF/1-propanol, obtained at ultrahigh scan rates, ref 53. [e] E_{pc} in DMF, ref 6. [f] E_{pc} in DMF, fully reversible value $E_{1/2} = -0.80$ V, ref 6. [g] $E°$ in water, ref 46.

with $E_{pc} = -0.71$ and -1.18 V versus NHE, respectively.[56] The former was observed exclusively at slow scan rates (0.1 V/s), whereas the latter predominated at much faster scan rates (≥50 V/s). Observation of a wave corresponding to reduction of the base-off form of **14** is surprising given the low pK_a of the dBzm group of **14** (2.4),[57] which predicts a $K(H_2O)$ of 6.3 × 10^{-4} for the base-on/base-off equilibrium. Presumably, the irreversible follow-up Co−C bond cleavage is sufficiently fast to "drive" the equilibrium toward the base-off form, allowing the observation of its reduction. This follow-up reaction was found to involve either homolytic or heterolytic cleavage of the Co−C bond depending on the conditions.[56] Despite its more positive potential by ca. 100 mV, cob(I)alamin readily reduced the base-off form of **14**.

The pK_a values of the dBzm group in **2** and **3** (2.3 and 2.4, respectively)[12] are very similar to that of **14**, raising the question of whether the base-off forms of the chlorinated vinylcobalamins could be the redox-active species in the reductive dehalogenation. The results of calculations of the vertical electron attachment energies for base-off organocobalamins are presented alongside the base-on results in Table 6.

While the calculated EA_{vert} values for the base-off models of the methyl-, vinyl-, and chlorovinylcobalamins correlate very well with the corresponding base-on values, those calculated for the dichlorovinyl and trichlorovinyl congeners are much larger than expected. The reason for this deviation is immediately evident upon examination of the orbitals to which the extra electron is attached in the cobalamin model series. While the SOMO remains the corrin ring π_8* in the one-electron reduced methyl, vinyl, and chlorovinyl models, the SOMO in the dichlorovinyl and trichlorovinyl congeners is σ_{Co-C}*. This suggests that two chlorine atoms are required to drop σ_{Co-C}* below π_8* in the base-off vinylcobalamins. In the base-on dichlorovinyl and trichlorovinyl cobalamins, σ_{Co-C}* still lies above π_8* due to the strong destabilization by the nitrogen lone pair electrons on the axial imidazole ligand.[58] This concept is illustrated schematically in Figure 3.

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(56) Tinembart, O.; Walder, L.; Scheffold, R. *Ber. Bunsen-Ges. Phys. Chem.* **1988**, *92*, 1225−1231.
(57) Brown, K. L.; Hakimi, J. M.; Nuss, D. M.; Montejano, Y. D.; Jacobsen, D. W. *Inorg. Chem.* **1984**, *23*, 1463−1471.

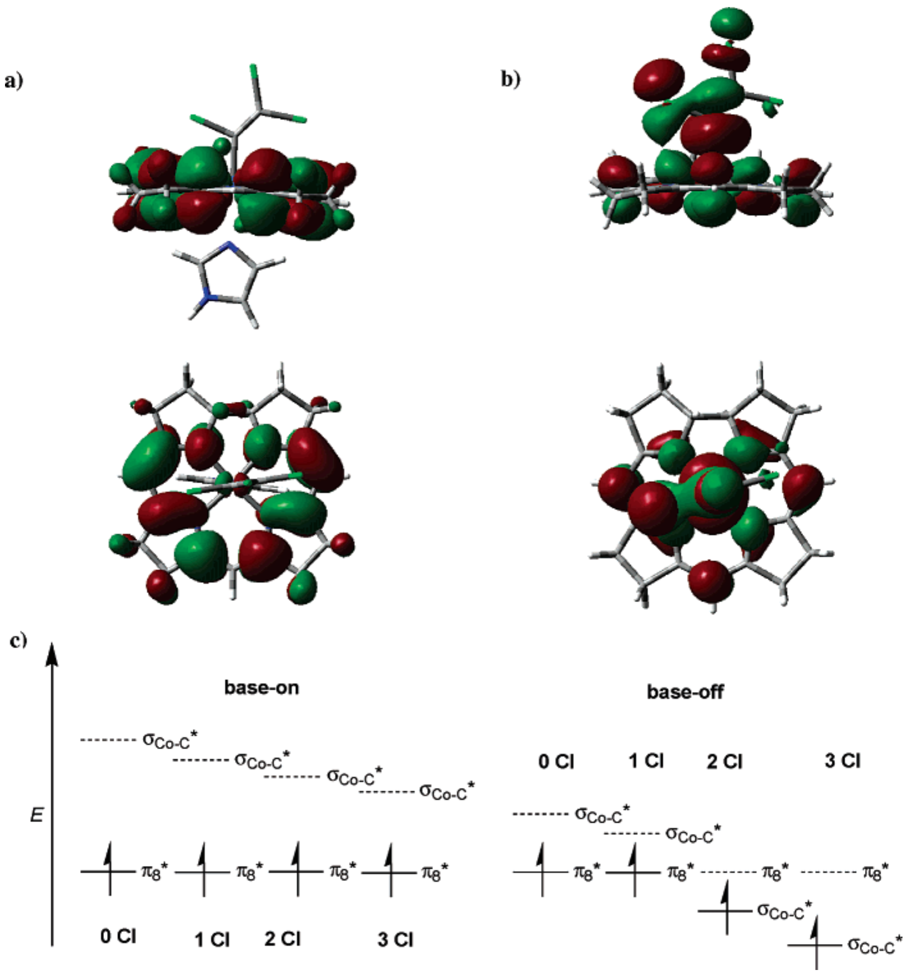

Figure 3. (a) Side and top views of the SOMO in the base-on trichlorovinylcob(II)alamin model. (b) Side and top views of the SOMO in the base-off trichlorovinylcob(II)alamin model. (c) Schematic representation of the relative ordering of the corrin π_8* and the $\sigma_{\mathrm{Co-C}}$* orbitals as a function of chlorine substitution in the vinylcob(II)alamin models.

Relaxation of the one-electron-reduced base-off geometries maintains the same lowest energy electronic configurations and yields the standard reduction potentials given in Table 6. The calculated values of $E°$ for the base-off forms of the methyl-, vinyl-, and (*Z*)-chlorovinylcobalamin models drop slightly to −1.85, −1.82, and −1.74 V, respectively. These values are less negative than the base-on potentials by 170, 210, and 130 mV, respectively, a rather modest change, but not unexpected since the electron is still attached to the corrin ring π_8* orbital. On the other hand, the change in electronic configuration on going from the base-on to base-off form of the dichlorovinyl and trichlorovinyl congeners drops the calculated standard reduction potentials by 710−870 mV and 1.15 V, respectively. The calculated values for all three isomers of the dichlorovinylcobalamin model ($E° = -1.02$ to -1.13 V) are slightly more positive than the calculated value for the model $\mathrm{Co^{II}/Co^{I}}$ couple ($E° = -1.20$ V), and that for trichlorovinylcobalamin is substantially more positive ($E° = -0.72$ V).

It is noteworthy that we calculate $E°$ for the base-on and base-off forms of the L*CoR model of **14** to be −1.99 and −1.31 V, respectively.[59] Reinforcing the importance of the base-on/base-off equilibrium, the basis for the large drop in the calculated $E°$ for **14** and presumably the explanation for the drop in the experimental E_{pc}[56] are again the change in electronic configuration: the SOMO in the base-off form of the model of **14** is $\sigma_{\mathrm{Co-C}}$*, whereas in the base-on form it is π_8*. Importantly, the calculated $E°$ for the base-off form of **14** is 110 mV more negative than the calculated $\mathrm{Co^{II}/Co^{I}}$ couple of B_{12}, in excellent agreement with the experimental observations ($\Delta E_{\mathrm{pc}} = 100$ mV). Thus, like **14** the base-off forms of the trichloro- and dichlorovinylcobalamins should also be reduced by cob(I)alamin (and by inference $\mathrm{Ti^{III}}$).

Mechanism of Reductive Cleavage of the Co−C Bond in Chlorinated VinylCobalamins. While the electrochemistry for vinylcobalamin is reversible at high scan rates (>1 V/s), that for (*Z*)-chlorovinylcobalamin is irreversible,[6] suggesting fast and irreversible follow-up chemistry. Mechanistic studies by Scheffold and co-workers have shown that following the reduction

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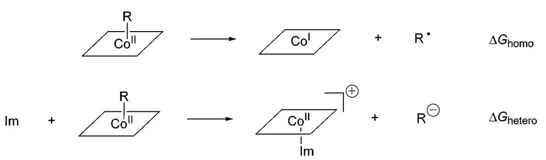
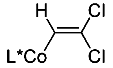
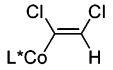
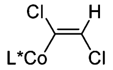
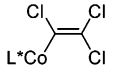
(58) Since the corrin is substituted with two (electron-donating) methyl groups directly attached to the ring π-system in cobalamins, the energy of the π_8* orbital would be relatively higher than in the models used in this work (the other substituents may also have a small effect on the energy of this orbital) and may be sufficient to drop the $\sigma_{\mathrm{Co-C}}$* orbital below π_8* for the base-off monochlorinated vinylcobalamins, which can account for the relatively rapid reduction of (*Z*)-chlorovinylcobalamin that we observed experimentally.[6,12] Along similar lines, since dBzm is a weaker ligand than Im, the energy of $\sigma_{\mathrm{Co-C}}$* in the base-on chlorinated vinylcobalamins may actually lie lower than that for the ring-substituted π_8*. For the influence of the axial base and corrin substituents on the energy levels of the orbitals of organocobalamins, see also refs 21e,f.

(59) The calculated difference of 680 mV in E^{o} is larger than the difference in E_{pc} of 470 mV determined experimentally in DMSO by Scheffold and co-workers.[56]

Table 7. Aqueous-Phase Free Energies for Homolysis and Heterolysis of the Base-Off Dichlorovinyl- and Trichlorovinylcob(II)alamin Models (kcal/mol)[a]



L*Co-R		ΔG_{homo}	ΔG_{hetero} [b]
10		26.3	-35.3
11		27.6	5.7
12		24.3	2.9
13		27.9	0.0

[a] Calculated from (U)B3LYP/6-31G(d)/TZV energies and thermochemical corrections and COSMO solvation energies obtained at the same level of theory (see the Theoretical Methods). [b] If water were to occupy the fifth coordination site of cob(II)alamin in the initial heterolysis (or ligand substitution) product, these free energy changes would be ca. 2.4 kcal/mol larger. See ref 61.

of base-off **14**, cleavage of the Co−C bond can occur homolytically or heterolytically depending on the conditions.[56] Indeed, calculated solution-phase free energies for homolysis and heterolysis of the base-off form using our model for **14** (L*CoR) are similar, 7.4 and 3.1 kcal/mol, respectively, and thus, the competition should be easily manipulated by the conditions (e.g., a good proton donor to trap the anion or a good H-atom donor to trap the radical).

We also calculated the free energy changes for these possibilities for the one-electron-reduced models of dichlorovinyl- and trichlorovinylcobalamins (Table 7).[60] Since the base-off cob(III)alamins are more easily reduced than the base-on forms and do not require a ligand-to-metal charge transfer prior to Co−C bond cleavage (vide supra), we focus on the calculated free energies for homolysis and heterolysis of these complexes.[60] In each case, heterolysis is the thermodynamically preferred mode of Co−C bond cleavage.[61] The calculated free energy for heterolysis is very negative for 2,2-dichlorovinylcobalamin (−35.3 kcal/mol), which results in an unbound anion (see also Table 4) and hence eliminates chloride concerted with cleavage of the Co−C bond. The calculated free energy changes are small (0−5.7 kcal/mol) for those cobalamins yielding bound vinyl anions upon heterolysis. These calculated free energy changes in combination with the calculated reduction potentials for the base-off complexes and taken in the context of the results of Scheffold with **14** (vide supra) suggest that reductive heterolysis of the dichlorovinyl- and trichlorovinylcobalamins catalyzed by the Co^I form of B_{12} should occur readily despite the fact that the equilibrium constant is expected to favor the base-on form by ca. 10^3−10^4. The more positive free energies calculated for heterolysis of the (*E*)- and (*Z*)-dichlorovinylcobalamins combined with their more negative reduction potentials relative to that of trichlorovinylcobalamin are consistent with their observation by mass spectrometry[8] and in model studies.[9]

Implications for the Mechanism of Dechlorination of PCE and TCE by Vitamin B_{12}. The theoretical studies presented herein provide important insights into the vitamin B_{12}-catalyzed reduction of PCE and TCE that could not be obtained to date by experimental studies. With respect to the reason behind the lack of detection of **1**, the calculations support two explanations. First, on the basis of the calculated reduction potential for the trichlorovinyl radical, both cob(I)alamin and the sacrificial reductant titanium(III) citrate are thermodynamically competent to effect reduction to the corresponding anion. This reduction may compete with the diffusion-controlled combination of the trichlorovinyl radical and cob(II)alamin (Scheme 1) and will reduce, if not prevent, the formation of **1**.[62] A second possibility was not anticipated previously. We had suggested that complex **1** might be reduced under the reaction conditions, preventing its detection. However, the calculations indicate that reduction of **1** by Co^I or Ti^{III} is quite unfavorable. On the other hand, reduction of its base-off form should be very facile and may account for consumption of **1** once it is formed. Preparation of authentic **1** under nonreducing conditions[63] will be required to verify this pathway.

It is worthwhile to compare the abiotic B_{12}-dependent dechlorination of PCE with its enzymatic counterpart. When the fully reduced protein from *Dehalobacter restrictus* was reacted with PCE, Co^{II} formation was observed,[64] suggesting a one-electron-transfer mechanism analogous to stopped-flow results on the abiotic reaction.[4] The kinetics of the enzymatic reaction indicate that the enzyme accelerates the rate by a factor of ca. 4500.[12,65] If the mechanism of the enzymatic dehalogenation is similar to that suggested here for the nonenzymatic system, the enzyme may accelerate the overall reaction simply by binding the B_{12} cofactor in the base-off form in the active site, such that the putative trichlorovinylcobalamin intermediate is easier to reduce by one of the two iron sulfur clusters present in the dehalogenases characterized to date[66] ($E° \approx -0.48$ V).[64] Indeed, in the sole dehalogenase enzyme system for which data are available, the cobalamin is bound in a base-off form.[64]

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(60) For calculations on the other models as well as the base-on series, see the Supporting Information, Table S12.

(61) Heterolysis of the one-electron-reduced base-off intermediate can be viewed as a ligand substitution reaction where Im (or dBzm) replaces the (chlorinated) vinyl anion as the single axial ligand. In aqueous solution, it is possible that water plays a role in this reaction as the initial nucleophile. Given that $K(H_2O)$ for cob(II)alamin is 1.7×10^{-2},[46] this would make the calculated heterolysis free energies more endergonic by ca. 2.4 kcal/mol.

(62) Comparing the driving force for reduction of the trichlorovinyl radical by cob(I)alamin ($\Delta G_{\text{rxn}}° = 23.06\Delta E° \approx -25$ kcal/mol) with that corresponding to its combination with cob(II)alamin to yield **1** ($-\Delta G_{\text{BDE(Co−C)}}° \approx -20$ kcal/mol, obtained from the ΔH value in Table 2 corrected by including $T\Delta S$ and $\Delta\Delta G_{\text{solvation}}$) would suggest that reduction is the thermodynamically more favorable of the two pathways. On the other hand, comparison of the driving force for reduction of the (*Z*)-dichlorovinyl radical by cob(I)alamin ($\Delta G_{\text{rxn}}° = 23.06\Delta E° \approx -22$ kcal/mol) with that corresponding to its combination with cob(II)alamin to yield the corresponding dichlorovinylcobalamin ($-\Delta G_{\text{BDE(Co−C)}}° \approx -28$ kcal/mol) would suggest that radical combination is the thermodynamically more favorable of the two pathways for the dichlorinated vinylcobalamins, explaining why they are detected.

(63) Puchberger, M.; Konrat, R.; Kräutler, B.; Wagner, U.; Kratky, C. *Helv. Chim. Acta* **2003**, *86*, 1453−1466.

(64) (a) Schumacher, W.; Holliger, C.; Zehnder, A. J.; Hagen, W. R. *FEBS Lett.* **1997**, *409*, 421−425 (b) Maillard, J.; Schumacher, W.; Vazquez, F.; Regeard, C.; Hagen, W. R.; Holliger, C. *Appl. Environ. Microbiol.* **2003**, *69*, 4628−4638.

(65) Neumann, A.; Siebert, A.; Trescher, T.; Reinhardt, S.; Wohlfarth, G.; Diekert, G. *Arch. Microbiol.* **2002**, *177*, 420−426.

(66) Wohlfarth, G.; Diekert, G. *Curr. Opin. Biotechnol.* **1997**, *8*, 290−295.

Whether the corrinoid is truly 4-coordinate in its Co^{II} state in the enzyme or whether an axial base is present that does not give magnetic hyperfine interaction with cobalt[67] is presently unresolved.

In addition to providing important new conceptual insights and thermodynamic data, the computations are in good agreement with experimental observations. First, they explain the results obtained when the B_{12}-dependent reduction of PCE was conducted in mixtures of H_2O and 2-d_1-2-propanol.[1d,4] These studies showed that the product TCE contained both hydrogen and deuterium. The theoretical studies indicate that, after the trichlorovinyl radical is formed, it partitions between reduction by Co^I/Ti^{III} to the anion followed by protonation and deuterium atom abstraction from 2-d_1-^{i}PrOH (BDE(TCE) $\gg$ BDE(C−D) bond; see the Supporting Information). Theory also accounts for the observation of acetylene and chloroacetylene and not dichloroacetylene.[1f,g] All vinyl radicals studied here should be readily reduced to their corresponding anions under the conditions of reductive dechlorination. While a very low barrier for chloride elimination from the (*Z*)-dichlorovinyl anion to yield chloroacetylene was calculated, the (*E*)-dichlorovinyl and trichlorovinyl anions face much larger activation energies to do so. Hence, protonation of the trichlorovinyl anion will be favored over elimination, and no dichloroacetylene should be formed. Finally, the calculated thermodynamic preference of the chlorinated vinylcobalamins to undergo heterolytic Co−C bond cleavage upon reduction, which can be driven even further when combined with a concerted expulsion of chloride and formation of acetylene, is in complete agreement with the experimental observations with the authentic (*Z*)-chlorovinylcobalamin complex.[12]

Theoretical Methods

Bond Dissociation Enthalpies. The gas-phase Co−C BDEs in the models of methylcobalamin (**5**) and the vinylcobalamins **6**−**13** were calculated from geometries using the combination of Becke's hybrid gradient-corrected exchange functional and the correlation functional of Lee, Yang, and Parr, conventionally referred to as the B3LYP density functional.[15] This approach was applied with 6-31G(d) basis sets[16] for C, N, H, and Cl and Ahrlich's TZV basis set for Co.[17] Pure (five) d functions were employed in these calculations. Stationary points were characterized as minima by analytic frequency calculations, and the derived vibrational data were scaled by 0.9806[68] and used to calculate zero-point energies and thermochemical corrections to the enthalpy and free energy at 298 K. Single-point calculations at the B3LYP minima were also carried out using the same basis sets and combinations of either Becke's pure or hybrid exchange functional with the '86 correlation functional of Perdew (denoted B3P86 and BP86, respectively).[32] The C−H BDEs in methane and the (chlorinated) ethylenes were calculated using both DFT and coupled-cluster theory at the CCSD(T) level. The DFT calculations employed the B3LYP functional with a 6-311+G(2d,2p) basis set, whereas the CCSD(T) calculations were done with an augmented cc-pVTZ basis set using B3LYP/6-311+G(2d,2p) minima and corresponding thermochemical corrections. In the DFT calculations, the electronic energy of the hydrogen atom was set to its exact value of −0.500000 hartree and either a spin-restricted or unrestricted wave function for open-shell species as indicated. All calculations were done with either the Gaussian-98 or Gaussian-03 suite of programs.[69]

Electron Attachment Energies and Standard Reduction Potentials of Chlorinated Vinyl Radicals, Proton Affinities of Chlorovinyl Anions, and pK_a Values of Chlorinated Ethylenes. All calculations were performed at both the B3LYP/6-311+G(2d,2p) and CCSD(T)/aug-cc-pVTZ levels of theory. Vertical electron attachment energies do not include zero-point energy corrections; they are simply differences in electronic energies. Adiabatic electron attachment energies are gas-phase electronic energy changes for the reaction $R^- \rightarrow R\bullet + e^-$. Proton affinities are gas-phase free energy changes for the reaction $R{-}H \rightarrow R^- + H^+$. Electron affinities of the vinyl radicals and proton affinities of the vinyl anions were converted to aqueous-phase standard reduction potentials ($E°$ versus the NHE)[70] and pK_a values, respectively, with solvation free energies in water (dielectric constant $\epsilon = 78.3$) calculated using the SM5.42R/AM1 method of the AMSOL program package.[41]

Redox Chemistry of Chlorinated Cobalamins. Gas-phase geometries were optimized and vibrational frequencies were calculated for the models of **5** and the vinylcobalamins **6**−**13** at the B3LYP/6-31G(d) level with the TZV basis set for Co. Vertical electron attachment energies were calculated as described above. Standard reduction potentials versus the NHE were obtained as described above including solvation free energies in water calculated at the B3LYP/ 6-31G(d) level using the COSMO solvation model as it is implemented in Gaussian-03. Aqueous-phase free energies of homolysis and heterolysis of both the base-on and base-off Co^{II} complexes were calculated by finding the differences in the aqueous solvation free energy-corrected gas-phase free energies of the participants in the reactions described in the title of Table 7.

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(70) Gas-phase electron affinities, $\Delta G_g°$, where the standard state is defined for 298 K and 1 atm, are calculated for $A\bullet + e^- \rightarrow A^-$, and then converted to corresponding aqueous-phase electron affinities, $\Delta G_{aq}°$, by adding the calculated $\Delta\Delta G_{hyd}^* = \Delta G_{hyd}^*(A^-) - \Delta G_{hyd}^*(A\bullet)$. This is converted to a standard reduction potential versus the NHE, by first combining $\Delta G_{aq}°$ with the absolute potential, $G_{NHE}°$, of the hydrogen electrode process producing one proton, $^1/_2H_{2,g} \rightarrow e^-_g + H^+_{aq}$, which is 4.44 eV,[45] and computing $E°$ in volts from the Nernst equation.

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Supporting Information Available: Tables containing the DFT- and CCSD(T)-calculated C−H BDEs and pK_a values of chlorinated ethylenes as well as the DFT-calculated thermodynamic data for homolytic and heterolytic cleavage of the Co−C bond of base-on organocobalamins and selected base-off compounds, and Cartesian coordinates of all relevant optimized geometries and the corresponding energies, thermochemical corrections, and solvation energies where applicable (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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